Quino[1,2-*c*]quinazolines. II. Synthesis of 12,13-Dihydro-11b*H*-quino-[1,2-*c*]quinazolines *via* the Versatile Intermediates 2-(2-Amino-4,5-dimethoxyphenyl)-6,7-disubstituted-1,2,3,4-tetrahydroquinolines

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Received July 2, 1980

The versatile intermediates 2-(2-amino-4,5-dimethoxyphenyl)-6,7-dimethoxy-1,2,3,4-tetrahydroquinoline (**2a**) and 6-(2-amino-4,5-dimethoxyphenyl)-5,6,7,8-tetrahydro[1,3]dioxolo[4,5-*g*]quinoline (**2b**) were used in the preparation of a wide variety of 12,13-dihydro-11b*H*-quino[1,2-*c*]quinazolines by reaction with triethyl orthoformate, cyanogen bromide, urea and carbon disulfide in pyridine. Reaction of the thio and keto products with methyl iodide and phosphorus oxychloride, respectively, gave the requisite methylthio and chloro derivatives. Novel Reissert type reactions occurred when the intermediates **2a,b** were reacted with acetic anhydride or benzoyl chloride. The attempted dehydrogenation of 12,13-dihydro-2,3,9,10-tetramethoxy-11b*H*-quino[1,2-*c*]quinazoline (**3a**) is also reported.

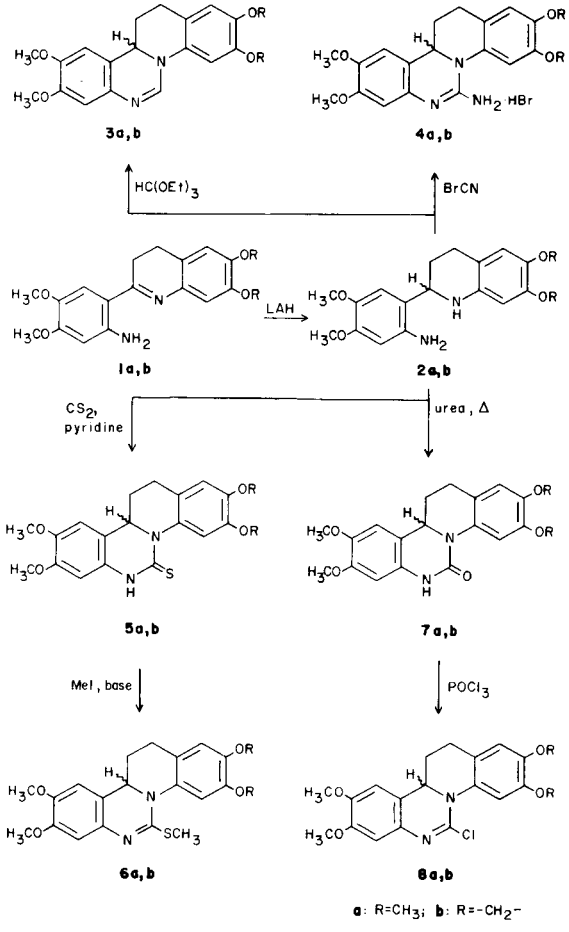
J. Heterocyclic Chem., **17**, 1665 (1980).

As a continuation of our research concerning the synthesis of quino[1,2-*c*]quinazolines as analogs of the potent antitumor benzo[*c*]phenanthridine alkaloids nitidine and fagaronine (1), the synthesis of 2-(2-amino-4,5-dimethoxyphenyl)-6,7-disubstituted-1,2,3,4-tetrahydroquinolines (**2a,b**), to be used as versatile synthons for the preparation of 12,13-dihydro-11b*H*-quino[1,2-*c*]quinazolines, was desired. These unsaturated quino[1,2-*c*]quinazolines are of further interest due to the narcotic activity exhibited by chelidonine (2), a benzo[*c*]phenanthridine alkaloid which is unsaturated in the B and C rings.

The synthesis of the intermediates **2a,b** is shown in Scheme I, and was accomplished by reduction of the imines **1a,b** with lithium aluminum hydride in tetrahydrofuran. The synthesis of the starting compounds **1a,b** can be achieved in three steps from readily available starting materials (1). Two enantiomeric products are possible for both **2a** and **2b** due to the chiral C-2 carbon in the quinoline ring. Two enantiomeric products are also possible for all of the compounds synthesized *via* **2a,b** shown in Scheme I. All of these compounds gave sharp melting points and only one spot on tlc using several solvent systems as eluents. However, no attempt was made to determine the exact configurations of these products or to separate any enantiomeric mixtures which may have been formed.

