The nonselectivity shown by the *E* lithium enolates[1,3,4,7a] is probably a result of these two opposite trends, but it is more difficult to rationalize because of lithium–enolate aggregation in ethereal solvents.[22]

The "normal" behavior can therefore be defined as follows: *both (E)- and (Z)-enolates prefer syn aldols under kinetic control* (tin–, zirconium–, and titanium–enolates and enol borates).

The "abnormal" behavior ((*E*)-enolates give anti aldols under kinetic control) *is due to the steric hindrance of the cation* and is more pronounced with enol borinates than with lithium–enolates.

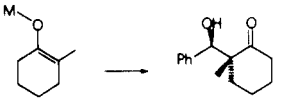
Therefore our calculations shed new light on the enolate selectivity and on the aldol transition-state conformations.

Our transition-state models could possibly also give some aid to rationally design new chiral auxiliaries so that enantiomerically pure aldols can be easily obtained.[23]

Acknowledgment. This work was made possible by the financial support of Ministero Pubblica Istruzione (40% and 60%). We thank P. Pugni for comments and assistance.

Registry No. 1, 100020-83-5; 3, 97231-14-6; (1-cyclopentenyloxy)(dibutyl)boron, 100020-84-6; (1-cyclopentenyloxy)(dimethyl)boron, 100020-85-7; benzaldehyde, 100-52-7; 2-(α-hydroxybenzyl)cyclopentanone (isomer 1), 43108-70-9; 2-(α-hydroxybenzyl)cyclopentanone (isomer 2), 43108-71-0; 3-(α-hydroxybenzyl)-2-butanone (isomer 1), 75600-09-8; 3-(α-hydroxybenzyl)-2-butanone (isomer 2), 81640-13-3.

(21) The experiments performed by Kuwajima and Nakamura[7a] and by Hoffman[13] using cyclohexanone and 2-methylcyclohexanone enolates are nicely interpreted by our model. Cyclohexanone enolates are syn selective (enol borates > 9:1;[8,13] trichlorotitanium–enolate 89:11[7a]), nonselective (lithium–enolate ca. 1:1[7a]), or slightly anti selective (enol borinate 67:33[7a]). In the case of 2-methylcyclohexanone, the substitution of the hydrogen with the methyl disfavors the twist-boat leading to the syn aldol because of the 1,2-methyl–hydrogen interaction (compare Charts III and IV). Therefore all the previously mentioned enolates become anti selective: lithium–enolate, ca. 3:1;[7a] enol borinate, >200:1;[7a] trichlorotitanium enolate, ca. 9:1;[7a] enol borate, >20:1.[13]



(22) THF–solvated lithium–enolates are known to be tetrameric (see: Amstutz, R.; Schweizer, W. B.; Seebach, D.; Dunitz, J. D. *Helv. Chim. Acta* **1981**, *64*, 2617). The O–Li group can then be considered a rather large group. For this kind of discussion, see: Heathcock, C. H.; Henderson, M. A.; Oare, D. A.; Sanner, M. A. *J. Org. Chem.* **1985**, *50*, 3019. Heathcock, C. H.; Oare, D. A. *J. Org. Chem.* **1985**, *50*, 3022.

(23) Part of this work was presented as an invited lecture (C. Gennari) at the IXth International Symposium on "Synthesis in Organic Chemistry", Oxford, July 22–25 1985.

Defined Dimensional Alterations in Enzyme Substrates. General Synthetic Methodology for the Bent Dihydro-*lin*-benzopurines

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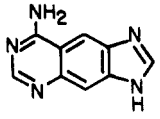
Received July 19, 1985

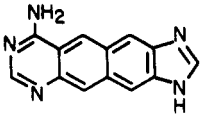
The use of cycloaddition reactions for the synthesis of partially reduced heterocyclic systems has been shown to be an attractive approach to dihydrobenzimidazoles, dihydroquinazolines, and dihydro-*lin*-benzopurines. The first representatives of the bent dihydro-*lin*-benzopurines to be synthesized were 4,9-dihydroimidazo[4,5-*g*]-quinazoline-2,8(1*H*,7*H*)-dione (**20**) and 4,9-dihydro-*lin*-benzouric acid (**21**).

