Intramolecular Diels–Alder Reactions of 6-Azalumazines and 6-Azapterins. A Facile Route to 6,7-Annulated 5-Deazapteridines

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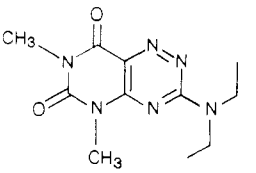
6-Azalumazines and 6-azapterins with dienophilic side chains tethered to the 7-position undergo remarkably facile intramolecular Diels–Alder reactions to yield novel 6,7-annulated 5-deazapteridines.

The utility of intramolecular Diels–Alder reactions of 1,2,4-triazines[1] to give fused pyridines, fused pyrimidines, and fused pyrazines has been extensively explored by our laboratory and others.[2] We have also described a synthetic route to 5-deazapteridines that involves intermolecular Diels–Alder reactions of 6-azalumazines and 6-azapterins with electron-rich dienophiles, where the reaction takes place with unexpected ease across the bridgehead 4a and C-7 positions.[3] We report herein the successful union of these two methodologies that permits a facile preparation of 6,7-annulated 5-deazapteridines.

We reported some years ago that 1,3-dimethyl-7-chloro-6-azalumazine underwent nucleophilic displacement of the 7-chloro group when treated with hydrazine.[4] We have now utilized an analogous displacement reaction of the more readily accessible 1,3-dimethyl-7-(methylthio)-6-azalumazine (**1**)[5] for the introduction of a variety of dienophilic side chains, as summarized in Table I. The oxygen-tethered side chains (**2a–d**) result from the room-temperature reaction of **1** with the appropriate alkoxides in THF/methylene chloride, whereas preparation of the nitrogen-tethered side chain (**2e**) requires several days of refluxing in methylene chloride with 4-amino-1-butyne.[2e]

The room-temperature ^{1}H NMR spectrum of the 7-(3-butynylamino)-tethered species **2e** is indicative of a ~3:1 mixture of conformational isomers, a consequence of a relatively high barrier of rotation about the exocyclic nitrogen–C7 bond. The nonuniformity of the mixture is due to the asymmetry of the substitution (i.e., H and butynyl) on the exocyclic nitrogen. High-temperature ^{1}H NMR (Me_2SO-d_6) has shown coalescence of the NH proton signals between 80 and 90 °C. Restricted rotation of the 7-diethylamino substituent in **3** is also evident from its NMR spectrum.



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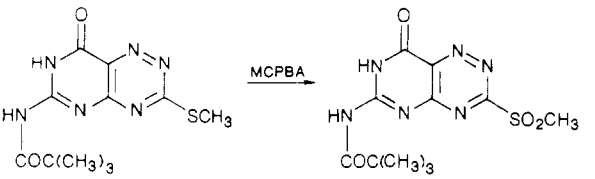
Heating the 1,3-dimethyl-7-substituted-6-azalumazines **2a–e** in the indicated solvents provides the 6,7-annulated 5-deazalumazine derivatives **4a–e** (see Table I). The buttressing effect[6] of a substituent immediately adjacent to the tethering atom (the Thorpe–Ingold effect) appears to be particularly effective with these intramolecular Diels–Alder reactions involving 1,2,4-triazines.[2d]

We have successfully extended the above concept to the preparation of several new 6,7-fused 5-deazapterins. Since 7-(methylthio)-6-azapterin, in common with all simple pterin derivatives, is extraordinarily insoluble in most organic solvents, it was converted to its 2-pivaloyl derivative, which is readily soluble even in methylene chloride.[3] Although 2-pivaloyl-7-(methylthio)-6-azapterin (**5**) surprisingly proved to be unreactive toward alkoxides or amines,[7] its derived methyl sulfone **6** (readily prepared by MCPBA oxidation of **5** in methylene chloride solution)



5 **6**

underwent the desired displacement with 2 equiv of the requisite nucleophile (alkoxide or amine; 2 equiv are required because of initial deprotonation at position 3 of the sulfone substrate by the first equivalent of the nucleophile). Heating the resulting 7-substituted 6-azapterin derivatives **7** in the appropriate solvent then led to the 6,7-fused 5-deazapterins **8** summarized in Table II.

In earlier work, we demonstrated that intramolecular Diels–Alder reactions of 1,2,4-triazine derivatives carrying a tethered dienophilic side chain at position 3 were strongly inhibited by the presence of substituents at C-6, the terminus of the azadiene system.[2e] It is thus remarkable that the intramolecular Diels–Alder reactions of **2a–e** and **7a–e** proceed with such ease. We attribute this unexpected ease of cycloaddition to activation of the 1,2,4-triazine ring by the annulated electron-withdrawing pyrimidine ring.

(1) For a recent comprehensive review of Diels–Alder reactions of heterocyclic azadienes, see: Boger, D.L. *Chem. Rev.* **1986**, *86*, 781.

