[Chem. Pharm. Bull. 22(9)2069—2074(1974)]

UDC 547.835.1.04 : 547.556.8.02

The Crystal Structure of the Bromoacetylated Dimer-A synthesized by the Reaction of Acridine with Hydroxylamine-O-sulfonic Acid

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(Received February 19, 1974)

The structure of the bromoacetylated dimer-A (BADA) benzene solvate; $C_{30}H_{26}O_2N_6Br_2 \cdot C_6H_6$ has been determined by X-ray diffraction method in order to elucidate the dimer-A structure; $(C_{13}H_{12}N_3)_2$ obtained by the reaction of acridine with hydroxylamine-O-sulfonic acid (NH_2OSO_3H, HAS).

The crystals; BADA·C_6H_6 are triclinic with space group P_1^- and the unit-cell dimensions are a=9.167, b=10.618, c=10.379Å, α=99.60, β=119.61, γ=95.21°. One formula unit is contained in the cell. The crystal structure was solved by the heavy-atom method and refined by the block-matrix least-squares method including anisotropic thermal parameters. The final *R* value for 1106 non-zero observed structure factors was 0.07.

BADA was found to be a benzalazine derivative, 2,2′-(2-bromoacetylaminoanilino)-benzalazine. On the basis of the result obtained by the present determination and the comparison of ultraviolet and nuclear magnetic resonance spectra, the structure of dimer-A has been established.

In the previous publication,[2)] we showed a novel one-step synthesis of 5H-dibenzo[*b*, *e*]-[1,4]diazepine derivatives involving a ring expansion from acridinium salts by use of a reaction with hydroxylamine-O-sulfonic acid (NH_2OSO_3H, HAS) as shown in Chart 1.

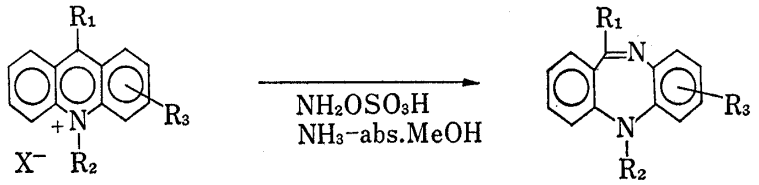


Chart 1

In this paper, we wish to present the interesting results of the reaction of acridine itself with HAS. Treatment of acridine with HAS in methanol containing ammonium hydroxide at room temperature afforded a product, mp 254—255° in 10.2% yield as shown in Chart 2.

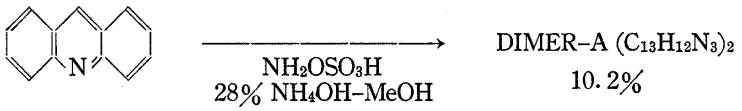


Chart 2

The elemental analysis, mass spectrum *m/e*: 420 (M^+) and nuclear magnetic resonance (NMR) spectrum which is mentioned below suggested this product to have a dimeric structure, $(C_{13}H_{12}N_3)_2$. It was named as dimer-A tentatively. But it seems to be difficult to determine the structure of dimer-A mainly on the basis of chemical and spectral data.

Therefore, the present X-ray crystallographical study of a heavy-atom derivative of dimer-A was undertaken.

1) Location: *Hongo 7-3-1, Bunkyo-ku, Tokyo.*
2) M. Hirobe and T. Ozawa, *Tetrahedron Letters*, **47**, 4493 (1971).

Experimental

Various attempts to prepare a suitable heavy-atom derivative of dimer-A for X-ray structure analysis failed, because of the very labile nature of dimer-A in acidic solutions.

It was finally succeeded to obtain the bromoacetylated dimer-A (BADA) by treatment with freshly synthesized bromoacetic anhydride in dry benzene. It gave fine yellow needles when recrystallized from dichloromethane, but recrystallization from benzene yielded well developed transparent yellow plates containing benzene as a solvent of crystallization. The latter crystals were uzed for the X-ray work.

