

Figure 1. Stereodrawing of **2**. The thermal ellipsoids are scaled at the 50% probability level. The disordered methyl of the ethyl side chain is shown only in one of its conformations.

(3)°;  $d_{\text{obsd}} = 1.10$ ;  $d_{\text{calcd}} = 1.16 \text{ g cm}^{-3}$ ;  $Z = 2$ . A total of 4393 reflections (1027 unobservedly weak) was measured on a Hilger-Watts model Y290 full circle diffractometer with Cu K $\alpha$  radiation ( $2\theta < 140^\circ$ ).

The structure was solved by the symbolic addition method.<sup>10</sup> Hydrogen atoms were located from a difference Fourier calculated after refinement of the heavier atoms. The full structure was refined by block diagonal least squares (ten blocks) with isotropic temperature factors for the hydrogen atoms and anisotropic thermal parameters for all other atoms. The final  $R$  is 5.4%.

In the crystal the terminal methyl of the ethyl side chain is disordered. Accordingly, atomic multipliers of 0.5 were assigned to the disordered atoms. The conformation of **2** in the solid state is shown in Figure 1. Both phenyl rings are planar to within  $\pm 0.02 \text{ \AA}$ . The angle between the normals to the two phenyl rings is  $120^\circ$ . The methoxyl carbon and oxygen atoms lie approximately in the plane of their respective phenyl rings. The dihedral angles between the planes of the methoxyls ( $\text{C}_{\text{Me}}\text{-O-C}_\phi$ ) and their respective phenyl planes from 4 to  $8^\circ$ .

With the establishment of the correct stereochemistry and molecular framework of **2** there remained only to convert the two substituted benzene rings to the maleic anhydride systems of byssochlamic acid. This was accomplished by cleavage of the tetramethyl ether with boron tribromide in methylene chloride<sup>11</sup> to the unstable bishydroquinone which, without purification, was submitted to oxidation, first with potassium permanganate in aqueous glyme at  $0^\circ$  for 1.5 hr and, finally, with lead tetraacetate in acetic acid containing some water, at  $55^\circ$  for 30 min. The crystalline product ( $\sim 13\%$  overall from **2**) obtained after preparative tlc on silica gel<sup>12</sup> and trituration, first with 95% ethanol, and then with pentane, had mp  $127\text{--}129^\circ$ . Its structure as ( $\pm$ )-byssochlamic acid (**1**) was established by its elemental analysis, and by comparison with the natural

substance<sup>13</sup> which showed identical tlc behavior in three different solvent systems, as well as identity of the ir, uv, nmr, and mass spectra ( $m/e$  332.1263).<sup>14</sup>

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(13) We thank Professor D. H. R. Barton (Imperial College, London) and J. E. Baldwin (King's College, London) for making natural byssochlamic acid available to us.

(14) Final atomic and anisotropic thermal parameters for **2** will appear following these pages in the microfilm edition of this volume of the journal. Single copies may be obtained from the Business Operations Office, Books and Journals Division, American Chemical Society, 1155 Sixteenth St., N.W., Washington, D. C. 20036, by referring to code number JACS-72-4735. Remit check or money order for \$3.00 for photocopy or \$2.00 for microfiche.

Gilbert Stork,\* Jacob M. Tabak

Department of Chemistry, Columbia University  
New York, New York 10027

John F. Blount

Hoffmann-LaRoche Inc.  
Nutley, New Jersey 07110

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## A Novel Synthesis of Purine $\beta$ -D-Nucleosides via Purine 8,5'-S-Anhydronucleosides

Sir:

We have developed a simple and superior procedure for the synthesis of purine 8,5'-S-anhydronucleosides which are found to be of considerable utility as chemical precursors for the preparation of purine  $\beta$ -D-nucleosides.<sup>1</sup> This novel synthetic procedure requires the easily accessible adenine derivatives of type III which bear a D-pentofuranos-5-yl group at position 8 as a key intermediate.

