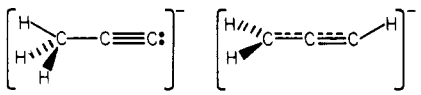
tonation of the carbonyl carbon results in a structure possessing a localized lone pair (41) orthogonal to the π system of the molecule. Likewise, for propene the allyl anion is preferred to a localized, vinyl-type anion. This is consistent with the result of a previous detailed theoretical and experimental study.[10k]

The most stable conjugate base of propyne, however, is predicted, in agreement with previous calculations,[10h] to be the propynyl anion (42) rather than the delocalized



42 43

species 43. Gas-phase experiments suggest[40] that the propargyl anion (43) is less stable than 42 but that the difference in stabilities could be considerably less than the figure of 5 kcal mol^{-1} obtained theoretically. This result suggests that the gain in stabilization in going from an sp^2 to an sp lone pair is considerable and is mirrored in the empirical linear relationship between pK_a and the percentage of s character of the lone pair in the series acetylene, ethylene, cyclopropane, and ethane.[2a]

Conclusions

Several important points emerge from this study.

(i) Relative acidities of substituted methanes XCH_3 are qualitatively well described by the 4-31G and 6-31G* basis sets. There is a substantial quantitative improvement in moving to 6-31G*, but deficiencies remaining even at this level suggest that further improvements in the basis set, e.g., addition of diffuse functions, may be required to obtain quantitatively accurate results. Electron correlation at the MP2 level with the 6-31G* basis set does not lead to improved results for the systems examined.

(ii) It appears that many of the prevalent ideas concerning the influence of substituents on carbanion stability as derived from experimental data (primarily acidities) in solution are well founded. The importance of charge dispersion through interaction with a π system is well recognized (exemplified by the acidity of protons α to a carbonyl group) and confirmed by this study. The inductive stabilization of carbanions (i.e., through the σ bond) is also confirmed, though our data suggest that, in contrast to the situation for the corresponding carbocations, π stabilization is considerably more effective than σ stabilization.

(iii) For systems XCH_3 offering competing sites of deprotonation, it is found that deprotonation at CH_3 is generally favored when X is an electropositive or unsaturated group while deprotonation at X is favored by electronegative substituents and by C≡CH.

Acknowledgment. We thank Professor P. v. R. Schleyer for helpful exchanges of information.

Registry No. CH_4, 74-82-8; $LiCH_3$, 917-54-4; $HBeCH_3$, 6917-55-1; H_2BCH_3, 12538-96-4; H_3CCH_3, 74-84-0; H_2NCH_3, 74-89-5; $HOCH_3$, 67-56-1; FCH_3, 593-53-3; $NCCH_3$, 75-05-8; O_2NCH_3, 75-52-5; $H_3CCH_2CH_3$, 74-98-6; $H_2C{=}CHCH_3$, 115-07-1; $HC{\equiv}CCH_3$, 74-99-7; F_3CCH_3, 420-46-2; $OHCCH_3$, 75-07-0; $C_6H_5CH_3$, 108-88-3; CH_3^-, 15194-58-8; $LiCH_2^-$, 55169-83-0; $HBeCH_2^-$, 74215-19-3; $H_2BCH_2^-$, 74215-20-6; $H_3CCH_2^-$, 25013-41-6; $H_2NCH_2^-$, 74215-21-7; $HOCH_2^-$, 55830-71-2; FCH_2^-, 60291-31-8; $NCCH_2^-$, 21438-99-3; $O_2NCH_2^-$, 18137-96-7; $H_3CCH_2CH_2^-$, 59513-13-2; $H_2C{=}CHCH_2^-$, 1724-46-5; $HC{\equiv}CCH_2^-$, 31139-07-8; $F_3CCH_2^-$, 27774-96-5; $OHCCH_2^-$, 64723-93-9; $C_6H_5CH_2^-$, 18860-15-6.