(2) For references to intramolecular Diels–Alder reactions of monocyclic 1,2,4-triazines, see the following. Dienophilic substituent tethered to positions 3 or 6 (nitrogen extrusion): (a) Taylor, E. C.; Macor, J. E. *Tetrahedron Lett.* **1985**, *26*, 2419. (b) Taylor, E. C.; Macor, J. E. *Tetrahedron Lett.* **1986**, *27*, 431. (c) Taylor, E. C.; French, L. G. *Tetrahedron Lett.* **1986**, *27*, 1967. (d) Taylor, E. C.; Macor, J. E. *Tetrahedron Lett.* **1986**, *27*, 2107. (e) Taylor, E. C.; Pont, J. L. *Tetrahedron Lett.* **1987**, *28*, 379. (f) Taylor, E. C.; Macor, J. E. *J. Org. Chem.* **1987**, *52*, 4280. (g) Taylor, E. C.; Macor, J. E.; Pont, J. L. *Tetrahedron* **1987**, *43*, 5145. (h) Taylor, E. C.; Pont, J. L.; Warner, J. C. *Tetrahedron* **1987**, *43*, 5159. (i) Seitz, G.; Dietrich, S. *Arch. Pharm.* **1984**, *317*, 379. (j) Seitz, G.; Gorge, L.; Dietrich, S. *Tetrahedron Lett.* **1985**, *26*, 4355. (k) Seitz, G.; Dietrich, S. *Arch. Pharm.* **1985**, *318*, 1048 and 1051. (l) Seitz, G.; Dietrich, S.; Gorge, L.; Richter, J. *Tetrahedron Lett.* **1986**, *27*, 2747. Dienophilic substituent tethered to position 5 (nitrile extrusion): (m) Taylor, E. C.; Pont, J. L. *J. Org. Chem.* **1987**, *52*, 4287.

(3) Taylor, E. C.; McDaniel, K. F.; Warner, J. C. *Tetrahedron Lett.* **1987**, *28*, 1977.

(4) Taylor, E. C.; Sowinski, F. *J. Org. Chem.* **1975**, *40*, 2329.

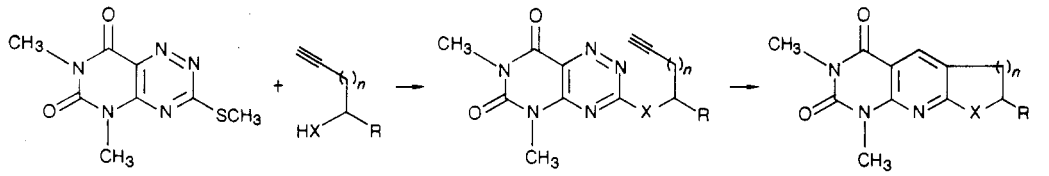
(5) Heinisch, L.; Ozegowski, W.; Muhlstadt, M. *Chem. Ber.* **1964**, *97*, 5.

(6) Fischer, K.; Hünig, S. *J. Org. Chem.* **1987**, *52*, 564.

(7) Alkoxides and amines both deprotonated **5** at position 3; however, subsequent displacement of the 7-methylthio group with excess nucleophile was not observed.

0022-3263/88/1953-0800$01.50/0

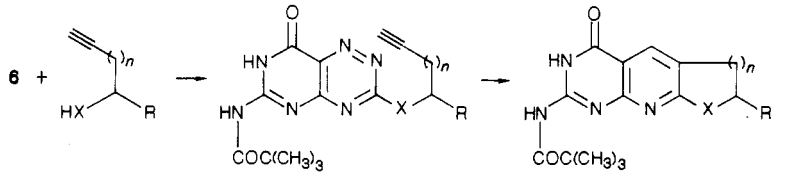
Table I. Intramolecular Diels-Alder Reactions of 6-Azalumazines



1 2 4

	X	R	n	% yield	reactn temp (°C)	reactn time	% yield
a	O	H	1	72	156	69 h	85
b	O	Et	1	67	156	10.5 h	100
c	O	Ph	1	76	156	6 h	60
d	O	H	2	62	180.5	102 h	98
e	NH	H	1	73	180.5	6 days	67

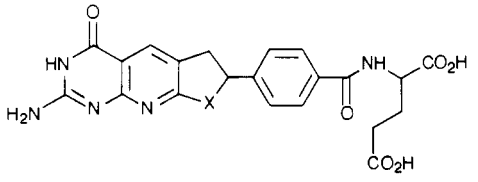
Table II. Intramolecular Diels-Alder Reactions of 6-Azapterins



7 8

	X	R	n	% yield	reactn temp (°C)	reactn time	% yield
a	O	H	1	75	156	29 h	84
b	O	Et	1	22	156	6 h	65
c	O	Ph	1	20	156	14 h	85
d	O	H	2	16	180.5	2 weeks	55
e	NH	H	1	89	180.5	92.5 h	3

We are currently exploring applications of this new methodology to the preparation of 5-deazafolic acid derivatives with a 7,10-heteroatom bridge, e.g. **9**.