Reaction of adenine-8-thiol (I)<sup>2</sup> (sodium salt) with 5-iodo-5-deoxy-1,2-O-isopropylidene- $\beta$ -D-xylofuranose (IIa),<sup>3</sup> methyl 5-iodo-5-deoxy-2,3-O-isopropylidene- $\beta$ -D-ribofuranoside (IIb),<sup>4</sup> and methyl 5-tosyloxy-5-deoxy-

(10) I. L. Karle and J. Karle, *Acta Crystallogr.*, **16**, 969 (1963).

(11) J. F. W. McOmie and M. L. Watts, *Chem. Ind. (London)*, 1658 (1963).

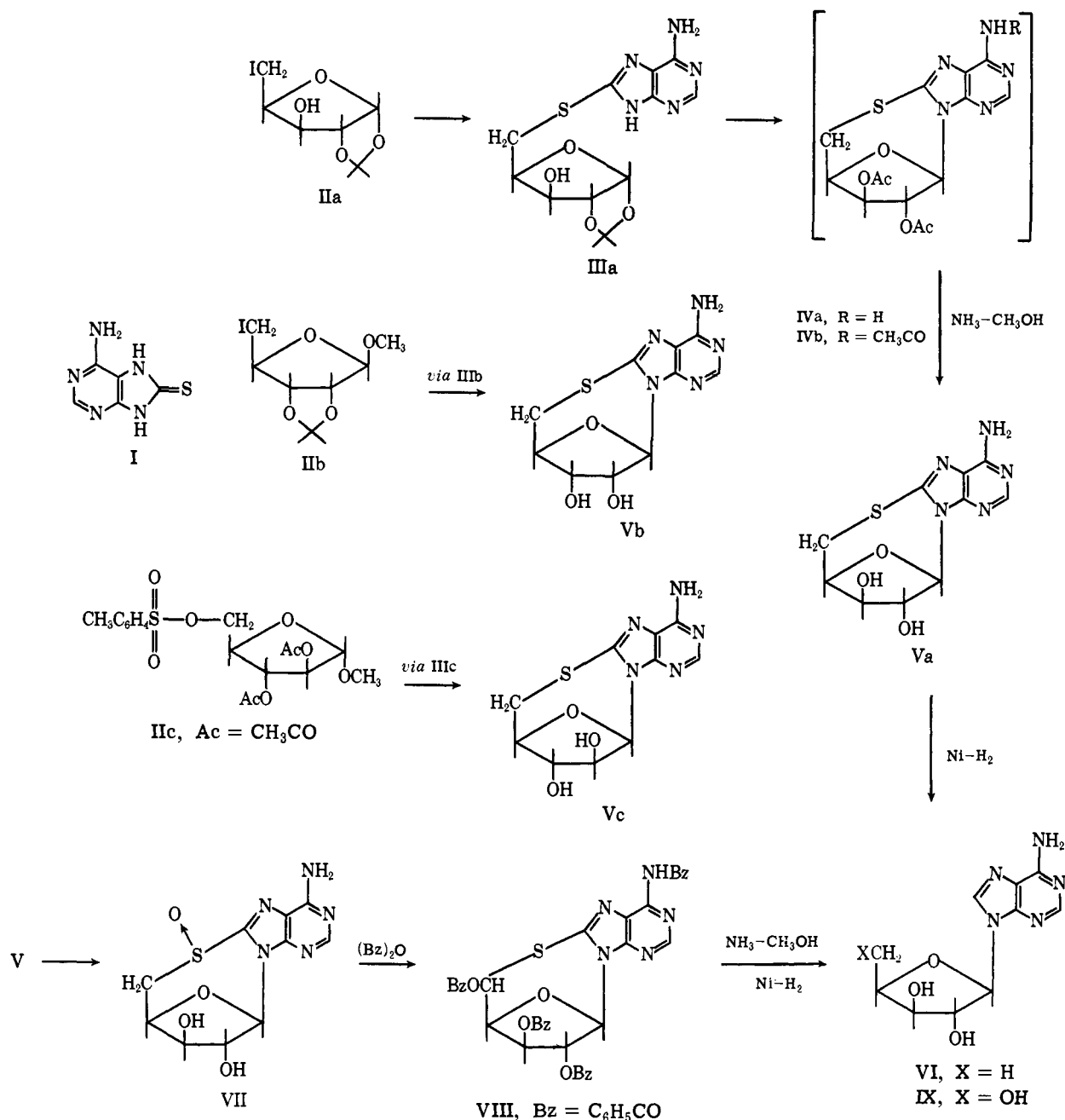
(12) Developed twice with 4% acetic acid-benzene. The synthetic byssochlamic acid was recovered by stirring the corresponding band with 5% aqueous NaOH, followed by acidification and ether extraction.

