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The X-ray Crystal Structure of the Molecular Complex 8-Bromo-9-ethyladenine–5-Allyl-5-isobutylbarbituric Acid

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Crystals of the hydrogen-bonded 1:1 complex 8-bromo-9-ethyladenine–5-allyl-5-isobutylbarbituric acid, $C_{18}H_{24}BrN_7O_3$, have the space group $P2_1/c$ with the unit-cell parameters $a=13{\cdot}732$ (3), $b=25{\cdot}685$ (19), $c=15{\cdot}132$ (4) Å and $\beta=123{\cdot}56$ (1)°, with eight complexes per unit cell. Intensity data were measured with an automated diffractometer using graphite-monochromated Cu $K\alpha$ radiation. The structure was solved by the heavy-atom technique and was refined by full-matrix least-squares procedures to a final discrepancy index of $R=0{\cdot}129$ based on the 2318 observed unique reflections. Both of the unlike adenines and one of the barbiturates associate through Watson–Crick-type base pairing to form six-molecule-long hydrogen-bonded ribbons of heterocycles. These ribbons terminate at both ends with adenine residues whose amino groups participate in only one of the two hydrogen bonds they have the potential to form. The second barbiturate does not participate in base-pairing interactions but rather makes a single hydrogen bond to the N(3) atom of each of the unlike adenines. This barbiturate ring is inclined by over 60° to the planes of the adenine rings. There is no precedent among the 36 published crystal structures containing base pairs for either of these hydrogen-bonding anomalies. Hence this structure constitutes further evidence that barbiturates are poor hydrogen-bond acceptors. The crystal structure assumes a complicated pattern in which layers containing the base-paired ring molecules alternate with regions containing the non-base-paired barbiturate rings together with the hydrocarbon substituents to the rings. These latter regions are quite loosely packed. This accounts for the observed disorder of the hydrocarbon substituents to the barbiturates and hence the relatively large discrepancy index of the refined structure.

Introduction

Adenine–barbiturate complexes were first studied by Kyogoku, Lord & Rich (1968). They reported that in $CHCl_3$ solution the association constants of these hydrogen-bonded complexes, as determined by IR measurements, were an order of magnitude greater than those of the closely analogous adenine–uracil complexes. This conclusion prompted several crystallographic studies of adenine–barbiturate complexes in an effort to elucidate the structural basis of their high binding strength. The N–H···O hydrogen bonds in these crystal structures (Kim & Rich, 1968; Voet & Rich, 1972; Voet, 1972), in which the oxygen atom was that of a barbiturate carbonyl group and the NH group was from adenine, were often found to be extremely long and are therefore, presumably, weak (Nakamoto, Margoshes & Rundle, 1955). In the complex 9-ethyladenine–parabanic acid–oxaluric acid monohydrate (Shieh & Voet, 1975), the parabanic acid molecule, which is chemically related to the barbiturates, appears to avoid all hydrogen-bonding acceptor interactions. These studies suggest that the conjugation of several carbonyl groups drastically reduces their hydrogen-bonding acceptor affinities (Voet, 1972; Shieh & Voet, 1975). A similar conclusion was reached by Gartland & Craven (1974) in their survey of N–H···O hydrogen bonds in which the oxygen atom belonged to a barbiturate with nonpolar C(5) substituents and the N–H group belonged to some other type of molecule.

The present study was initiated in order to further elucidate the hydrogen-bonding properties of crystalline adenine–barbiturate complexes. A bromine atom substituted at the 8-position of an adenine residue sterically prevents the formation of a Hoogsteen complex. Hence it was expected that the structure of the title complex would resemble that of the complex phenobarbital–(8-bromo-9-ethyladenine)$_2$ (Kim & Rich, 1968). It will be seen below that these expectations were, in part, borne out but that there are several unique features in the structure that further emphasize that carbonyl groups on barbiturates are poor hydrogen-bond acceptors.

Experimental

Colorless tabular crystals of 8-bromo-9-ethyladenine–5-allyl-5-isobutylbarbituric acid (*A*.*B*) were grown by the slow evaporation of a 50% aqueous ethanol solution of 8-bromo-9-ethyladenine (Cyclo Chemical) and 5-allyl-5-isobutylbarbituric acid (butalbital, a gift of Sandoz Pharmaceuticals) in equimolar ratio. The ultraviolet absorption spectrum of an aqueous solution of a washed crystal suggested that the crystals contained 8-bromo-9-ethyladenine and 5-allyl-5-iso-

butylbarbituric acid in approximately equimolar amounts.

Systematic absences of the $0k0$ reflections for k odd and of the $h0l$ reflections for l odd in the Weissenberg and precession photographs of a crystal of *A*.*B* indicate that its space group is $P2_1/c$. All subsequent X-ray measurements were made with a Picker FACS-I diffractometer equipped with a pyrolytic graphite monochromator and employing Cu $K\alpha$ radiation (λ= 1·5418 Å). The parameters of the unit cell, as determined from the angular positions of 12 reflections, are presented in Table 1.

Table 1. *Crystal data for 8-bromo-9-ethyladenine–5-allyl-5-isobutylbarbituric acid*

$C_{18}H_{24}BrN_7O_3$	V=4447·49 Å^3
F.W. 466·35	d_{obs}=1·400 g cm^{-3}
a=13·732 (3) Å	d_{calc}=1·393
b=25·685 (19)	μ(Cu $K\alpha$)=3·08 mm^{-1}
c=15·132 (4)	$F(000)$=2112
β=123·56 (1)°	
Space group $P2_1/c$	
Z=8	

The crystal density (Table 1), as determined by flotation in a mixture of cyclohexane and CCl_4 is in good agreement with the calculated density for the unit cell containing eight molecules each of 8-bromo-9-ethyladenine and 5-allyl-5-isobutylbarbituric acid.

The X-ray diffraction data were measured to the limit 2θ=125° using the θ–2θ scan mode, a scan rate of 1° min^{-1}, and a scan width of 1·2°. Stationary background counts of 20 s duration each were taken at both limits of each scan.

Structure determination and refinement

The measured intensities, I, were corrected for Lorentz and polarization effects. No absorption corrections were made. Standard deviations, $\sigma(I)$, were calculated (Stout & Jensen, 1968) assuming an instrumental instability factor of 0·03. Of the 5236 measured unique reflections, 2318 had $I>2{\cdot}33\sigma(I)$ and hence were considered observed. The great majority of the 2918 unobserved reflections occurred at high Bragg angles as is expected for a disordered structure (see below).

