photolyzed for 1 h, using a 200-W medium-pressure Hg vapor lamp. The solution was poured into a mixture of 200 mL of 1:1 cold water and pentane. The pentane layer was separated, and the aqueous layer was extracted with another 100 mL of pentane. The pentane extracts were combined, washed with 50 mL of cold water, and dried over anhydrons sodium sulfate. Most of the solvent was removed on a rotary evaporator and the rest of the solvent was removed at −30 °C using a high vacuum. MS and ^{1}H NMR were identical with those of pyrazole 14 (15 mg, 28% yield).

Low-Temperature Photolysis of the Sodium Salt of the Tosylhydrazone 15 through a Pyrex Filter with a 200-W Mercury Lamp. The above experiment was repeated, but the solution was photolyzed in an ice bath through a Pyrex filter with the 200-W medium-pressure Hg vapor lamp. GC/MS analysis of the product showed a single peak at 12.8 min with a molecular ion peak of 156 (31–33% yield). The ^{1}H NMR spectrum of this product was identical with that of diene **12**.

Registry No. **4**, 13380-66-0; **5**, 28860-69-7; **6**, 20061-84-1; **6**-*d*, 81121-06-4; **7**, 81121-07-5; **7**-*d*, 81121-08-6; **8**, 81121-09-7; **8** Li, 81176-65-0; **8**-*d*, 81132-92-5; **8**-*d* Li, 81177-13-1; **9**, 26333-43-7; **9**-*d*, 81121-10-0; **10**, 63162-54-9; **10**-*d*, 81176-66-1; **11**, 40644-06-2; **12**, 63064-34-6; **13**, 81121-11-1; **14**, 81121-12-2; **15**, 81121-13-3; **15** Li, 81176-67-2; **15** Na, 81176-68-3; **20**, 81121-14-4; **22**, 81121-15-5; **33**, 81176-69-4.

Synthesis of 2,5-Disubstituted 3,6-Diamino-1,4-benzoquinones

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A general synthetic approach to a wide variety of 2,5-disubstituted 3,6-diamino-1,4-benzoquinones was developed. Bromanil was diaminated with ammonia, and adjacent NH_2 and OH groups were protected as benzoxazoles by treatment with a carboxylic acid chloride followed by a polyphosphate ester cyclization–dehydration. The resulting 2,5-dibromobenzobis(oxazoles) were monolithiated by halogen–metal exchange with *n*-butyllithium and then reacted with a variety of electrophiles. The remaining bromide was replaced in a similar fashion. Alternatively the second bromide was replaced by reaction with π allylnickel halide complexes. The benzoxazole protecting group could be hydrolyzed with zinc(II) chloride/HCl–aqueous ethanol under an inert atmostphere. Air oxidation of the resulting hydroquinone under neutral conditions gave the desired 2,5-disubstituted 3,6-diamino-1,4-benzoquinone in good to excellent overall yield. This method was used to synthesize precursors to the basic ring system of the mitomycin antineoplastic antibiotics. Acid hydrolysis of the benzoxazole protecting group under oxidizing conditions resulted in the production of 2,5-disubstituted 3,6-dihydroxy-1,4-benzoquinone. Methylation followed by reaction with ammonia gave the desired diaminoquinone.

Introduction

A number of palladium-assisted heterocyclization reactions have been developed in these laboratories[1-7] with the long-range intent of application in the synthesis of pyrroloindoloquinone ring systems found in the mitomycin antineoplastic antibiotics.[8] For these processes, specifically alkylated 3,6-diaminoquinones were required as substrates. Although the parent compound 2,5-diamino-1,4-benzoquinone has long been known,[9,10] there is, as yet, no general synthetic approach to 2,5-disubstituted 3,6-diamino-1,4-benzoquinones, in spite of many recent studies concerning the synthesis of substituted quinones.[10-14] An attractive starting point for the synthesis of these compounds is 2,5-dibromo-3,6-diamino-1,4-hydroquinone (1), readily available from the reaction of bromanil with ammonia.[15a] This compound has the amino groups in the desired positions, and the halogens are, in principle, reactive in a number of alkylation processes. In this paper a general approach to the desired tetrasubstituted benzoquinones from this precursor is presented.

Results and Discussion

Two major problems faced in synthesis using diaminoquinones as intermediates are the high reactivity of this system toward a variety of reagents and the insolubility of these substrates in common organic solvents. A general approach to the practical management of both of these problems is to block both the amino and the quinone groups and then carry out substitution chemistry at the 2,5-dibromo positions. Thus, 2,5-dibromo-3,6-diamino-1,4-benzoquinone was reduced with sodium dithionite, and a number of attempts to introduce difunctional protecting groups were made. Surprisingly, protecting groups normally used for *o*-dihydroxy aromatics such as methylenedioxy, acetonide, dialkylsilyl, and carbonate groups failed to produce the corresponding aminal or carbamate compounds from 1 (eq 1). In contrast, conversion of 1 to the