(1) M. Ikehara, *Accounts Chem. Res.*, **2**, 47 (1969).

(2) R. K. Robins, *J. Amer. Chem. Soc.*, **80**, 6671 (1958).

(3) R. A. Leven and A. L. Raymond, *J. Biol. Chem.*, **102**, 317 (1933).

(4) N. J. Leonard and K. L. Carraway, *J. Heterocycl. Chem.*, **3**, 485 (1966).



2,3-diacetyl-D-arabinofuranoside (IIc), mp 152–154°, in boiling methyl Cellosolve, afforded IIIa,<sup>5</sup> IIIb,<sup>5</sup> and IIIc,<sup>5</sup> in good yields (80% yield) (see Scheme I). Treatment of IIIa (6 mmol) with a mixture of acetic anhydride (16 ml) and glacial acetic acid (20 ml) in the presence of concentrated sulfuric acid (2 ml), followed by deacetylation, afforded colorless needles (Va, 44% yield): mp 267–269°;  $[\alpha]_D^{25} +30^\circ$ ;  $\lambda_{\text{max}}^{\text{H}_2\text{O}}$  239 ( $\epsilon$  10,000), 286 ( $\epsilon$  20,700), 287.5 (sh,  $\epsilon$  18,600), and 295 nm (sh,  $\epsilon$  13,800).

The ultraviolet absorption spectrum of Va was unaltered between pH 7 and 12 consistent with the absence of a dissociable group on N-9. Raney nickel treatment of Va afforded the known<sup>6</sup> 9-(5-deoxy-D-xylofuranosyl)-

adenine (VI): mp and mmp 228–229°;  $\lambda_{\text{max}}^{\text{pH } 1}$  261 nm;  $R_f$  0.58 in solvent A.<sup>7</sup> On the basis of elemental analysis and uv spectral data along with results on the Raney nickel treatment, the 8,5'-anhydro-9-( $\beta$ -D-xylofuranosyl)adenine-8-thiol structure is assigned to Va.

Similar treatment of IIIb and IIIc afforded the corresponding nucleosides Vb (mp 225–226°, downy crystals, 35% yield)<sup>8</sup> and Vc (mp 195–197°, colorless needles, 59% yield).

It is noteworthy that the predominant products isolated from the reactions of III–V were 9-substituted adenines as shown by the conversion of Va to VI. It is also evident that the anhydronucleosides V formed from III possess the  $\beta$ -D configuration irrespective of

(5) Satisfactory elementary analyses were obtained for these compounds and those with melting points listed herein. IIIb and IIIc are 8-alkylthioadenines of type IIIa derived from IIb and IIc, respectively.

(6) E. J. Reist, V. J. Bartuska, D. F. Calkins, and L. Goodman, *J. Org. Chem.*, **30**, 3401 (1965); we are grateful to Professor L. Goodman for providing us with an authentic sample of VI.

(7) *i*-C<sub>5</sub>H<sub>7</sub>OH-NH<sub>4</sub>OH-H<sub>2</sub>O (7:1:2, v/v).

(8) Anhydronucleoside Vb has been prepared by an alternative method: M. Ikehara, M. Kaneko, and M. Sagai, *Chem. Pharm. Bull.*, **6**, 1151 (1968). Physical properties (melting point, uv spectrum, and  $R_f$  values) of our sample are identical with reported values.

the nature of the D-pentoses attached to position 8 in III or the configuration of their blocking groups at C-2'.