The reaction of the intermediates **2a,b** with a variety of cyclizing agents is also shown in Scheme I. Reaction of **2a,b** with triethyl orthoformate gave the quino[1,2-*c*]-quinazolines **3a,b**, which are unsubstituted at the 6-position. Compounds **2a,b** also led to the amino hydrobromides **4a,b** on reaction with cyanogen bromide. The synthesis of the thiones **5a,b** was accomplished by the reaction of **2a,b** with carbon disulfide in pyridine. These compounds were subsequently used in the reaction with methyl iodide and sodium hydroxide to give the methylthio derivatives **6a,b**. Finally, fusion of **2a,b** with urea gave **7a,b**, which were reacted with phosphorus oxychloride as shown. In this last sequence the reaction of **7b** did not lead to the successful formation of **8b**.

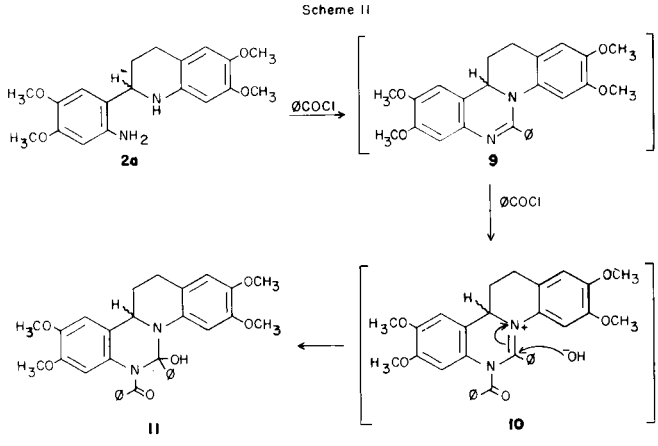
Scheme I



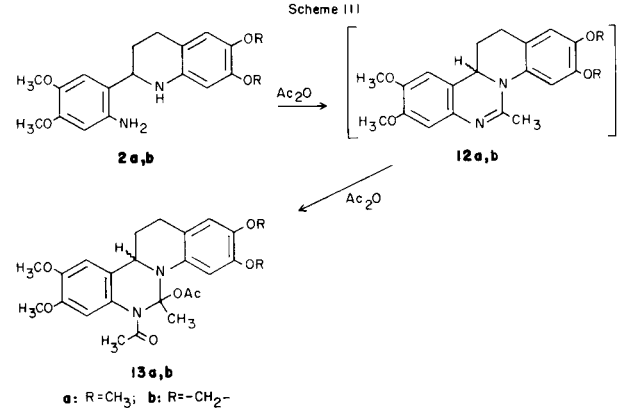
The attempted synthesis of the phenyl derivative **9** from

0022-152X/80/081665-05$02.25

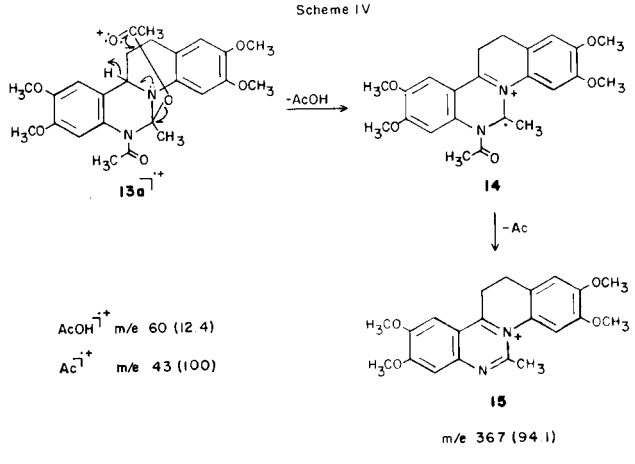
Scheme II



Scheme III



Scheme IV



2a is shown in Scheme II. Reaction of **2a** with benzoyl chloride gave a crystalline solid, which did not exhibit spectral data indicative of the formation of **9**. The ir spectrum showed the presence of a carbonyl group (1660 cm^{-1}) and a hydroxyl group (3200 cm^{-1}). The nmr indicated the reaction product contained two phenyl groups (m, δ 7.3-7.7) and further confirmed the presence of a hydroxyl group (s, δ 8.35). Based on these results, **11** was proposed as the correct structure for the reaction product. This proposed structure was further confirmed by elemental analysis and mass spectral data (parent peak = M - benzoyl; base peak = parent peak - OH).