The crystal of dimensions $0.516 \times 0.490 \times 0.090$ mm was mounted on the goniometer of a four-circle X-ray diffractometer with the c axis coincident with the φ axis. Diffraction intensities were measured by Ni-filtered Cu $K\alpha$ radiation utilizing the ω-2θ scan technique up to $2\theta = 90°$. The scanning speed was 4°/min in 2θ. No absorption correction was applied and a total of 1106 structure factors having the net intensities above the 3σ level were obtained out of 1394 accessible reflections within the same angular range.

Table I. The Final Atomic Parameters and Their Standard Deviations

	x	y	z	B11	B22	B33	B12	B13	B23
BR(1)	0.4788	0.0803	0.1496	0.0219	0.0236	0.0160	0.0052	0.0080	0.0072
	(2)	(2)	(2)	(3)	(3)	(3)	(2)	(3)	(2)
C(1)	0.5132	0.0805	0.3486	0.0230	0.0245	0.0118	0.0048	0.0094	0.0046
	(18)	(16)	(15)	(34)	(26)	(24)	(24)	(24)	(21)
C(2)	0.7010	0.1193	0.4791	0.0268	0.0135	0.0116	0.0017	0.0098	0.0033
	(18)	(13)	(14)	(34)	(20)	(23)	(21)	(24)	(17)
O(3)	0.7266	0.1341	0.6094	0.0302	0.0245	0.0157	0.0043	0.0142	0.0059
	(13)	(11)	(10)	(24)	(17)	(17)	(16)	(17)	(14)
N(4)	0.8248	0.1283	0.4439	0.0175	0.0110	0.0123	0.0034	0.0103	0.0027
	(12)	(9)	(11)	(21)	(13)	(17)	(13)	(16)	(12)
C(5)	1.0048	0.1650	0.5454	0.0186	0.0092	0.0101	0.0044	0.0090	0.0033
	(15)	(11)	(13)	(27)	(16)	(20)	(16)	(20)	(14)
C(6)	1.0847	0.1782	0.7072	0.0285	0.0094	0.0089	0.0056	0.0075	0.0039
	(17)	(12)	(13)	(33)	(16)	(21)	(19)	(22)	(15)
C(7)	1.2639	0.2129	0.7934	0.0284	0.0122	0.0155	0.0083	0.0073	0.0052
	(19)	(13)	(16)	(36)	(19)	(26)	(21)	(26)	(18)
C(8)	1.3618	0.2394	0.7278	0.0225	0.0132	0.0183	0.0066	0.0067	0.0019
	(18)	(14)	(16)	(32)	(20)	(27)	(20)	(25)	(19)
C(9)	1.2796	0.2252	0.5681	0.0221	0.0116	0.0153	0.0073	0.0081	0.0017
	(17)	(13)	(15)	(31)	(18)	(25)	(19)	(24)	(17)
C(10)	1.1014	0.1874	0.4805	0.0200	0.0076	0.0126	0.0057	0.0093	0.0043
	(15)	(11)	(13)	(27)	(15)	(21)	(16)	(21)	(15)
N(11)	1.0198	0.1681	0.3162	0.0196	0.0099	0.0075	0.0042	0.0074	0.0037
	(12)	(9)	(10)	(22)	(12)	(15)	(13)	(15)	(11)
C(12)	0.9496	0.2634	0.2432	0.0152	0.0072	0.0093	0.0016	0.0063	0.0022
	(14)	(11)	(13)	(25)	(14)	(19)	(15)	(19)	(13)
C(13)	0.9182	0.3729	0.3158	0.0197	0.0084	0.0135	0.0032	0.0083	0.0027
	(16)	(11)	(14)	(28)	(15)	(22)	(17)	(22)	(15)
C(14)	0.8464	0.4675	0.2387	0.0240	0.0122	0.0128	0.0071	0.0084	0.0038
	(17)	(13)	(14)	(32)	(18)	(23)	(19)	(23)	(16)
C(15)	0.8060	0.4546	0.0857	0.0318	0.0111	0.0140	0.0075	0.0083	0.0035
	(19)	(13)	(15)	(38)	(19)	(24)	(22)	(26)	(17)
C(16)	0.8367	0.3450	0.0143	0.0236	0.0130	0.0120	0.0062	0.0070	0.0015
	(17)	(13)	(14)	(32)	(19)	(23)	(20)	(23)	(17)
C(17)	0.9066	0.2485	0.0882	0.0126	0.0079	0.0088	0.0037	0.0039	0.0021
	(14)	(11)	(12)	(24)	(15)	(19)	(15)	(18)	(14)
C(18)	0.4723	0.4386	0.3565	0.0602	0.0208	0.0307	−0.0027	0.0262	0.0028
	(29)	(19)	(23)	(69)	(30)	(42)	(36)	(47)	(28)
C(19)	0.6207	0.4429	0.4861	0.0386	0.0178	0.0487	0.0071	0.0289	0.0111
	(24)	(17)	(25)	(49)	(27)	(53)	(29)	(45)	(31)
C(20)	0.6545	0.4998	0.6259	0.0332	0.0216	0.0372	−0.0008	0.0112	0.0136
	(23)	(18)	(23)	(46)	(29)	(45)	(29)	(38)	(30)
C(21)	0.9288	0.1415	0.0007	0.0160	0.0113	0.0136	0.0056	0.0085	0.0033
	(15)	(12)	(14)	(26)	(17)	(22)	(17)	(21)	(16)
N(22)	0.9980	0.0480	0.0538	0.0162	0.0104	0.0076	0.0011	0.0051	−0.0011
	(12)	(9)	(10)	(20)	(14)	(17)	(14)	(16)	(11)

