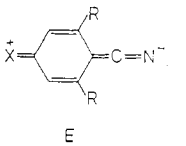
importance in unsaturated systems has been repeatedly stressed.[37]

For acetophenones **2**, the normal resonance effect observed at both C(α) and C(1) can be explained[1b-d] on the basis of the prevalence of conjugative interactions between the aromatic moiety and the acetyl group, which are enhanced by +R and reduced by -R substituents. On the other hand, in DM-**2** the change of the resonance scale and the shift of ρ_R toward negative values suggest (i) remarkable analogies with methyl benzoates **3** and DM-**3** and (ii) a prevalence of π-polarization over through-conjugation in determining the C(α) chemical shift also in DM-**2**. The analogies between the DM-**2** and **3** series find strong substantiation in the comparison of the plots of the C(α) chemical shifts of **3** vs those of **2** or DM-**2**: while scattering of points is observed in the former case (r = 0.550), a satisfactory linear correlation (r = 0.972, slope = 0.89 ± 0.08) is obtained between the C(α) chemical shifts of **3** and DM-**2**.[38]

Finally, the behavior of benzonitriles **1** and DM-**1**, characterized by a reverse resonance effect of 4-substituents on the cyano carbon, can suggest tight analogies between the CN and the COOR groups. These analogies could hinge upon a large polarizability of the CN group and/or a scarce importance of canonical structures such as E, because of their cumulene character.[39]



E

R = H, Me

Further studies are in progress in order to confirm the picture herein and to shed some light onto the reasons for the different behavior of unhindered acetophenones and alkyl benzoates, with particular regard to the reasonable possibility that the conjugation within the COOR group play a role in limiting the conjugation of the same group with the aromatic ring.

Acknowledgment is made to MPI and CNR for financial support.

Registry No. DM-**1b**, 114820-10-9; DM-**16**·HBF_4, 114820-19-8; DM-**1c**, 19111-77-4; DM-**1c**(amide), 114820-17-6; DM-**1d**, 2571-52-0; DM-**1e**, 6575-13-9; DM-**1f**, 14659-61-1; DM-**1g**, 5757-66-4; DM-**1i**, 114820-11-0; DM-**1j**, 31664-87-6; DM-**2b**, 83759-88-0; DM-**2b**·HBF_4, 114820-21-2; DM-**2c**, 60999-76-0; DM-**2d**, 1667-01-2; DM-**2e**, 2142-76-9; DM-**2f**, 114820-12-1; DM-**2g**, 53379-63-8; DM-**2i**, 114820-13-2; DM-**2j**, 114820-14-3; **3a**, 1202-25-1; **3b**, 619-45-4; **3c**, 121-98-2; **3d**, 99-75-2; **3e**, 93-58-5; **3f**, 403-33-8; **3g**, 619-42-1; **3h**, 2967-66-0; **3i**, 3609-53-8; **3j**, 619-50-1; DM-**3b**, 79909-92-5; DM-**3b**·HBF_4, 114820-23-4; DM-**3c**, 37934-88-6; DM-**3d**, 2282-84-0; DM-**3c**, 14920-81-1; DM-**3f**, 14659-60-0; DM-**3g**, 90841-46-6; DM-**3i**, 114820-15-4; DM-**3j**, 114820-16-5; biacetyl, 431-03-8.

(37) Pople, J. A.; Gordon, M. *J. Am. Chem. Soc.* **1967**, *89*, 4253. Fliszar, S. *J. Am. Chem. Soc.* **1972**, *94*, 7386.

(38) As expected, a very good linear correlation (r = 0.995; slope = 0.80 ± 0.03) was obtained by plotting the C(α) chemical shifts of DM-**3** vs those of the corresponding DM-**2**.

(39) The minor importance of the cumulene-type structure in the VB description of the acetonitrile anion was evidenced by the SCF + CI computations. See: Delbecq, F. *J. Org. Chem.* **1984**, *49*, 4838.

Diels-Alder Reactions of 7-Azalumazines. Synthesis of Condensed Lumazines and 8-Deazalumazines

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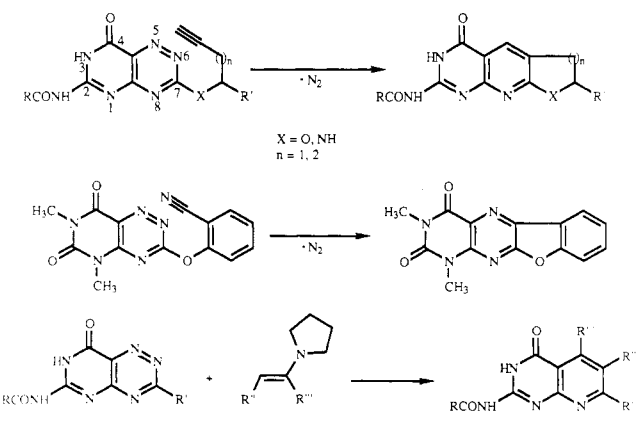
7-Azalumazines tethered at the C6 position with a series of dienophilic side chains undergo intramolecular Diels-Alder reactions to provide 6,7-annulated lumazines and 8-deazalumazines. The rates of these cycloaddition reactions are markedly faster than for previously reported cycloadditions of isomeric C7-tethered 6-azalumazines. On the other hand, 7-azalumazines do not undergo intermolecular Diels-Alder reactions with enamine dienophiles, whereas under identical conditions, 6-azalumazines react readily. Reasons for this striking reversal in reactivity observed for inter- and intramolecular Diels-Alder reactions of 6- vs 7-azalumazines are discussed.