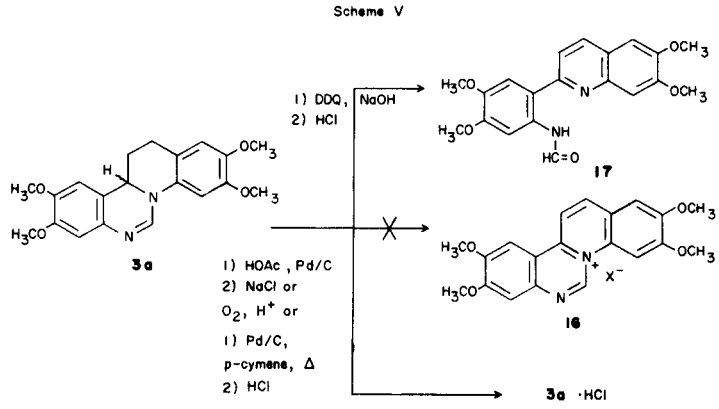
A proposed pathway for the formation of **11** from **2a** is shown in Scheme II. Following the reaction of **2a** with one mole of benzoyl chloride to give the requisite phenyl derivative **9**, reaction with an additional mole of benzoyl chloride would lead to the formation of **11** *via* the benzoyl derivative **10** in a Reissert type reaction where the normal nucleophilic cyano group is replaced by a hydroxyl group. The product **11** thus possesses a pseudo-base type structure (3). Psuedo-base formation is known to be a competing reaction in the Reissert reaction involving isoquinolines, quinolines and phthalazines (4). Further, analogous to the formation of **11**, the attempted acetylation of 3-methylimidazo[1,5-*a*]pyrazine in either acetic anhydride or acetyl chloride is reported to give the pseudo-base 7-acetyl-8-hydroxy-3-methyl-7,8-dihydroimidazo[1,5-*a*]pyrazine (5). Thus, formation of the unexpected product **11** is not without precedence in the literature. Reaction of **2b** with benzoyl chloride under the same reaction conditions did not give an isolated product.

Reaction of **2a,b** with acetic anhydride also gave Reissert type reaction products **13a,b** rather than the desired methyl derivatives **12a,b** as shown in Scheme III. These products were isolated as white crystalline solids and exhibited spectral data indicative of the structures **13a,b**. The ir spectra showed the presence of a carbonyl group (1705 cm^{-1} for both **13a** and **13b**) and the nmr showed three methyl absorptions (**13a**: δ 2.12, 2.28, 2.63; **13b**: δ 2.03, 2.15, 2.48) for the two acetyl methyl groups and the ring substituent methyl group in each of the two products. Again, elemental analysis further confirmed the formation of **13a,b**. As shown in Scheme III, the suggested pathway for this reaction involves conversion of the intermediates **12a,b** into **13a,b** *via* a Reissert type reaction similar to that discussed in Scheme II.

The mass spectrum of **13a** gives further evidence for the proposed structure and also indicates the formation of fragmentation ions *via* a McLafferty type rearrangement (6), involving a seven-membered rather than a six-membered cyclic transition state. As shown in Scheme IV, rearrangement of the molecular ion of **13a** followed by the loss of an acetyl group would account for the observed parent peak at m/e 367 (94). The molecular ion of the acetyl group accounts for the base peak at m/e 43. The mass spectrum of **13b** shows similar fragmentation patterns.

Several unsuccessful attempts were made to synthesize the aromatic quino[1,2-*c*]quinazolinium derivative **16** from **3a** as shown in Scheme V. The simultaneous aromatization and quaternization of benzo[*c*]phenanthridines and related compounds has been reported to occur by catalytic dehydrogenation in acid or by air oxidation in acid (7-10). However, catalytic dehydrogenation of **3a** in acetic acid,

Scheme V



followed by treatment with sodium chloride, and air oxidation of **3a** in ethanol containing a catalytic amount of hydrochloric acid yielded only the hydrochloride salt of the starting material. This compound was also isolated in the attempted dehydrogenation of **3a** with palladium on carbon in refluxing *p*-cymene, following the work up with hydrogen chloride. The quaternization of benzo[*c*]phenanthridine alkaloids has also been reported to occur by oxidation with 2,3-dichloro-5,6-dicyano-1,4-benzoquinone (DDQ) in a two phase reaction in benzene and aqueous sodium hydroxide, followed by work up in hydrochloric acid (11,12). These same reaction conditions led to the ring opening and aromatization of **3a** to give the quinoline derivative **17**, presumably *via* nucleophilic attack of hydroxide ion at the C-6 carbon atom. In analogous reactions, the C-2 carbon atom of quinazoline 3-oxides is known to be susceptible to nucleophilic attack giving ring enlarged products (13).