(40) Depuy, C. H.; Bierbaum, V. M.; Flippin, L. A.; Grabowski, J. J.; King, G. K.; Schmitt, R. J. *J. Am. Chem. Soc.* **1979**, *101*, 6443. Depuy, C. H.; Bierbaum, C. A.; Flippin, L. A.; Grabowski, J. J.; King, G. K.; Schmitt, R. J.; Sullivan, S. A. *Ibid.* **1980**, *102*, 5012.

Synthesis of *lin*-Benzofervenulin, *lin*-Benzotheophylline, and *lin*-Benzocaffeine

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The synthesis of 7,9-dimethylpyrimido[5,4-*g*]-1,2,4-benzotriazine-6,8(7*H*,9*H*)-dione (3) as the *lin*-benzo-separated analogue of fervenulin is reported in five steps from 7-chloro-2,4(1*H*,3*H*)-quinazolinedione. The preparation of *lin*-benzotheophylline (11) is described as arising from 1,3-dimethyl-7-hydrazino-6-nitro-2,4(1*H*,3*H*)-quinazolinedione (9) in a procedure originally designed to give 3. Methylation of 11 is shown to yield two products, one of which is *lin*-benzocaffeine (18).

The broad-spectrum antibiotic fervenulin (1) possesses the unique pyrimido[5,4-*e*]-1,2,4-triazine (i.e., 7-azapteridine) nucleus and has aroused considerable attention due to its interesting biological and chemical properties.[1] Stimulated by this, Leonard's recent successes[2] with benzo-separated purines [e.g., *lin*-benzoadenine (2)],[3] and our interest in the similarly separated pteridines,[4] *lin*-benzofervenulin[5] [7,9-dimethylpyrimido[5,4-*g*]-1,2,4-benzotri-

(1) For leading references to fervenulin see the introductory paragraphs of: (a) Taylor, E. C.; Sowinski, F. *J. Org. Chem.* **1975**, *40*, 2321; (b) Billings, B. K.; Wagner, J. A.; Cook, P. D.; Castle, R. N. *J. Heterocycl. Chem.* **1975**, *12*, 1221; (c) Yoneda, F.; Nagamatsu, T. *Bull. Chem. Soc. Jpn.* **1975**, *48*, 2884; (d) Yamaguchi, H.; Kuwata, R.; Yoneda, F. *J. Heterocycl. Chem.* **1978**, *15*, 615.

(2) Leonard, N. J. *Heterocycles* **1979**, *12*, 129.

(3) See, for example: Leonard, N. J.; Scopes, D. I. C.; Van Der Lijn, P.; Barrio, J. *Biochemistry* **1978**, *17*, 3677; Kauffman, R. F.; Lardy, H.; Barrio, J. R.; Barrio, M. D. C. G.; Leonard, N. J. *Ibid.* **1978**, *17*, 3686.

(4) Christ, W. J.; Schneller, S. W. "Abstracts of Papers", 7th International Congress of Heterocyclic Chemistry, Tampa, FL, Aug 12-17, 1979; International Society of Heterocyclic Chemistry: Tampa, FL, 1979; No. M1515B. Christ, W. J.; Schneller, S. W. "Abstracts of Papers", 179th National Meeting of the American Chemical Society, Houston, TX, Mar 23-28, 1980; American Chemical Society: Washington, DC, 1980; ORGN 13. Christ, W. J.; Schneller, S. W. "Abstracts of Papers", 2nd Chemical Congress of the North American Continent, Las Vegas, NE, Aug 24-29, 1980; American Chemical Society: Washington, DC, 1980; ORGN 176.

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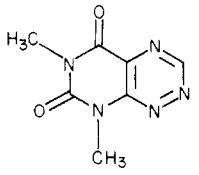

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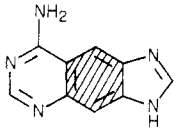

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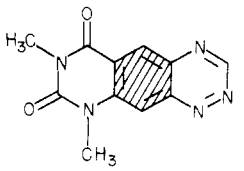
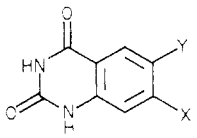


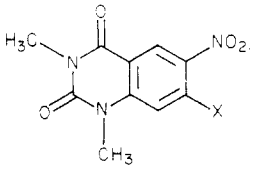
3

azine-6,8(7*H*,9*H*)-dione (**3**)] was established as an intriguing synthetic goal.