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Experimental Section

General. Melting points are uncorrected and were determined in open capillary tubes by using a Thomas-Hoover apparatus for temperatures below 250 °C and a Meltemp apparatus for temperatures above 250 °C. Room-temperature ^{1}H NMR data were obtained with a General Electric QE300 300 MHz instrument, and chemical shifts are reported in ppm downfield from TMS. High-temperature ^{1}H NMR data were obtained with a Bruker WM250 250 MHz instrument. Mass spectral data were obtained by Dr. Dorothy Little on a Kratos MS50TC spectrometer. Elemental analyses were performed by Eli Lilly and Co., Indianapolis, IN. Column chromatography was performed on Merck silica gel 60 (240–400 mesh). Preparative TLC was carried out on Analtech silica gel GF uniplates (1500 μm).

Materials. Commercial reagents were utilized without further purification. All of the acetylenic alcohols utilized in this work were purchased from Farchan Laboratories, Gainesville, FL. Anhydrous solvents were distilled before use—tetrahydrofuran from benzophenone ketyl, methylene chloride and dimethylformamide from calcium hydride.

Synthesis of 7-Alkoxy-1,3-dimethyl-6-azalumazines 2a–d from 1,3-Dimethyl-7-(methylthio)-6-azalumazine. General Procedure. To a suspension of sodium hydride (2.7 mmol) in 30 mL of anhydrous tetrahydrofuran was added the desired acetylenic alcohol (2.5 mmol). After the initial effervescence subsided, a solution of 1,3-dimethyl-7-(methylthio)-6-azalumazine[5] (1) (2.5 mmol) in 30 mL of anhydrous methylene chloride was added, and the reaction was subsequently followed by TLC to completion. The solution was filtered through a pad of silica gel followed by elution with 1:1 ethyl acetate/methylene chloride. The filtrate was evaporated under reduced pressure to yield **2a–d**. Trituration with ether, unless otherwise noted, gave the solid product in pure form.

7-(3-Butynyloxy)-1,3-dimethyl-6-azalumazine (2a): obtained as a pale tan powder in 72% yield; mp 150.5–151.5 °C (effervescence); ^{1}H NMR ($CDCl_3$) δ 4.79 (t, J = 7.0 Hz, 2 H), 3.66 (s, 3 H), 3.54 (s, 3 H), 2.85 (dt, J_1 = 6.9 Hz, J_2 = 2.7 Hz, 2 H), 2.09 (t, J = 2.9 Hz, 1 H); HRMS calcd for $C_{11}H_{11}N_5O_3$, m/z 261.0862, found m/z 261.0852.

7-[(1-Ethyl-3-butynyl)oxy]-1,3-dimethyl-6-azalumazine (2b): obtained as a white solid in 67% yield; mp 134.5–135.5 °C (effervescence); ^{1}H NMR ($CDCl_3$) δ 5.53 (quintet, J = 6.0 Hz, 1 H), 3.65 (s, 3 H), 3.54 (s, 3 H), 2.78–2.75 (m, 2 H), 2.06–1.97 (m, 3 H), 1.06 (t, J = 7.4 Hz, 3 H); HRMS calcd for $C_{13}H_{15}N_5O_3$, m/z 289.1175, found m/z 289.1154.

Anal. Calcd for $C_{13}H_{16}N_5O_3$: C, 53.97; H, 5.23; N, 24.21. Found: C, 54.13; H, 5.29; N, 24.12.

1,3-Dimethyl-7-[(1-phenyl-3-butynyl)oxy]-6-azalumazine (2c): obtained as a viscous oil in 76% yield; ^{1}H NMR ($CDCl_3$) δ 7.54–7.50 (m, 2 H), 7.39–7.29 (m, 3 H), 6.33 (t, J = 6.0 Hz, 1 H), 3.55 (s, 3 H), 3.47 (s, 3 H), 3.11–2.95 (m, 2 H), 2.03 (t, J = 3.0 Hz, 1 H); HRMS calcd for $C_{17}H_{15}N_5O_3$, m/z 337.1175, found m/z 337.1159.

1,3-Dimethyl-7-(4-pentynyloxy)-6-azalumazine (2d): obtained as an off-white solid in 62% yield; mp 119–120 °C; ^{1}H NMR ($CDCl_3$) δ 4.78 (t, J = 6.2 Hz, 2 H), 3.65 (s, 3 H), 3.54 (s, 3 H), 2.48 (dt, J_1 = 6.8 Hz, J_2 = 2.6 Hz, 2 H), 2.18–2.10 (m, 2 H), 2.00 (t, J = 2.7 Hz, 1 H); HRMS calcd for $C_{12}H_{13}N_5O_3$, m/z 275.1018, found m/z 275.1020.