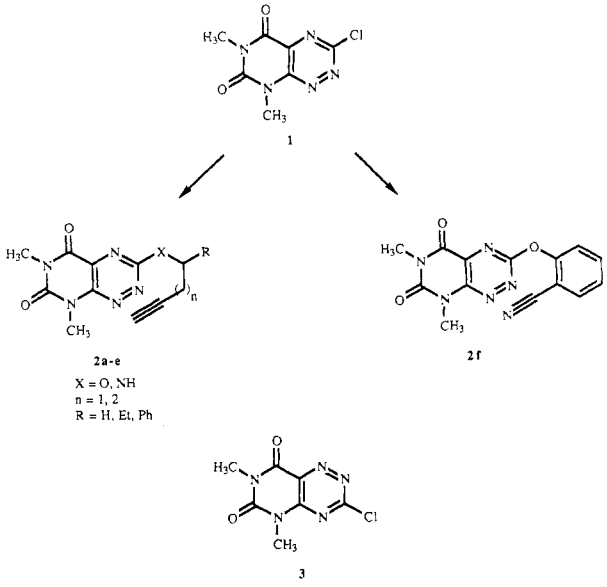
We have previously reported a number of facile intramolecular Diels-Alder reactions of 6-azapterins and 6-azalumazines (pyrimido[4,5-*e*]-1,2,4-triazines) with dienophilic side chains tethered to C7 of the azapteridine skeleton that give access to an array of 6,7-annulated 5-deazapteridines and lumazines.[1,2] Analogous intermolecular inverse electron demand Diels-Alder reactions of 6-azapteridines with enamines have also been described that similarly provide a wide selection of 5-deazapteridines (Scheme I).[3] Derivatives of this latter ring system are of intense current interest as antimetabolites of the folate family of enzyme cofactors,[4] and some (e.g., DDATHF[5]) exhibit extraordinary antimitotic activity against a broad range of solid tumors.[6-11] We report herein our studies

Scheme I

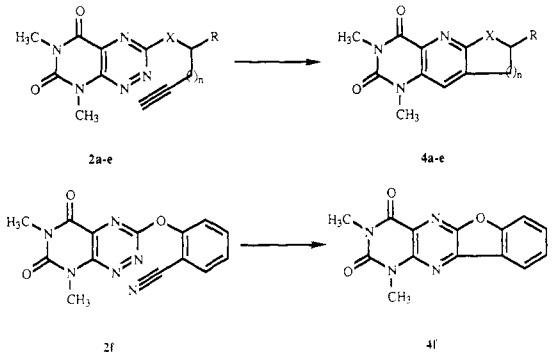


(1) Taylor, E. C.; Pont, J. L.; Warner, J. C. *Tetrahedron* **1987**, *43*, 5159.
(2) Taylor, E. C.; Pont, J. L.; Warner, J. C. *J. Org. Chem.* **1988**, *53*, 800.
(3) Taylor, E. C.; McDaniel, K. F.; Warner, J. C. *Tetrahedron Lett.* **1987**, *28*, 1977.
(4) Palmer, D. C.; Skotnicki, J. S.; Taylor, E. C. In *Progress in Medicinal Chemistry*; Ellis, G. P., ed.; Elsevier: New York, in press.

Scheme II



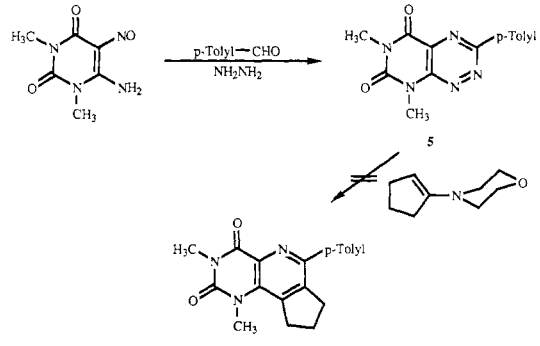
Scheme III



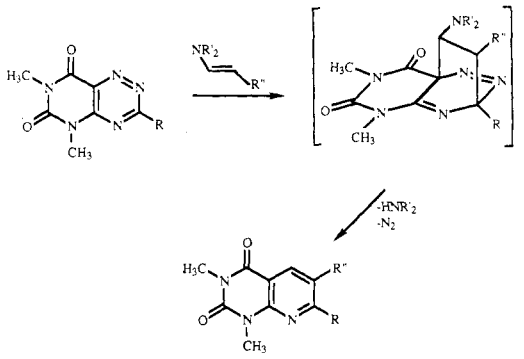
of isomeric 7-azalumazines in both intra- and intermolecular Diels–Alder reactions and a discussion of the contrasting trends in reactivity these 7-azalumazines display in relation to their 6-azalumazine isomers.