Naturally occurring, modified, and substituted purines have been subjected to close scrutiny by scientists seeking to establish structure–biological activity relationships. The need for more information defining the active sites of enzymes that require purines as substrates or cofactors has led to the synthesis of an ordered series of compounds which we refer to as dimensional probes.[1] These compounds retain both the pyrimidine and imidazole rings present in purines, but they are separated by intervening chemical frameworks. The formal insertion of a benzene ring (actually four additional carbons) into the middle of the adenine ring system leads to a molecule referred to as *lin*-benzoadenine (**1**), and of a naphthalene ring (actually an eight-carbon insertion) to an analogue referred to as *lin*-naphthoadenine (**2**). We have previously described their syntheses, along with the corresponding ribonucleosides, and their biochemical activity.[2]

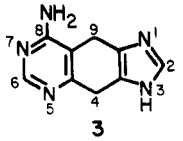
A compound related to **1**, the biochemically active analogue of adenine, is the 4,9-dihydro derivative **3**, which could give a different type of information. Its bent



1



2



3

structure poses the question as to whether the contributing terminal rings of adenine, namely, the pyrimidine and

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(1) (a) Leonard, N. J. *Acc. Chem. Res.* **1982**, *15*, 128. (b) Leonard, N. J. *Heterocycles* **1979**, *12*, 129. (c) Keyser, G. E.; Leonard, N. J. *J. Org. Chem.* **1976**, *41*, 3529. (d) Scopes, D. I. C.; Barrio, J. R.; Leonard, N. J. *Science (Washington, D.C.)* **1977**, *195*, 296. (e) Leonard, N. J.; Scopes, D. I. C.; VanDerLijn, P.; Barrio, J. R. *Biochemistry* **1978**, *17*, 3677. (f) Kauffman, R. F.; Lardy, H. A.; Barrio, J. R.; Barrio, M. del C., Leonard, N. J. *Biochemistry* **1978**, *17*, 3686. (g) Keyser, G. E.; Leonard, N. J. *J. Org. Chem.* **1979**, *44*, 2989. (h) Leonard, N. J.; Keyser, G. E. *Proc. Natl. Acad. Sci. U.S.A.* **1979**, *76*, 4262. (i) Moder, K. P.; Leonard, N. J. *J. Am. Chem. Soc.* **1982**, *104*, 2613.

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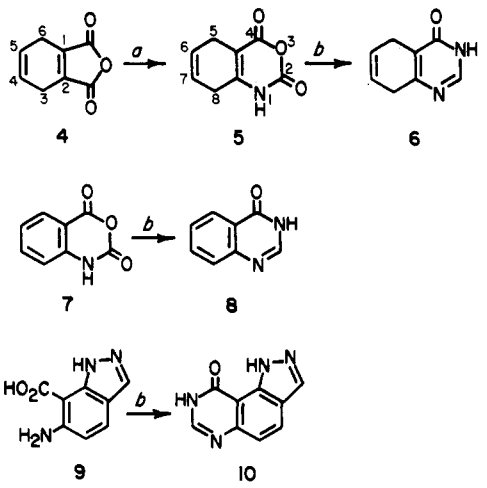
Scheme I[a]



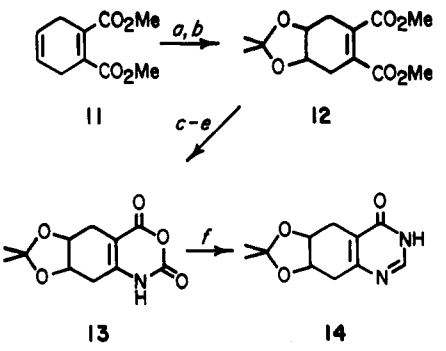
[a] **a**, $(CH_3)_3SiN_3$; **b**, formamidine acetate.

imidazole, must be coplanar, especially in those systems where the reactivity of **1** has shown that they need not be contiguous. The 4,9-dihydro-*lin*-benzopurines bear the same relation to the corresponding *lin*-benzopurines that dihydroanthracene, with a 148° angle between the planes of the terminal rings,[3] bears to anthracene. We set out first to synthesize the heterocyclic subunits, i.e., the dihydroquinazolines and dihydrobenzimidazoles, in order to judge their stability and then to develop synthetic methodology adaptable to the dihydro-*lin*-benzopurines.

Results and Discussion

These systems can be thought of retrosynthetically as derivatives of 1,4-cyclohexadienes, which are generally synthesized in either of two ways. The first method is by reduction of fully aromatic compounds. Tricyclic relatives of the benzimidazoles having 6:6:5 ring systems are not readily reduced in the central ring, and quinazolines are often reduced in the pyrimidine ring.[4] More importantly, under Birch reduction conditions, benzyl-substituted precursors to *lin*-benzoadenine (**1**) could be debenzylated without evidence of reduction in the heterocyclic ring system.[2a] The second, more feasible method of obtaining 1,4-cyclohexadienes is via a Diels–Alder reaction of dienes with acetylenic dienophiles. The most reasonable starting materials for the synthesis of the dihydroquinazolines were the cycloadducts from butadiene and derivatives of acetylenedicarboxylic acid in which one of the two C–C bonds would have to be converted to a C–N bond. Among the rearrangement reactions considered for this purpose, the Hoffman,[5] Lossen,[6] or Curtius[7] rearrangements, the first of these was not fully investigated because the requisite diamide precursor was not readily available. Although requisite precursors for the Lossen rearrangement were available by synthesis, the dihydroquinazolines could not

Scheme II[a]



[a] **a**, OsO_4, *N*-methylmorpholine *N*-oxide; **b**, acetone, $HClO_4$; **c**, NaOH; **d**, EtOC≡CH; **e**, $(CH_3)_3SiN_3$; **f**, formamidine acetate.

be obtained in preparatively useful yields. We therefore concentrated our efforts toward the use of the Curtius rearrangement.