(1) L. S. Hegedus, G. F. Allen, and E. L. Waterman, *J. Am. Chem. Soc.*, **98**, 2674 (1976).
(2) D. E. Korte, L. S. Hegedus, and R. K. Wirth, *J. Org. Chem.*, **42**, 1329 (1977).
(3) L. S. Hegedus, G. F. Allen, and D. J. Olsen, *J. Am. Chem. Soc.*, **100**, 5800 (1978).
(4) L. S. Hegedus, G. F. Allen, and D. J. Olsen, *J. Am. Chem. Soc.*, **102**, 3503 (1980).
(5) R. Odle, B. Blevins, M. Ratcliff, and L. S. Hegedus, *J. Org. Chem.*, **45**, 2709 (1980).
(6) L. S. Hegedus, P. M. Winton, and S. Varaprath, *J. Org. Chem.*, **46**, 2215 (1981).
(7) J. J. Bozell and L. S. Hegedus, *J. Org. Chem.*, **46**, 2561 (1981).
(8) For recent reviews on the mitomycins see K. Takahashi and T. Kametani, *Heterocycles*, **9**, 293 (1978); *ibid*, **13**, 411 (1979). For a recent total synthesis of several mitomycins see Y. Kishi, F. Nakatsubo, A. J. Ocuyza, and T. Fukuyama, *J. Am. Chem. Soc.*, **99**, 8115 (1977).
(9) F. Kehrman and G. Betsch, *Ber. Dtsch. Chem. Ges.*, **30**, 2095 (1897); H. W. Moore, H. R. Shelden, and D. F. Shellhamer, *J. Org. Chem.*, **34**, 1999 (1969).
(10) P. Germeraad and H. W. Moore, *J. Org. Chem.*, **39**, 774 (1974).
(11) P. Germeraad, W. Weyler, Jr., and H. W. Moore, *J. Org. Chem.*, **39**, 781 (1974).
(12) G. J. Sinta, R. W. Franck, and R. J. Kempton, *J. Org. Chem.*, **39**, 3739 (1974).
(13) K. A. Parker and S.-K. Kang, *J. Org. Chem.*, **44**, 1536 (1979).
(14) H. W. Moore, Y.-L. Sing, and R. S. Sidhiv, *J. Org. Chem.*, **45**, 5057 (1980).
(15) (a) L. F. Fieser and E. T. Martin, *J. Am. Chem. Soc.*, **57**, 1844 (1935). (b) Polyphosphate ester is prepared by refluxing phosphorous pentoxide in diethyl ether and chloroform, followed by solvent removal. See Louis F. Fieser and M. Fieser, "Reagents for Organic Synthesis", Vol 1, Wiley, New York, 1967, pp 892–894.

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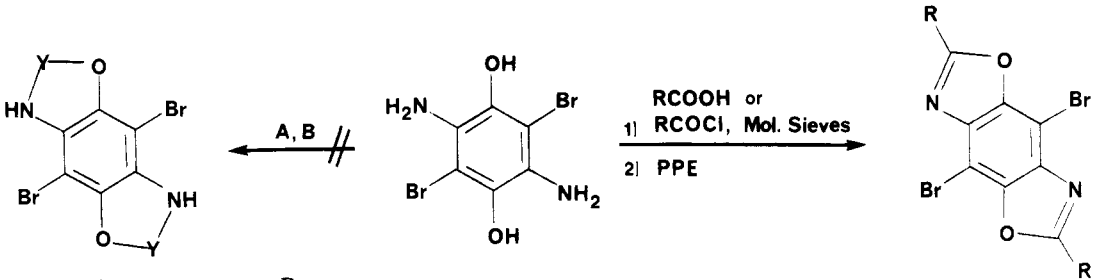


(1)

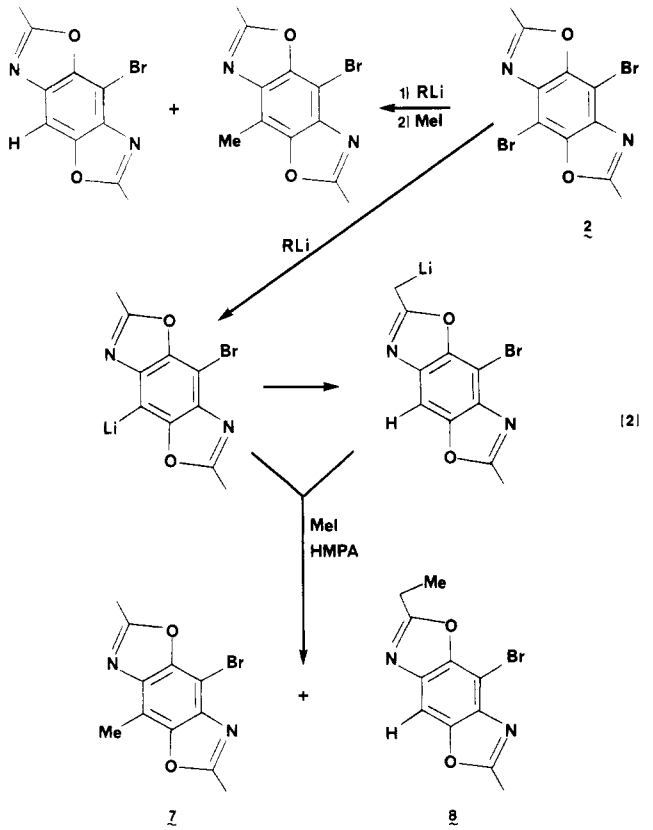
Y	A	B
CH_2	CH_2I_2	K_2CO_3
$[CH_3]_2C$	$[CH_3]_2CO$	mol. sieve
Ph_2Si	Ph_2SiCl_2	Py
CO	$COCl_2$	K_2CO_3

1

R = Me	61%	2
Et	76%	3
i-Pr	52%	4
Ph	82%	5
CF_3	46%	6

benzobis(oxazole) proceeded readily upon treatment with a carboxylic acid and polyphosphate ester (PPE)[15b] or upon conversion of 1 to its corresponding diamide, followed by PPE-assisted cyclization and dehydration (eq 1). With the exception of the insoluble phenylbenzoxazole **5**, compounds **2–6** were stable, soluble materials suitable for further reaction at the 2- and 5-positions.