The requisite C6-(dienophile-tethered) 7-azalumazine Diels–Alder precursors (**2a–f**) were obtained by reaction of 6-chloro-1,3-dimethyl-7-azalumazine (**1**)[12] with a series of nucleophilic side chain dienophiles (Scheme II). This nucleophilic displacement reaction was very slow and required several days at room temperature. Analogous displacement reactions with the isomeric 7-chloro-1,3-dimethyl-6-azalumazine (**3**), on the other hand, were usually complete in 1 h under identical conditions.[1] This considerable deviation in reactivity is clearly consistent with

Scheme IV



Scheme V



the nature of the functionality on the triazine ring para to the chloro substituent ($N(CH_3)CO$ vs $CON(CH_3)$).

The Diels–Alder precursors (**2a–f**) were heated in a range of refluxing high-boiling solvents to afford the 6,7-annulated 8-deazalumazines (**4a–e**) and the 6,7-annulated lumazine (**4f**). The times required for the Diels–Alder reactions of **2a–f** are compared in Scheme III with the times required at the same temperature for the isomeric 6-azalumazine systems.[1,2] It is immediately evident that *intra*molecular cycloaddition of the 6-tethered 7-azalumazines proceeds much more readily than in the case of the isomeric 6-aza system, especially with the nitrile tethered species (**2f**).[13] Since the reason for this deviation in behavior was not immediately obvious, we were led to compare the facility with which these isomeric systems underwent *inter*molecular Diels–Alder reactions with enamines.

1,3-Dimethyl-6-*p*-tolyl-7-azalumazine (**5**) was prepared by condensation of 6-amino-1,3-dimethyl-5-nitrosouracil with the hydrazone of *p*-tolualdehyde (generated in situ).[14] Surprisingly, reaction of **5** with 1-morpholinocyclopentene generated none of the anticipated Diels–Alder product (**6**) (Scheme IV). Even with reaction temperatures as high as 210 °C, the azalumazine (**5**) was recovered unchanged, while the enamine underwent complete decomposition. This result is in striking contrast to the ease with which 1,3-dimethyl-7-*p*-tolyl-6-azalumazine reacts with enamines.[3] Thus, while 6-azalumazines display greater *inter*molecular Diels–Alder reactivity than the corresponding 7-aza isomers, this order of reactivity appears to be reversed for *intra*molecular Diels–Alder reactions.

Both the recalcitrance of 7-azalumazines and the reactivity of 6-azalumazines in intermolecular Diels–Alder reactions with enamines can be rationalized in terms of

(5) 5,10-Dideaza-5,6,7,8-tetrahydrofolic acid; see: (a) Taylor, E. C.; Fletcher, S. R.; Beardsley, G. P.; Moran, R. G. *J. Med. Chem.* **1985**, *28*, 914. (b) Taylor, E. C.; Wong, G. S. K.; Fletcher, S. R.; Harrington, P. J.; Beardsley, G. P.; Shih, C. J. In *Chemistry and Biology of Pteridines*; Cooper, B. A.; Whitehead, V. M., Eds.; Walter de Gruyter: Berlin, 1986; p 61.

(6) Moran, R. G.; Taylor, E. C.; Beardsley, G. P. *Proc. Am. Assoc. Cancer Res.* **1985**, *26*, 231.

(7) Beardsley, G. P.; Taylor, E. C.; Grindey, G. B.; Moran, R. G. In *Chemistry and Biology of Pteridines*; Cooper, B. A., Whitehead, V. M., Eds.; Walter de Gruyter: Berlin, 1986; p 953.

(8) Beardsley, G. P.; Taylor, E. C.; Shih, C.; Poore, G. A.; Grindey, G. B.; Moran, R. G. *Proc. Am. Assoc. Cancer Res.* **1986**, *27*, 259.

(9) Moran, R. G.; Taylor, E. C.; Beardsley, G. P. *Proc. Am. Assoc. Cancer Res.* **1987**, *28*, 274.

(10) Pizzorno, G.; Moroson, B. A.; Cashmore, A. C.; Taylor, E. C.; Beardsley, G. P. *Proc. Am. Assoc. Cancer Res.*, in press.

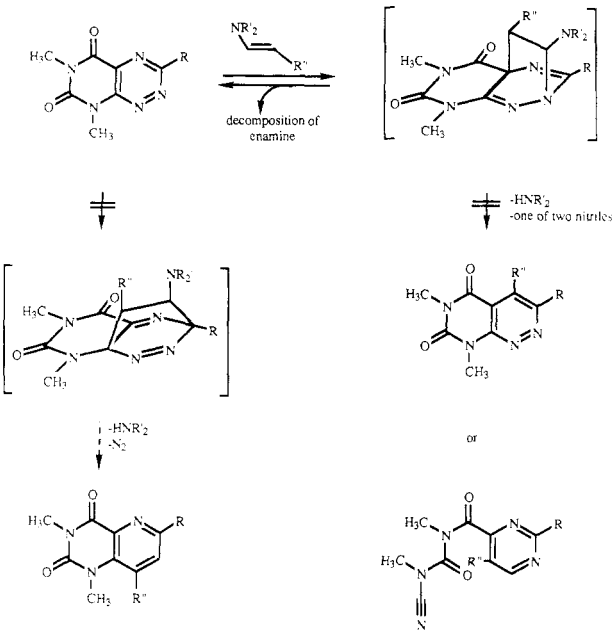
(11) Beardsley, G. P.; Moroson, B. A.; Taylor, E. C.; Moran, R. G. *J. Biol. Chem.*, in press.