One of the most useful variants of the Curtius rearrangement of dicarbonyl compounds is the conversion of five-membered-ring cyclic anhydrides to oxazinedione ring systems by treatment with trimethylsilyl azide, Me_3SiN_3.[8] 3,6-Dihydrophthalic anhydride (**4**) was synthesized by the reaction of acetylenedicarboxylic acid with butadiene.[9] Treatment of **4** with Me_3SiN_3 resulted in rearrangement to 5,8-dihydroisatoic anhydride (**5**). The oxidized compound corresponding to this, isatoic anhydride (**7**), has been thoroughly investigated in its conversion to various quinazolines and serves as a useful model.[10] In order to avoid isomerization and/or aromatization of the dihydro moiety in **5**, we sought a milder technique for pyrimidine ring formation than had been used previously (Scheme I). The stable salt formamidine acetate had been shown to be useful for the synthesis of pyrimidines,[11] but its reaction with isatoic anhydride had not been investigated. In fact, when isatoic anhydride (**7**) was heated with formamidine acetate in ethanol, quinazolin-4(3*H*)-one (**8**) was isolated in >80% yield. Extension of this reaction to 5,8-dihydroisatoic anhydride gave 5,8-dihydroquinazolin-4-(3*H*)-one (**6**) in 62% yield. There was no evidence of aromatization on the basis of the ^{13}C and ^1H NMR spectra and the mass spectrum. The retention of the unconjugated disposition of the double bonds was shown by the presence of four doubly allylic protons in the ^1H NMR spectrum.

The scope of the ring closure with formamidine acetate was readily capable of extension since anthranilic acid, methyl anthranilate, and anthranilamide all reacted to give **8**. Further generality of this reaction with respect to substituted isatoic anhydrides and anthranilic acids is shown in Table I (see Experimental Section). Of particular interest is the reaction of the substituted indazole **9** with formamidine acetate. This intermediate in the synthesis of *prox*-benzoisoallopurinol (**10**)[12] suffered extensive decarboxylation to 6-aminoindazole when heated with formamide at 180 °C in an attempt at direct synthesis. This difficulty has now been eliminated by heating **9** with an excess of formamidine acetate in ethanol, with the resulting isolation of *prox*-benzoisoallopurinol (**10**), an extended analogue of isoallopurinol, in >80% yield. This compound

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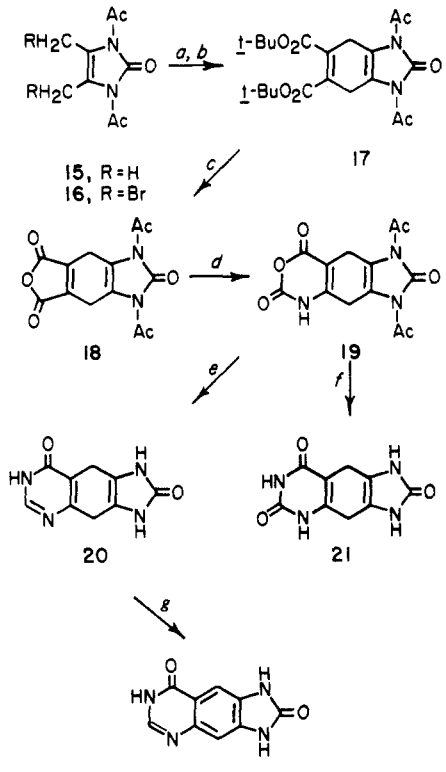
Scheme III[a]



[a] **a**, NBS; **b**, NaI, DMF, *t*-BuOOCC≡CCOO-*t*-Bu; **c**, TsOH, toluene; **d**, $(CH_3)_3SiN_3$; **e**, formamidine acetate; **f**, H_2NCONH_2; **g**, *p*-chloranil.

is an active substrate for and an alternative-substrate inhibitor of xanthine oxidase.[12]

The suitability of the general approach to the synthesis of 6,7-disubstituted dihydroquinazolines was investigated briefly. The dihydroxylation of Diels–Alder product dimethyl 3,6-dihydrophthalate (**11**)[9] with osmium tetraoxide and *N*-methylmorpholine *N*-oxide followed by protection of the diol as the isopropylidene derivative provided **12** (Scheme II). Saponification, dehydration with ethoxyacetylene, and rearrangement with trimethylsilyl azide effected conversion to the substituted tetrahydroisatoic anhydride **13**, and subsequent treatment with formamidine acetate yielded compound **14**. The substituents at the 6,7 positions of **14** were not amenable, however, for annelation of an imidazole. Since the methodology for annelating the pyrimidine ring was already in place, we turned to the alternative route of constructing the dihydrobenzimidazole unit prior to addition of the pyrimidine ring.