Crystal data

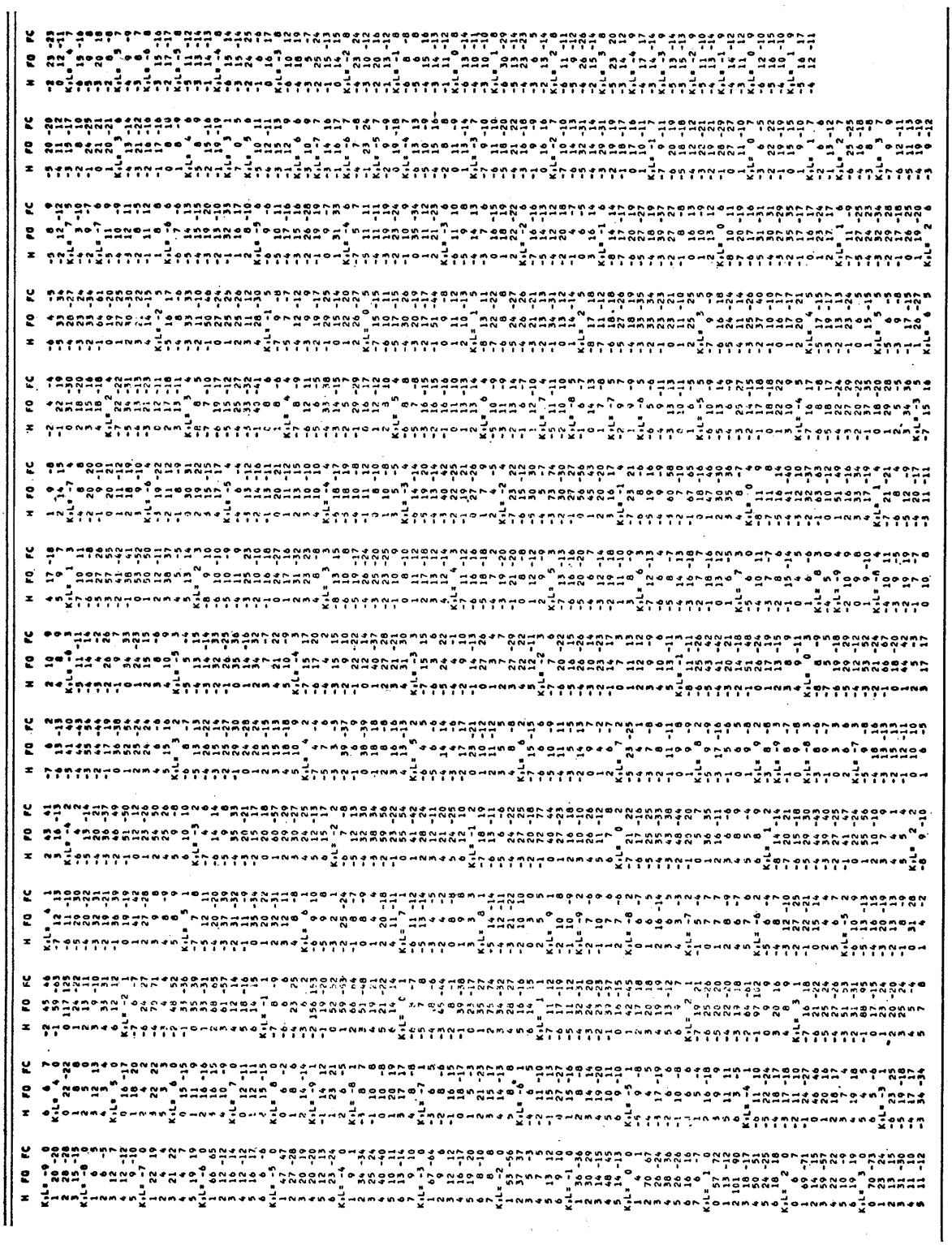
Bromoacetylated dimer-A (BADA) benzene solvate;
$C_{30}H_{26}O_2N_6Br_2 \cdot C_6H_6$, mp 180° (decomp.)
MW. 662.386, FW. 740.496

