H, s, OCH_3), 3.2–2.7 (3 H, complex m, allylic), 1.08 (3 H, d, $J \approx 6$ Hz, allylic CH_3). Hydrolysis of the diene **3b** by the procedure used for the conversion of **4a** to **1a** afforded the known 5-methylcyclohexane-1,3-dione: 76% yield based on **8b** (12.6 g, from ethyl acetate); mp 124–125 °C (lit.[6] mp 127–128 °C).

1,5-Dimethoxy-3,6-dimethyl-1,4-cyclohexadiene (4b) and 2,5-Dimethylcyclohexane-1,3-dione (2c). The diene **3b** (924 mg, 5.8 mmol) was methylated (CH_3I, 0.91 g, 6.4 mmol) and then worked up by the procedure described above for the conversion of **3a** to **4a**. The crude product appeared pure by NMR: δ 4.5 (2 H, m, vinyl), 3.50 (6 H, s, OCH_3), 3.1–2.5 (2 H, m, allylic), 1.19 and 1.18 (3 H, 2 overlapping d, $J \approx 6$ Hz, ~2:1 ratio of one of the allylic methyls of two stereoisomers), 1.03 (3 H, d, $J \approx 6$ Hz, second allylic methyl of both stereoisomers). Hydrolysis (1 M HCl) of **4b** as described above for preparing **1a** from **4a** afforded an 80% yield (650 mg from **3b**; crystallization from water) of dione **2c**, mp 168.5–171 °C (lit.[3d] mp 170–172 °C). A sample of **2c** prepared by the literature[3d] procedure had a melting point of 169–171 °C (from ethyl acetate). Both samples of **2c** exhibited identical NMR spectra.

3-Ethyl-2,4-dimethoxy-1,4-cyclohexadiene (4c) and 2-Ethylcyclohexane-1,3-dione (2a). For alkylation of **3c**[4] (1.262 g, 9.01 mmol), the procedure used for the preparation of **4a** was followed except that ethyl iodide (1.90 g, 12.2 mmol) was used. Workup and Kugelrohr distillation [bp 70–72 °C (3.0 mm)] afforded 1.263 g (83% yield) of **4c**: NMR δ 4.7 (2 H, m, olefinic), 3.50 (6 H, s, OCH_3), 2.8 (3 H, m, allylic), 1.9–1.5 (2 H, m, ethyl CH_2), 0.68 (3 H, t, $J \approx 6.2$ Hz); calcd for $C_{10}H_{16}O_2$ m/e 168.1151, found m/e 168.1138. Hydrolysis (by the procedure described above for preparing **1a**) of **4c** afforded after crystallization (ethyl acetate) the pure diketone **2a**: 92% yield (78% based on **3c**); mp 173–176 °C (lit.[3b] mp 172–175 °C). The NMR spectrum of **2a** proved to be identical with that of an authentic specimen prepared in this laboratory by the literature procedure.[3b]

3-Isopropyl-2,4-dimethoxy-1,4-cyclohexadiene (4d) and 2-Isopropylcyclohexane-1,3-dione (2b). For alkylation of **3c** (700 mg), the procedure used for the preparation of **4a** was followed except that isopropyl bromide (0.8 mL) was used as the alkylating agent. Workup and Kugelrohr distillation [bp 76–79 °C (3.2 mm)] afforded a 71% yield of **4d**: NMR δ 4.7 (2 H, m, olefinic), 3.50 (6 H, s, OCH_3), 2.7 (3 H, m, allylic), 2.1 (1 H, m, isopropyl methine), 0.89 (6 H, d, $J \approx 6$ Hz, $C(CH_3)_2$); calcd for $C_{11}H_{18}O_2$ m/e 182.1307, found m/e 182.1304. Hydrolysis with aqueous HCl by the above procedure afforded after crystallization a 90% yield (64% based on **3c**) of pure diketone **2b**: mp 143–145 °C (from ethyl acetate), mp 139–142 °C (from water) (lit.[7] mp 140–143 °C).