A direct route to the dihydro-*lin*-benzopurine ring system was again based on $4^{\pi} + 2^{\pi}$ cycloaddition. Dienes with heteroatoms attached to the 2 or 3 position are well-known, but none with nitrogen at both positions has been described.[13] The most advantageous diene to use would be one already containing an imidazole ring and consisting of an *o*-xylylene type[14] that can be generated nonthermally under Finkelstein reaction conditions.[2c,15] 1,3-Diacetyl-4,5-dimethylimidazolin-2(1*H*)-one (**15**)[16] was treated with 2 equiv of NBS with radical initiation to produce the dibromo compound **16** in good yield.[17] Compound **16** was submitted to Finkelstein reaction conditions (NaI) and treated with di-*tert*-butyl acetylenedicarboxylate in DMF to give **17** (Scheme III). Isolation of the substituted dihydrobenzimidazolinone **17** in 77% overall yield from **15** was representative of other possible trapping reactions (e.g., methyl propiolate, dimethyl acetylenedicarboxylate) of the intermediate bis(methylene)imidazolinone. The reactivity of this intermediate was not predictable since a diene fused to a five-membered ring was reported to have decreased utility in cycloaddition reactions.[18]

The decomposition of di-*tert*-butyl 1,2-dicarboxylic esters has the advantage of giving cyclic anhydrides directly, without resorting to alkaline saponification, by heating in a melt with a catalytic amount of *p*-toluenesulfonic acid.[19] Application of this procedure to **17** failed because of the high melting point (200–201 °C) of the diester, but by heating **17** with a catalytic amount of TsOH in benzene or toluene, 2 equiv of isobutylene and 1 equiv of water were lost. When the solution was cooled, the crystalline anhydride **18** was deposited in 85% yield. While this anhydride was insoluble in trimethylsilyl azide, the Curtius rearrangement could be carried out with an excess of the azide in refluxing acetonitrile to give the substituted dihydroisatoic anhydride **19**. Conversion of **19** to the dihydro-*lin*-benzopurinedione **20** was possible if a solution of **19** in *N*-methylpyrrolidone was deoxygenated prior to the addition of formamidine acetate and heated at 100 °C for 1 h. The NMR spectrum confirmed the presence of only one aromatic proton and four doubly allylic protons in the same range as that observed for **6** and for the precursors **17–19** in this series.

The substituted dihydroisatoic anhydride **19** proved to be useful for the synthesis of 4,9-dihydro-*lin*-benzouric acid. Brief reaction of **19** with urea in a melt at 180 ± 5 °C gave 4,9-dihydro-*lin*-benzouric acid (**21**) in 73% yield. The preservation of the methylene groups was indicated by the single NMR peak at δ 3.42, and the composition was confirmed by the high-resolution mass spectrum. The major peak in the low-resolution electron-impact mass spectrum was indicative of an aromatization process under the conditions of the determination.

It was possible to aromatize the central ring of 4,9-dihydroimidazo[4,5-*g*]quinazoline-2,8(1*H*,7*H*)-dione (**20**) by heating with *p*-chloranil in glacial acetic acid. The structure of the product (**22**) was established by the appearance of two additional aromatic protons in the ^1H NMR spectrum with concomitant loss of the methylene signals, by the new absorption maxima appearing at a longer wavelength in the UV spectrum, and by the low- and high-resolution mass spectra. *lin*-Benzouric acid, bearing oxygen substitution at the 2, 6, and 8 positions, had been identified previously as the final enzymatic oxidation product of *lin*-benzohypoxanthine (and *lin*-benzoxanthine) with xanthine oxidase.[2b]

The stability of the ring system present in dihydro-*lin*-benzoadenine (**3**) has been demonstrated by the synthesis of compounds **20** and **21**. Adaptation of Finkelstein reaction conditions to imidazoles unsubstituted at C-2 could provide a viable route to compound **3** and its derivatives. Model compounds **20** and **21** have the potential to be

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Table I. Synthesis of Substituted Quinazolin-4(3*H*)-ones

starting material	quinazolin-4(3*H*)-one	yield, %	reactn time, h	solvent[a]	mp, °C found	mp, °C lit.
6-chloroisatoic anhydride	6-Cl	87	2	M	263	264–265[21]
4-chloroanthranilic acid	7-Cl	89	1.5	M	253	252–254[20]
5-iodoanthranilic acid	6-I	87	2	E	268	269–271[23]
5-methylanthranilic acid	6-CH_3	83	1	M	258	254–255[21]
4-nitroanthranilic acid	7-NO_2	77	8	M	265	263–266[21]
anthranilic acid	H	81	3	E	216	215–216[22]
methylanthranilate	H	63	6	E	216	215–216[22]
anthranilamide	H	86	1	E	216	215–216[22]

[a] M = methyl cellosolve, E = ethanol.

inhibitors of the enzyme xanthine oxidase, and testing of this possibility is in order.