A required intermediate in proposed mitomycin synthetic studies was the diaminoquinone having an allyl group in the 2-position and a methyl group in the 5-position (**13**). Reaction of benzobis(methyloxazole) (**2**) with *n*-butyl-, *tert*-butyl-, or methyllithium, followed by methyl iodide, produced mixtures of alkylated as well as protonated products under a variety of conditions (eq 2). It was



2 (2)

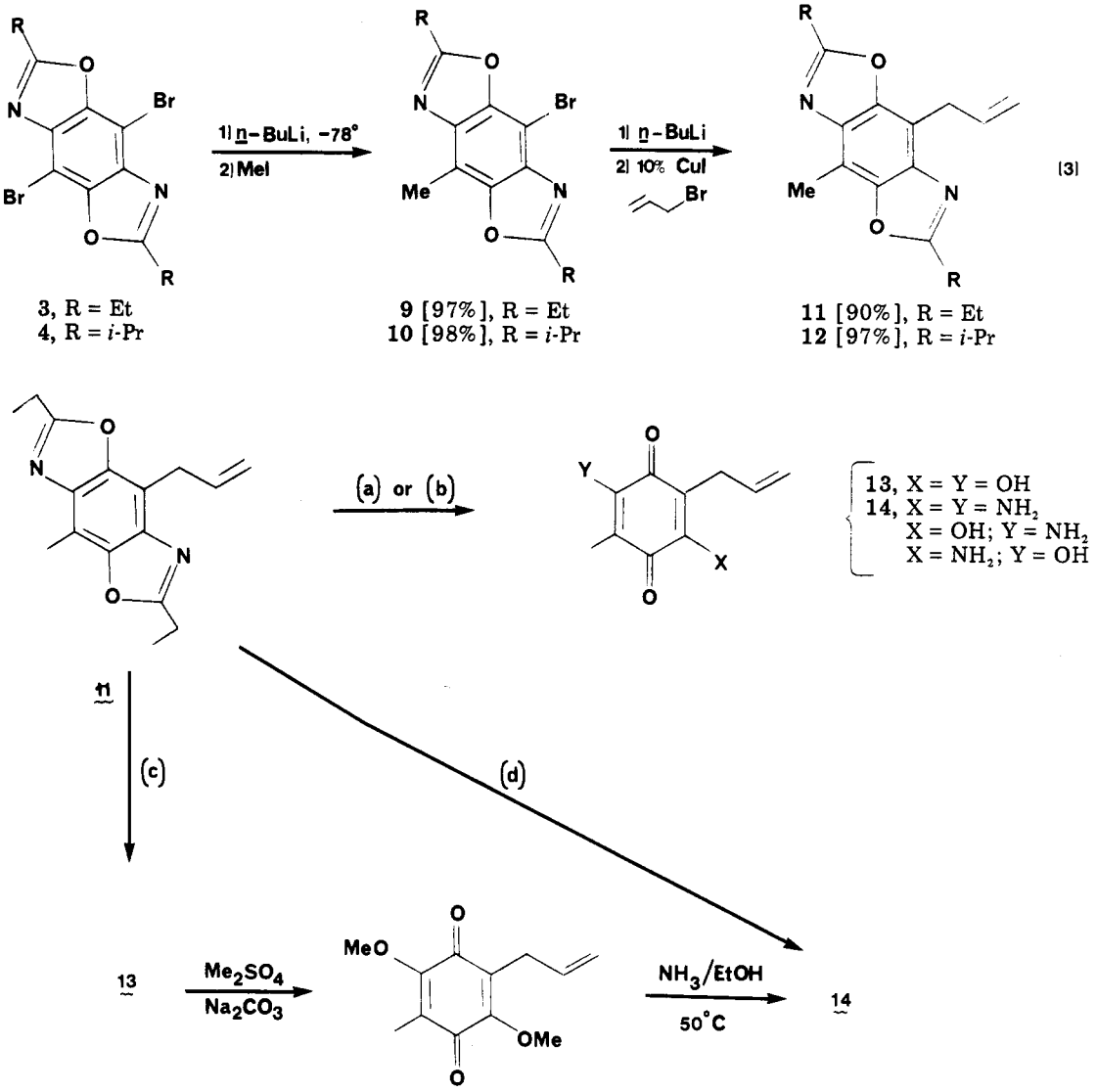
7 8

initially thought that the protonated product resulted from incomplete reaction of the aryllithium compound with methyl iodide. For facilitation of this process, hexamethylphosphoramide [HMPA, $(Me_2N)_3PO$] was added to the aryllithium reagent prior to methyl iodide addition. This resulted in alkylation at the aryl position (**7**) as well as at a benzoxazole methyl position (**8**) (eq 2). Apparently, metal–halogen exchange proceeds rapidly and is followed by irreversible proton transfer from a benzoxazole methyl group to the aryllithium. Alkylation at the methyl benzoxazole position only occurs in the presence of HMPA, whereas arene ring alkylation occurs under all conditions tried.

For suppression of this internal proton transfer, both the ethyl and isopropyl benzobis(oxazoles) **3** and **4** were carried through the halogen–metal exchange alkylation process (eq 3). Internal proton transfer was not a problem with these substrates because of the low acidity of the benzoxazole alkyl group proton. High yields of alkylation were realized with both **3** and **4**. Introduction of the allyl group was effected in a similar manner, although the use of a copper(I) catalyst and more severe reaction conditions was required to ensure high yields. Attempts to alkylate the (trifluoromethyl)benzobis(oxazole) (**6**) resulted instead in attack of the *n*-butyllithium at the highly electrophilic benzoxazole C=N groups, resulting in decomposition of the substrate.