(12) Taylor, E. C.; Sowinski, F. *J. Org. Chem.* **1975**, *40*, 2321.

(13) While a rigorous kinetic analysis was not performed, careful monitoring of reaction progress by TLC (disappearance of starting material) provided a means for an estimate of relative rates.

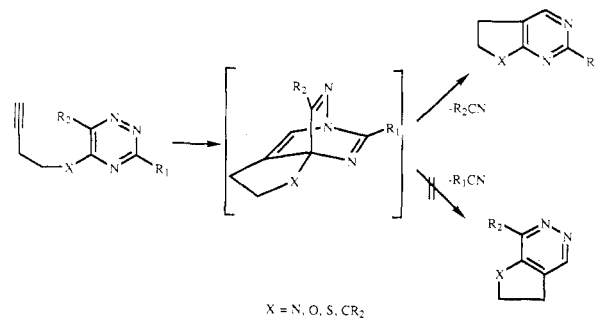
(14) Yoneda, F.; Nagamatsu, T. *Bull. Chem. Soc. Jpn.* **1975**, *48*, 2884.

Scheme VI



a substituent-directing effect. Enamine dienophiles should undergo site-specific and regiospecific cycloaddition favoring bond formation between the enamine β-carbon (the atom with the greatest electron density of the enamine) and the most electron deficient site of the 1,2,4-triazine ring. With 6-azalumazines, this dictates regiospecific C4′–C7 cycloaddition leading smoothly (following nitrogen elimination from the initial cycloadduct) to 5-deazalumazines (Scheme V).[15] With the isomeric 7-azalumazine system, cycloaddition across C6–C8′ could hypothetically lead to an 8-deazalumazine. However, no 8-deazalumazine product is observed presumably because the most electron deficient sites in this system are at C4′ and at N7 (illustrated in Scheme VI with one of the two possible cycloaddition pathways). The initial cycloadduct derived from such a cycloaddition (across C4′–N7) could either revert to starting materials or extrude either of two possible nitriles to yield a pyridazine (loss of HCN) or a pyrimidine (ring fission at C8′) (Scheme VI). There are no known examples of nitrile extrusion from C3, N4 of a 1,2,4-triazine derivative in a N2–C5 cycloaddition reaction; the few reactions that have been documented to undergo such a cycloaddition lose a nitrile derived from C6–N1 (Scheme VII), a reaction clearly impossible for 5,6-fused 1,2,4-triazines such as 7-azalumazines.[16–19] Thus, the

Scheme VII



presumption is that any cycloadduct derived from an intermolecular Diels–Alder reaction of 7-azalumazines with enamines collapses back to starting materials. As higher temperatures or extended reaction times are used in an attempt to coerce cycloaddition, enamine decomposition results.

In the analogous *intra*molecular Diels–Alder reactions of 6- and 7-azalumazines, however, the directing effect of electron-withdrawing groups is of negligible importance; cycloaddition is sterically constrained to proceed in well-defined modes. With 7-tethered 6-azalumazines, cycloaddition can only occur across C4′–C7 to provide annulated 5-deazalumazines, while the isomeric 6-tethered 7-azalumazines give 8-deazalumazines by cycloaddition across C6–C8′.

Consideration of possible resonance structures for 6- and 7-azalumazines suggests that the azadiene moiety of the latter is more electron deficient than the azadiene component in the former ring system (see Scheme VIII). Our experimental observations that intramolecular Diels–Alder reactions of 7-azalumazines proceed more readily than comparable reactions with their 6-aza isomers is consistent with the generally accepted assumption that such reactions are governed by inverse electron-demand considerations.[20]

Experimental Section

General Procedures. Melting points were determined in open capillary tubes with a Thomas-Hoover apparatus and are uncorrected. ^{1}H NMR data were obtained with a General Electric QE300 300-MHz instrument and chemical shifts are reported in ppm downfield from TMS. 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. Anhydrous solvents were distilled before use: *tetrahydrofuran from benzophenone ketyl and methylene chloride* and dimethylformamide from calcium hydride.