The use of cycloaddition reactions for the synthesis of partially reduced heterocyclic systems has been shown to be an attractive approach to dihydrobenzimidazoles, dihydroquinazolines, and dihydro-*lin*-benzopurines. Extension to the synthesis of other compounds in these series and as an alternate route to *lin*-benzopurines can be readily envisaged.

Experimental Section

General Comments. Thin-layer chromatography was performed on Merck precoated silica gel f-254 plates with fluorescent backing. NMR spectra were recorded on a Varian Associates EM-390 or XL-200 or on a Nicolet NTC-360 spectrometer. Melting points were determined on a Büchi melting point apparatus and are uncorrected. UV absorption spectra were obtained on a Beckman Acta MVI spectrophotometer. Electron-ionization mass spectra (EIMS) were obtained on a Varian MAT CH-5 instrument, high-resolution electron-ionization mass spectra (HREIMS) were obtained on a Varian MAT-731 high-resolution spectrometer coupled with a 620i computer and a STATOS recorder, and fast atom bombardment mass spectra (FABMS) and high-resolution mass spectra (HRFABMS) were obtained on a VG ZAB-1F instrument equipped with a high field magnet and a VG 11/250 data system, all by J. Carter Cook and his staff. Microanalyses were performed by Josef Nemeth and his staff, who also weighed samples for electronic absorption spectra.

5,8-Dihydroisatoic Anhydride (5). 3,6-Dihydrophthalic anhydride (4)[9] (6.0 g, 40 mmol) and trimethylsilyl azide (10 mL, 86 mmol) were stirred at 20 °C with the exclusion of moisture. The reaction mixture was heated slowly until strong evolution of nitrogen was observed (50–60 °C) and alternately heated or cooled to keep a moderate rate of gas evolution. After 2 h, the solution was cooled to 20 °C and treated with ethanol (2 mL). After further cooling to 0 °C, the precipitate was filtered to provide **5** (4.1 g, 61%) as a white powder of analytical purity: mp 187–189 °C dec; mass spectrum, m/z 165 (M^+); NMR ($(CD_3)_2SO$) δ 3.10 (s, 4, CH_2), 5.80 (s, 2, CH).

Anal. Calcd for $C_8H_7NO_3$: C, 58.18; H, 4.27; N, 8.48. Found: C, 58.04; H, 4.19; N, 8.31.

5,8-Dihydroquinazolin-4(3*H*)-one (6). To a solution of 5,8-dihydroisatoic anhydride (**5**) (560 mg, 3.6 mmol) in methyl cellosolve (15 mL) was added formamidine acetate (416 mg, 4 mmol). The solution was heated at reflux for 1.5 h and then evaporated in vacuo. The residue was recrystallized from ethyl acetate as silky white needles of **6** (310 mg, 62%): mp 214–215 °C; mass spectrum, m/e 148 (M^+); NMR ($(CD_3)_2SO$) δ 3.05 (br, 4, CH_2), 5.72 (s, 2, CH), 8.80 (s, 1, pyrimidine-H).

Anal. Calcd for $C_8H_8N_2O$: C, 64.85; H, 5.44; N, 18.91. Found: C, 64.96; H, 5.32; N, 19.18.

Quinazolin-4(3*H*)-one (8). To a solution of isatoic anhydride (**7**) (500 mg, 3.1 mmol) in ethanol (10 mL) was added formamidine acetate (450 mg, 4.3 mmol). The solution was heated at reflux for 3 h and allowed to come to room temperature. The reaction mixture was diluted with water (5 mL), and filtration yielded white needles of **8** (420 mg, 81%): mp 216–217 °C (Table I).

General Procedure for the Preparation of Quinazolin-4-(3*H*)-ones with Formamidine Acetate. A mixture of the anthranilic acid derivative (2 mmol) and formamidine acetate (2.5 mmol) was heated in methyl cellosolve or ethanol (20 mL) at reflux for the period of time indicated in Table I. When the solution was cooled, the product crystallized and the solution was diluted with water (10 mL) and filtered. If crystallization did not occur, the solvent was evaporated and the residue was triturated with water (10 mL) and filtered to give the desired product.