With the properly dialkylated substrate available in high yield, it remained to remove the protecting group to regenerate the free diaminobenzoquinone. This proved more difficult than anticipated. Although simple benzoxazoles hydrolyze readily[16,17] and the dibromobenzobis(oxazole) **2** hydrolyzed with 2 N HCl, the dialkylbenzobis(oxazoles) **11** and **12** were considerably more resistent to hydrolysis. These compounds were inert to 2 N HCl and produced intractable tars with 4 and 6 N HCl and with 20% HBr. Trimethylsilyl iodide (TMSI), which promotes ester hydrolysis,[18] simply added HI to the double bond of the allyl group in **11**. The observation that nickel(II) salts complexed benzoxazoles at both oxygen and nitrogen[19] and gave rate enhancements of 10^7 in the hydrolysis of nitriles[20] suggested their use for the hydrolysis of compound **11**. Treatment of **11** with 2.5 equiv of nickel(II) chloride in 50% aqueous ethanolic HCl (0.1–2 N) resulted in slow, incomplete hydrolysis. Addition of iron(III) chloride to the hydrolysis system (to oxidize the hydroquinone to the quinone as it is formed) resulted in complete hydrolysis of **11**, but the product was a mixture of all possible amino-, hydroxy-, and aminohydroxyquinones. The same general product mixture was obtained with copper(II) chloride alone, whereas copper(II) chloride (3 equiv) followed by

(16) K. J. Morgan, P. F. Jackson, and A. M. Turner, *J. Chem. Soc. Perkin Trans 2*, 1582 (1972).
(17) V. F. Smith, Jr., and G. L. Schmir, *J. Am. Chem. Soc.*, **97**, 3171 (1975).
(18) G. A. Olah, *J. Org. Chem.*, **44**, 1247 (1979).
(19) E. J. Duff and M. N. Hughes, *J. Chem. Soc. A*, 477 (1969).
(20) R. Breslow, R. Fairweather, and J. Keana, *J. Am. Chem. Soc.*, **89**, 2135 (1967).



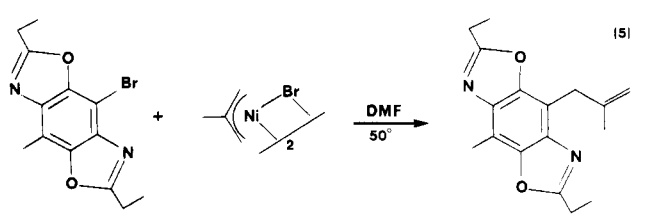
(a) $NiCl_2$, H_2O/EtOH, 2 N HCl, $FeCl_3$
(b) $CuCl_2$, H_2O/EtOH, 2 N HCl
(c) $CuCl_2$, H_2O/EtOH, 2 N HCl; $FeCl_3$
(d) $ZnCl_2$, H_2O/EtOH, HCl; Na_2CO_3; O_2

iron(III) chloride (1 equiv) produced dihydroxyquinone **13** cleanly (eq 4).

The hydroxyquinone products resulted from acid-catalyzed replacement of NH_2 by OH in the quinone product.[21,22] In contrast, aminohydroquinones are stable to amine displacement reactions under acidic conditions. Thus, hydrolysis of **11** under an argon atmosphere (to prevent quinone formation) in 50% aqueous ethanolic HCl (~2 N) in the presence of zinc(II) chloride (3 equiv), followed by neutralization (Na_2CO_3) and air oxidation gave the desired diaminoquinone **14** in 97% isolated yield, >95% pure by NMR spectroscopy. (Compound **14** was also produced from **13** by O-methylation followed by treatment with ammonia.[23,24]) This step culminates a nine-step synthetic sequence that produces **14** in 27% overall yield from benzoquinone, which is easily carried out on a multigram scale. The first six steps are carried out sequentially without any purification necessary. Thus, this procedure affords an efficient route to the desired tetrasubstituted quinones. Furthermore, the benzobis(oxazoles) **15** and **9** are versatile intermediates for the synthesis of a variety 2,5-disubstituted 3,6-diamino-1,4-benzoquinones as shown in Scheme I.

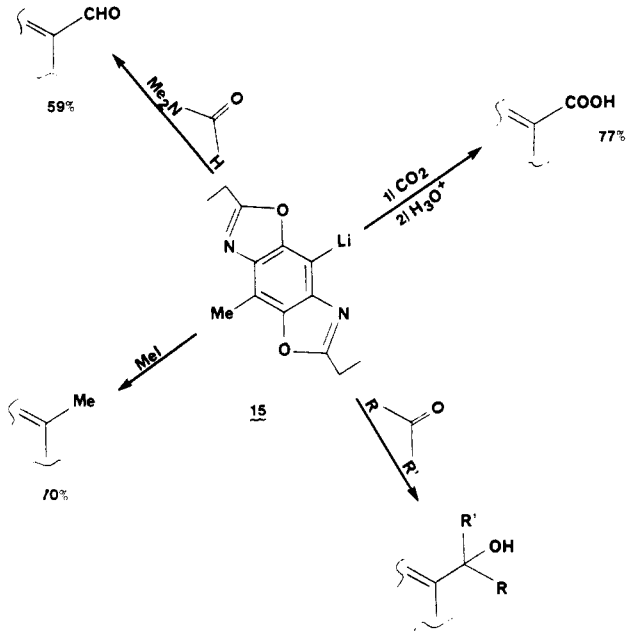
The lithiated benzobis(oxazole) **15** reacted cleanly with carbon dioxide to give the carboxylic acid, with methyl iodide to give the dimethylbenzobis(oxazole), and with dimethyl formamide to give the aldehyde. It was also generally reactive toward aldehydes and ketones, even relatively hindered ones such as acetophenone, producing the alcohols in reasonable yields.