8,5'-Anhydronucleosides of type V are useful intermediates for the synthesis of purine nucleosides of the  $\beta$ -D configuration. Thus, oxidation of Va with an equivalent amount of *N*-bromosuccinimide in aqueous solution afforded the corresponding sulfoxide (VII, monohydrate) in 67% yield (*Anal.* Found: C, 38.41; H, 3.90; N, 22.01; S, 10.07): uv  $\lambda_{\max}^{\text{H}_2\text{O}}$  262 nm;  $\lambda_{\max}^{\text{pH } 1}$  262 nm;  $\lambda_{\max}^{\text{pH } 11}$  265 nm; ir 1040 and 1080  $\text{cm}^{-1}$  (sulfoxide);  $R_f$  in solvent A,<sup>7</sup> 0.29. Treatment of VII (80 mg) with benzoic anhydride<sup>9</sup> at 80° for 10 hr and then at 100° for another 10 hr afforded (after removal of benzoic acid and the excess anhydride with ether) VIII (85 mg; 45% yield;  $\lambda_{\max}^{\text{EtOH}}$  299, 227 nm; absorbance ratio at two maxima, 1:5.5; homogeneous in tlc;  $R_f$  0.38<sup>10</sup>). The product VIII (80 mg) was treated with methanolic ammonia at room temperature and subsequently treated with Raney nickel, affording 9- $\beta$ -D-xylofuranosyladenine (IX, 14 mg, 62% yield). This sample was indistinguishable from an authentic sample prepared by a reported method<sup>11</sup> on the criteria of melting point, uv, and  $R_f$  in two solvent systems (*viz.*  $R_f$  0.45 in solvent A,<sup>7</sup> *cf.*  $R_f$  of VI in the same solvent system, 0.58). Since reaction conditions of each step were not optimized, the overall yield of IX must be improved.

A logical extension of the present work would be a preparation of 2'-deoxyadenosine, which is now in progress in our laboratories.

(9) Pummerer rearrangement: R. Pummerer, *Chem. Ber.*, 43, 1401 (1910).

(10) Silica gel, solvent  $\text{CHCl}_3$ -EtOH (70:5, v/v).

(11) W. W. Lee, A. P. Martinez, G. L. Tong, and L. Goodman, *Chem. Ind. (London)*, 2007 (1963).

Yoshihisa Mizuno,\* Chisato Kaneko  
Yuji Oikawa, Takao Ikeda, Tokuo Itoh

Faculty of Pharmaceutical Sciences, Hokkaido University  
Sapporo, Japan

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## Structural Consequences of 2,8 Bridging of the Semibullvalene Nucleus<sup>1</sup>

Sir:

Historically, semibullvalene can be regarded as the molecule which, because of its unique structural and geometric features, approaches most closely the realization of homoaromatic<sup>2</sup> cyclic delocalization (of six electrons) in a neutral species. However, a ring current is not observed<sup>3</sup> and the semibullvalene transition state appears to reside some 2.3–3.6 kcal/mol in potential energy above the well-known classical structures.<sup>4</sup> Both EH and MINDO/2 calculations have demonstrated that the placement of substituents on **1** will result in pronounced imbalances of the ground-state equilibrium;<sup>4a,b,5</sup>

(1) Part X of the series entitled Silver(I) Ion Catalyzed Rearrangements of Strained  $\sigma$  Bonds. For paper IX, see L. A. Paquette and L. M. Leichter, *J. Amer. Chem. Soc.*, 94, 3653 (1972).

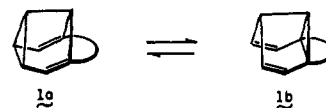
(2) S. Winstein, *Chem. Soc., Spec. Publ.*, No. 21, 5 (1969).