Anal. Calcd for $C_{12}H_{13}N_5O_3$: C, 52.36; H, 4.76; N, 25.44. Found: C, 52.12; H, 4.62; N, 25.43.

7-(3-Butynylamino)-1,3-dimethyl-6-azalumazine (2e). To a stirred solution of 1,3-dimethyl-7-(methylthio)-6-azalumazine (1) (0.68 g, 2.85 mmol) in anhydrous methylene chloride (25 mL) was added 4-amino-1-butyne[2e] (0.30 g, 4.35 mmol) at once. The resultant mixture was heated at reflux under nitrogen for 53 h. After this time, the reaction mixture was cooled to 0 °C and vacuum filtered to afford **2e** as a pale beige solid (0.54 g, 73%):

mp 213–215 °C (effervescent dec); ^{1}H NMR ($CDCl_3$) δ 6.81 (br s, 0.73 H), 5.95 (br s, 0.27 H), 3.96 (q, J = 6.3 Hz, 0.54 H), 3.73 (q, J = 6.4 Hz, 1.46 H), 3.60 (s, 2.19 H), 3.54 (s, 0.81 H), 3.51 (s, 3 H), 2.65–2.58 (m, 2 H), 2.09 (t, J = 2.4 Hz, 1 H); ^{1}H NMR (Me_2SO-d_6) δ 9.09 (br t, J = 5.7 Hz, 0.71 H), 8.53 (br t, J = 5.7 Hz, 0.29 H), 3.65 (q, J = 6.6 Hz, 0.58 H), 3.48 (q, J = 6.7 Hz, 1.42 H), 3.38 (s, 2.13 H), 3.33 (s, 0.87 H), 3.24 (s, 3 H), 2.85 (t, J = 2.3 Hz, 1 H), 2.51–2.46 (m, 2 H); HRMS calcd for $C_{11}H_{12}N_6O_2$, m/z 260.1021, found m/z 260.1009.

7-(Diethylamino)-1,3-dimethyl-6-azalumazine (3). A stirred solution of 7-chloro-1,3-dimethyl-6-azalumazine[8] (0.79 g, 3.47 mmol) in anhydrous methylene chloride (45 mL) was treated with diethylamine (0.75 mL, 7.25 mmol) at once. The resultant mixture was stirred under nitrogen for 2.5 h. After this period, the reaction mixture was successively washed with water (2 × 50 mL) and brine (50 mL), then dried (anhyd $MgSO_4$) and evaporated under reduced pressure to yield 7-(diethylamino)-1,3-dimethyl-6-azalumazine as a pale yellow solid (0.92 g, quantitative): mp 158–159 °C; ^{1}H NMR ($CDCl_3$) δ 3.98 (q, J = 7.1 Hz, 2 H), 3.68 (q, J = 7.1 Hz, 2 H), 3.55 (s, 3 H), 3.49 (s, 3 H), 1.34–1.25 (m, 6 H); ^{1}H NMR (Me_2SO-d_6) δ 3.86 (q, J = 6.7 Hz, 2 H), 3.62 (q, J = 6.7 Hz, 2 H), 3.36 (s, 3 H), 3.24 (s, 3 H), 1.22–1.15 (m, 6 H); HRMS calcd for $C_{11}H_{16}N_6O_2$, m/z 264.1334, found m/z 264.1339.

Anal. Calcd for $C_{11}H_{16}N_6O_2$: C, 49.99; H, 6.10; N, 31.80. Found: C, 49.70; H, 5.91; N, 31.50.

Intramolecular Diels–Alder Reactions of 2a–e. General Procedure. A suspension of the azalumazine (**2a–e**) in the given solvent (ca. 0.2 M) was heated at reflux. The reaction was followed by TLC until completion. The high boiling solvent was removed by filtration of the reaction mixture through a pad of silica gel followed by washing with hexanes; subsequent elution of the silica gel with 1:1 ethyl acetate/methylene chloride (unless otherwise noted) followed by evaporation under reduced pressure gave the fused 5-deazalumazines **4a–e**.

1,3-Dimethyl-1,2,3,4,6,7-hexahydro[3′,2′:5,6]pyrido[2,3-*d*]pyrimidine-2,4-dione (4a): carried out in bromobenzene (bp 156 °C) for 69 h; white needles, 85% yield; mp 196–197 °C; ^{1}H NMR ($CDCl_3$) δ 8.21 (s, 1 H), 4.79 (t, J = 8.6 Hz, 2 H), 3.66 (s, 3 H), 3.47 (s, 3 H), 3.34 (t, J = 8.6 Hz, 2 H); HRMS calcd for $C_{11}H_{11}N_3O_3$, m/z 233.0800, found m/z 233.0800.

Anal. Calcd for $C_{11}H_{11}N_3O_3$: C, 56.65; H, 4.75; N, 18.02. Found: C, 56.46; H, 4.74; N, 18.07.