The bromobenzobis(oxazole) **9** reacted with π-(2-methylallyl)nickel bromide to produce allylated product by an alternative route (eq 5). Since a variety of functionalized π-allylnickel halide complexes is known,[25] this



(21) H. Ulrich and R. Richter, in lqtHouben-Weyl Methoden der Organische Chemie", E. Müller, Ed, Vierte Auflage, Band VII/3a, Teil 1, Georg Thieme Verlag, Stuttgart, West Germany, 1977, pp 204–209.
(22) H. W. Moore and R. H. Shelden, *J. Org. Chem.*, **33**, 4019 (1968).
(23) W. K. Anslow and H. Raistrick, *J. Chem. Soc.*, 1446 (1939).
(24) Abdel-Megued Osman, *J. Am. Chem. Soc.*, **79**, 966 (1957).

Scheme I. Reactions of Lithiated Benzobis(oxazole) 15 with Electrophiles



R	R'	% yield
Et	H	61
n-Pr	H	59
Ph	H	46
Me	Me	74
Et	Et	75
Ph	Me	51

reaction should permit the introduction of functionalized olefinic side chains at this position of **9**. Reactions with other organometallic reagents were less successful. Dialkylcuprates resulted in halogen–metal exchange rather than an alkylation and simply reduced the bromo compound to the corresponding arene.[26] Attempted palladium(0)-catalyzed carbonylation[27] led to no reaction, and the bromobenzobis(oxazole) **9** was recovered unchanged. This may have been due to both the general lack of reactivity of aryl bromides in these processes and the sterically hindered nature of compound **9**.

In summary, this benzobis(oxazole) approach offers a general route to 2,5-disubstituted 3,6-diamino-1,4-benzoquinone precursors. The use of these compounds in synthetic approaches to the mitomycins will be presented in future reports from these laboratories.

Experimental Section

Materials. All solvents were freshly distilled and stored under argon. THF and ether were distilled from Na/benzophenone. DMF was distilled from CaH_2 under reduced pressure (20 mm). Acetonitrile and CH_2Cl_2 were distilled from P_2O_5. Allyl bromide and methyl iodide were all washed with Na_2SO_3 solution and $NaHCO_3$ solution, dried (K_2CO_3 and $MgSO_4$), and distilled through a copper helix. They were stored under argon in brown bottles. Benzoquinone was purified by sublimation. Copper iodide was Alfa ultrapure grade and was used without purification. PPE (polyphosphate ester) was prepared by literature methods.[15b,24]

General. All melting points are uncorrected. ^1H NMR spectra (60 MHz) were measured with a Varian Model T-60 or with a Model EM-360; ^1H NMR spectra (100 MHz) were recorded with either a JEOL MH100 or a JEOL FX100, all using tetramethylsilane as an internal standard and all reported in δ. Infrared spectra were recorded on a Beckmann Acculab 3 spectrophotometer and are reported in cm^{-1}. Medium-pressure liquid chromatography was performed at 10–60 psi (damped system) with Ace-Mischler columns packed with Woelm type 260 silica gel. Samples 0.05–1.0 g were run on a 2.2 × 30 cm column, 0.75–4 g on a 3.7 × 35 cm column, and 4–20 g on a 4.7 × 45 cm column. The products were detected by an ISCO-UA5 detector at 254 nm. Analyses were performed by Midwest Microanalytical Labs, Indianapolis, IN.

Preparation of Bromanilic Acid. In a 500-mL round-bottomed three-necked flask, benzoquinone (15 g, 139 mmol) was dissolved in 150 mL of acetic acid and brought to reflux. To this boiling solution, 3.56 mL (694 mmol) of bromine in 30 mL of acetic acid was added dropwise over the period of 1 h via an addition funnel. After the bromine addition, the reaction mixture was kept at reflux for an additional 2 h. (Care should be taken that solid does not sublime and plug the condenser.) The reaction was cooled, 100 mL of water was added, and the mixture was filtered. The solid was washed with water and ethanol and air dried to give 49.8 g (85%) of a light yellow powder, mp 244 °C (lit. mp 244 °C).[29]

Preparation of Bromanil. Bromanilic acid (49.8 g, 117 mmol) was slurried into 200 mL of acetic acid. Chromium trioxide (24 g, 240 mmol) was added portionwise to the stirred bromanilic acid solution. The reaction was then warmed at 50 °C for 1 h, after which ice was added and the mixture was filtered. The yellowish crystals were slurried in ethanol and filtered to give 47.4 g (112 mmol) (95%) of yellow powder: mp 303–304 (lit.[30] mp 300 °C); IR (Nujol) 1690 (s, C=O), 1680 (s, C=O), 1570 (m), 1550 (m), 700 (m) cm^{-1}.

Preparation of 2,5-Diamino-3,6-dibromoquinone. Bromanil (13.6 g, 32.1 mmol) was slurried into 70 mL of absolute ethanol in a three-necked 250-mL round-bottomed flask fitted with two septa and a Friedrich's condenser with a balloon fitted at the top. Ammonia was admitted via a large needle through one of the septa into the system at reflux. Ammonia was admitted as often as needed to keep the balloon full. The mixture was maintained at reflux for 8 h. The solution was then cooled, vacuum filtered, and washed successively with water, ethanol, and then ether. The red solid was air dried to give 7 g (74%) of red powder. Due to insolubility, this material was used without further purification; IR (Nujol) 3480 (s, N–H), 3320 (s, N–H), 3240 (s, N–H), 3180 (s, N–H), 1600 (s, br, C=O) cm^{-1}.

Preparation of 2,5-Diamino-3,6-dibromohydroquinone (1). 2,5-Diamino-3,6-dibromoquinone (2 g, 6.76 mmol) was mixed with $Na_2S_2O_4$ (2.8 g, 16.1 mmol) in 60 mL of H_2O and warmed under nitrogen until the red color of the starting material had disappeared. The mixture was filtered, and the off-white crystals were washed with H_2O and ethanol and air dried to give 1.81 g (90%) of the desired product. This material was used without purification; IR (Nujol) 3390 (m, NH, OH), 3310 (m, OH, NH) cm^{-1}.