triclinic space group P_1^-

$a=9.167$ (5)	$b=10.618$ (5)	$c=10.379$ (5) Å
$\alpha=99.60$ (3)	$\beta=119.61$ (3)	$\gamma=95.21$ (3)°
$U=848.1$Å^3,	$Dx=2.59$ g·cm^{-3},	$Z=1$

The structure was solved by the heavy atom method and refined by the block-matrix least-squares method to an R value of 0.07. The refinement was carried out allowing to anisotropic thermal parameters

TABLE II. Observed and Calculated Structure Factors



for each atom and the unit weight for each reflection. Hydrogen atoms were not included in the refinement. The final atomic parameters are given in Table I and the observed and calculated structure factors are listed in Table II.

Discussion of the Structure

The molecule takes a dimer form with its center coincident with the center of symmetry of the lattice. It consists of a benzalazine, two aminoaniline and two bromoacetyl groups and the chemical structure can be formulated as 2,2′-(2-bromoacetylaminoanilino)-benzalazine- (Fig. 1 and Fig. 2). Bond lengths and angles are shown in Fig. 2 and Fig. 3. The standard deviations of these values were estimated to be σ(Br—C)=0.017Å, σ(distances between light atoms)=0.025Å, σ(C—C—Br)=1.1°, σ(angles formed by light atoms)=1.3°.

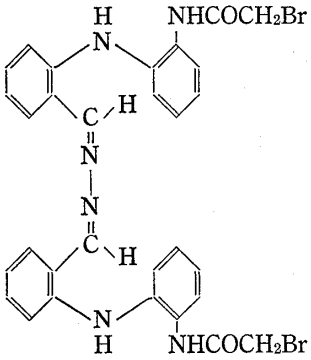


Fig. 1. BADA

The structure of benzalazine group of BADA resembles that found in the crystal of benzalazine.[3] The bond lengths and angles of their benzalazine groups are compared in Table III. These values as well as the planarity of the benzalazine group shown in Table IV indicate the conjugated structure of the benzalazine group as in the case of benzalazine itself.[3]

The least-squares planes through various groups of atoms and the deviations of atoms from the plane are shown in Table IV.

The benzalazine group takes a planar conformation as is expected from the conjugated structure mentioned above. However this conjugated system does not extend to the *o*-phenylene diamine group since the bond length C(10)–N(11) (1.45Å) is almost that of the single bond and the plane of the *o*-phenylene diamine group makes an angle of 75° 40′ to the *o*-toluidine group, the torsion angles C(13)–C(12)–N(11)–C(10) and C(12)–N(11)–C(10)–C(5) being −14.3° and 84.4° respectively.