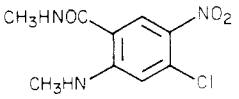
Thus, nitration of 7-chloro-2,4(1*H*,3*H*)-quinazolinedione (**4**)[6] gave 7-chloro-6-nitro-2,4(1*H*,3*H*)-quinazolinedione (**5**).



4, X = Cl; Y = H
5, X = Cl; Y = NO_2
6, X = $NHNH_2$; Y = NO_2



7, X = Cl
9, X = $NHNH_2$
10, X = NHNHCHO
17, X = NHN=$CHOC_2H_5$
20, X = $NHCH_3$

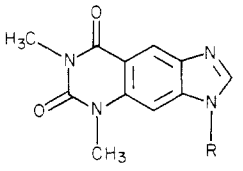


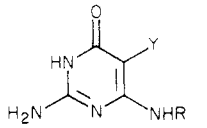
8

Since numerous attempts to convert **5** into **6** with hydrazine led to complex mixtures, **5** was next methylated with tetraethylammonium hydroxide/dimethyl sulfate to produce 7-chloro-1,3-dimethyl-6-nitro-2,4(1*H*,3*H*)-quinazolinedione (**7**). Compound **8** was the only product isolated when the methylation of **5** was conducted with sodium hydroxide/dimethyl sulfate.

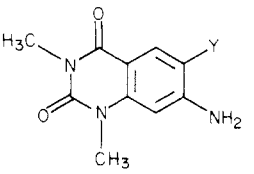
Pursuant to the synthesis of **3**, **7** was converted into **9** with hydrazine. Hydrogenation of **9** in 97% formic acid at elevated pressures was then foreseen as leading to **3** but instead produced the formylated derivative **10** and *lin*-benzotheophylline (**11**). Isolation of **11** was not surprising in view of the report[7] that the reduction of 2-amino-6-hydrazino-5-nitro-4(3*H*)-pyrimidinone (**12**) gave **13** rather than the expected **14**. Thus, hydrogenation of **9** must have yielded **15** which underwent subsequent ring closure to **11** upon reaction with formic acid. Support for this route to **11** was achieved by amination of **7** to **16**, which, following catalytic hydrogenation in 97% formic acid, became **11**, identical in all respects with the **11** synthesized from **9**.

Since **10** (also obtainable from **9** and refluxing formic acid) possessed all of the structural components for **3** as well as a hydrazino "protecting" formyl group, high-pressure hydrogenation of **10** in methanol was conducted and found to give the desired 7,9-dimethylpyrimido[5,4-*g*]-1,2,4-benzotriazine-6,8(7*H*,9*H*)-dione (*lin*-benzo-





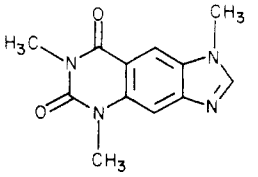
12, R = NH_2; Y = NO_2
13, R = H; Y = NH_2
14, R = Y = NH_2



15, Y = NH_2
16, Y = NO_2

fervenulin, **3**). In light of a number of problems with **10** (purification, solubility, thermal instability), a more convenient route to **3** was developed by hydrogenation of the ethoxymethylene derivative **17**, the product from **9** and triethyl orthoformate.