Synthesis of 6-Alkoxy-1,3-dimethyl-7-azalumazines (2a–d) from 6-Chloro-1,3-dimethyl-7-azalumazine (1). General Procedure. To a suspension of sodium hydride (1.02 equiv) in anhydrous tetrahydrofuran was added the desired acetylenic alcohol (1.01 equiv). After the initial effervescence subsided, a solution of 6-chloro-1,3-dimethyl-7-azalumazine (1)[12] (1.00 equiv) in 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

(15) Because the diene and dienophilic components of this reaction type are of opposite polarities, it would seem likely that a Diels–Alder reaction between the two would proceed in a stepwise fashion via discrete zwitterionic intermediates. However, ynamine dienophiles, unlike enamines, undergo almost exclusive N2–C5 cycloadditions (cf. ref 16), an observation that itself has been rationalized in terms of a stepwise mechanism (ref 19). Thus, it can be assumed that Diels–Alder reactions of 1,2,4-triazines with enamines are for the most part probably concerted processes. The nature of the mechanism of the Diels–Alder reaction remains a subject of inquiry. For a flavor of this, see: Dewar, M. J. S.; Olivella, S.; Stewart, J. J. P. *J. Am. Chem. Soc.* **1986**, *108*, 5771.

(16) (a) Neunhoeffer, H.; Lehmann, B. *Liebigs Ann. Chem.* **1977**, 1413. (b) Adler, J.; Böhnisch, V.; Neunhoeffer, H. *Chem. Ber.* **1978**, *111*, 240.

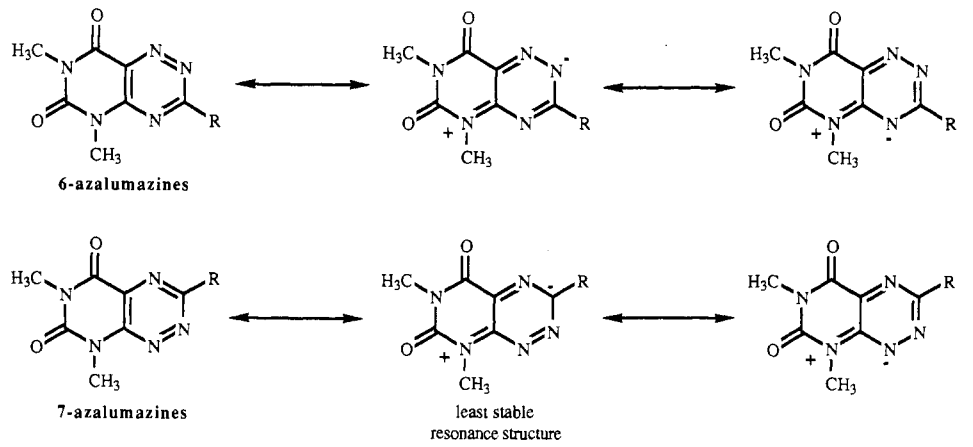
(17) Taylor, E. C.; Pont, J. L. *J. Org. Chem.* **1987**, *52*, 4287.

(18) We are currently extending this concept to isoelectronic monocyclic 1,2,4-triazines, which since free of the constraints associated with 5,6-fusion to the 1,2,4-triazine skeleton, should readily undergo N2–C5 cycloaddition with subsequent nitrile loss to afford pyrimidines. This would represent the first example of an N2–C5 cycloaddition of an enamine dienophile with a 1,2,4-triazine derivative.

(19) Boger, D. L.; Weinreb, S. N. *Hetero Diels–Alder Methodology in Organic Synthesis*; Academic: New York, 1987; p 324.

(20) MNDO calculations (ref 21) on some model 6- and 7-azalumazines provided LUMO coefficient values that are supportive of these substituent-directed modes of intermolecular cycloaddition. Furthermore, calculations reveal that LUMO energies of model 7-azalumazines are consistently lower than for isomeric 6-azalumazines, supporting the experimental observation that the former azadienes are more reactive than the latter in intramolecular inverse electron demand Diels–Alder reactions.

Scheme VIII



ethyl acetate/methylene chloride. The filtrate was evaporated under reduced pressure to yield the 6-alkoxy-1,3-dimethyl-7-azalumazines (**2a–d**). Trituration with ether, unless otherwise noted, gave the solid product in pure form.

6-(3-Butynyloxy)-1,3-dimethyl-7-azalumazine (2a): obtained as a yellow solid, yield 31%, mp 142–143 °C (effervescence); ^{1}H NMR ($CDCl_3$) δ 4.74 (t, J = 6.7 Hz, 2 H), 3.88 (s, 3 H), 3.56 (s, 3 H), 2.84 (dt, J_1 = 6.7 Hz, J_2 = 2.7 Hz, 2 H), 2.06 (t, J = 2.7 Hz, 1 H); HRMS calcd for $C_{11}H_{11}N_5O_3$ m/z 261.0862, found m/z 261.0870.

6-[(1-Ethyl-3-butynyl)oxy]-1,3-dimethyl-7-azalumazine (2b): obtained as a crude greenish orange oil, yield 40%; ^{1}H NMR ($CDCl_3$) δ 5.45–5.37 (m, 1 H), 3.86 (s, 3 H), 3.56 (s, 3 H), 2.74 (dd, J_1 = 5.7 Hz, J_2 = 3.4 Hz, 2 H), 2.06–1.98 (m, 2 H), 1.05 (t, J = 7.4 Hz, 3 H); HRMS calcd for $C_{13}H_{15}N_5O_3$ m/z 289.1175, found m/z 289.1168.