The two unique bromine atoms in the structure were located by analysis of the Patterson map. The discrepancy index at this point was R=0·499. The remaining 56 unique non-hydrogen atoms in the structure were located using the heavy-atom technique as modified by Woolfson (1956) in a series of successive electron density maps. The side groups of the barbiturates were quite poorly resolved in these maps and hence were located with considerable difficulty.

The structure was refined by the full-matrix least-squares method in which the quantity minimized was $\sum w(|F_o|-|F_c|)^2$. Here the summation is over the 2318 observed reflections and $w=I/\sigma^2(I)=1/\sigma^2(F_o)$. The atomic scattering factors were taken from Cromer & Waber (1965). The overall scale factor together with all atomic positional and isotropic thermal parameters was refined to convergence. This was followed by a similar procedure in which the anisotropic thermal parameters were varied but in which the refinements were carried out on half the unique structure at a time, due to limitations of the computer memory. The agreement indices are presented in Table 2 for both the isotropic and the anisotropic refinement models.* The hypothesis that only the isotropic refinement of this structure is significant is strongly rejected at the 0·005 confidence level by the R-ratio test (Hamilton, 1965). The final parameter shifts were of the order of their estimated standard deviations for the atoms of the barbiturate side groups and somewhat less than this for the other atoms of the structure.

Table 2. *Agreement indices*

	Anisotropic observed data	Aniso-tropic* all data	Isotropic observed data
$R=\frac{\sum\|\|F_o\|-\|F_c\|\|}{\sum\|F_o\|}$	0·129	0·203	0·226
$R_w=\left[\frac{\sum w(\|F_o\|-\|F_c\|)^2}{\sum w\|F_o\|^2}\right]^{1/2}$	0·153	0·181	0·235
Goodness of fit: $\left[\frac{\sum w(\|F_o\|-\|F_c\|)^2}{(m-n)}\right]^{1/2}$	2·002	-	2·861
Number of observations, m	2318	5236	2318
Number of parameters, n	523	523	233

* The refinement model is based on the 2318 observed reflections only.

The final atomic parameters of the structure are presented in Table 3. The difference Fourier map did not reveal the presence of any hydrogen atoms. However it contained considerable positive and negative density in the vicinity of the hydrocarbon substituents to the rings. This, together with the large agreement indices of the refined structure, the distorted geometry of the hydrocarbon residues (see below), and the large and sometimes unrealistic thermal parameters and standard deviations of their component atoms, clearly indicates that these side groups are disordered in some manner. Several unsuccessful attempts were made to fit the data to various models in which the barbiturate side groups were statistically disordered. Least-squares refinements of these models invariably caused the various overlapping and fractionally weighted side groups to coalesce into a structure much like that de-

* A list of structure factors has been deposited with the British Library Lending Division as Supplementary Publication No. SUP 31660 (28 pp., 1 microfiche). Copies may be obtained through The Executive Secretary, International Union of Crystallography, 13 White Friars, Chester CH1 1NZ, England.

scribed by the final parameters. These models caused little variation in the agreement indices. Hence it appears that the atoms of the hydrocarbon substituents are continuously disordered about the positions indicated by the final parameters.

The molecular structures

The molecular configuration of an asymmetric unit of the complex together with the atomic numbering system used in this report is illustrated in Fig. 1. The covalent bond distances and angles of the structure are presented in Fig. 2. These data indicate that the covalent bonding parameters of the adenine and the barbiturate residues are in reasonable agreement with the corresponding averages of similar structures (Voet & Rich, 1970) although there are regions in these rings that appear to be somewhat distorted. Fig. 2 also shows that the hydrocarbon substituents to the rings all exhibit considerable distortion. These distortions are un-

Table 3. *Positional and thermal parameters for the complex 8-bromo-9-ethyladenine–5-allyl-5-isobutylbarbituric acid*

The positional parameters are expressed as fractions of unit-cell edges. The anisotropic temperature factors have the functional form $T=\exp[-(h^2\beta_{11}+k^2\beta_{22}+l^2\beta_{33}+2hk\beta_{12}+2hl\beta_{13}+2kl\beta_{23})\times 10^{-3}]$. Standard deviations as determined from the variance-covariance matrix of the final cycles of least-squares refinement are given in parentheses and refer to the least significant digits of their corresponding parameters.

8-Bromo-9-ethyladenine 1 (*A*1)

	x	y	z	β_{11}	β_{22}	β_{33}	β_{12}	β_{13}	β_{23}
N(1)	0·6902 (18)	0·4457 (10)	1·2422 (18)	4 (2)	2 (1)	8 (2)	−1 (1)	3 (2)	−1 (1)
C(2)	0·5969 (23)	0·4282 (13)	1·2491 (24)	7 (3)	3 (1)	8 (3)	0 (1)	6 (3)	−1 (1)
N(3)	0·5967 (18)	0·4315 (10)	1·3381 (21)	3 (2)	3 (1)	8 (2)	−1 (1)	4 (2)	−1 (1)
C(4)	0·6931 (24)	0·4508 (11)	1·4238 (27)	6 (3)	1 (1)	8 (3)	1 (1)	6 (3)	1 (1)
C(5)	0·7925 (23)	0·4673 (11)	1·4242 (26)	5 (3)	1 (1)	7 (3)	0 (1)	5 (3)	0 (1)
C(6)	0·7875 (23)	0·4631 (12)	1·3323 (25)	6 (3)	1 (1)	8 (3)	−1 (1)	5 (3)	−1 (1)
N(7)	0·8773 (17)	0·4867 (10)	1·5239 (18)	5 (2)	3 (1)	5 (2)	−2 (1)	3 (2)	−1 (1)
C(8)	0·8321 (23)	0·4801 (13)	1·5811 (20)	7 (3)	3 (1)	3 (2)	−1 (1)	1 (2)	−2 (1)
N(9)	0·7179 (17)	0·4579 (10)	1·5224 (18)	4 (2)	2 (1)	4 (2)	−1 (1)	2 (2)	−2 (1)
N(6)	0·8806 (16)	0·4758 (9)	1·3241 (15)	7 (2)	2 (1)	7 (2)	−2 (1)	6 (2)	−1 (1)
Br	0·9072 (3)	0·4944 (2)	1·7204 (3)	9 (0)	5 (0)	8 (0)	−3 (0)	6 (0)	−2 (0)
C(1′)	0·6501 (22)	0·4404 (16)	1·5693 (22)	5 (3)	4 (1)	5 (3)	−3 (2)	5 (2)	−3 (2)
C(2′)	0·6646 (32)	0·3872 (15)	1·6027 (32)	20 (5)	1 (1)	22 (5)	0 (2)	16 (4)	1 (2)