Prompted by the considerable biological significance of caffeine,[8] this study was extended to the methylation of **11** as a means to the benzo-separated caffeine **18**. Such



18

an alkylation produced two, isomeric (i.e., by microanalysis and ^1H NMR) monomethyl derivatives, separable by silica gel column chromatography. The second fraction was identified as **19** by comparing its spectral and chromatographic properties with those for the compound prepared by the reaction of **7** with anhydrous methylamine (to give **20**) followed by catalytic hydrogenation in formic acid. By comparison with the results[9] of the alkylation reactions of theophylline, the only structure possible for the initial chromatographic fraction is the desired *lin*-benzocaffeine (**18**). Interestingly, under a laboratory UV–visible light unit, **18** has a vivid purple fluorescence whereas **19** exhibits a blue fluorescent property. These are characteristics reminiscent of the benzo-separated purines described by Leonard.[2,10]

Experimental Section

General Methods. All melting points were obtained on a Thomas-Hoover or a Mel-Temp melting point apparatus and are uncorrected. Infrared spectra were recorded on a Beckman AccuLab 3 spectrophotometer, and the ^1H NMR spectra were determined at 60 MHz with a Varian EM-360 spectrometer and are reported in parts per million downfield from Me_4Si as an internal standard. The spin multiplicities are indicated by the symbols s (singlet), d (doublet), t (triplet), q (quartet), m (multiplet), and br (broad). Elemental analyses were performed by M-H-W Laboratories.

7-Chloro-2,4(1*H*,3*H*)-quinazolinedione (4). Russo and Ghelardoni[6] employed 2-amino-4-chlorobenzoic acid and urea to prepare compound **4**. However, here it was more advantageous

(5) See: Leonard, N. J.; Morrice, A. G.; Sprecker, M. A. *J. Org. Chem.* **1975**, *40*, 356 for an explanation of the use of the "linear" and "benzo" terms as prefixes in defining a particular dimensional analogue.
(6) Russo, F.; Ghelardoni, M. *Ann. Chim. (Rome)* **1966**, *56*, 839.
(7) Temple, C., Jr.; Kussner, C. L.; Montgomery, J. A. *J. Org. Chem.* **1971**, *36*, 3502.
(8) Ritchie, J. M. In "The Pharmacological Basis of Therapeutics", 5th ed.; Goodman, L. S., Gilman, A., Eds.; MacMillan: New York, 1975; Chapter 19.
(9) For a recent reference see: Holý, A., Vaněček, M. *Collect. Czech. Chem. Commun.* **1979**, *44*, 2550.
(10) See references 1 and 2 of: Foster, R. H., Leonard, N. J. *J. Org. Chem.* **1980**, *45*, 3072.

to employ methyl 2-amino-4-chlorobenzoate[11] (10 g, 0.05 mol; prepared from 2-amino-4-chlorobenzoic acid[12] and diazomethane) and urea (20 g, 0.33 mol) which were ground to a fine powder and then heated at 220 °C for 1 h. Water (500 mL) was added to the hot reaction mixture, and the solid that resulted was washed with $CHCl_3$ and dried to give 7.8 g (0.04 mol, 80%) of **4** following recrystallization from glacial AcOH: mp 360–362 °C (lit.[6] mp 360–362 °C); ^1H NMR (Me_2SO-d_6) δ 7.18 (m, 2 H), 7.82 (d, 1 H, J = 4 Hz), 10.18 (br s, 2 H, H-1 and H-3).

7-Chloro-6-nitro-2,4(1*H*,3*H*)-quinazolinedione (5). To a solution of 5 mL of concentrated H_2SO_4 in which 1 g (5.1 mmol) of **4** had been dissolved and cooled to −10 °C was added 0.2 mL of fuming HNO_3 under stirring. The mixture was then heated on a steam bath for 10 min and subsequently poured over 200 mL of stirred crushed ice. The precipitated product was isolated by filtration, dried, and recrystallized from glacial AcOH to give 1.04 g (0.43 mmol, 85%) of **5** as a light yellow powder: mp 335 °C; IR (KBr) 1710 (C=O), 1600 (NO_2), 1330 (NO_2) cm^{-1}; ^1H NMR (Me_2SO-d_6) δ 7.30 (s, 1 H, H-8), 8.48 (s, 1 H, H-5), 11.72 (br s, 2 H, H-1 and H-3).