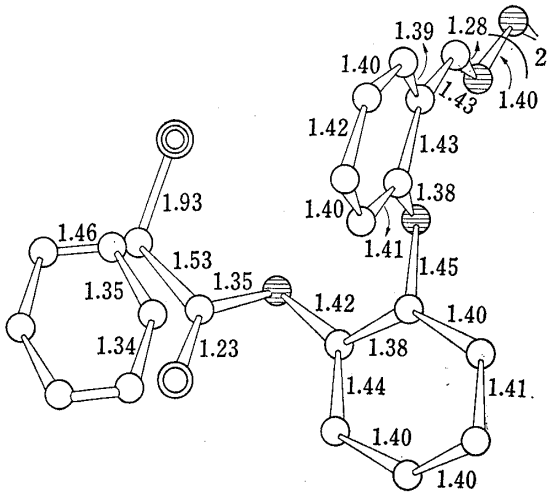


Fig. 2. Conformation of the BADA Molecule
The Bond lengths are also shown in Å unit.

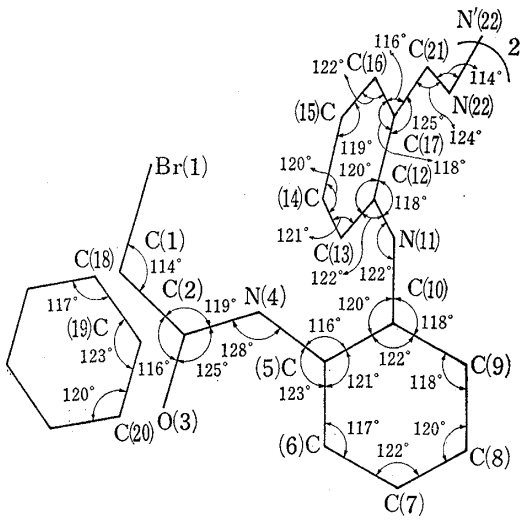


Fig. 3. Bond Angles in Degrees

A projection of the crystal structure along the b axis is shown in Fig. 4. The intermolecular short contacts less than 3.7Å are also shown in Fig. 4. No unusnal short contacts are found between the molecules. The benzene molecule is enclosed in the structure as a solvent of crystallization.

3) U.C. Sinha, *Acta Cryst.*, **B26**, 889 (1970).

Table III. Bond Lengths and Angles of the Benzalazine Groups

	BADA (present study)	Benzalazine[3]
C═C (benzene ring)[a]	1.408Å	1.386Å
C (17)—C (21)	1.427	1.465±0.018
C (21)=N (22)	1.282	1.264±0.017
N (22)—N (22′)	1.398	1.380±0.014
C═C═C (benzene ring)[a]	120.0°	120.0°
C (16)—C (17)—C (21)	116.4	119.0
C (12)—C (17)—C (21)	125.2	122.0
C (17)—C (21)—N (22)	124.1	122.5
C (21)—N (22)—N (22′)	114.1	115.0

a) mean value

Table IV. The Least-Squares Planes through Various Groups and the Deviations of Atoms from Each Plane

I	*o*-Toluidine		$0.8334X+0.4982Y-0.2392Z=7.720$[a]	
	C (12)	0.005Å	C (17)	0.001
	C (13)	−0.005	C (21)	−0.013
	C (14)	−0.012	N (11)	0.007
	C (15)	0.007	N (22)[b]	0.037
	C (16)	0.009		
II	*o*-Phenylene diamine group		$-0.2728X+0.9619Y+0.0176Z=-0.457$[a]	
	C (5)	0.009Å	C (10)	0.012
	C (6)	−0.004	N (4)	0.014
	C (7)	−0.031	N (11)	−0.034
	C (8)	0.013	C (2)[b]	0.206
	C (9)	0.021	C (12)[b]	1.102
III	Acetylamine group		$-0.2232X+0.9686Y-0.1096Z=-0.197$[a]	
	C (1)	−0.005Å	N (4)	−0.006
	C (2)	0.017	Br[b]	0.263
	O (3)	−0.006	C (5)[b]	0.037

dihedral angles between I and II=75°40′
II and III=7°50′

a) Atoms marked with an asterisk are not included in the least-squares calculation.
b) X, Y and Z form an orthogonal set of axis measured in Å unit with $Z||C$, $Y||$ [b] and X lies in (010).