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Registry No. 1a, 80753-98-6; **1b**, 49673-64-5; **2a**, 18456-78-5; **2b**, 3401-01-2; **2c**, 61621-47-4; **3a**, 80753-99-7; **3b**, 28495-21-8; **3c**, 37567-78-5; **4a**, 80754-00-3; **4b**, 54118-01-3; **4c**, 54117-99-6; **4d**, 80754-01-4; **5**, 91-10-1; **6** (R = *t*-Bu), 6766-84-3; **7** (R = *t*-Bu), 80754-02-5; **8b**, 4179-19-5; 5-methylcyclohexane-1,3-dione, 4341-24-6.

Regioselective Diamine–Dialdehyde Condensation. Annelated Azepinopurine

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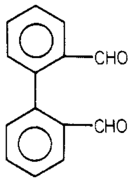
Diamine–dialdehyde condensations provide a valuable entry into heteroannulenes and condensed heterocyclic series.[1] The method has been studied in terms of bis Schiff bases vs. bicyclic "hydride shift" products. It may be illustrated by the double condensations of biphenyl-2,2′-dicarboxaldehyde (**1**, Chart I): it reacted with 2,2′-diaminobiphenyl to give 9,20-diazatetrabenzo[*a*,*c*,*g*,*i*]dodecene (**2**)[2,3] and with *o*-phenylenediamine to give 15*H*-dibenzo[*c*,*e*]benzimidazo[2,1-*a*]azepine (**3**).[4] We describe here the condensation of **1** and 4,5-diaminopyrimidine (**4**), an unsymmetrical heterocyclic diamine. α-Dicarbonyl compounds (including glyoxal) have previously been condensed with **4** and its derivatives to give pteridines.[5,6a]

Chart I



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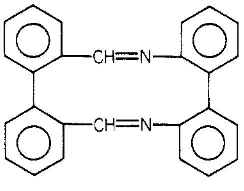

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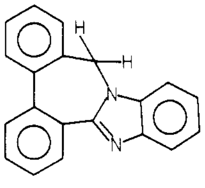

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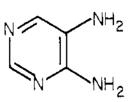

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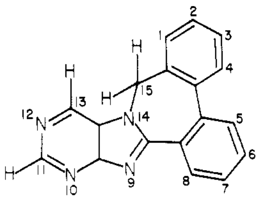

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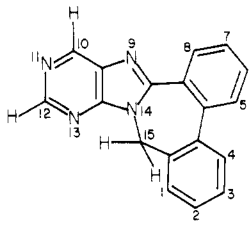

6

The reaction of **1** and **4** was conducted in boiling acetic acid. The bicyclic "hydride shift" structure of the product was concluded from the ^1H NMR spectrum (in CF_3CO_2H) which showed an AB quartet at 5.92 and 5.26 ppm ($J = 14$ Hz) due to two aliphatic geminal protons. Two isomeric "hydride shift" products may account for the spectroscopic data: 15*H*-dibenzo[3,4:5,6]azepino[2,1-*f*]purine (**5**) and 15*H*-dibenzo[3,4:5,6]azepino[1,2-*e*]purine (**6**). In **5**, the origin of the azepino nitrogen is the 5-amino group of **4**, while in **6**, it is the 4-amino group of **6**. Compound **5** is a 7*H*-purine derivative while **6** is a 9*H*-purine derivative. The decision between **5** and **6** was based on the results of the X-ray crystallographic investigation. The evidence established the structure of the product as **5**.