Anal. Calcd for $C_8H_4ClN_3O_4$: C, 39.77; H, 1.67; N, 17.39. Found: C, 39.74; H, 1.94; N, 17.10.

7-Chloro-1,3-dimethyl-6-nitro-2,4(1*H*,3*H*)-quinazolinedione (7). To a mechanically stirred mixture of 5 g (21 mmol) of **5**, 50 mL of H_2O, and 30.49 g (42 mmol) of 20% tetraethylammonium hydroxide at room temperature was added excess dimethyl sulfate portionwise. This mixture was warmed at 60 °C for 1 h, and the resulting yellow solid was isolated by filtration, washed with H_2O, and air-dried to give 5 g (19 mmol, 90%) of **7** which was recrystallized from aqueous Me_2SO as light yellow plates: mp 181–182 °C; IR (KBr) 1720 (C=O) cm^{-1}; ^1H NMR (Me_2SO-d_6 at 127 °C) δ 3.36 (s, 3 H, CH_3), 3.46 (s, 3 H, CH_3), 7.54 (s, 1 H, H-8), 8.40 (s, 1 H, H-5).

Anal. Calcd for $C_{10}H_8ClN_3O_4$: C, 44.54; H, 2.99; N, 15.58. Found: C, 44.37; H, 3.05; N, 15.50.

4-Chloro-2-(methylamino)-5-nitro-*N*-methylbenzamide (8). A mixture of 1 g (4.15 mmol) of **5**, 50 mL of 10% aqueous NaOH, and 1.05 g (8.3 mmol) of dimethyl sulfate was refluxed for 40 min. The yellow solid which resulted was isolated by filtration, dried, and recrystallized from ethanol to give **8** (0.61 g, 2.49 mmol, 60%) as bright yellow needles: mp 203–204 °C; IR (KBr) 3410 (NH), 1650 (C=O) cm^{-1}; ^1H NMR (Me_2SO-d_6) δ 2.65 (d, 3 H, J = 4 Hz, NH), 2.85 (d, 3 H, J = 4 Hz, CH_3), 6.6 (s, 1 H, H-3), 8.3 (s, 1 H, H-6), 8.6 (br q, 2 H, 2 NH).

Anal. Calcd for $C_9H_{10}ClN_3O_3$: C, 44.37; H, 4.14; N, 17.25. Found: C, 44.44; H, 4.10; N, 17.14.

1,3-Dimethyl-7-hydrazino-6-nitro-2,4(1*H*,3*H*)-quinazolinedione (9). To a stirred mixture of 1 g (3.7 mmol) of **7** in 35 mL of absolute EtOH was added, dropwise and under N_2 at room temperature, 3.2 mL of 95% hydrazine hydrate. The resultant mixture was refluxed for 18 h and cooled, and the red solid that formed was isolated by filtration, dried, and recrystallized from dimethylformamide to give 0.7 g (2.63 mmol, 71%) of **9** as red needles: mp 278–279 °C; IR (KBr) 1690 (C=O), 1440 (NO_2) cm^{-1}; ^1H NMR (Me_2SO-d_6) δ 3.25 (s, 3 H, CH_3), 3.45 (s, 3 H, CH_3), 4.75 (br s, 2 H, NH_2), 7.13 (s, 1 H, H-8), 8.60 (s, 1 H, H-5), 9.25 (br s, 1 H, NH).

Anal. Calcd for $C_{10}H_{11}N_5O_4$: C, 45.29; H, 4.18; N, 26.41. Found: C, 45.19; H, 4.15; N, 26.60.