Thus, 2-(2-amino-4,5-dimethoxyphenyl)-6,7-disubstituted-1,2,3,4-tetrahydroquinolines were shown to be versatile intermediates for the synthesis of quino[1,2-*c*]quinazolines. Further research concerning the synthesis of benzo[*c*]phenanthridine alkaloid analogs is currently in progress in our laboratory.

EXPERIMENTAL

Ir spectra were obtained in potassium bromide discs on a Beckman Acculab 2 spectrophotometer. ^{1}H nmr spectra were obtained on a Varian EM 390 spectrometer in the solvents as indicated. Chemical shifts are reported in ppm, from TMS as an internal standard and are given in δ units. Mass spectra were obtained on a Hewlett-Packard model 5980A mass spectrometer. Elemental analyses were obtained from MHW Laboratories, Phoenix, Arizona. Melting points were determined on a Thomas-Hoover melting point apparatus and are uncorrected.

2-(2-Amino-4,5-dimethoxyphenyl)-6,7-dimethoxy-1,2,3,4-tetrahydroquinoline (**2a**).

To a cold stirring mixture of 4.6 g. (0.0134 mole) of **1a** (1) in 400 ml. of tetrahydrofuran (stirring in an ice bath), 1.3 g. of lithium aluminum hydride was slowly added. Following the addition the mixture was stirred in the ice bath under an atmosphere of nitrogen for an additional 0.5 hour. The reaction mixture was then stirred at room temperature for 4 hours, after which time successive portions of water and 10% aqueous potassium hydroxide were added to decompose the excess lithium aluminum hydride. The mixture was then filtered and the resulting white precipitate was washed with chloroform. The filtrates were dried over sodium sulfate; evaporation of the solvent gave a yellow-brown oil which was recrystallized from benzene-cyclohexane (1:1) giving 4.17 g. (90%) of fine yellow needles, m.p. 87-89°; ir: 3380 (NH_2), 1230, 1205 and 1010 (C-O-CH_3); nmr (DMSO-d_6): 1.8-2.12 (m, H-3, 2H), 2.6-2.9 (m, H-4, 2H), 3.69, 3.71, 3.73 and 3.76 (4 singlets, OCH_3, 12H), 4.22-4.47 (m, H-2, 1H), 4.72 (broad, NH_2, 2H), 5.37 (broad, NH, 1H), 6.37, 6.4, 6.57 and 6.82 (4 singlets, aromatic, 4H); ms: 344 (M^+, 100), 329 (M-CH_3, 16).

Anal. Calcd. for $C_{19}H_{24}N_2O_4$: C, 66.26; H, 7.02; N, 8.13. Found: C, 66.57; H, 7.11; N, 7.91.

6-(2-Amino-4,5-dimethoxy)-5,6,7,8-tetrahydro[1,3]dioxolo[4,5-*g*]quinoline (**2b**).

Compound **2b** was synthesized from **1b** in 84% yield in a manner similar to the preparation of **2a**, and was obtained as white needles after recrystallization from ethanol, m.p. 186°; ir: 3300 and 3210 (NH_2); nmr (DMSO-d_6): 1.7-1.97 (m, H-7, 2H), 2.4-2.8 (m, H-8, 2H), 3.55 and 3.62 (2 singlets, OCH_3, 6H), 4.12-4.3 (m, H-6, 1H), 4.6 (broad, NH_2, 2H), 5.37 (broad, NH, 1H), 5.73 (s, -OCH_2O-, 2H), 6.22, 6.3, 6.43 and 6.72 (4 singlets, aromatic, 4H); ms: 328 (M^+, 70), 313 (M-CH_3, 11), 178 (100).

Anal. Calcd. for $C_{18}H_{20}N_2O_4$: C, 65.84; H, 6.14; N, 8.53. Found: C, 65.99; H, 6.10; H, 8.51.

12,13-Dihydro-2,3,9,10-tetramethoxy-11b*H*-quino[1,2-*c*]quinazoline (**3a**).

A solution of 1.0 g. (2.90 mmoles) of **2a** in 40 ml. of triethyl orthoformate was refluxed for 0.5 hour, after which the excess triethyl orthoformate was removed *in vacuo*. The resulting solid residue was treated with decolorizing carbon and recrystallized from ethyl acetate giving 0.65 g. (63%) of tan plates, m.p. 168-169° dec.; ir: 1255 and 1010 (C-O-CH_3); nmr (DMSO-d_6): 2.05-2.28 (m, H-12, 2H), 2.7-2.95 (m, H-13, 2H), 3.67, 3.69 and 3.72 (3 singlets, OCH_3, 12H), 4.58-4.77 (m, H-11b, 1H), 6.53, 6.67 and 6.8 (3 singlets, aromatic, 4H), 7.49 (s, H-6, 1H); ms: 354 (M^+, 100), 339 (M-CH_3, 36).