Preparation of the Bis(propionamido)hydroquinone Precursor to 3. The aminohydroquinone 1 (6.7 g, 22.5 mmol), pripionyl chloride (4.1 mL, 47.0 mmol), and 25 mL (solid volume) of molecular sieves were mixed with 90 mL of dry degassed THF under an argon atmosphere. The mixture was not magnetically stirred but rather swirled manually about every 15 min for 2 h. The mixture was heated to reflux and cooled. The mixture was filtered through a Büchner funnel without filter paper to remove the molecular sieves. The THF slurry was concentrated and water was added and the mixture filtered. The crystals were washed with a very small portion of methanol to give 7.01 g (76% yield) of the slightly pink amido hydroquinone. The material was used without further purification; IR (Nujol) 3310 (m, NH, OH), 1630 (s, C=O), 1580 (s), 1405 (m), 1320 (m), 1260 (m), 1200 (m), 1080 (w), 1020 (w), 950 (m), 910 (w), 810 (m) cm^{-1}.

General Procedure for the Preparation of Benzobis(oxazoles) by the Reaction of Aminohydroquinones with a Carboxylic Acid in PPE. The hydroquinone was mixed with

(25) For reviews see L. S. Hegedus, *J. Organomet. Chem. Libr.*, **1**, 329 (1976); M. F. Semmelhack, *Org. Reac.*, **19**, 115 (1972).
(26) G. Posner, *Org. React.* (N.Y.), **22**, 253 (1975).
(27) J. K. Stille and P. Kwang Wong, *J. Org. Chem.*, **40**, 532 (1975).
(28) Y. Kanoaka, T. Hamada, and O. Yonemitsu, *Chem. Pharm. Bull.*, **18**, 587 (1970).
(29) E. Sarauw, *Justis Liebigs Ann. Chem.*, **209**, 126 (1881).
(30) S. Levy and G. Schultz, *Justis Liebigs Ann. Chem.*, **210**, 159 (1881).

Table I. Reaction of Aminohydroquinones with Carboxylic Acids in PPE

compd	1, g, mmol	carboxylic acid, g/mL; mmol	PPE, g	temp, °C	yield, g, %
2	2.24, 7.50	acetic, 1.17 mL; 15.0	10.0	110	1.16, 45
3	1.50, 5.0	propionic, 2 mL	10	100	0.187, 10
4	3.00, 10.0	isobutyric, 2.5 mL	20	90-100	1.78, 52
5	2.24, 7.50	benzoic, 1.85 g; 15.0	10	110	0
6	3.00, 10.0	trifluoroacetic, 1.6 mL; 20.8	13.4	110	2.11, 46

Table II. Reaction of Amido Hydroquinones with PPE

product	starting amide, g (mmol)	PPE, g	temp, °C	yield, g, %
2	acetamide, 2.87 (7.5)	5	110	1.57, 61
3	propanamide, 5.62 (13.7)	40	110-150	3.90, 76
5	benzamide, 2.81 (5.6)	20	130	2.15, 82

PPE (1.3–2.0 g PPE/mmol hydroquinone) under an inert atmosphere. The carboxylic acid (2 equiv) was added and the mixture vigorously stirred either magnetically or mechanically. The reaction mixture was heated for approximately 1 h at 100–130 °C. The reaction mixture was cooled, and concentrated ammonium hydroxide was added until the mixture was basic. In cases where a precipitate formed, the mixture was filtered and washed with water and methanol to give the benzoxazole. In some cases, the mixture was extracted with chloroform. The chloroform was washed with saturated sodium bicarbonate, dried ($MgSO_4$), treated with activated charcoal, and concentrated to give the benzoxazoles (Table I).

General Procedure for the Preparation of Benzobis(oxazoles) by the Action of PPE on Amido Hydroquinones. The amido hydroquinone was mixed with PPE under an inert atmosphere. The mixture was stirred and heated (~100 °C) for 1 h. The mixture was cooled and made basic with either saturated sodium bicarbonate solution or concentrated ammonium hydroxide (best method). The mixture was either filtered and the residue washed with water and methanol or extracted ($CHCl_3$), dried (K_2CO_3), and treated with activated charcoal to give the desired benzoxazoles (Table II).

Spectral data of 2: NMR ($CDCl_3$) δ 2.73 (s); IR (Nujol) 1610 (s, O—C=N), 1335 (s), 1280 (w), 1190 (s), 1040 (w), 1030 (w), 990 (m), 910 (m), 873 (m), 720 (w), 660 (w) cm^{-1}. Anal. ($C_{10}H_6Br_2O_2N_2$) C, H, N.

Spectral data of 3: The material was used without purification to prepare **9**; NMR ($CDCl_3$) δ 1.50 (t, J = 8 Hz, 6, CH_3), 3.09 (q, J = 8 Hz, 4, CH_2); mp 216–218 °C; IR ($CDCl_3$) 3150 (w), 2990 (m), 2940 (w), 2880 (w), 1595 (s, O—C=N), 1480 (w), 1440 (w), 1370 (m), 1310 (m), 1160 (m), 980 (m), 850 (m), 610 (m) cm^{-1}.

Spectral data of 4: NMR ($CDCl_3$) δ 1.50 (d, J = 7 Hz, 12, CH_3), 3.33 (septet, J = 7 Hz, 2, N=C—CH); IR (Nujol) 1590 (s, O—C=N), 1550 (w), 1440 (m), 1365 (m), 1330 (m), 1250 (m), 1205 (w), 1180 (m), 1130 (m), 1100 (m), 1050 (w), 985 (m), 925 (m), 875 (m), 865 (s), 740 (m), 720 (w) cm^{-1}. Anal. ($C_{14}H_{14}Br_2N_2O_2$) C, H, N.