8-Bromo-9-ethyladenine 2 (*A*2)

	x	y	z	β_{11}	β_{22}	β_{33}	β_{12}	β_{13}	β_{23}
N(1)	0·2860 (17)	0·4096 (10)	0·6775 (20)	6 (2)	2 (1)	8 (2)	0 (1)	4 (2)	1 (1)
C(2)	0·2807 (22)	0·4045 (13)	0·5873 (27)	5 (2)	2 (1)	8 (3)	0 (1)	0 (2)	−2 (1)
N(3)	0·1859 (25)	0·3822 (10)	0·4992 (23)	15 (3)	2 (1)	17 (3)	0 (1)	14 (3)	0 (1)
C(4)	0·0946 (25)	0·3689 (13)	0·5105 (27)	11 (3)	2 (1)	9 (3)	0 (1)	6 (3)	0 (1)
C(5)	0·0994 (19)	0·3776 (11)	0·6005 (22)	3 (2)	2 (1)	8 (3)	0 (1)	2 (2)	0 (1)
C(6)	0·2042 (23)	0·3990 (13)	0·6929 (23)	10 (3)	3 (1)	6 (3)	1 (1)	5 (2)	1 (1)
N(7)	−0·0046 (22)	0·3591 (11)	0·5870 (25)	9 (2)	2 (1)	15 (3)	1 (1)	8 (2)	1 (1)
C(8)	−0·0619 (23)	0·3438 (14)	0·4882 (31)	6 (2)	3 (1)	12 (3)	−2 (1)	2 (3)	−3 (2)
N(9)	−0·0144 (19)	0·3485 (11)	0·4292 (24)	6 (2)	4 (1)	18 (4)	−3 (1)	9 (3)	−4 (1)
N(6)	0·2157 (18)	0·4019 (11)	0·7832 (20)	9 (2)	3 (1)	12 (2)	0 (1)	6 (2)	0 (1)
Br	−0·2189 (3)	0·3200 (2)	0·4220 (4)	9 (0)	5 (0)	16 (0)	−2 (0)	7 (0)	−1 (0)
C(1′)	−0·0778 (24)	0·3378 (14)	0·2995 (26)	9 (3)	2 (1)	15 (3)	0 (1)	7 (2)	−1 (1)
C(2′)	−0·0608 (26)	0·2917 (17)	0·3004 (28)	10 (3)	3 (1)	12 (4)	−1 (1)	3 (3)	−3 (2)

5-Allyl-5-isobutylbarbituric acid 1 (*B*1)

	x	y	z	β_{11}	β_{22}	β_{33}	β_{12}	β_{13}	β_{23}
N(1)	0·6493 (20)	0·4444 (11)	1·0398 (18)	3 (2)	3 (1)	6 (2)	−1 (1)	2 (2)	−2 (1)
C(2)	0·5415 (36)	0·4404 (15)	0·9544 (34)	16 (5)	3 (1)	13 (5)	0 (2)	13 (5)	−1 (2)
N(3)	0·5193 (18)	0·4421 (11)	0·8554 (20)	6 (2)	3 (1)	6 (2)	0 (1)	3 (2)	0 (1)
C(4)	0·6025 (38)	0·4485 (16)	0·8371 (33)	19 (6)	3 (1)	11 (4)	2 (2)	12 (5)	2 (2)
C(5)	0·7349 (32)	0·4546 (24)	0·9270 (25)	6 (4)	8 (2)	0 (3)	−2 (2)	1 (3)	−1 (2)
C(6)	0·7384 (29)	0·4519 (14)	1·0251 (29)	7 (3)	3 (1)	7 (3)	−1 (2)	2 (3)	−2 (2)
O(2)	0·4612 (14)	0·4346 (9)	0·9661 (13)	5 (2)	5 (1)	5 (2)	0 (1)	3 (1)	0 (1)
O(4)	0·5777 (15)	0·4468 (11)	0·7451 (18)	6 (2)	5 (1)	8 (2)	0 (1)	4 (2)	0 (1)
O(6)	0·8365 (17)	0·4568 (10)	1·1123 (16)	7 (2)	5 (1)	6 (2)	0 (1)	4 (2)	0 (1)
C(1′)	0·8075 (46)	0·4311 (42)	0·9142 (36)	12 (6)	11 (4)	8 (4)	5 (4)	6 (4)	0 (4)
C(2′)	0·7695 (57)	0·3703 (37)	0·9274 (72)	13 (7)	6 (3)	36 (11)	4 (4)	5 (7)	−7 (5)
C(3′)	0·6846 (54)	0·3349 (20)	0·8776 (66)	30 (10)	2 (1)	54 (14)	0 (3)	28 (10)	1 (3)
C(4′)	0·8496 (75)	0·3369 (35)	0·9322 (90)	39 (15)	7 (3)	84 (23)	−2 (6)	15 (15)	2 (6)
C(5′)	0·7850 (55)	0·5153 (36)	0·9111 (40)	23 (8)	10 (3)	12 (5)	−7 (5)	15 (6)	−2 (4)
C(6′)	0·7213 (40)	0·5458 (28)	0·9117 (59)	9 (5)	5 (2)	22 (8)	0 (2)	2 (5)	−4 (3)
C(7′)	0·7895 (62)	0·5797 (28)	0·9840 (42)	37 (11)	9 (3)	14 (6)	−1 (4)	13 (7)	−1 (3)

Table 3 (*cont.*)