1,3-Dimethyl-6-[(1-phenyl-3-butynyl)oxy]-7-azalumazine (2c): obtained as a yellow oil, yield 84%; ^{1}H NMR ($CDCl_3$) δ 7.56–7.54 (m, 2 H), 7.38–7.28 (m, 3 H), 6.35 (t, J = 6.7 Hz, 2 H), 2.00 (t, J = 2.6 Hz, 1 H), 3.79 (s, 3 H), 3.50 (s, 3 H), 3.01 (dt, J_1 = 6.6 Hz, J_2 = 2.6 Hz, 2 H); HRMS calcd for $C_{17}H_{15}N_5O_3$ m/z 337.1175, found m/z 337.116.

1,3-Dimethyl-6-(4-pentynyloxy)-7-azalumazine (2d): obtained as a pale orange solid, yield 23%, mp 115–117 °C; ^{1}H NMR ($CDCl_3$) δ 4.73 (t, J = 6.0 Hz, 2 H), 3.87 (s, 3 H), 3.55 (s, 3 H), 2.49 (dt, J_1 = 7.0 Hz, J_2 = 2.6 Hz, 2 H), 2.16–2.11 (m, 2 H), 1.98 (t, J = 2.5 Hz, 1 H); HRMS calcd for $C_{12}H_{13}N_5O_3$ m/z 275.1018, found m/z 275.1107.

6-(3-Butynylamino)-1,3-dimethyl-7-azalumazine (2e). To a stirred solution of **1** (0.25 g, 1.10 mmol) in 15 mL of anhydrous tetrahydrofuran was added 4-amino-1-butyne[22] (0.18 g, 2.61 mmol) at once. The resultant mixture was heated at reflux under nitrogen for 5.5 h. After this time, the reaction mixture was cooled to room temperature and filtered through a silica gel pad followed by elution with anhydrous tetrahydrofuran. Evaporation under reduced pressure gave 0.29 g (100%) of an orange solid: mp 162–164 °C (effervescent dec); ^{1}H NMR ($CDCl_3$) δ 6.00 (br s, 1 H), 3.87–3.77 (m, 2 H), 3.82 (s, 3 H), 3.53 (s, 3 H), 2.62 (dt, J_1 = 6.4 Hz, J_2 = 2.7 Hz, 2 H), 2.05 (t, J = 2.6 Hz, 1 H); HRMS calcd for $C_{11}H_{12}N_6O_2$ m/z 260.1021, found m/z 260.1024. Anal. Calcd for $C_{11}H_{12}N_6O_2$: C, 50.77; H, 4.65; N, 32.29. Found: C, 50.76; H, 4.66; N, 32.12.

6-(2-Cyanophenoxy)-1,3-dimethyl-7-azalumazine (2f). A stirred suspension of sodium hydride (0.12 g, 3.00 mmol, 60% oil dispersion) in 15 mL of anhydrous tetrahydrofuran was treated with a suspension of 2-cyanophenol (0.31 g, 2.64 mmol) in 10 mL of anhydrous tetrahydrofuran. After the initial effervescence subsided, a solution of **1** (0.60 g, 2.64 mmol) in 10 mL of anhydrous methylene chloride was added rapidly to the mixture, which was subsequently stirred at room temperature for 5 days. After this period, the reaction mixture was evaporated under reduced pressure and the residual orange oil was taken up in methylene chloride and filtered through a silica gel pad. Further elution with 1:1 ethyl acetate/methylene chloride afforded 0.76 g (93%) of a flaky orange solid: mp 63–66 °C; ^{1}H NMR ($CDCl_3$) δ 7.79–7.71 (m, 2 H), 7.47–7.40 (m, 2 H), 3.87 (s, 3 H), 3.56 (s, 3 H); HRMS calcd for $C_{14}H_{10}N_6O_3$ m/z 310.0814, found m/z 310.0814. Anal. Calcd for $C_{14}H_{10}N_6O_3$: C, 54.20; H, 3.25; N, 27.09. Found: C, 54.19; H, 3.38; N, 26.96.

Intramolecular Diels–Alder Reactions of 4a–e. General Procedure. A suspension of the C6-tethered 7-azalumazine (**2a–e**) in the indicated 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 6,7-annulated 8-deazalumazine (**4a–e**).

1,3-Dimethyl-1,2,3,4,7,8-hexahydrofuro[3′,2′:5,6]pyrido-[3,2-*d*]pyrimidine-2,4-dione (4a): carried out in bromobenzene (bp 156 °C) for 6 h to give yellow needles, yield 90%, mp 293–294 °C; ^{1}H NMR ($CDCl_3$) δ 7.50 (d, J = 1.3 Hz, 1 H), 4.74 (t, J = 8.6 Hz, 2 H), 3.52 (s, 3 H), 3.61 (s, 3 H), 3.42 (dt, J_1 = 8.6 Hz, J_2 = 1.3 Hz, 2 H); HRMS calcd for $C_{11}H_{11}N_3O_3$ m/z 233.0800, found m/z 233.0797. Anal. Calcd for $C_{11}H_{11}N_3O_3$: C, 56.65; H, 4.75; N, 18.02. Found: C, 56.29; H, 4.67; N, 17.83.