1,3-Dimethyl-7-ethyl-1,2,3,4,6,7-hexahydrofuro[3′,2′:5,6]pyrido[2,3-*d*]pyrimidine-2,4-dione (4b): carried out in bromobenzene as solvent for 10.5 h; white solid, yield quantitative; mp 190.5–191 °C; ^{1}H NMR ($CDCl_3$) δ 8.17 (s, 1 H), 5.00–4.90 (m, 1 H), 3.66 (s, 3 H), 3.47 (s, 3 H), 3.43–3.34 (m, 1 H), 2.99–2.90 (m, 1 H), 1.99–1.77 (m, 2 H), 1.09 (t, J = 7.4 Hz, 3 H); HRMS calcd for $C_{13}H_{15}N_3O_3$, m/z 261.1113, found m/z 261.1089.

Anal. Calcd for $C_{13}H_{16}N_3O_3$: C, 59.76; H, 5.79; N, 16.08. Found: C, 59.48; H, 5.73; N, 15.89.

1,3-Dimethyl-7-phenyl-1,2,3,4,6,7-hexahydrofuro[3′,2′:5,6]pyrido[2,3-*d*]pyrimidine-2,4-dione (4c): carried out in bromobenzene as solvent for 6 h; **4c** precipitated out of the cooled reaction mixture as a white solid in 60% yield; mp 254–255 °C; ^{1}H NMR ($CDCl_3$) δ 8.23 (s, 1 H), 7.42–7.37 (m, 5 H), 6.01–5.95 (m, 1 H), 3.80–3.71 (m, 1 H), 3.69 (m, 3 H), 3.48 (s, 3 H), 3.35–3.27 (m, 1 H); HRMS calcd for $C_{17}H_{15}N_3O_3$, m/z 309.1113, found m/z 309.1092.

Anal. Calcd for $C_{17}H_{15}N_3O_3$: C, 66.01; H, 4.89; N, 13.59. Found: C, 65.79; H, 4.83; N, 13.39.

1,3-Dimethyl-1,2,3,4,6,7-hexahydro-8*H*-pyrano[3′,2′:5,6]pyrido[2,3-*d*]pyrimidine-2,4-dione (4d): reaction carried out in *o*-dichlorobenzene (bp 180.5 °C) as solvent for 102 h; white needles, 98% yield; mp 205–207 °C; ^{1}H NMR ($CDCl_3$) δ 8.16 (s, 1 H), 4.48 (t, J = 5.2 Hz, 2 H), 3.65 (s, 3 H), 3.47 (s, 3 H), 2.89 (t, J = 6.3 Hz, 2 H), 2.13–2.05 (m, 2 H); HRMS calcd for $C_{12}H_{13}N_3O_3$, m/z 247.0957, found m/z 247.0947.

Anal. Calcd for $C_{12}H_{13}N_3O_3$: C, 58.30; H, 5.30; N, 17.00. Found: C, 58.03; H, 5.39; N, 17.20.

1,3-Dimethyl-1,2,3,4,6,7-hexahydropyrrolo[3′,2′:5,6]pyrido[2,3-*d*]pyrimidine-2,4-dione (4e): carried out in *o*-dichlorobenzene as solvent for 6 days; pale tan needles, 67% yield; mp 303–307 °C dec; ^{1}H NMR ($CDCl_3$) δ 7.88 (s, 1 H), 5.14 (br s, 1 H), 3.79 (t, J = 8.6 Hz, 2 H), 3.60 (s, 3 H), 3.45 (s, 3 H), 3.15 (t, J = 8.7 Hz, 2 H); HRMS calcd for $C_{11}H_{12}N_4O_2$, m/z 232.0960, found m/z 232.0956.

7-(Methylsulfonyl)-2-pivaloyl-6-azapterin (6). A stirred suspension of 7-(methylthio)-2-pivaloyl-6-azapterin (0.53 g, 1.80 mmol) in anhydrous methylene chloride (40 mL) was treated with *m*-chloroperoxybenzoic acid (0.89 g, 4.13 mmol, 80–85% technical solid) at once. The resultant mixture was stirred under nitrogen for 4.5 h. After this period, the reaction mixture was evaporated under reduced pressure, and the residual yellow solid was triturated with ether to afford 7-(methylsulfonyl)-2-pivaloyl-6-azapterin (**6**) as a yellow solid: mp >300 °C; ^{1}H NMR ($CDCl_3$) δ 12.75 (br s, 1 H), 9.07 (br s, 1 H), 3.55 (s, 3 H), 1.42 (s, 9 H); HRMS calcd for $C_{11}H_{14}N_6O_4S$, m/z 326.0797 (M^+), 247.0943 (CH_3SO_2), found m/z 326.0814 (M^+), 247.0935 (CH_3SO_2).