Anal. Calcd. for $C_{20}H_{22}N_2O_4$: C, 67.78; H, 6.26; N, 7.90. Found: C, 67.94; H, 6.24; N, 7.82.

The hydrochloride salt was prepared as explained in the discussion.

Anal. Calcd. for $C_{20}H_{22}N_2O_4$·HCl: C, 61.46; H, 5.93; N, 7.17. Found: C, 61.57; H, 6.09; N, 7.09.

5,6-Dihydro-2,3-dimethoxy-4b*H*-[1,3]dioxolo[4',5':6,7]quino[1,2-*c*]quinazoline (**3b**).

Compound **3b** was synthesized from **2b** in 48% yield in a manner similar to the preparation of **3a**, and was obtained as pink needles after treatment with decolorizing carbon and recrystallization from ethanol, m.p. 195-196° dec.; ir: 1220 and 1040 (C-O-CH_3); nmr

(DMSO-d_6): 2.15-2.35 (m, H-5, 2H), 2.78-2.92 (m, H-6, 2H), 3.75 (s, OCH_3, 6H), 4.62-4.8 (m, H-4b, 1H), 5.97 (s, $-OCH_2O-$, 2H), 6.6, 6.72, 6.73 and 6.93 (4 singlets, aromatic, 4H), 7.43 (s, H-13, 1H); ms: 337 (M-1, 100), 103 (13) and 102 (7) (characteristic quinazoline fragmentation) (14).

Anal. Calcd. for $C_{19}H_{18}N_2O_4$: C, 67.45; H, 5.36; N, 8.28. Found: C, 67.73; H, 5.43; N, 8.48.

6-Amino-12,13-dihydro-2,3,9,10-tetramethoxy-11b*H*-quino[1,2-*c*]quinazoline Hydrobromide (**4a**).

To a stirring mixture of 0.5 g. (1.45 mmoles) of **2a** in 10 ml. of absolute ethanol, 0.16 g. (1.51 mmoles) of cyanogen bromide was added at room temperature. The mixture was then stirred at room temperature for 2 hours, after which time the cloudy pink solution was cooled in an ice bath and filtered. The resulting pink precipitate was recrystallized from ethanol-water giving 0.3 g. (46%) of pink needles, m.p. 282-284° dec.; ir: 3500 and 3400 (NH_2); nmr (DMSO-d_6): 2.18-2.32 (m, H-12, 2H), 2.89-3.1 (m, H-13, 2H), 3.72, 3.73, 3.75 and 3.78 (4 singlets, OCH_3, 12H), 4.6-4.8 (m, H-11b, 1H), 6.7-6.92 and 6.97 (3 singlets, aromatic, 4H), 7.6-7.95 (broad, NH_2, 2H).

Anal. Calcd. for $C_{20}H_{23}N_3O_4 \cdot HBr$: C, 53.34; H, 5.37; N, 9.33. Found: C, 53.26; H, 5.46; N, 9.07.

13-Amino-5,6-dihydro-2,3-dimethoxy-4b*H*[1,3]dioxolo[4′,5′:6,7]quino-[1,2-*c*]quinazoline Hydrobromide (**4b**).

Compound **4b** was synthesized from **2b** in a manner similar to the preparation of **4a**, except that the reaction was run in refluxing ethanol. The product was obtained in 25% yield as pink needles after treatment with decolorizing carbon and recrystallization from ethanol, m.p. 187-190° dec.; ir: 3340 (NH_2); nmr (DMSO-d_6): 1.9-2.3 (m, H-5, 2H), 2.8-3.05 (m, H-5, 2H), 3.71 and 3.73 (2 singlets, OCH_3, 6H), 4.5-4.75 (m, H-4b, 1H), 6.03 and 6.06 (2 singlets, $-OCH_2O-$, 2H), 6.68, 6.87, 6.92 and 6.95 (4 singlets, aromatic, 4H), 7.6-8.2 (broad, NH_2, 2H) (15).

Anal. Calcd. for $C_{19}H_{19}N_3O_4 \cdot HBr \cdot 2H_2O$: C, 48.52; H, 5.14; N, 8.93. Found: C, 48.95; H, 4.89; N, 9.12.

12,13-Dihydro-2,3,9,10-tetramethoxy-11b*H*-quino[1,2-*c*]quinazoline-6-(7*H*)thione (**5a**).