1,3-Dimethyl-7-ethyl-1,2,3,4,7,8-hexahydrofuro[3′,2′:5,6]-pyrido[3,2-*d*]pyrimidine-2,4-dione (4b): carried out in bromobenzene for 4.5 h to give **4b** as a white solid, yield 44%, mp 213–214 °C; ^{1}H NMR ($CDCl_3$) δ 7.45 (s, 1 H), 4.93–4.84 (m, 1 H), 3.59 (s, 3 H), 3.51 (s, 3 H), 3.49–3.43 (m, 1 H), 3.06–2.98 (m, 1 H), 1.89–1.72 (m, 2 H), 1.06 (t, J = 7.4 Hz, 3 H); HRMS calcd for $C_{13}H_{15}N_3O_3$ m/z 261.1113, found m/z 261.1104. Anal. Calcd for $C_{13}H_{15}N_3O_3$: C, 59.76; H, 5.79; N, 16.08. Found: C, 59.97; H, 5.49; N, 16.13.

1,3-Dimethyl-7-phenyl-1,2,3,4,7,8-hexahydrofuro-[3′,2′:5,6]pyrido[3,2-*d*]pyrimidine-2,4-dione (4c): carried out in bromobenzene for 3.5 h to give beige plates, yield 87%, mp 212–213 °C; ^{1}H NMR ($CDCl_3$) δ 7.49 (s, 1 H), 7.40–7.33 (m, 5 H), 5.99–5.93 (m, 1 H), 3.91–3.82 (m, 1 H), 3.60 (s, 3 H), 3.53 (s, 3 H), 3.39–3.31 (m, 1 H); HRMS calcd for $C_{17}H_{15}N_3O_3$ m/z 309.1113, found m/z 309.1107. Anal. Calcd for $C_{17}H_{15}N_3O_3$: C, 66.01; H, 4.89; N, 13.58. Found: C, 66.23; H, 4.89; N, 13.52.

1,3-Dimethyl-1,2,3,4,8,9-hexahydro-7*H*-pyrano[3′,2′:5,6]-pyrido[3,2-*d*]pyrimidine-2,4-dione (4d): carried out in *o*-dichlorobenzene (bp 180.5 °C) for 56.5 h to give **4d** as a white solid, yield 100%, mp 233.5–239 °C; ^{1}H NMR ($CDCl_3$) δ 7.35 (s, 1 H), 4.41 (t, J = 5.1 Hz, 2 H), 3.58 (s, 3 H), 3.51 (s, 3 H), 2.99 (t, J = 6.5 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 247.0956. Anal. Calcd for $C_{12}H_{13}N_3O_3$: C, 58.29; H, 5.30; N, 17.00. Found: C, 58.01; H, 5.22; N, 16.82.

1,3-Dimethyl-1,2,3,4,7,8-hexahydropyrrolo[3′,2′:5,6]-pyrido[3,2-*d*]pyrimidine-2,4-dione (4e): carried out in *o*-dichlorobenzene as solvent for 49 h to give a dark tan solid, yield 71%, mp >300 °C dec; ^{1}H NMR ($CDCl_3$) δ 7.26 (s, 1 H), 5.56 (br s, 1 H), 3.79 (t, J = 8.0 Hz, 2 H), 3.58 (s, 3 H), 3.51 (s, 3 H), 3.23 (t, J = 8.0 Hz, 2 H); HRMS calcd for $C_{11}H_{12}N_4O_2$ m/z 232.0960, found m/z 232.0962.

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1,3-Dimethyl-1,2,3,4-tetrahydrobenzofuro[2',3':5,6]pyrazino[2,3-*d*]pyrimidine-2,4-dione (4f). A stirred solution of **2f** (0.50 g, 1.61 mmol) in 10 mL of nitrobenzene was heated at reflux for 54 h. After this period, the reaction mixture was filtered through a silica gel pad, eluting successively with methylene chloride and 1:1 methylene chloride/ethyl acetate. The second fraction was evaporated under reduced pressure, and the residual burnt sienna soil was triturated with methylene chloride to afford 0.21 g of a pale tan solid. The filtrate was passed through a silica gel column, eluting with 1:1 ethyl acetate/methylene chloride to give 0.16 g of additional solid. The products were combined to give 0.37 g (82%) of a tan solid: mp 298–300 °C; ^{1}H NMR ($CDCl_3$) δ 8.26 (d, J = 8.1 Hz, 1 H), 7.82–7.73 (m, 2 H), 7.57–7.52 (m, 1 H), 3.89 (s, 3 H), 3.60 (s, 3 H); HRMS calcd for $C_{14}H_{10}N_4O_3$ m/z 282.0753, found m/z 282.0751. Anal. Calcd for $C_{14}H_{10}N_4O_3$: C, 59.57; H, 3.57; N, 19.85. Found: C, 59.35; H, 3.64; N, 19.71.