Synthesis of 7-Alkoxy-2-pivaloyl-6-azapterins (7a–c) from 7-(Methylsulfonyl)-2-pivaloyl-6-azapterin (6). General Procedure. To a suspension of sodium hydride (2.5 mmol) in 30 mL of anhydrous tetrahydrofuran was added the desired acetylenic alcohol (2.5 mmol). After the initial effervescence subsided, a suspension of 7-(methylsulfonyl)-2-pivaloyl-6-azapterin (**6**) (1.25 mmol) in 30 mL of anhydrous methylene chloride was added, and the reaction was subsequently followed by TLC to completion. Unless otherwise noted, the reaction mixture was subsequently washed with two portions of water and one portion of brine, respectively, then dried (anhydrous $MgSO_4$), and evaporated under reduced pressure to yield **7a–c**. Trituration with ether afforded the solid product in pure form.

7-(3-Butynyloxy)-2-pivaloyl-6-azapterin (7a): obtained as an off-white solid in 75% yield; mp 215–215.5 °C (effervescence); ^{1}H NMR ($CDCl_3$) δ 12.37 (br s, 1 H), 8.58 (br s, 1 H), 4.71 (t, J = 7.0 Hz, 2 H), 2.84 (dt, J_1 = 7.0 Hz, J_2 = 2.8 Hz, 2 H), 2.06 (t, J = 2.8 Hz, 1 H), 1.37 (s, 9 H); HRMS calcd for $C_{14}H_{16}N_6O_3$, m/z 316.1283, found m/z 316.1289.

7-[(1-Ethyl-3-butynyl)oxy]-2-pivaloyl-6-azapterin (7b): obtained as a pale yellow solid in 22% yield; mp 132–134 °C (effervescence); ^{1}H NMR ($CDCl_3$) δ 12.33 (br s, 1 H), 8.52 (br s, 1 H), 5.42 (quintet, J = 6.0 Hz, 1 H), 2.74 (dd, J_1 = 5.9 Hz, J_2 = 2.7 Hz, 2 H), 2.07–1.96 (m, 3 H), 1.36 (s, 9 H), 1.04 (t, J = 7.4 Hz, 3 H); HRMS calcd for $C_{16}H_{20}N_6O_3$, m/z 344.1596, found m/z 344.1592.

Anal. Calcd for $C_{16}H_{20}N_6O_3$: C, 55.81; H, 5.85; N, 24.40. Found: C, 55.64; H, 5.98; N, 24.60.

7-[(1-Phenyl-3-butynyl)oxy]-2-pivaloyl-6-azapterin (7c): obtained as a slightly yellow solid (after filtration through a silica gel pad with 5% methanol/methylene chloride as eluent) in 20% yield; mp 136–138 °C (effervescence); ^{1}H NMR ($CDCl_3$) δ 12.32 (br s, 1 H), 8.43 (br s, 1 H), 7.58–7.55 (m, 2 H), 7.41–7.31 (m, 3 H), 6.41 (t, J = 6.0 Hz, 1 H), 3.14–2.90 (m, 2 H), 1.99 (t, J = 2.8 Hz, 1 H), 1.35 (s, 9 H); HRMS calcd for $C_{20}H_{20}N_6O_3$, m/z 392.1596, found m/z 392.1628.

Anal. Calcd for $C_{20}H_{20}N_6O_3$: C, 61.22; H, 5.14; N, 21.42. Found: C, 61.17; H, 5.22; N, 21.49.

7-(4-Pentynyloxy)-2-pivaloyl-6-azapterin (7d). A stirred suspension of sodium hydride (0.09 g, 3.0 mmol, 80% oil dispersion) in anhydrous dimethylformamide (10 mL) was treated with 4-pentyn-1-ol (0.23 g, 2.73 mmol) at once. When the initial effervescence subsided, a suspension of **6** (0.43 g, 1.32 mmol) in anhydrous DMF (25 mL) was added rapidly to the reaction mixture. The resultant mixture was stirred under nitrogen for 14 h. After this period, water (35 mL) was added to the reaction mixture which was subsequently acidified with concentrated HCl (0.6 mL). After further addition of water (35 mL), the mixture was extracted with methylene chloride (75 mL), and the extract was washed successively with water (2 × 50 mL) and brine (50 mL), then dried (anhyd $MgSO_4$), and evaporated under reduced pressure to afford a yellow oil. This oil was filtered through a silica gel pad, eluting with 1:1 ethyl acetate/methylene chloride. The filtrate was evaporated under reduced pressure to afford a yellow solid. Trituration of this material in ether yielded 7-(4-pentynyloxy)-2-pivaloyl-6-azapterin (**7d**) as a pale yellow solid (0.07 g, 16%): mp 187–190 °C (effervescent dec); ^{1}H NMR ($CDCl_3$) δ 12.35 (br s, 1 H), 8.60 (br s, 1 H), 4.68 (t, J = 6.2 Hz, 2 H), 2.48 (dt, J_1 = 7.0 Hz, J_2 = 2.6 Hz, 2 H), 2.17–2.09 (m, 2 H), 1.98 (t, J = 2.6 Hz, 1 H), 1.36 (s, 9 H); HRMS calcd for $C_{15}H_{18}N_6O_3$,

(8) Taylor, E. C.; Sowinski, F. *J. Am. Chem. Soc.* **1968**, *90*, 1374.

m/z 330.1440, found m/z 330.1428.