Consider the structures of **5** and **6**. They differ (inter alia) in the positions of the atoms of the pyrimidine rings: N(10) and N(12) in **5** became C(10) and C(12) in **6**, while C(11) and C(13) in **5** became N(11) and N(13) in **6**. The X-ray scattering power of carbon and nitrogen atoms does not differ significantly. Therefore, the distinction between

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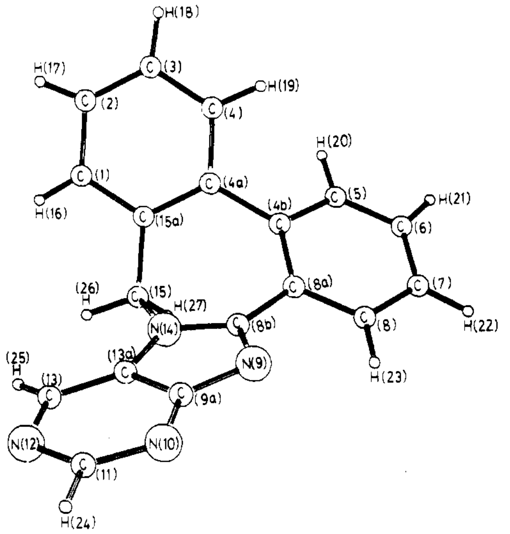


Figure 1. Crystal structure of 15*H*-dibenzo[3,4:5,6]azepino-[2,1-*f*]purine (**5**).

5 and **6** relies mainly on the locations of the two hydrogen atoms of the pyrimidine ring: H(24) and H(25) bonded to C(11) and C(13) in **5** and to C(10) and C(12) in **6**. The difference map did not show any peak which could be interpreted as an H atom around the peaks due to atoms number 10 and 12. Hence, these two peaks are assigned as nitrogen atoms and not carbon atoms. Thus the condensation product is **5** (Figure 1) and not **6**. The packing of **5** in the crystalline state is mainly via weak van der Waals and coulombic contacts.

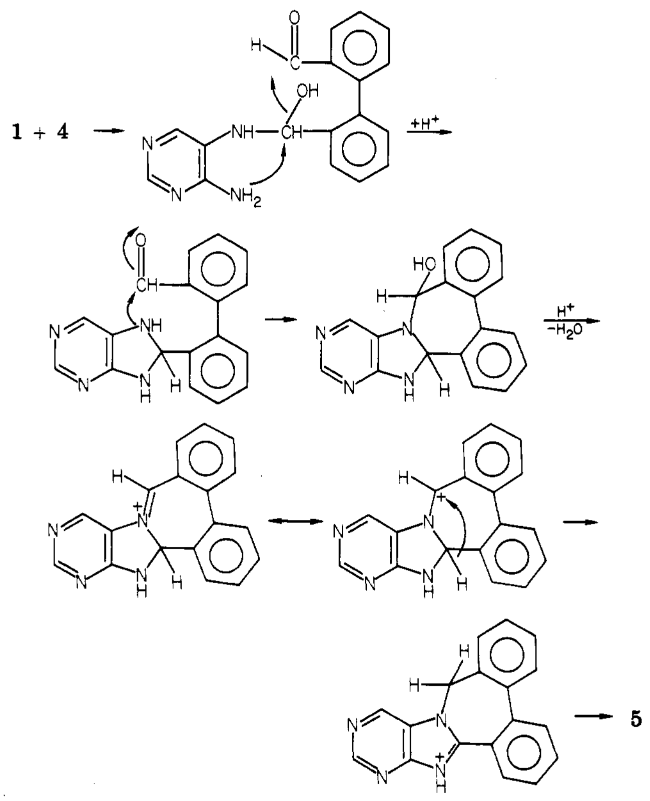
Scheme I describes a mechanism which accounts for the preferred formation of **5** in the condensation of **1** and **4**. A crucial point in this mechanism is inherent in the relative nucleophilicity of the two amino groups of **4**. It has previously been shown that 4,5-diaminopyrimidines were selectively formylated and acylated at the 5-position.[6b-8] Thus the 5-amino group in these diamines seems to be a stronger nucleophile than the 4-amino group. The first step in the condensation of **1** and **4** is the nucleophilic attack by the 5-amino group of **4** at a carbonyl carbon of **1**. This is followed by an intramolecular nucleophilic (Michael type) attack by the less active 4-amino group to give the 8-substituted purine intermediate 2′-[(7,8-dihydro-8-purinyl)methyl]biphenyl-2-carbaldehyde. The second amine–aldehyde condensation is intramolecular and involves preferentially the dihydropurine 7-nitrogen rather than the dihydropurine 9-nitrogen. This nucleophilic nitrogen also enhances the hydride shift to its neighboring electrophilic center (C-15).