5,7-Dimethylimidazo[4,5-*g*]quinazoline-6,8(5*H*,7*H*)-dione (*lin*-Benzotheophylline, 11). Method A. A mixture of 4.8 g (19.2 mmol) of **16** (whose preparation is given below) in 300 mL of 97% formic acid, to which 0.89 g of 10% palladium on charcoal had been added under N_2, was shaken under 52 psi of H_2 for 3 h. The catalyst was removed by filtration and the filtrate refluxed for 2 h under N_2. The formic acid was then evaporated in vacuo and 50 mL of 97% formic acid and 50 mL of toluene were added to the residue. This mixture was then refluxed for 1 h under N_2, and the solvents were again removed in vacuo. To the resultant residue was added 50 mL of toluene, and the mixture was then evaporated in vacuo to give 3.5 g (15.2 mmol, 79%) of crude **11**. This product was purified by being dissolved first in 1 N NaOH solution, treated with activated charcoal, reprecipitated with glacial AcOH, and finally recrystallized for analysis from dimethylformamide to give **11** as a white powder: mp 289–292 °C; IR (KBr) 1690 (C=O) cm^{-1}; ^1H NMR (Me_2SO-d_6 at 128 °C) δ 3.28 (s, 3 H, CH_3), 3.50 (s, 3 H, CH_3), 7.12 (s, 1 H, H-9), 8.18 (s, 1 H, H-4), 8.22 (s, 1 H, H-2), 8.35 (s, 1 H, NH).

Anal. Calcd for $C_{11}H_{10}N_4O_2$: C, 57.39; H, 4.38; N, 24.34. Found: C, 57.25; H, 4.15; N, 24.47.

Method B. Compound **9** (1 g, 3.77 mmol) was placed in 50 mL of 97% formic acid to which 0.2 g of 10% palladium on charcoal was added under N_2, and the resultant mixture was treated with 50 psi of H_2 for 3 h. Use of the same reaction workup as in method A gave a low yield of **10** along with a considerable amount of **11**. These compounds were identified by comparison (TLC, IR, ^1H NMR) to authentic samples prepared by other routes described herein. They were separated by digesting the mixture with 1 N NaOH solution (dissolves **11**), filtering to isolate **10**, and acidifying the filtrate with glacial AcOH to precipitate **11**. The yields here were not quantitated since **10** and **11** were available by more attractive means.

7-Amino-1,3-dimethyl-6-nitro-2,4(1*H*,3*H*)-quinazolinedione (16). To 50 mL of 1-butanol, which had been saturated at room temperature with anhydrous ammonia, was added 3.5 g (13 mmol) of **7**, and this mixture was heated at 120 °C in a Parr stainless-steel reaction vessel for 24 h. After the solution was cooled, the precipitated yellow product was isolated by filtration (2.27 g, 9.1 mmol, 69.8%) and purified by recrystallization from dimethylformamide as yellow amorphous crystals of **16**: mp 321–323 °C; IR (KBr) 3310 (NH_2), 1720 (C=O); ^1H NMR (Me_2SO-d_6 at 128 °C) δ 3.22 (s, 3 H, CH_3), 3.32 (s, 3 H, CH_3), 6.64 (s, 1 H, H-8), 7.48 (br s, 2 H, NH_2), 8.55 (s, 1 H, H-5).

Anal. Calcd for $C_{10}H_{10}N_4O_4$: C, 48.00; H, 4.03; N, 22.39. Found: C, 47.81; H, 3.90; N, 22.25.

1,3-Dimethyl-7-(2-formylhydrazino)-6-nitro-2,4-(1*H*,3*H*)-quinazolinedione (10). A mixture of 1 g (3.77 mmol) of **9** was refluxed in 97% formic acid for 1 h. The formic acid was then evaporated to dryness in vacuo, and the yellow-orange residue was washed with water and isolated by filtration. This material was recrystallized from Me_2SO to give 0.99 g (3.39 mmol, 90%) of **10** as orange needles: mp 314–316 °C; IR (KBr) 1700 (C=O) cm^{-1}; ^1H NMR (Me_2SO-d_6) δ 3.20 (s, 3 H, CH_3), 3.39 (s, 3 H, CH_3), 6.62 (s, 1 H, H-8), 8.09 (s, 1 H, CHO), 8.55 (s, 1 H, H-5), 9.40–9.70 (br s, 2 H, NH).