7-(3-Butynylamino)-2-pivaloyl-6-azapterin (7e). A stirred suspension of **5** (0.58 g, 1.78 mmol) in anhydrous methylene chloride (40 mL) was treated with 4-amino-1-butyne[16] (0.31 g, 4.49 mmol) at once. The resultant mixture was stirred under nitrogen for 23.5 h. After this period, the reaction mixture was washed with water (2 × 50 mL) followed by brine (1 × 50 mL), dried (anhyd $MgSO_4$), and evaporated under reduced pressure to afford a pale yellow solid. Trituration of this material in ether yielded 7-(3-butynylamino)-2-pivaloyl-6-azapterin (**7e**) as a fine yellow solid (0.50 g, 89%); mp 227–228 °C (effervescent dec); ^1H NMR ($CDCl_3$) δ 12.08 (br s, 1 H), 8.37 (br s, 1 H), 6.83 (br s, 1 H), 3.74 (q, J = 6.4 Hz, 2 H), 2.59 (dt, J_1 = 6.5 Hz, J_2 = 2.6 Hz, 2 H), 2.07 (t, J = 2.7 Hz, 1 H), 1.34 (s, 9 H); HRMS calcd for $C_{14}H_{17}N_7O_2$, m/z 315.1443, found m/z 315.1426.

Anal. Calcd for $C_{14}H_{17}N_7O_2$: C, 53.33; H, 5.43; N, 31.09. Found: C, 53.13; H, 5.52; N, 31.38.

Intramolecular Diels–Alder Reactions of 7a–e. General Procedure. A suspension of the azapterin **7a–e** in the given solvent (ca 0.2 M) was heated at reflux. The reaction was followed by TLC until completion. The high boiling solvent was removed by fitration of the reaction mixture through a pad of silica gel followed by washing with hexanes; subsequent elution of the silica gel with 1:1 acetonitrile/methylene chloride followed by evaporation under reduced pressure gave the fused 5-deazapterins **8a–e** without further purification (unless otherwise noted).

2-(Pivaloylamino)-3,4,6,7-tetrahydrofuro[3′,2′:5,6]pyrido[2,3-*d*]pyrimidin-4-one (8a): carried out in bromobenzene as solvent for 29 h; white solid, 48% yield; mp 265 °C (slow dec); ^1H NMR ($CDCl_3$) δ 11.94 (br s, 1 H), 8.25 (br s, 1 H), 8.23 (s, 1 H), 4.77 (t, J = 8.6 Hz, 2 H), 3.35 (t, J = 8.4 Hz, 2 H), 1.33 (s, 9 H); HRMS calcd for $C_{14}H_{16}N_4O_3$, m/z, 288.1222, found m/z 288.1223.

2-(Pivaloylamino)-7-ethyl-3,4,6,7-tetrahydrofuro[3′,2′:5,6]pyrido[2,3-*d*]pyrimidin-4-one (8b): carried out in bromobenzene as solvent for 6 h; white flakes, 65% yield; mp 176–178 °C; ^1H NMR ($CDCl_3$) δ 11.95 (br s, 1 H), 8.32 (br s, 1 H), 8.20 (s, 1 H), 4.98–4.91 (m, 1 H), 3.45–3.37 (m, 1 H), 3.01–2.92 (m, 1 H), 1.99–1.76 (m, 2 H), 1.33 (s, 9 H), 1.07 (t, J = 7.4 Hz, 3 H); HRMS calcd for $C_{16}H_{20}N_4O_3$, m/z 316.1535, found m/z 316.1519.

Anal. Calcd for $C_{16}H_{20}N_4O_3$: C, 60.75; H, 6.37; N, 17.71. Found: C, 60.52; H, 6.24; N, 17.74.

2-(Pivaloylamino)-7-phenyl-3,4,6,7-tetrahydrofuro[3′,2′:5,6]pyrido[2,3-*d*]pyrimidin-4-one (8c): carried out in bromobenzene as solvent for 14 h; white solid, 85% yield; mp 183–184 °C; ^1H NMR ($CDCl_3$) δ 12.00 (br s, 1 H), 8.46 (br s, 1 H), 8.25 (s, 1 H), 7.40 (m, 5 H), 5.98 (m, 1 H), 3.83–3.75 (m, 1 H), 3.36–3.28 (m, 1 H), 1.33 (s, 9 H); HRMS calcd for $C_{20}H_{20}N_4O_3$, m/z 364.1535, found m/z 364.1536.