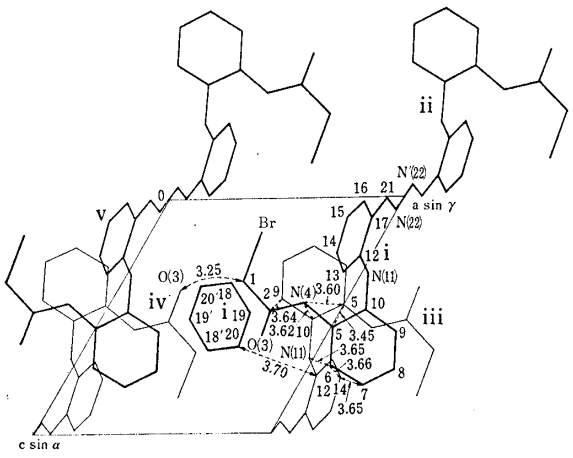


Fig. 4. Projection of the Crystal Structure along the b Axis

Intermolecular short contacts are also shown. The equivalent positions are; i at x, y, z; ii at 2-x, -y, -z; iii at 2-x, -y, 1-z; iv at 1-x, -y, 1-z.

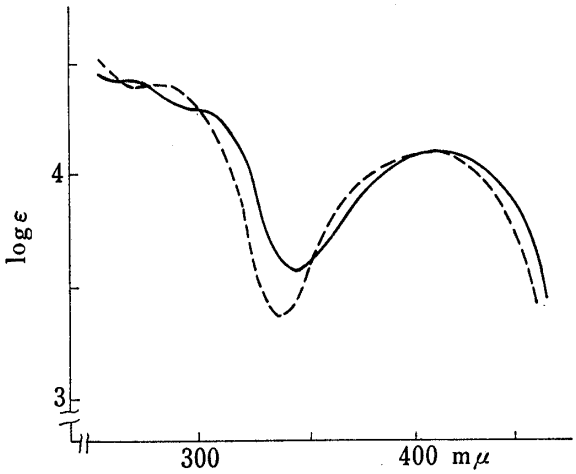


Fig. 5. Comparison of the UV Spectra (in $CHCl_3$) of Dimer-A (——) and BADA (----)

The ultraviolet (UV) spectra of BADA and dimer-A showed a close resemblance at the long wavelength region as shown in Fig. 5.

Further, the NMR spectrum of BADA benzene solvate (in dimethyl sulfoxide (DMSO)) exhibited the peaks of 0.04 τ (2H, two singlets, two NH), 1.04 τ (1H, singlet, methine), 2.4—3.4 τ (11H, multiplet, aromatic protons involving three protons of solvating benzene) and 5.96 τ (2H, singlet, methylene ($-CH_2-Br$).

On the other hand, the peaks of 0.34 τ (1H, singlet, NH), 1.06 τ (1H, singlet, methine), 2.4—3.6 τ (8H, multiplet, aromatic protons) and 5.18 τ (2H, singlet, NH_2) were observed in the NMR spectrum (in DMSO) of dimer-A.

These NMR spectra indicate that the signals of NH group at 0.04 τ and methylene group ($-CH_2-Br$) at 5.96 τ of BADA benzene solvate have been newly revealed as the result of the bromoacetylation of the NH_2 group of dimer-A which was observed at 5.18 τ, and the chemical shifts of aromatic and methine protons have been scarcely changed by the bromoacetylation.

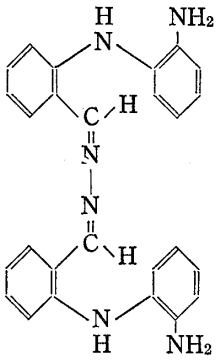


Fig. 6. Dimer–A

By comparison of their UV and NMR spectra, it has been concluded that the basic structure of dimer-A did not change by bromoacetylation and the structure of dimer-A could be formulated as 2,2′-(2-aminoanilino)-benzalazine (Fig. 6).

On the basis of the result of the present study, the reaction product of acridine with HAS in the presence of ammonium hydroxide has been fully clarified.

Full accounts of chemical study will be published in a separate paper.