5-Allyl-5-isobutylbarbituric acid 2 (*B*2)

	x	y	z	β_{11}	β_{22}	β_{33}	β_{12}	β_{13}	β_{23}
N(1)	0·2825 (17)	0·3428 (12)	0·3781 (20)	7 (2)	1 (1)	13 (3)	−1 (1)	6 (2)	−1 (1)
C(2)	0·3529(26)	0·3800 (16)	0·3738 (28)	6 (3)	3 (1)	12 (3)	−2 (1)	5 (2)	0 (2)
N(3)	0·4271 (17)	0·3573 (12)	0·3418 (16)	6 (2)	2 (1)	9 (2)	−2 (1)	6 (2)	−3 (1)
C(4)	0·4408 (25)	0·3090 (14)	0·3323 (23)	12 (3)	1 (1)	10 (3)	−2 (1)	7 (3)	−1 (1)
C(5)	0·3605 (28)	0·2633 (13)	0·3341 (30)	13 (3)	1 (1)	15 (4)	−1 (1)	10 (3)	0 (1)
C(6)	0·2745 (27)	0·2951 (19)	0·3597 (28)	7 (3)	3 (1)	16 (4)	2 (2)	9 (3)	3 (2)
O(2)	0·3512 (18)	0·4236 (11)	0·3908 (20)	10 (2)	3 (1)	16 (3)	−2 (1)	9 (2)	−1 (1)
O(4)	0·5117 (17)	0·2938 (9)	0·3137 (16)	12 (2)	4 (1)	16 (2)	−2 (1)	12 (2)	−3 (1)
O(6)	0·2094 (20)	0·2607 (10)	0·3619 (22)	16 (3)	3 (1)	27 (3)	−3 (1)	17 (3)	−1 (1)
C(1′)	0·4300 (30)	0·2225 (17)	0·4114 (33)	10 (3)	4 (1)	17 (5)	0 (2)	10 (3)	0 (2)
C(2′)	0·5305 (39)	0·2454 (21)	0·5292 (31)	15 (6)	6 (2)	10 (4)	2 (2)	6 (4)	3 (2)
C(3′)	0·5952 (54)	0·2003 (27)	0·5929 (40)	34 (10)	9 (2)	13 (5)	7 (4)	5 (6)	1 (3)
C(4′)	0·4845 (43)	0·2640 (27)	0·5833 (36)	21 (7)	11 (3)	14 (4)	−2 (3)	8 (4)	2 (3)
C(5′)	0·2898 (34)	0·2408 (19)	0·2265 (35)	14 (4)	5 (1)	14 (4)	−6 (2)	8 (3)	−7 (2)
C(6′)	0·2080 (43)	0·2808 (23)	0·1311 (46)	16 (5)	6 (2)	10 (5)	−2 (3)	2 (5)	−4 (3)
C(7′)	0·1476 (65)	0·2713 (30)	0·0650 (53)	47 (11)	7 (2)	18 (8)	0 (4)	−18 (8)	−7 (4)

doubtedly artifacts of the refinement process attributable to the disorder in the crystal structure.

Both adenine rings and both barbiturate rings are planar within experimental error as can be seen from the planarity data in Table 4. The two hydrocarbon side groups on each of the barbiturates, together with the barbiturate atom C(5), can be considered to be a 6-methyl-1-heptene molecule that is disubstituted at its 4 position. On both barbiturates, this hydrocarbon chain assumes a conformation that is nearly fully extended in the direction normal to the plane of its attached barbiturate ring.

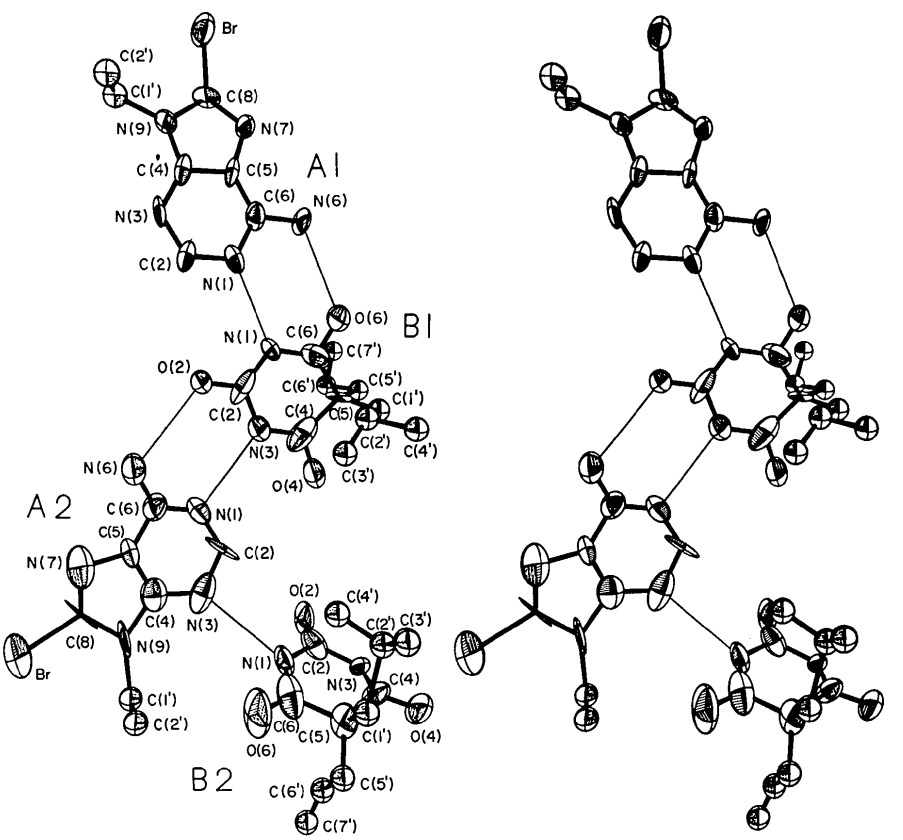

Fig. 1. A stereographic view of an asymmetric unit of the crystalline complex 8-bromo-9-ethyladenine–5-allyl-5-isobutylbarbituric acid. All atoms but those of the hydrocarbon side groups are illustrated as thermal ellipsoids at the 50% probability level. The atoms of the hydrocarbon side groups are shown as spheres of an arbitrary radius for the sake of clarity. Hydrogen bonds are represented by thin lines.