A mixture of 1.0 g. (2.90 mmoles) of **2a**, 4 ml. of carbon disulfide and 20 ml. of pyridine was refluxed for 2.5 hours, after which time the reaction mixture was poured into an excess of ice water. The resulting yellow floculent precipitate was triturated in ethanol giving 0.83 g. (74%) of a white product, m.p. 303-305° dec.; ir: 3200 (NH); nmr (DMSO-d_6): 2.0-2.25 (m, H-12, 2H), 2.8-3.0 (m, H-13, 2H), 3.68, 3.7 and 3.72 (3 singlets, OCH_3, 12H), 4.5-4.7 (m, H-11b, 1H), 6.72, 6.73, 6.82 and 7.22 (4 singlets, aromatic, 4H), 11.73 (s, NH, 1H); ms: 386 (M^+, 100).

Anal. Calcd. for $C_{20}H_{22}N_2O_4S$: C, 62.16; H, 5.74; H, 7.25; S, 8.30. Found: C, 62.33; H, 5.71; N, 7.08; S, 8.43.

5,6-Dihydro-2,3-dimethoxy-4b*H*-[1,3]dioxolo[4′,5′:6,7]quino[1,2-*c*]quinazoline-13-(14*H*)thione (**5b**).

Compound **5b** was synthesized from **2b** in 47% yield in a manner similar to the preparation of **5a**, and was obtained as white needles after treatment with decolorizing carbon and recrystallization in ethanol, m.p. 258-259° dec.; ir: 3200 (NH); nmr (DMSO-d_6): 1.97-2.25 (m, H-5, 2H), 2.72-2.98 (m, H-6, 2H), 3.7 (s, OCH_3, 6H), 4.52-4.75 (m, H-4b, 1H), 6.02 and 6.07 (2 singlets, $-OCH_2O-$, 2H), 6.69, 6.72, 6.82 and 7.08 (4 singlets, aromatic, 4H), 10.68 (s, NH, 1H).

Anal. Calcd. for $C_{19}H_{18}N_2O_4S$: C, 61.61; H, 4.90; N, 7.56; S, 8.66. Found: C, 61.83; H, 4.73; N, 7.68; S, 8.51.

12,13-Dihydro-2,3,9,10-tetramethoxy-6-methylthio-11b*H*-quino[1,2-*c*]-quinazoline (**6a**).

To a stirring suspension of 0.50 g. (1.29 mmoles) of **5a** in 20 ml. of 10% aqueous sodium hydroxide, 5 ml. of methyl iodide was added and the mixture was heated at 95-100° for 3 hours with vigorous stirring. After evaporation of the excess methyl iodide *in vacuo*, the aqueous residue was extracted with chloroform and the extracts were washed with water until neutral to *p*H paper. The extracts were then dried over sodium sulfate and following removal of the chloroform *in vauco*, the resulting solid residue was triturated in boiling ethanol giving 0.33 g. (64%) of light yellow crystals, m.p. 172-173°; ir: 1230 and 1020 (OCH_3); nmr (deuteriochloroform): 1.8-2.09 (m, H-12, 2H), 2.4 (s, SCH_3, 3H), 2.8-3.0 (m, H-13, 2H), 3.8, 3.81 and 3.86 (3 singlets, OCH_3, 12H), 4.28-4.48 (m, H-11b, 1H), 6.43, 6.58, 6.72 and 6.85 (4 singlets, aromatic 4H); ms: 400 (M^+, 60), 341 (M-SCH_3, 100).

Anal. Calcd. for $C_{21}H_{24}N_2O_4S$: C, 62.98; H, 6.04; N, 7.00; S, 8.01. Found: C, 63.30; H, 6.16; N, 6.79; S, 7.80.

5,6-Dihydro-2,3-dimethoxy-13-methylthio-4b*H*-[1,3]dioloxo[4′,5′:6,7]-quino[1,2-*c*]quinazoline (**6b**).

Compound **6b** was synthesized from **5b** in 66% yield in a manner similar to the preparation of **6a**, and was obtained as white crystals after recrystallization from ethanol, m.p. 182°; ir: 1225 and 1020 (C-O-CH_3); nmr (deuteriochloroform): 1.78-2.1 (m, H-5, 2H), 2.48 (s, SCH_3, 3H), 2.83-3.0 (m, H-6, 2H), 3.85 and 3.9 (2 singlets, OCH_3, 6H), 4.3-4.5 (m, H-4b, 1H), 5.97 (s, $-OCH_2O-$, 2H), 6.5, 6.61, 6.79 and 6.85 (4 singlets, aromatic, 4H), ms: 337 (M-SCH_3, 100).

Anal. Calcd. for $C_{20}H_{20}N_2O_4S$: C, 62.46; H, 5.24; N, 7.28; S, 8.34. Found: C, 62.51; H, 5.09; N, 7.20; S, 7.96.