Dimethyl 2,2-Dimethyl-3a,4,7,7a-tetrahydro-1,3-benzodioxole-5,6-dicarboxylate (12). To a solution of 2.5% osmium tetraoxide in *tert*-butyl alcohol (3.0 mL), *N*-methylmorpholine *N*-oxide (10.5 g, 76 mmol), and water (30 mL) in tetrahydrofuran (75 mL) at 0 °C was added 15 g (76 mmol) of dimethyl 3,6-dihydrophthalate (**11**)[9] during 30 min. When the resulting solution came to room temperature, it was stirred for 30 h. The volatiles were removed in vacuo, and the residue was dissolved in ethyl acetate (500 mL). The organic layer was extracted with 1 N HCl (2 × 250 mL). The acidic washes were back-extracted with hot ethyl acetate (3 × 250 mL). The combined organic layers were dried (Na_2SO_4) and evaporated to yield a viscous oil. The residue was dissolved in acetone (400 mL) and treated with perchloric acid (3 mL). After 30 min, sodium bicarbonate (3 g) was added, and the acetone was removed under reduced pressure. The residue was treated with water (200 mL) and extracted with ethyl acetate (3 × 100 mL). The combined organic extracts were dried (Na_2SO_4) and evaporated to dryness in vacuo. The residue was recrystallized from cyclohexane to give **12** (6.4 g, 31%) as white plates: mp 76 °C; NMR ($CDCl_3$) δ 1.35 (s, 3, CH_3), 1.45 (s, 3, CH_3), 2.45 (br, 4, CH_2), 3.70 (s, 6, OCH_3), 4.40 (br, 2, CH).

Anal. Calcd for $C_{13}H_{18}O_6$: C, 57.77; H, 6.71. Found: C, 57.82; H, 6.71.

2,2-Dimethyl-3a,4,7,7a-tetrahydro-1,3-benzodioxole-5,6-dicarboxylic Acid. To a solution of dimethyl 2,2-dimethyl-3a,4,7,7a-tetrahydro-1,3-benzodioxole-5,6-dicarboxylate (**12**) (780 mg, 2.9 mmol) in 8 mL of tetrahydrofuran was added 0.25 N NaOH (50 mL). The heterogeneous mixture was stirred at 20 °C for 5 h. The mixture was acidified to pH 2 and extracted with 5 × 50 mL of ethyl acetate. The combined extracts were dried with sodium sulfate and evaporated in vacuo. The residue was dried at 60 °C for 12 h to give 678 mg (93%) of a white solid which was used directly in the next step: mp 132–133 °C; NMR ($(CD_3)_2SO$) δ 1.60 (s, 6, CH_3), 2.62 (br, 4, CH_2), 4.70 (s, 2, CH), 12.15 (br, 2, CO_2H).

2,2-Dimethyl-3a,4,9,9a-tetrahydro-1,3-dioxolo[4.5-*g*](3,1)-benzoxazine-6,8-dione (13). To a suspension of 2,2-dimethyl-3a,4,7,7a-tetrahydrobenzodioxole-5,6-dicarboxylic acid (635 mg, 2.5 mmol) in methylene chloride (30 mL) was added ethoxyacetylene (1.5 mL, 20 mmol). The solution was heated at reflux for 20 h and filtered. The filtrate was evaporated in vacuo to leave an orange oil that was suspended in trimethylsilyl azide (2.5 mL, 22 mmol). The mixture was heated to 50 °C and then alternately heated or cooled to keep a moderate evolution of nitrogen. After 1 h the mixture was diluted with chloroform (10 mL) and ethanol (1 mL). The white solid was collected in three crops to give 365 mg (61%) of **13**: mp 194–195 °C; mass spectrum, m/z 239 ($M^+ - CH_3$); NMR ($(CD_3)_2SO$) δ 1.53 (s, 6, CH_3), 2.95 (br, 4, CH_2), 4.90 (br, 2, CH), 8.82 (br, 1, NH).

Anal. Calcd for $C_{11}H_{13}NO_5$: C, 55.23; H, 5.48; N, 5.86. Found: C, 54.99; H, 5.57; N, 5.82.

2,2-Dimethyl-3a,4,9,9a-tetrahydrodioxolo[4,5-*g*]-quinazolin-8(7*H*)-one (14). To a solution of compound **13** (635 mg, 2.7 mmol) in ethanol (15 mL) was added formamidine acetate (335 mg, 3.3 mmol). The mixture was refluxed for 4.5 h and the solvent was evaporated under reduced pressure. The residue was

extracted with ethyl acetate and filtered, and the filtrate was cooled to −20 °C to precipitate **14** as colorless plates (220 mg, 36%): mp 197–198 °C; mass spectrum, m/z 222 (M^+), 207 ($M^+ - CH_3$); NMR ($(CD_3)_2SO$) δ 1.35 (s, 3, CH_3), 1.50 (s, 3, CH_3), 2.78 (br, 4, CH_2), 4.73 (br, 2, CH), 8.10 (s, 1, pyrimidine-H).