2-(Pivaloylamino)-3,4,6,7-tetrahydro-8*H*-pyrano[3′,2′:5,6]pyrido[2,3-*d*]pyrimidin-4-one (8d): carried out in *o*-dichlorobenzene as solvent for 2 weeks; pale yellow crystals, 55% yield; mp 256–258 °C dec, ^1H NMR ($CDCl_3$) δ 11.94 (br s, 1 H), 8.40 (br s, 1 H), 8.18 (s, 1 H), 4.47 (t, J = 5.2 Hz, 2 H), 2.92 (t, J = 6.4 Hz, 2 H), 2.12–2.04 (m, 2 H), 1.33 (s, 9 H); HRMS calcd for $C_{15}H_{18}N_4O_3$, m/z 302.1379, found m/z 302.1365.

2-(Pivaloylamino)-3,4,6,7-tetrahydropyrrolo[3′,2′:5,6]pyrido[2,3-*d*]pyrimidin-4-one (8e): carried out in *o*-dichlorobenzene as solvent for 92.5 h, tan solid (after purification by preparative TLC using 1:1 acetonitrile/methylene chloride as eluent), 3% yield; mp 214–219 °C dec; ^1H NMR ($CDCl_3$) δ 12.08 (br s, 1 H), 8.18 (br s, 1 H), 8.15 (s, 1 H), 4.19 (t, J = 8.2 Hz, 2 H), 3.10 (t, J = 8.3 Hz, 2 H), 1.86 (br s, 1 H), 1.35 (s, 9 H); HRMS calcd for $C_{14}H_{17}N_5O_2$, m/z 287.1382, found m/z 287.1374.

Registry No. 1, 7271-94-5; **2a**, 111934-33-9; **2b**, 111934-34-0; **2c**, 111934-35-1; **2d**, 111934-36-2; **2e**, 111934-37-3; **3**, 111934-38-4; **4a**, 111934-39-5; **4b**, 111934-40-8; **4c**, 111934-41-9; **4d**, 111934-42-0; **4e**, 111934-43-1; **5**, 111934-44-2; **6**, 111934-45-3; **7a**, 111934-46-4; **7b**, 111934-47-5; **7c**, 111934-48-6; **7d**, 111934-49-7; **7e**, 111934-50-0; **8a**, 111934-51-1; **8b**, 111934-52-2; **8c**, 111934-53-3; **8d**, 111934-54-4; **8e**, 111934-55-5; 4-amino-1-butyne, 14044-63-4; 7-chloro-1,3-dimethyl-6-azalumazine, 54632-27-8; 4-pentyn-1-ol, 5390-04-5; 3-butyn-1-ol, 927-74-2; 5-hexyn-3-ol, 19780-84-8; α-2-propylbenzenemethanol, 1743-36-8.

Thermally Irreversible Photochromic Systems. Reversible Photocyclization of Diarylethene Derivatives

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The reversible photocyclization of 1,2-diarylethene derivatives having methyl-substituted heterocyclic rings has been found to constitute a photochromic system, which is both thermally irreversible and fatigue resistant. *cis*-1,2-Dicyano-1,2-bis(2,4,5-trimethyl-3-thienyl)ethene (**3d**) undergoes a photocyclization to produce the dihydro derivative of benzodithiophene (**4d**) with λ_{max} at 512 nm, which is stable for more than 12 h at 80 °C. The colored form reverts to the cis form on exposure to visible light (λ > 500 nm). The absorption maximum of the colored form shifts to 560 nm, when the cyano residues are replaced by an acid anhydride group. Upon irradiation with 405-nm light, the acid anhydride derivative, 2,3-bis(2,4,5-trimethyl-3-thienyl)maleic anhydride (**5**), cyclizes to the thermally stable dihydro form (**6**) with the quantum yield of 0.08 ± 0.01. No change in the visible absorption at 560 nm and the NMR spectrum is observed at 80 °C. Coloring and bleaching cycles can be repeated more than 100 times under deaerated conditions. Quantum yield for bleaching reaction has been found to depend on the wavelength of excitation. The quantum yield, 0.14 ± 0.02, at the excitation wavelength of 546 nm decreases to 0.04 at the wavelength of 633 nm. Both compounds do not show any thermochromic reaction even at 300 °C.

Introduction

Photochromism is defined as a reversible change in a chemical species between two forms having different absorption spectra,

$$A \underset{h\nu'}{\overset{h\nu}{\rightleftharpoons}} B$$

Organic compounds that possess the photochromic property have attracted a significant amount of attention from the view point of using them as optical memory media. Hirshberg mentioned, for the first time, that the cycle of photocoloring and photobleaching constituted a chemical memory model.[1] Despite favorable conditions provided

(1) Hirschberg, Y. *J. Am. Chem. Soc.* **1956**, *78*, 2304.

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