Table 4. *Deviations of atoms from the least-squares plane through the indicated atoms*

Adenine atom	Deviation for molecule *A*1 (Å)[a]	Deviation for molecule *A*2 (Å)[b]
N(1)	−0·03	0·02
C(2)	0·01	−0·02
N(3)	0·00	0·02
C(4)	0·00	0·02
C(5)	0·02	−0·03
C(6)	0·03	−0·01
N(7)	−0·02	0·01
C(8)	0·00	0·01
N(9)	0·01	−0·02
N(6)	0·10*	0·11*
Br	0·07*	−0·10*
C(1′)	0·18*	−0·20*
R.m.s. deviation	0·02	0·02

Barbiturate atom	Deviation for molecule *B*1 (Å)[c]	Deviation for molecule *B*2 (Å)[d]
N(1)	0·02	0·03
C(2)	0·05	0·01
N(3)	−0·04	−0·09
C(4)	−0·06	0·01
C(5)	0·02	0·02
C(6)	−0·02	−0·02
O(2)	0·07	0·03
O(4)	−0·07	0·03
O(6)	0·03	−0·02
R.m.s. deviation	0·05	0·04

* Atoms not included in calculating the least-squares plane.

(*a*), (*b*), (*c*), (*d*) refer to equations of least-squares planes: (*a*) $4{\cdot}0955x-23{\cdot}6069y+0{\cdot}7525z=-7{\cdot}4837$; (*b*) $3{\cdot}6248x-23{\cdot}5484y+1{\cdot}5700z=-7{\cdot}5625$; (*c*) $1{\cdot}6952x-25{\cdot}3789y+0{\cdot}1266z=-10{\cdot}1930$; (*d*) $2{\cdot}2864x-3{\cdot}6605y+10{\cdot}9103z=3{\cdot}4882$ Å.

The intermolecular associations

The crystal structure of *A*.*B* can be considered to be formed from a hierarchy of structural motifs. These motifs, some of which have quite unusual features, will be described in the order of their increasing complexity.

Both unique adenine molecules and barbiturate molecule *B*1 associate by hydrogen bonding to form extended ribbons of planar rings with the sequence *A*2–*B*1–*A*1–*A*1*–*B*1*–*A*2* (where the asterisks indicate the centrosymmetrically related molecules). This is illustrated in Fig. 3. Within these ribbons adenines *A*1 and *A*2 are each hydrogen-bonded to barbiturate *B*1 by a Watson–Crick-type association. In addition, adenine *A*1 forms a hydrogen-bonded cyclic dimer (*i.e.* molecules joined by two or more hydrogen bonds so as to form one or more rings) with a centrosymmetrically related adenine molecule, *A*1*, in a manner quite common for hydrogen-bonded adenine pairs (Voet & Rich, 1970; Voet, 1972). However, adenine *A*2 forms only one of the two hydrogen bonds that it has the potential to form [there is no possible acceptor group for such a second hydrogen bond that is within 4·0 Å of atom *A*2N(6)]. Failure to form a full complement of hydrogen bonds is rare in crystal structures in general and is without precedent among the 36 published crystal structures of base pairs (Voet & Rich, 1970; Sobell, 1971; Hsu & Craven, 1974).

The foregoing ribbon of hydrogen-bonded heterocyclic molecules has the form of an undulating plane. The mean planes of the two centrosymmetrically related (and hence parallel) adenine *A*1 molecules that form a cyclic dimer are 0·30 Å apart. The dihedral angles between the mean plane of barbiturate group *B*1 and those of adenine rings *A*1 and *A*2 are 14 and 15°, respectively. It is interesting to note that the dihedral angles between base-paired adenine and uracil rings are rarely greater than 10° (Voet & Rich, 1970) whereas those between base-paired adenine and barbiturate rings are all observed to be greater than 10° (Kim & Rich, 1968; Voet & Rich, 1972; Voet, 1972). The reasons for this phenomenon are not readily apparent.

Barbiturate molecule *B*2 does not join in the formation of hydrogen-bonded cyclic dimers. Rather it forms two single N–H···N hydrogen bonds in which atoms N(3) of both adenine residues *A*1 and *A*2 are the acceptor groups. Translationally related (by $z=1$) hydrogen-bonded ribbons of molecules of the previously described sort are thereby joined into planar strips that extend infinitely along the *z* direction. This structural feature can be seen in Fig. 3 and is schematically represented in Fig. 4(*a*).

The parameters describing the hydrogen bonds interconnecting this assemblage of molecules are all within the normal ranges for such interactions. The two N–H···O hydrogen bonds in the structure are both somewhat longer than the average for such interactions in agreement with the N–H···O distances reported in other crystal structures containing uracil or barbiturate residues in complex with adenine derivatives (Voet, 1972; Gartland & Craven, 1974).

Barbiturate *B*2 is more nearly perpendicular than parallel to the previously described ribbon of hydrogen-bonded molecules. The dihedral angles between the mean plane of barbiturate *B*2 and those of adenines *A*1 and *A*2 are 64 and 62°, respectively. This structural feature is also without precedent among the known crystal structures of base pairs (Voet & Rich, 1970; Sobell, 1971; Hsu & Craven, 1974).

Neighboring planar strips that are related by the translation (1,0,1) associate vertically in an overlapping manner much like that of shingles on a roof. A two to three-ply mat of hydrogen-bonded and stacked molecules is thereby formed that extends infinitely in the *x* and *z* directions and which is 7–11 Å thick along *y*. Such mats are centered at $y=0$ and $\frac{1}{2}$ according to the twofold screw symmetry of the unit cell. This assemblage of molecules is schematically illustrated in Fig. 4(*b*).

Within these mats of molecules adjacent parallel ribbons of hydrogen-bonded molecules associate vertically to form two to three-layered stacks of parallel

planar rings. This is illustrated in Fig. 5. Here it is seen that although these stacked ribbons lie directly over one another, their intermolecular interactions are largely characterized by a lack of overlap between neighboring rings. Such associations are typical of stacking interactions among purines and pyrimidines. The greatest amount of ring overlap in the structure is found in the stacking interactions between adenine rings *A*1 and *A*2. The relative orientation of the adenine rings in this interaction is almost identical to that found in the stacking interaction between two crystallographically non-equivalent 8-bromo-9-ethyladenine molecules in the crystal structure of the hydrogen-bonded complex phenobarbital–(8-bromo-9-ethyladenine)$_2$ (Kim & Rich, 1968) [see Fig. 11(*e*) of Bugg, Thomas, Rao & Sundaralingam, 1971]. The most intimate contact in this interaction is between the bromine atom of adenine *A*2 and the pyrimidine ring of adenine *A*1. The closest *A*2Br$\cdots$*A*1 ring contacts, *A*2Br$\cdots$*A*1N(3) $[x-1,y,z-1]$ and *A*2Br$\cdots$*A*1C(4) $[x-1,y,z-1]$ are 3·56 and 3·58 Å, respectively. The closest contact between light atoms in this stack, that between atom *A*2C(6) and *A*1N(6)$[1-x,1-y,2-z]$, is 3·38 Å. These distances are all near their respective minimal van der Waals contacts.