Anal. Calcd for $C_{11}H_{14}N_2O_3$: C, 59.45; H, 6.35; N, 12.60. Found: C, 59.70; H, 6.33; N, 12.59.

Di-*tert*-butyl 1,3-Diacetyl-1,2,4,7-tetrahydro-2-oxobenzimidazole-5,6-dicarboxylate (17). To a solution of compound **15**[16] (9.0 g, 46 mmol) in carbon tetrachloride (250 mL) was added 16.4 g (93 mmol) of *N*-bromosuccinimide and 20 mg of benzoyl peroxide. The mixture was heated at reflux for 40 min and cooled to 20 °C. The succinimide was filtered, and the solvent was removed under reduced pressure to afford **16**, a yellow, lachrymatory solid. Compound **16** was dissolved immediately in DMF (150 mL) and treated with 11.9 g (52.6 mmol) of di-*tert*-butyl acetylenedicarboxylate and 25 g of sodium iodide. The dark brown mixture was heated at 80 °C with stirring for 4 h and poured into 200 mL of 20% aqueous sodium bisulfite. The cooled solution was filtered and the solid was washed with cold water. The yellow solid was refluxed with acetone (50 mL), cooled, and filtered. Recrystallization was accomplished from 3:1 acetone/chloroform to give 14.85 g (77%) of **17** as a white powder: mp 200–201 °C dec; mass spectrum, m/z 420 (M^+), 308 ($M^+ - (C_4H_8)_2$), 290 ($M^+ - (C_4H_8)_2 - H_2O$); NMR ($CDCl_3$) δ 1.47 (s, 18, CH_3), 2.60 (s, 6, $COCH_3$), 3.71 (s, 4, CH_2).

Anal. Calcd for $C_{21}H_{28}N_2O_7$: C, 59.99; H, 6.71; N, 6.66. Found: C, 60.23; H, 6.72; N, 6.57.

1,3-Diacetyl-1,2,4,7-tetrahydro-2-oxobenzimidazole-5,6-dicarboxylic Anhydride (18). To a solution of **17** (1.5 g, 3.6 mmol) in dry toluene (12 mL) was added *p*-toluenesulfonic acid monohydrate (30 mg). The solution was heated at reflux for 1.5 h, during which time the solution turned light yellow. The reaction mixture was filtered hot and a light yellow solid crystallized upon cooling to give **18** (890 mg, 86%): mp 221–222 °C: mass spectrum, m/z 290 (M^+); 206 ($M^+ - (C_2H_2O)_2$); NMR ($(CD_3)_2SO$) δ 2.56 (s, 6, CH_3), 3.85 (s, 4, CH_2).

Anal. Calcd for $C_{13}H_{10}N_2O_6$: C, 53.80; H, 3.47; N, 9.65. Found: C, 53.76; H, 3.50; N, 9.58.

1,3-Diacetyl-4,9-dihydroimidazo[4,5-*g*](3,1)benzoxazine-2,6,8-trione (19). To a suspension of **18** (860 mg, 3.0 mmol) in dry acetonitrile (16 mL) at 45 °C was added trimethylsilyl azide (2 mL, 17 mmol). The solution was heated at reflux for 1 h. The solution was cooled to 0 °C and filtered to give, in two crops, **19** (570 mg, 64%) as an off-white powder: mp 262–263 °C; mass spectrum, m/z 305 (M^+), 221 ($M^+ - (C_2H_2O)_2$); NMR ($(CD_3)_2SO$) δ 2.53 (s, 6, CH_3), 3.64 (m, 4, CH_2), 11.40 (br, 1, NH).

Anal. Calcd for $C_{13}H_{11}N_3O_6$: C, 51.15; H, 3.63; N, 13.77. Found: C, 51.40; H, 3.81; N, 13.48.

4,9-Dihydroimidazo[4,5-*g*]quinazoline-2,8(1*H*,7*H*)-dione (20). A suspension of **19** (500 mg, 1.7 mmol) in *N*-methylpyrrolidone (15 mL) was saturated with nitrogen for 30 min. Then, formamidine acetate (500 mg, 4.8 mmol) was added and the reaction mixture was stirred at 100 °C for 1 h. After cooling, the mixture was filtered and washed with acetone (3 × 15 mL) and dried to give **20** as a yellow powder (300 mg, 60%): mp >300 °C; NMR (TFA) δ 3.90 (m, 4, CH_2), 9.40 (s, 1, CH); mass spectrum, m/z 204 (M^+); exact mass calcd for $C_9H_8N_4O_2$ 204.0646, obsd 204.0639.