Anal. Calcd for $C_{11}H_{11}N_5O_5$: C, 45.06; H, 3.78; N, 23.88. Found: C, 44.96; H, 3.77; N, 23.65.

1,3-Dimethyl-7-[2-(ethoxymethylene)hydrazino]-6-nitro-2,4(1*H*,3*H*)-quinazolinedione (17). Refluxing a mixture of 1 g (3.77 mmol) of **9** in 20 mL of triethyl orthoformate for 2 h gave 1.1 g (3.47 mmol, 91%) of crude **17** which was recrystallized from EtOH/petroleum ether (60–110 °C) to result in yellow needles of **17**: mp 235–237 °C; IR (KBr) 1710 (C=O) cm^{-1}; ^1H NMR ($CDCl_3$) δ 1.42 (t, 3 H, J = 4 Hz, CH_3), 3.40 (s, 3 H, CH_3), 3.54 (s, 3 H, CH_3), 4.24 (q, 2 H, J = 4 Hz, CH_2), 6.70 (s, 1 H, H-8), 7.12 (s, 1 H, =CH), 8.97 (s, 1 H, H-5), 11.00 (br s, 1 H, NH).

Anal. Calcd for $C_{13}H_{15}N_5O_5$: C, 48.60; H, 4.71; N, 21.80. Found: C, 48.37; H, 4.70; N, 21.81.

7,9-Dimethylpyrimido[5,4-*g*]-1,2,4-benzotriazine-6,8-(7*H*,9*H*)-dione (*lin*-Benzofervenulin, 3). A mixture of 3.77 mmol of either **10** or **17** in 50 mL of methanol, to which 5% palladium on charcoal had been added, was treated with 50 psi of H_2 for 3 h. At this point the catalyst was removed by filtration, and evaporation of the filtrate gave **3** (500 mg, 2.06 mmol, 54.5% from **10**; 600 mg, 2.47 mmol, 66.1% from **17**) which was recrystallized from Me_2SO as orange needles: mp 317–318 °C dec (with partial sublimation); IR (KBr) 1710 (C=O) cm^{-1}; ^1H NMR (Me_2SO-d_6) δ 3.30 (s, 3 H, CH_3), 3.63 (s, 3 H, CH_3), 8.23 (s, 1 H, H-5), 8.63 (s, 1 H, H-10), 9.93 (s, 1 H, H-3).

Anal. Calcd for $C_{11}H_9N_5O_2$: C, 54.32; H, 3.73; N, 28.79. Found: C, 54.45; H, 3.57; N, 29.00.

1,5,7-Trimethylimidazo[4,5-*g*]quinazoline-6,8(5*H*,7*H*)-dione (*lin*-Benzocaffeine, 18) and 3,5,7-Trimethylimidazo-[4,5-*g*]quinazoline-6,8(5*H*,7*H*)-dione (19). To a rapidly stirred solution of 0.69 g (3 mmol) of **11** dissolved in 40 mL of 0.2 N NaOH solution was added, dropwise, 1.5 g of dimethyl sulfate. The stirring was continued for 1 h, and the resulting white solid was

(11) Lutz, R. E.; Ashburn, G.; Freek, J. A.; Jordan, R. H.; Leake, N. H.; Martin, T. A.; Rowlett, R. J., Jr.; Wilson, J. W., III. *J. Am. Chem. Soc.* **1946**, *68*, 1285.

(12) Obtained commercially from Aldrich Chemical Co.

isolated by filtration, air dried, dissolved in a minimum amount of hot $CHCl_3$ and placed on a silica gel column. Elution of this column with $CHCl_3$–ethanol (95:5) and collection of the first purple fluorescent band gave 0.37 g (1.5 mmol, 50%) of **18**, which, upon recrystallization from Me_2SO, became white plates: mp 355–356 °C; IR (KBr) 1690 (C=O) cm^{-1}; ^1H NMR (Me_2SO-d_6 at 128 °C) δ 3.35 (s, 3 H, N-5 CH_3), 3.54 (s, 1 H, N-7 CH_3), 3.80 (s, 3 H, N-1 CH_3), 7.48 (s, 1 H, H-4), 8.14 (s, 1 H, H-2), 8.20 (s, 1 H, H-9).