The rather large spaces between the above described mats of heterocycles are filled by the rings of barbiturates *B*2 and by the hydrocarbon substituents to the heterocycles as is indicated schematically in Fig. 4(*b*). However, these spaces are not efficiently filled as is suggested by the rather low density of the crystal (Table 1; other crystalline complexes of base pairs with elemental compositions similar to that of the present complex are generally reported to have densities in the range 1·5–1·7 g cm^{-3}). Indeed, barbiturate ring *B*2 makes no intermolecular contacts less than 4·0 Å, except for the regions about the two hydrogen bonds that it forms with adenines *A*1 and *A*2. This inefficient packing accounts for the disorder of the hydrocarbon substituents to the barbiturates. A similar phenomenon

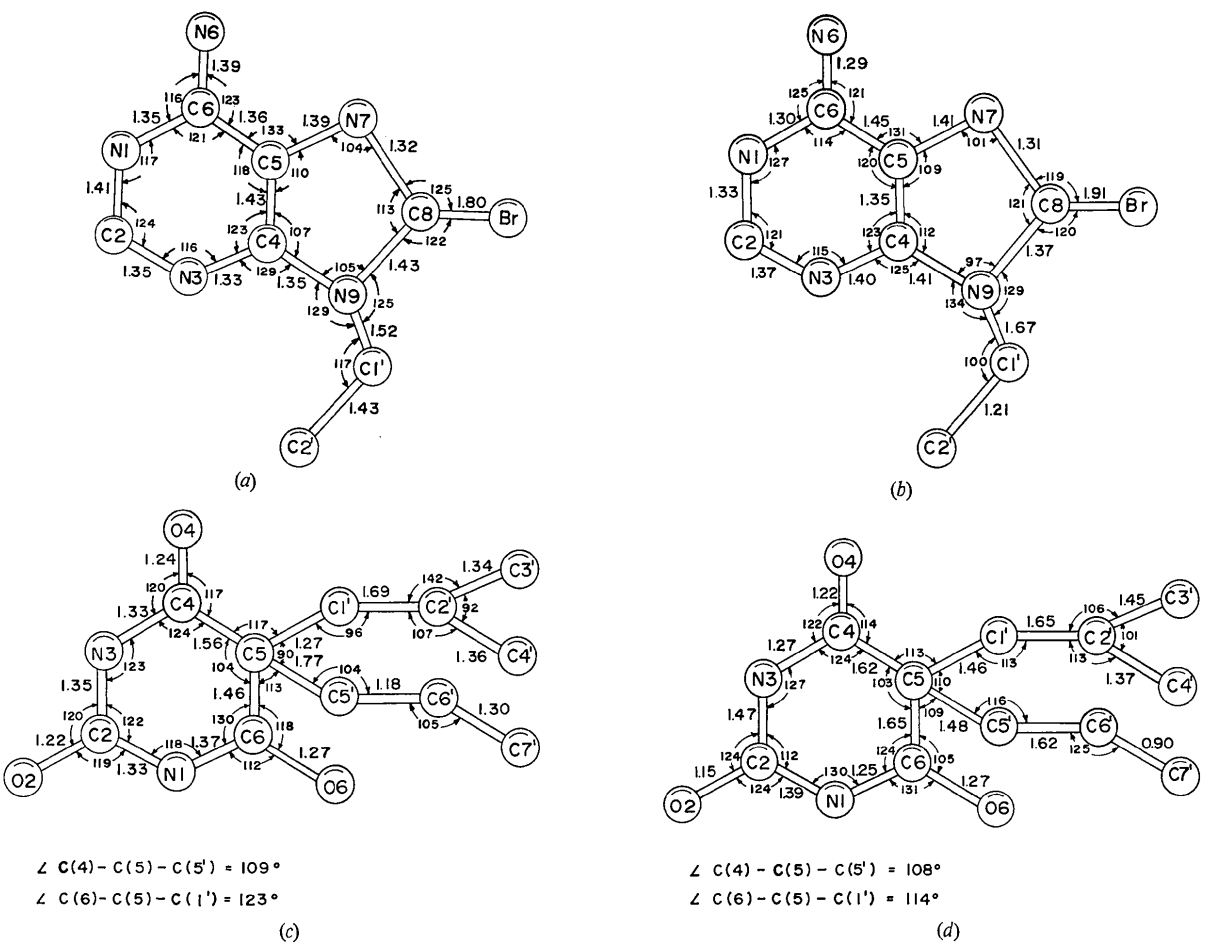

Fig. 2. The covalent bond distances (Å) and angles (°) of (*a*) 8-bromo-9-ethyladenine 1, (*b*) 8-bromo-9-ethyladenine 2, (*c*) 5-allyl-5-isobutylbarbituric acid 1 and (*d*) 5-allyl-5-isobutylbarbituric acid 2. The average standard deviations of these quantities are 0·04 Å and 3°, respectively, for ring distances and angles and are 0·08 Å and 5°, respectively, for distances and angles involving the hydrocarbon side groups.

has been described by Smit & Kanters (1974) in the crystal structure of 5-ethyl-5-(1,3-dimethylbutyl)barbituric acid. Despite the looseness of the crystal structure of *A.B* there is no indication that it incorporates any solvent of crystallization.