4,9-Dihydro-*lin*-benzouric Acid (21). A mixture of 25 mg (0.082 mmol) of 1,3-diacetyl-4,9-dihydroimidazo[4,5-*g*](3,1)-benzoxazine-2,6,8-trione (**19**) and 75 mg (1.25 mmol) of urea was ground in a mortar and deoxygenated with dry nitrogen in a two-necked reaction flask for 1–3 h. The reaction flask was placed in an oil bath at 180 ± 5 °C for 2–3 min, during which time the solid mixture melted and became slightly yellow. The mixture was cooled nearly to room temperature, absolute ethanol (2 mL) was added, and the heterogeneous mixture was heated briefly to the boiling point. The light yellow substance that separated was collected and dried at 40 °C in an Abderhalden drying pistol (13.2 mg, 73%): mp >300 °C; NMR ($(CD_3)_2SO$) δ 3.42 (s, CH_2); UV max (H_2O, neutral) 258 nm, 322 sh; (pH 11) 276 nm, 326; (pH 1) 260 nm; (EtOH) 260 nm, 324 sh; (DMF) 320 nm; mass spectrum (10 eV), m/z (relative intensity) 220 (M^+, 37), 219 ($M^+ - 1$, 69), 218 ($M^+ - 2$, 100); exact mass calcd for $C_9H_8N_4O_3$ 220.0596, obsd 220.0591.

Imidazo[4,5-*g*]quinazoline-2,8(1*H*,7*H*)-dione (22). To a boiling suspension of 5.0 mg (0.024 mmol) of 4,9-dihydroimidazo[4,5-*g*]quinazoline-2,8(1*H*,7*H*)-dione (**20**) in glacial acetic acid (2 mL) was added dropwise a solution of 6.0 mg (0.024 mmol) of *p*-chloranil in glacial acetic acid (1 mL) during 2 min. The reaction mixture was heated at reflux for 8 h and then cooled to room temperature. The solid material that deposited was collected and washed on a fritted glass funnel with boiling ethyl ether (5 × 3 mL portions), leaving an off-white substance (2.0 mg, 40%): mp >300 °C; NMR ($(CD_3)_2SO$) δ 12.00 (br s, 1, N7-H), 11.14 (s, 1, N1-H), 11.02 (s, 1, N3-H), 7.94 (s, 1, 6-H), 7.52 (s, 1, 9-H), 7.09 (s, 1, 4-H); (after D_2O shake) δ 7.96 (s, 1, 6-H), 7.59 (s, 1, 9-H), 7.17 (s, 1, 4-H); UV max (H_2O, pH 11) 252 nm, 318, 331; (EtOH) 245, 314, 327; ($(CH_3)_2SO$) 319, 332; mass spectrum (10 eV), m/z (relative intensity) 202 (M^+, 100), 174 ($M^+ - CO$, 10.4), 147 ($M^+ - HCN - CO$, 35.6), 131 (8.3), 119 (27.6), 104 (4.7), 92 (20.7), 77 (4.2), 54 (1.0), 43 (1.5); exact mass calcd for $C_9H_6N_4O_2$ 202.0491, obsd 202.0487.

Registry No. **4**, 4773-89-1; **5**, 99966-38-8; **6**, 99966-39-9; **7**, 118-48-9; **8**, 491-36-1; **11**, 14309-54-7; **12**, 99966-46-8; **13**, 99966-48-0; **14**, 99966-49-1; **15**, 21265-71-4; **16**, 99966-41-3; **17**, 99966-40-2; **18**, 99966-42-4; **19**, 99966-43-5; **20**, 100019-69-0; **21**, 99966-44-6; **22**, 99966-45-7; 6-chloroisatoic anhydride, 4743-17-3; 6-chloroquinazolin-4(3*H*)-one, 16064-14-5; 7-chloroquinazolin-4(3*H*)-one, 31374-18-2; 6-iodoquinazolin-4(3*H*)-one, 16064-08-7; 6-methylquinazolin-4(3*H*)-one, 19181-53-4; 7-nitroquinazolin-4(3*H*)-one, 20872-93-9; 2,2-dimethyl-3a,4,7,7a-tetrahydrobenzodiazole-5,6-dicarboxylic acid, 99966-47-9; trimethylsilyl azide, 4648-54-8; formamidine acetate, 3473-63-0; 4-chloroanthranilic acid, 89-77-0; 5-iodoanthranilic acid, 5326-47-6; 5-methylanthranilic acid, 2941-78-8; 4-nitroanthranilic acid, 619-17-0; anthranilic acid, 118-92-3; methyl anthranilate, 134-20-3; anthranilamide, 88-68-6; di-*tert*-butyl acetylenedicarboxylate, 66086-33-7; urea, 57-13-6.