1,3-Dimethyl-6-*p*-tolyl-7-azalumazine (5). A mixture of 6-amino-1,3-dimethyl-5-nitrosouracil[14] (1.64 g, 8.9 mmol), *p*-tolylaldehyde (1.20 g, 11.1 mmol), and anhydrous hydrazine (0.32 g, 10.0 mmol) in 50 mL of dimethylformamide was heated at reflux for 5 h. After this period, the solvent was removed by distillation, and the residue was triturated with ethanol. Recrystallization from isopropyl alcohol gave 1.54 g (61%) of a yellow solid: mp 291–292 °C; ^{1}H NMR δ 2.47 (s, 3 H), 3.59 (s, 3 H), 3.94 (s, 3 H), 7.37 (d, J = 8.2 Hz, 2 H), 8.49 (d, J = 8.2 Hz, 2 H); HRMS calcd for $C_{14}H_{13}N_5O_2$ m/z 283.1069, found m/z 283.1069. Anal. Calcd for $C_{14}H_{13}N_5O_2$: C, 59.36; H, 4.63; N, 24.72. Found: C, 59.11; H, 4.69; N, 24.45.

Registry No. **1**, 18969-84-1; **2a**, 114996-94-0; **2b**, 114996-95-1; **2c**, 114996-96-2; **2d**, 114996-97-3; **2e**, 114996-98-4; **2f**, 114996-99-5; **4a**, 114997-00-1; **4b**, 114997-01-2; **4c**, 114997-02-3; **4d**, 114997-03-4; **4e**, 114997-04-5; **4f**, 114997-05-6; **5**, 65358-01-2; $HO(CH_2)_2C{\equiv}CH$, 927-74-2; $HOCH(Et)CH_2C{\equiv}CH$, 19780-84-8; $HOCH(Ph)CH_2C{\equiv}CH$, 1743-36-8; $HO(CH_2)_2C{\equiv}CMe$, 5390-04-5; 4-amino-1-butyne, 14044-63-4; 2-cyanophenol, 611-20-1; 6-amino-1,3-dimethyl-5-nitrosouracil, 6632-68-4; *p*-tolylaldehyde, 104-87-0; hydrazine, 302-01-2.

π-Acceptor-Induced Reactions: Unusual Selectivity in Bond-Cleavage Reactions through the Use of Photochemical Excitation

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Bond-cleavage reactions of benzyl ether (BE) and 4,4'-dicyanobenzyl ether (DCBE) can be induced in the presence of various π-acceptor compounds. π-Acceptors used in this study are 2,3,5,6-tetrafluoro-7,7,8,8-tetracyanoquinodimethane ($TCNQF_4$), 2,3-dichloro-5,6-dicyano-1,4-benzoquinone (DDQ), and 7,7,8,8-tetracyanoquinodimethane (TCNQ). The products of these reactions are the corresponding benzaldehydes and benzyl alcohols regardless of the π-acceptors used in this study. Activation of these reactions can be achieved either thermally or photochemically. The relative reactivities of benzyl phenyl ether (BPE) and BE with these π-acceptors have been determined for both thermal and photochemical activation. BE is more reactive under all conditions than BPE. The selectivity of the BE bond-cleavage reaction initiated by photochemical excitation of DDQ is increased by 2 orders of magnitude when compared to thermal activation. $\Delta\Delta H^{\ddagger}$s for the bond-cleavage reactions of BE and BPE as induced by DDQ and $TCNQF_4$ have been determined. These results are interpreted with respect to the stability of the ionic intermediates and the tightness of ion pairing.

Introduction

Even though the transfer of electrons occurs in almost all chemical reactions, the dynamics of electron transfer are probably the least understood of all chemical processes. Given the importance of electron-transfer processes in a large variety of chemical reactions such as photosynthesis[1] and bond-cleavage reactions,[2] a great deal of theoretical[3] and experimental work[4] has been directed toward a better understanding of the relative rates of electron-transfer processes and the chemical processes that occur around them.[5]

A long-standing question concerns the interactions of quinones with various hydride donors.[6-10] The reactions of quinones have attracted a great deal of attention because of their role in a large variety of chemical and biochemical processes. The possible interactions of quinones with various hydrides are shown in eq 1. Although quinones

$$DH + Q \rightleftarrows DH{\cdots}Q \rightleftarrows DH^{\bullet+}/Q^{\bullet-} \rightleftarrows D^{\bullet}/QH^{\bullet} \rightleftarrows D^{+}/QH^{-} \quad (1)$$

are generally regarded to be good hydride acceptors,[8] a critical question concerns whether this reaction occurs in a single reaction step or in a stepwise fashion.[9,10] A continuum of reaction possibilities exist that form part of what electrochemists have referred to as an electrochemical, chemical, electrochemical (ECE) mechanism.[10] For a chemical oxidizing reagent, in which the oxidation is occurring in solution through single electron transfer (SET) reagents, geminate ion pairs are produced when electrons are transferred from the substrate to the oxidant. Proton transfer would lead to a geminate radical pair, while a

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