Both unique bromine atoms make closer than van der Waals contacts with oxygen atoms of neighboring barbiturate rings. The *A*2Br···*B*2O(4)[$x-1,y,z$] and the *A*1Br···*B*1O(6)[$2-x,1-y,3-z$] distances are 3·18 and 3·24 Å, respectively (the latter transformation relates the two halves of the hydrogen-bonded ribbon of heterocycles). The Br···O minimal van der Waals contact is 3·35 Å (Pauling, 1960). The C–Br···O angles associated with these close contacts are 173 and 132° for *A*2C(8)–*A*2Br–*B*2O(4)[$x-1,y,z$] and *A*1C(8)–*A*1Br –*B*1O(6)[$2-x,1-y,3-z$], respectively. The near linearity of the former angle suggests that the close *A*2Br···*B*2O(4)[$x-1,y,z$] contact is an association of the type that Hassel (1970) described as a charge-transfer interaction. The poor linearity of the latter Br···O interaction together with the relatively large errors in the bond distances suggest that the close *A*1Br···*B*1O(6)[$2-x,1-y,3-z$] contact can be attributed to the packing requirements necessary to maintain the integrity of the hydrogen-bonded ribbon of ring molecules. There are no other notably close interatomic contacts within the crystal structure.

Discussion

The most striking feature of the present structure is the nearly perpendicular disposition of barbiturate rings *B*2 with respect to the ribbons of base-paired molecules. Consideration of the 36 reported crystal structures containing base pairs (Voet & Rich, 1970; Sobell, 1971) leads to the expectation that all of the bases in a crystalline complex of stoichiometry $(A.B)_2$ will associate to form endless ribbons of hydrogen-bonded heterocycles in which the repeating motif is ···*A*2 . *B*2 . *A*1 . *B*1···. In the structure of *A.B* all of the hetero base-pairing

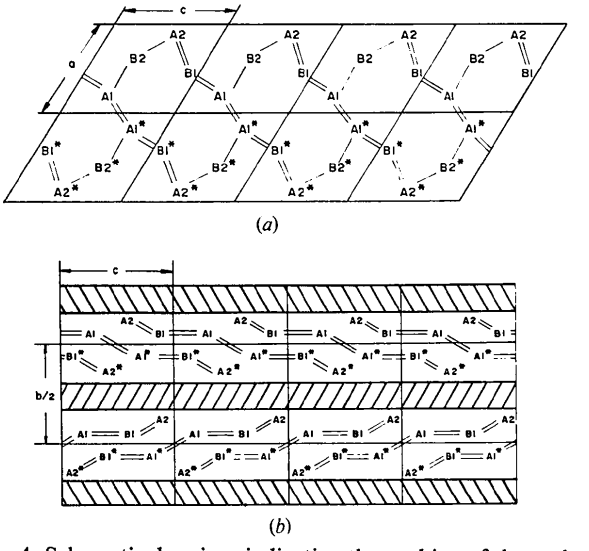

Fig. 4. Schematic drawings indicating the packing of the molecules of the complex *A.B* into its crystal structure. (*a*) View along the *b* axis illustrating the pattern of association of a hydrogen-bonded layer of heterocycles. (*b*) View along the *a* axis indicating the vertical packing mode of the hydrogen-bonded layers of heterocycles. Hydrogen bonds are represented by thin lines. The regions of the crystal structure containing the hydrocarbon side groups together with the rings of barbiturates *B*2 are represented by hatched areas.

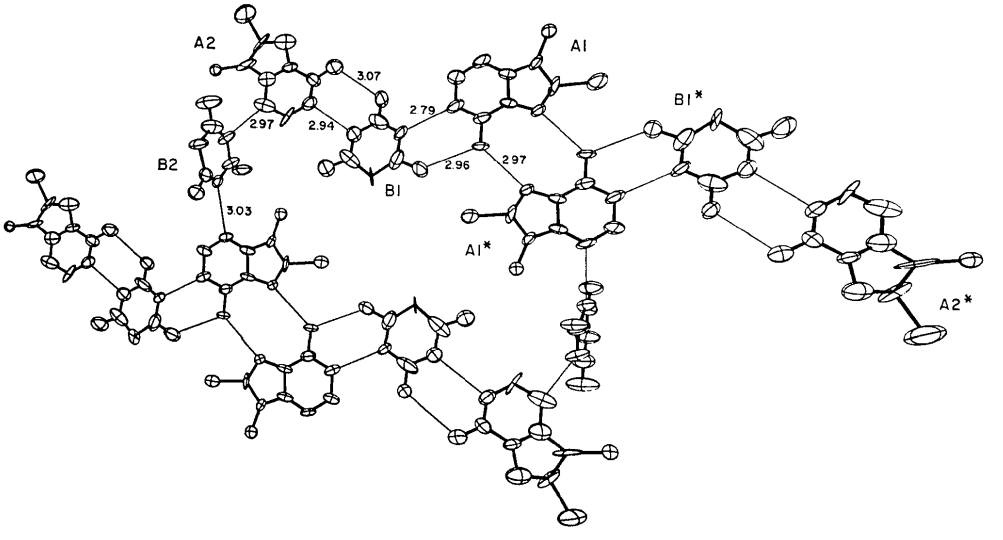

Fig. 3. A perspective drawing illustrating the hydrogen-bonding interactions in the crystalline complex 8-bromo-9-ethyladenine–5-allyl-5-isobutylbarbituric acid. All atoms are shown but atoms C(1′) of the adenine residues are illustrated as thermal ellipsoids at the 50% probability level. Atoms C(1′) of the adenine residues are represented by spheres of arbitrary radii. The other atoms of the hydrocarbon side groups have been omitted for the sake of clarity. Hydrogen bonds are represented by thin lines. The lengths of the unique hydrogen bonds are given in Å.

interactions must be of the Watson–Crick type because Hoogsteen pairing is prevented by steric interference with the 8-substituent bromine atoms of the adenine residues. Nevertheless model building studies using space filling (*CPK*) models indicate that there would be no obvious steric objection to the formation of any of several such Watson–Crick paired assemblies.

Previous structural studies of crystalline complexes of adenine derivatives with barbiturates (Voet, 1975) as well as those of other crystals incorporating barbiturates (Gartland & Craven, 1974) have shown that N–H···O hydrogen bonds, in which the acceptor is a barbiturate carbonyl group, tend to be abnormally long. Several of those hydrogen bonds are so long (3·3–3·4 Å) as to be essentially non-existent (Hamilton & Ibers, 1968). In other crystal structures containing barbiturates or barbiturate derivatives (Shieh & Voet, 1975; Bolton, 1964) the barbiturates do not participate as hydrogen-bonding acceptors. This information is consistent with the hypothesis that barbiturates are poor hydrogen-bonding acceptors (Voet, 1972; Gartland & Craven, 1974; Voet, 1975).