12,13-Dihydro-2,3,9,10-tetramethoxy-11b*H*-quino[1,2-*c*]quinazolin-6-(7*H*)-one (**7a**).

Compound **2a** (0.6 g., 1.74 mmoles) was fused with 2.0 g. of urea at 160-180° for 0.5 hour, after which time the mixture was poured into an excess of water. The crude product was filtered and recrystallized from ethanol giving 0.4 g. (62%) of white needles, m.p. 252-254° dec.; ir: 3200 (NH), 1660 (C=O); nmr (DMSO-d_6): 1.85-2.2 (m, H-12, 2H), 2.77-2.95 (m, H-13, 2H), 3.66, 3.67 and 3.7 (3 singlets, OCH_3, 12H), 4.4-4.6 (m, H-12b, 1H), 6.45, 6.67, 6.8 and 7.02 (4 singlets, aromatic, 4H), 9.18 (s, NH, 1H); ms: 370 (M^+, 100), 355 (M-CH_3, 46), 118 (phenylisocyanate, 2) (16).

Anal. Calcd. for $C_{20}H_{22}N_2O_5$: C, 64.85; H, 5.99; N, 7.56. Found: C, 64.89; H, 5.94; N, 7.42.

5,6-Dihydro-2,3-dimethoxy-4b*H*-[1,3]dioxolo[4′,5′:6,7]quino[1,2-*c*]quinazolin-13-(14*H*)one (**7b**).

Compound **7b** was synthesized from **2b** in 45% yield in a manner similar to the preparation of **7a**, and was obtained as orange-pink needles after treatment with decolorizing carbon and recrystallization from ethanol, m.p. 275-277° dec.; ir: 3200 (NH), 1670 (C=O); nmr (DMSO-d_6): 1.92-2.2 (m, H-5, 2H), 2.75-2.95 (m, H-6, 2H), 3.7 (s, OCH_3, 6H), 4.42-4.6 (m, H-4b, 2H), 5.95 (s, $-OCH_2O-$, 2H), 6.47, 6.67, 6.82 and 6.92 (4 singlets, aromatic, 4H), 9.28 (s, NH, 1H); ms: 354 (M^+ 100), 339 (M-CH_3, 30).

Anal. Calcd. for $C_{19}H_{18}N_2O_5$: C, 64.40; H, 5.12; N, 7.91. Found: C, 64.31; H, 5.19; N, 7.81.

6-Chloro-12,13-dihydro-2,3,9,10-tetramethoxy-11b*H*-quino[1,2-*c*]quinazoline (**8a**).

A mixture of 0.4 g. of **7a** in 4 ml. of phosphorus oxychloride was heated on a steam bath for 1 hour, after which time the orange-red solution was added to a mixture of 35 ml. of ice, 25 ml. of concentrated ammonia and 30 ml. of chloroform. The aqueous layer was washed with 30 ml. of chloroform and the chloroform extracts were washed with aqueous sodium chloride and dried over sodium sulfate. The chloroform was then removed *in vacuo* and the resulting oil was recrystallized in ethanol giving 0.16 g. (38%) of pink needles, m.p. 161-162°; ir: 1245 and 1030 (C-O-CH_3); nmr (deuteriochloroform): 2.15-2.5 (m, H-12, 2H), 2.9-3.2 (m, H-13, 2H), 3.91 (s, OCH_3, 12H), 4.6-4.85 (m, H-11b, 1H), 6.52, 6.65 and 6.82 (3 singlets, aromatic, 4H); ms: 388 (M^+, 27), 389 (M+1, 8), 390 (M+2, 11), 353 (M-Cl, 100).

Anal. Calcd. for $C_{20}H_{21}ClN_2O_4$: C, 61.78; H, 5.44; N, 7.20. Found: C, 61.83; H, 5.72; N, 6.68.

7-Benzoyl-12,13-dihydro-6-hydroxy-2,3,9,10-tetramethoxy-6-phenyl-11b*H*-quino[1,2-*c*]quinazoline (**11**).

A mixture of 0.6 g. (1.74 mmoles) of **2a** and 4 ml. of benzoyl chloride

was refluxed for 2 hours. On cooling, the precipitated product was collected, triturated with light petroleum ether and recrystallized from ethanol-ethyl acetate, giving 0.2 g. (21%) of yellow crystals, m.p. 237° dec.; ir: 3200 (OH), 1660 (C=O); nmr (DMSO-d_6): 1.8-2.0 (m, H-12, 2H), 3.0-3.2 (m, H-13, 2H), 3.6, 3.65, 3.82 and 3.92 (4 singlets, OCH_3, 12H), 4.0-4.15 (m, H-11b, 1H), 6.55-6.75 (2 singlets, aromatic, 2H), 7.25-7.75 (m, aromatic, 12H), 8.35 (s, OH, 1H); ms: 430 (M-OH, benzoyl, 100) (15).