Anal. Calcd for $C_{12}H_{12}N_4O_2$: C, 59.01; H, 4.95; N, 22.94. Found: C, 59.26; H, 5.02; N, 23.06.

Following removal of **18** from the column, elution with methanol gave a second blue fluorescent material which, upon evaporation of the methanol, gave 0.22 g (0.9 mmol, 30%) of **19**, identical in all respects (TLC, IR, ^1H NMR) with **19** obtained from **20** described below.

1,3-Dimethyl-7-(methylamino)-6-nitro-2,4(1*H*,3*H*)-quinazolinedione (20). A mixture of 0.4 g (1.48 mmol) of **7** and 5 mL of anhydrous 1-butanol, which had been saturated with methylamine at room temperature, was heated in a sealed reaction vessel at 120 °C for 24 h. After the mixture was cooled, the bright yellow solid that resulted was isolated by filtration, washed with ether, and recrystallized from aqueous Me_2SO to give 0.32 g (1.4 mmol, 95%) of **20** as amorphous, yellow crystals: mp 327–329 °C; IR (KBr) 3325 (NH), 1705 (C=O) cm^{-1}; ^1H NMR (Me_2SO-d_6 at 138 °C) δ 3.00 (d, J = 3 Hz, 3 H, NCH_3), 3.20 (s, 3 H, N-1 CH_3), 3.40 (s, 3 H, N-3 CH_3), 6.25 (s, 1 H, H-8), 7.05 (m, 1 H, NH), 8.50 (s, 1 H, H-5).

Anal. Calcd for $C_{11}H_{12}N_4O_4 \cdot {}^1/_3H_2O$: C, 48.88; H, 4.71; N, 20.73. Found: C, 49.05; H, 4.65; N, 20.87.

3,5,7-Trimethylimidazo[4,5-*g*]quinazoline-6,8(5*H*,7*H*)-dione (19). To a mixture of 0.3 g (1.23 mmol) of **20** and 40 mL of 97% formic acid was added 0.1 g of 10% palladium on charcoal under N_2, and the resultant mixture was shaken under 52 psi of H_2 for 3 h. The catalyst was removed by filtration and the filtrate refluxed under N_2 for 2 h. The formic acid was then evaporated in vacuo, and to this residue was added a mixture of 20 mL of 97% formic acid and 20 mL of toluene. This mixture was refluxed 30 min. After azeotropic distillation of the formic acid and toluene to an oily residue, 20 mL of toluene was added and the mixture evaporated to dryness in vacuo. The gum that remained was triturated with petroleum ether (60–110 °C) to give 0.24 g (0.98 mmol, 80%) of **19** which was subsequently recrystallized from Me_2SO as white needles: mp 341–343 °C; IR (KBr) 1700 (C=O) cm^{-1}; ^1H NMR (Me_2SO-d_6 at 128 °C) δ 3.26 (s, 3 H, N-5 CH_3), 3.48 (s, 3 H, N-7 CH_3), 3.78 (s, 3 H, N-3 CH_3), 7.19 (s, 1 H, H-4), 8.03 (s, 1 H, H-9), 8.10 (s, 1 H, H-2).

Anal. Calcd for $C_{12}H_{12}N_4O_2$: C, 59.01; H, 4.95; N, 22.94. Found: C, 59.00; H, 5.03; N, 22.89.

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Registry No. **3**, 76822-65-6; **4**, 13165-35-0; **5**, 76822-66-7; **7**, 76822-67-8; **8**, 76822-68-9; **9**, 76822-69-0; **10**, 76822-70-3; **11**, 76822-71-4; **16**, 76822-72-5; **17**, 76822-73-6; **18**, 76832-42-3; **19**, 76822-74-7; **20**, 76822-75-8; methyl 2-amino-4-chlorobenzoate, 5900-58-3; urea, 57-13-6.