The prominent structural features of the present complex are also consistent with the above hypothesis. Only two of the possible twelve unique hydrogen-bond acceptor sites on the barbiturates participate in hydrogen bonding. In contrast, all six such sites on the adenine residues do so with the exception of atom *A*2N(7). However, the hydrogen-bonding capabilities of this latter position are significantly restricted due to the previously described steric interference with Hoogsteen pair formation.

In previously reported structures in which barbiturates or their derivatives have formed extremely long hydrogen bonds (Voet, 1972; Voet & Rich, 1972) or do not participate in hydrogen-bond formation (Shieh & Voet, 1975; Bolton, 1964), the barbiturates associate through dipole–dipole interactions between carbonyl groups. On the basis of these structures it could be argued that the hydrogen-bond acceptor capabilities of the barbiturates are not necessarily weak but that they are dominated by the presumably strong dipole–dipole interactions in which the barbiturates take part. However in the present structure, barbiturate *B*2, the molecule that accepts no hydrogen bonds, interacts quite loosely with its surrounding milieu. Hence this argument becomes considerably less convincing.

The experimental data concerning adenine–barbiturate complexes appear contradictory. Solution studies have shown that the association constants of adenine–barbiturate complexes are an order of magnitude greater than those of adenine–uracil complexes (Kyogoku, Lord & Rich, 1968). Yet crystallographic studies clearly indicate that N–H···O hydrogen bonds in which the acceptor group forms part of a barbiturate ring are significantly weaker than those in which the acceptor group is from a uracil derivative.

The simple electrostatic theory of hydrogen bonding leads to the expectation that the strong dipole moments generated by barbiturate carbonyl groups would render their affinity for hydrogen-bond formation particularly great. However, CNDO/2 molecular orbital calculations on 5,5-diethylbarbituric acid (Voet, 1972) suggest that the dipole moments of barbiturate carbonyl groups are no greater than those of uracil derivatives. Present day theory has not satisfactorily explained the barbiturates' observed lack of hydrogen-bond acceptor affinity nor has it accounted for the strength of the adenine–barbiturate association in a manner that is consistent with crystallographic observations. It remains for future studies, both theoretical and experimental, to resolve this apparent paradox.

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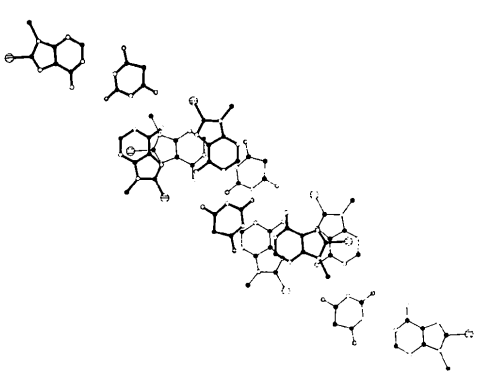

Fig. 5. A projection of two consecutive parallel ribbons of base-paired molecules onto the least-squares plane of adenine ring *A*1. This illustrates the ring stacking relationships within the crystal structure of *A.B.* Atoms are represented as circles of arbitrary radii with carbons as filled circles, nitrogen atoms as unfilled circles, oxygen atoms as shaded circles and bromine atoms as larger shaded circles.

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A Neutron-Diffraction Study of the 1:1 Molecular Complex of 7,7,8,8-Tetracyanoquinodimethane with *p*-Terphenyl*

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The 1:1 complex between 7,7,8,8-tetracyanoquinodimethane (TCNQ) and deuterated *p*-terphenyl forms dark red crystals, space group $P\bar{1}$, with one molecule of each component in the unit cell of dimensions $a = 8{\cdot}0189$ (5), $b = 8{\cdot}8927$ (5), $c = 8{\cdot}0264$ (5) Å, and $\alpha = 96{\cdot}413$ (3), $\beta = 95{\cdot}861$ (9), $\gamma = 102{\cdot}800$ (7)°. The structure was solved by fitting the transform of terphenyl-d to neutron-diffraction intensity data and was refined by least-squares methods, using 2614 unique reflections, to a final discrepancy index $R(F^2)$ of 0·042. All bond distances were determined to a precision of $\leq 0{\cdot}002$ Å. The structure consists of stacks in which TCNQ and terphenyl molecules alternate on centers of symmetry along the *a* axis. *p*-Terphenyl is an overcrowded molecule showing in-plane and out-of-plane deviations from the idealized planar conformation, the largest of which is a 12° torsion between the center and each end ring. The resultant distances between overcrowded deuterium atoms, 1·972 (2) and 1·985 (2) Å, are still less than the sum of van der Waals radii. An unusual pattern of incomplete deuteration was noted.

Introduction

Two main structure types of molecular complexes with TCNQ have been observed. In 'segregated stack' structures, approximately parallel molecules of the same kind occur in infinite stacks, while in 'mixed-stack' structures, molecules of two kinds alternate. Some charge-transfer complexes with TCNQ are good organic electrical conductors; although the segregated-stack arrangement seems to characterize the best conductors, mixed-stack structure determinations help to provide further understanding of TCNQ behavior.§ The structures of a number of mixed-stack charge-transfer complexes of TCNQ and planar aromatic compounds have been determined and are listed in Table 5.

The *p*-terphenyl complex with TCNQ has two features which are different from those with other planar aromatic compounds whose structures have been determined. The *p*-terphenyl molecule is longer than the TCNQ, so that there are several ways the two could overlap. The present structure determination shows that viewed perpendicular to the TCNQ plane the quinonoid *exo* double bonds center over the middle ring of terphenyl (see Fig. 1). Secondly, *p*-terphenyl in a planar conformation is an overcrowded molecule because the distance between the *ortho* bay§ hydrogen atoms is less than the sum of van der Waals radii. Rietveld, Maslen & Clews (1970) found that in crystals of *p*-terphenyl the molecule departs only slightly from planarity and the overcrowding is relieved by in-plane deformations. Baudour (1972) concluded that the planarity, however, did not necessarily correspond to the equilibrium configura-

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§ The present compound is an insulator: the conductivity at room temperature is less than 4×10^{-11} ohm^{-1} cm^{-1}.

§ We suggest the descriptive term '*ortho* bay' to designate a pair of positions on separate rings each *ortho* to and lying on the same side of the bond between the rings. Jones & Sowden (1975) have employed the term 'bay' in a similar connection.