Spectral data of 5: IR (Nujol) 1610 (m), 1590 (m), 1565 (s, O—C=N), 1490 (m), 1330 (m), 1320 (s), 1300 (w), 1290 (w), 1220 (s), 1170 (w), 1075 (w), 1055 (s), 1020 (s), 970 (m), 930 (w), 910 (m), 879 (s), 775 (m), 765 (m), 715 (s), 690 (s), 680 (m) cm^{-1}.

Due to insolubility, the material was not further purified and no NMR spectrum was recorded.

Spectral data of 6: IR (Nujol) 1615 (m, O—C=N), 1510 (w), 1400 (w), 1330 (m), 1240 (s), 1210 (s), 1180 (s), 1120 (s), 970 (m), 940 (w), 870 (s), 750 (m), 735 (m), 720 (m) cm^{-1}. Anal. ($C_{10}Br_2F_6N_2O_2$) C, H, N.

Preparation of Bromomethylbenzobis(ethyloxazole) (9). Dibromobenzobis(oxazole) (**3**) (1.00 g, 2.68 mmol) was dissolved in 100 mL of dry degassed THF under an argon atmosphere. The mixture was stirred and warmed until dissolution was complete. The solution was cooled to −78 °C (dry ice/isopropyl alcohol bath), a precipitate appeared, and the reaction was stirred 5 min longer. To the mixture was added n-butyllithium (1.30 mL of a 2.26 M hexane solution, 2.93 mmol) dropwise over a period of about 5 min. The mixture changed from a white slurry to an orange slurry and finally to a reddish amber homogeneous solution after about 45 min. After the solution was stirred for 1 h at −78 °C, methyl iodide (0.84 mL, 13.4 mmol) was added and the reaction mixture was allowed to warm to room temperature. The reaction mixture was stirred at room temperature for 24 h. After this period, the reaction mixture was a homogeneous red solution.

The reaction mixture was poured into a separatory funnel, and the reaction flask was washed with 100 mL of ether, which was also poured into the separatory funnel. The organic phase was washed with two 75-mL portions of saturated ammonium chloride solution and 75 mL of brine. The aqueous portions were back-extracted with 100 mL of ether. The organic portions were combined, dried ($MgSO_4$), treated with activated charcoal, and concentrated to give 0.845 g of a yellow solid. This represents a 102% crude yield, and NMR analysis shows a very small (1%) amount of protonation product.

This material may be used without further purification for the allylation reaction or it can be recrystallized from ether/hexane at −78 °C; mp 165–166 °C (82% yield); NMR ($CDCl_3$) δ 1.48 (t, J = 8 Hz, 6, CH_2CH_3, 2.65 (s, 3, Ar CH_3), 2.95 (q, J = 8 Hz, 4, CH_2); IR ($CDCl_3$) 1605 (s, O—C=N) cm^{-1}. Anal. ($C_{13}H_{13}BrN_2O_2$) C, H, N.

Preparation of Bromomethylbenzobis(isopropyloxazole) (10). The benzoxazole **10** was prepared as above by using the dibromobis(isopropylbenzoxazole) **4** (0.85 g, 2.09 mmol), n-butyllithium solution (0.83 mL, 2.75 M, 2.28 mmol), and methyl iodide (0.26 mL, 4.16 mmol) to give 0.693 g (98%) of the desired **10** as a brown oil. This material was used without purification to prepare **12**; NMR ($CDCl_3$) δ 1.50 (d, J = 7 Hz, 12, CH_3), 2.63 (s, 3, Ar CH_3), 3.29 (septet, J = 7 Hz, 2, CH); IR ($CDCl_3$) 1590 (s, O—C=N) cm^{-1}.

Preparation of Allylmethylbenzobis(ethyloxazole) (11). The bromomethylbis(benzoxazole) **9** (0.541 g, 1.75 mmol) was dissolved in 54 mL of dry degassed THF under an argon atmosphere. The solution was cooled to −78 °C (dry ice/acetone) and stirred for 7 min after formation of a precipitate. At this time n-butyllithium (0.85 mL, 1.92 mmol of a 2.26 M hexane solution) was added dropwise. After 10 min the reaction mixture was dark amber and homogeneous. The reaction mixture was allowed to stir 1 h and then allyl bromide (0.46 mL, 5.28 mmol) was added followed by enough copper(I) iodide to cover a spatula tip (approximately 10 mol %). The mixture was allowed to warm to room temperature. After 1.5 h, the reaction mixture was stirred at 45–50 °C for 18 h.

The reaction mixture was combined with 50 mL of ether and washed with two 50-mL portions of saturated ammonium chloride (until no blue color remained in the aqueous phase) and 50 mL of brine. The aqueous portions were back-extracted with 50 mL of ether. The red organic portions were combined, dried ($MgSO_4$), treated with activated charcoal, filtered, and concentrated to give 0.464 g of a yellow-amber oil. Medium-pressure liquid chromatography eluting with 3:2 hexane/ether gave 0.425 g (90%) of compound **11** as a pale yellow solid; mp 39–40 °C; NMR (CCl_4) δ 1.48 (t, J = 7.5 Hz, 6, CH_2CH_3), 2.65 (s, 3, Ar CH_3), 2.94 (q, J = 7.5 Hz, 4, CH_2CH_3), 3.87 (d, J = 5 Hz, 2, Ar CH_2), 4.9–5 (m, 2, C=CH_2), 5.8–6.5 (m, 1, C**H**=CH_3); IR (film) 1600 (vs, O—C=N) cm^{-1}. Anal. ($C_{16}H_{18}N_2O_2$) C, H, N.