(3) H. E. Zimmerman, R. W. Binkley, R. S. Givens, G. L. Grunwald, and M. A. Sherwin, *J. Amer. Chem. Soc.*, 91, 3316 (1969).

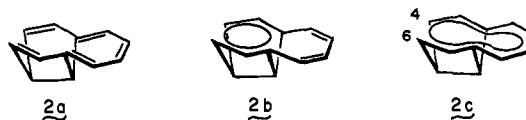
(4) (a) M. J. S. Dewar and W. W. Schoeller, *ibid.*, 93, 1481 (1971); (b) M. J. S. Dewar and D. H. Lo, *ibid.*, 93, 7201 (1971); (c) F. A. L. Anet and G. E. Schenk, *Tetrahedron Lett.*, 4237 (1970).

(5) R. Hoffmann and W.-D. Stohrer, *J. Amer. Chem. Soc.*, 93, 6941 (1971).

on this basis, annelation of the semibullvalene nucleus with a saturated polymethylene chain at positions 2 and 8 is expected to affect the position of equilibrium only by inductive stabilization and to favor **1a**, provided that the "belt" is sufficiently "loose." On the other hand, if the length of the bridge is sufficiently short, isomer **1b**

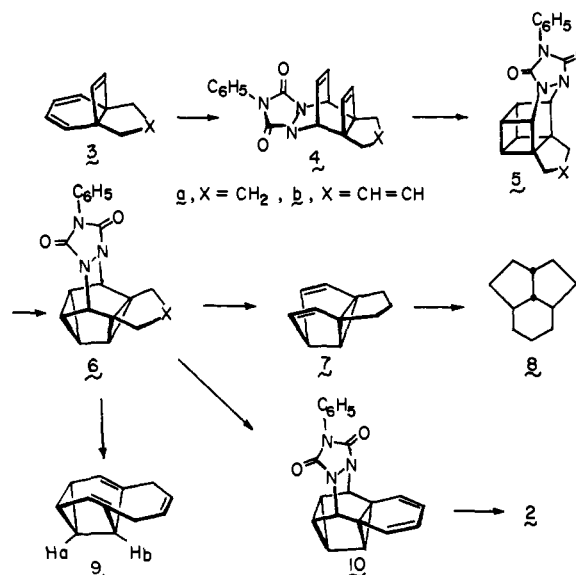


should be overwhelmingly favored in order to bypass the destabilization of **1a** arising from Bredt's rule violations. From the electronic viewpoint, similar bridging with a 1,3-butadienyl moiety could provide a molecule where the actual stable form could instead be the rigid pentaene **2a**, or one of the mesovalent Hückel-like species **2b** (six electron) or **2c** (ten electron). If



either of the latter structures were to result, reduction of the activation energy of the Cope rearrangement to a negative value<sup>5</sup> would be realized experimentally for the first time.

In design, the synthetic scheme is based upon the efficient preparation of semibullvalene realized earlier in this laboratory,<sup>6</sup> and proceeds by initial elaboration of the annelated 1,8-bishomocubanes **5a** and **5b**. [4.3.2]Propella-2,4,10-triene (**3a**)<sup>7</sup> readily underwent



Diels–Alder reaction with *N*-phenyltriazolinedione at  $-70^\circ$  to give **4a**, mp 253.5°.<sup>7</sup> That the cycloaddition had occurred virtually exclusively by underside attack<sup>8</sup> was established by acetone-sensitized photocyclization of **4a** to cubyl isomer **5a**, mp 204.5°,<sup>7</sup> in 92% yield.

(6) L. A. Paquette, *ibid.*, 92, 5765 (1970); see also R. Askani, *Tetrahedron Lett.*, 3349 (1970).

(7) Satisfactory analyses (combustion and mass spectrometric) have been obtained for all compounds described herein except **2** and **7** for which only accurate mass determinations are available. In both cases, air sensitivity precluded combustion analysis. In every instance, spectral data supported the structural assignments indicated.

(8) L. A. Paquette and G. L. Thompson, *J. Amer. Chem. Soc.*, in press.