Anal. Calcd. for $C_{33}H_{32}N_2O_6 \cdot 0.9H_2O$: C, 69.68; H, 5.99; N, 4.92. Found: C, 69.84; H, 5.51; N, 4.80.

7-Acetyl-6-acetyloxy-12,13-dihydro-2,3,9,10-tetramethoxy-6-methyl-11b*H*-quino[1,2-*c*]quinazoline (**13a**).

A mixture of 1.0 g. of **2a** in 25 ml. of acetic anhydride was refluxed for 12 hours, after which time the resulting solution was cooled and the acetic anhydride was removed *in vacuo* giving a yellow-brown oil. Recrystallization from ethanol gave 1.2 g. (48%) of white plates, which melted at 144° and then solidified in the melting point tube, melting finally at 172°; ir: 1705 (C=O); nmr (deuteriochloroform): 1.4-1.7 (m, H-12, 2H), 2.12, 2.28 and 2.63 (3 singlets, CH_3, 9H), 2.45-2.6 (m, H-13, 2H), 3.68, 3.8, 3.85 and 3.9 (3 singlets, OCH_3, 12H), 5.55 (t, H-11b, 1H, $J_{11b,12}$ = 9 Hz), 6.48, 6.52 and 6.8 (3 singlets, aromatic, 4H); ms: see Scheme IV.

Anal. Calcd. for $C_{25}H_{30}N_2O_7$: C, 63.82; H, 6.43; N, 5.95. Found: C, 63.60; H, 6.58; N, 5.33.

14-Acetyl-13-acetyloxy-5,6-dihydro-2,3-dimethoxy-13-methyl-4b*H*-[1,3]-dioxolo[4',5':6,7]quino[1,2-*c*]quinazoline (**13b**).

Compound **13b** was synthesized from **2b** in 36% yield in a manner similar to the preparation of **13a**, and was obtained as light yellow needles after treatment with decolorizing carbon and recrystallization from ethanol. Compound **13b** also showed unusual melting properties, melting first at 197°, solidifying in the melting point tube and finally melting at 211-212°; ir: 1705 (C=O); nmr (DMSO-d_6): 1.2-1.55 (m, H-5, 2H), 2.03, 2.15 and 2.48 (3 singlets, CH_3, 9H), 2.3-2.45 (m, H-6, 2H), 3.62 and 3.72 (2 singlets, OCH_3, 6H), 5.36 (t, H-4b, 1H, $J_{4b,5}$ = 7 Hz), 6.03 (s, OCH_2O-, 2H), 6.5, 6.85 and 7.25 (3 singlets, aromatic, 4H); ms: 454 (M^+, 4), 351 (corresponds to **16** in Scheme IV).

Anal. Calcd. for $C_{24}H_{26}N_2O_7$: C, 63.43; H, 5.77; N, 6.16. Found: C, 63.22; H, 6.00; N, 6.04.

2-(2-Formamido-4,5-dimethoxyphenyl)-6,7-dimethoxyquinoline (**17**).

To a vigorously stirring mixture of 0.32 g. (0.903 mmole) of **3a** in 15 ml. of benzene and 75 ml. of 10% aqueous sodium hydroxide, a solution of 0.9 g. (3.965 mmoles) of DDQ in 175 ml. of benzene was slowly added at room temperature. The two-phase reaction mixture was stirred at room temperature for 5 hours following the addition, during which time the dark reaction mixture turned light orange in color. The benzene layer was then separated, washed with water and dried over sodium sulfate. After removal of benzene *in vacuo*, the resulting yellow residue was recrystallized from benzene-cyclohexane giving 0.16 g. (48%) of yellow crystals, m.p. 208-209°; ir: 1670 (C=O); nmr (deuteriochloroform): 3.7-4.1 (m, OCH_3, 12H), 7.0 (s, HC=O, 1H), 7.24 (s, aromatic, 2H), 7.6 (d, H-3, 1H, $J_{3,4}$ = 8 Hz), 8.05 (d, H-4, 1H), 8.4 and 8.5 (2 singlets, aromatic, 2H), 12.6-12.8 (broad, NH, 1H); ms: 368 (M^+, 29), 325 (M-43, 100).

Anal. Calcd. for $C_{20}H_{20}N_2O_5$: C, 65.21; H, 5.47; N, 7.60. Found: C, 65.44; H, 5.66; N, 7.40.

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