Experimental Section

Melting points were taken on a Thomas-Hoover Unimelt capillary melting point apparatus and are uncorrected. Infrared spectra were recorded on a Perkin-Elmer Model 457 spectrometer in Nujol. Ultraviolet spectra were recorded on a Unicam Model SP800A spectrometer. ^{1}H NMR spectra were taken on a Varian HA-100D spectrometer at 100 MHz (Me$_4$Si internal reference). ^{1}H chemical shifts are reported in parts per million downfield from Me$_4$Si (δ units). Mass spectra were measured on a Varian MAT-311 double-focusing instrument operating at 70 eV by employing the direct-insertion technique. Microanalyses were performed at the Microanalysis Laboratory of The Hebrew University of Jerusalem.

15*H*-Dibenzo[3,4:5,6]azepino[2,1-*f*]purine (5). A solution of 2,2′-biphenyldicarbaldehyde (**1**; 1.05 g, 50 mmol) and 4,5-diaminopyrimidine (**4**; 0.56 g, 50 mmol) in glacial acetic acid (60 mL) was magnetically stirred and refluxed for 24 h. The solvent was evaporated under vacuum, and the residue was dissolved in chloroform (200 mL). The solution was passed through a short alumina column (25 cm), the chloroform was evaporated, and the residue was rechromatographed on an alumina column (300 g) by using a mixture of chloroform and ethyl acetate (3:1) as the eluent. The product was obtained as a light brown solid: 870 g; mp 305–310 °C. Recrystallization from benzene gave **5** as light brown needles: mp 317–319 °C; yield 35% (500 mg); IR (Nujol) ν_{max} 1610, 1600, 1570, 1515, 1420, 1350, 1320, 1300, 1255, 1225, 1210, 1160, 920, 800, 780, 755, 745 cm^{-1}; UV (CH$_2$Cl$_2$) λ_{max} 255 nm (ε 22 500), 298 (20 700); mass spectrum, *m/e* 284 (M$^{+}\cdot$); ^{1}H NMR (CF$_3$CO$_2$H) AB q δ 5.26, 5.29 (*J* = 14 Hz, 2 H, CH$_2$), 7.22–8.30 (m, 8 H, benzenoid), 9.52 (s, 1 H, purinoid, H-11), 10.15 (s, 1 H, purinoid, H-13). Anal. Calcd for $C_{18}H_{12}N_4$: C, 76.05; H, 4.23; N, 19.72. Found: C, 76.20; H, 4.39; N, 19.55.

Scheme I



Crystallography. 15*H*-dibenzo[3,4:5,6]azepino[2,1-*f*]purine (**5**: $C_{18}H_{12}N_9$; mp 317–319 °C) crystallizes in the orthorhombic space group P_{bca} with *a* = 18.804 (4), *b* = 12.220 (4), and *c* = 12.129 (3) Å with *Z* = 8 in a unit cell (d_c = 1.35 g cm^{-3}). X-ray data were collected on a computer-controlled Siemens diffractometer with C_4 Kα radiation. All C and N atoms of the molecule were located by direct methods.[9] All hydrogen atoms were located via the difference Fourier technique. Within 2651 independent reflections, 496 were treated as unobserved reflections. All atomic parameters were refired by a full-matrix least-squares method. The final *R* is 0.059 with the unobserved reflections excluded.

Acknowledgment. The crystallographic studies were carried out at the Weizmann Institute of Science, Rehovot, Israel.

Registry No. 1, 1210-05-5; 4, 13754-19-3; 5, 80484-73-7.

Supplementary Material Available: Tables I–V containing atomic fractional coordinates, thermal parameters, bond lengths, bond angles, and torsion angles of 15*H*-dibenzo[3,4:5,6]azepino-[2,1-*f*]purine (**5**) (5 pages). Ordering information is given on any current masthead page.

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