Preparation of Allylmethylbenzobis(isopropyloxazole) (12). The methylbromobenzoxazole **10** (0.693 g, 2.06 mmol) was treated as above with n-butyllithium solution (0.83 mL, 2.75 M, 2.28 mmol), a catalytic amount of CuI (~10 mol %), and allyl bromide (0.75 mL, 8.4 mmol) to give **12** as 0.61 g (97%) of an oil which eventually solidified; NMR (CCl_4) δ 1.49 (d, J = 7 Hz, 12, $CHCH_3$), 2.64 (s, 3, Ar CH_3), 3.19 (septet, J = 7 Hz, 2, $CH(CH_3)_2$), 3.82 (d, J = 6 Hz, 2, Ar CH_2), 4.85–5.3 (m, 2, CH=CH_2), 5.8–6.5 (m, 1, C**H**=CH_2); IR (neat) 1600 (vs, O—C=N) cm^{-1}. Anal. ($C_{18}H_{22}N_2O_2$) C, H, N.

Deprotection of Allylmethylbenzobis(ethyloxazole) (11) via Nickel(II)-Catalyzed Hydrolysis. Allylmethylbenzobis(ethyloxazole) (11) (0.124 g, 0.46 mmol) was dissolved in 10 mL of absolute ethanol. To this solution was added nickel(II) chloride (0.258 g, 1.08 mmol), and the mixture was stirred for 30 min. The pH was adjusted with 4 M sodium hydroxide until the solution just began to cloud (pH 6). The reaction mixture was heated to reflux for 4 h, and then iron(III) chloride (0.585 g, 2.16 mmol) was added and the mixture was kept at reflux for 12 h. The solution was cooled, a 4-fold excess of EDTA in 100 mL of water was added to the reaction mixture, and the mixture was stirred for 1 h. The mixture was washed 3 times with chloroform. The combined chloroform extracts were washed with a dilute solution of EDTA, dried ($MgSO_4$), and concentrated to give 0.111 g of an unidentified red solid. The *aqueous* portions were made acidic with 2 N HCl and extracted 3 times with chloroform. The chloroform portions were dried ($MgSO_4$) and concentrated to give a purple solid (0.072 g) which was an ~80% yield of a mixture of **13**, **14**, and mixed aminohydroxy quinones; NMR ($CDCl_3$) δ 1.93 (s, 3, CH_3), 3.17 (d, J = 6 Hz, 2, CH_2), 5.07 (m, 2, CH=CH_2), 5.73 (m, 1, C**H**=CH_2), 7.7 (br, NH); IR ($CDCl_3$) 3400 (M–H, OH), 1640 (C=O), 1600 (C=O) cm^{-1}; mass spectrum, m/e 192 (parent), strong P + 1 (193) and P + 2 (194).

Preparation of 6-Allyl-2,5-diamino-3-methyl-1,4-benzoquinone (14). To 0.264 g (0.97 mmol) of benzobis(ethyloxazole) **11** and 0.399 g (2.93 mmol) of anhydrous zinc chloride was added 10 mL of absolute ethanol. The resulting mixture was stirred to dissolve the solids, degassed, and placed under a static argon atmosphere. To this yellow, homogeneous solution was added 10 mL of argon-saturated 4 N HCl. The reaction mixture was heated at reflux until no trace of starting material could be detected by TLC (silica gel, 66:34 hexane/ethyl acetate), with 2 mL of fresh 4 N HCl being added every 24 h. Under these conditions the reaction went to completion in 96 h. When air was rigorously excluded from the system, the reaction mixture changed from yellow at the onset of the reflux, to deep purple as the reaction proceeded, and finally to a golden colored solution when no starting material remained. The resulting golden solution was allowed to cool to room temperature, after which small portions of anhydrous sodium carbonate were added until a small amount of solid remained undissolved. This mixture was then poured into an open beaker, and 20 mL of saturated aqueous EDTA solution was added. The mixture was stirred in the air for 5 h so that oxidation of the intermediate hydroquinone could take place. The resulting purple solution was continuously extracted with chloroform (30 mL), and the extract was dried (Na_2SO_4), filtered, and concentrated in vacuo. The residual purple solid (0.183 g, 97%) was sufficiently pure for further work but was recrystallized from acetone/hexane for characterization; mp none, 170–190 °C dec; IR (KBr) 3360, 3300, 3240 (m, br, NH_2), 1530 (s, C=O), 1380 (s), 770 (w) cm^{-1}; NMR ($CDCl_3$, 360 MHz) δ 1.79 (s, 3, CH_3), 3.12 (d, J = 6 Hz, 2, CH_2), 5.12 (m, 2, CH=CH_2), 5.24 (br, s, 2, NH_2), 5.41 (br, s, 2, NH_2), 5.74 (m, 1, C**H**=CH_2); UV ($CHCl_3$) 331 (log ϵ 4.37), 498 (log ϵ 2.34) nm; mass spectrum, m/e 192 (parent). Anal. ($C_{10}H_{12}N_2O_2$) C, H, N.

The diaminoquinone **14** was also prepared from the dimethoxyquinone (eq 4). A solution of 30.71 mg (0.14 mmol) of 6-allyl-2,5-dimethoxy-3-methyl-1,4-benzoquinone in 3 mL of ammonia-saturated ethanol was heated at 52 °C, in an argon-filled sealed tube for 3 h. The resulting purple solution was cooled and concentrated in vacuo. The residual purple solid (28 mg) was dissolved in acetone (2 mL) and filtered. The pure diaminoquinone (11.2 mg, 42%) was then precipitated by the addition of 5 volumes of hexane (10 mL). The material obtained by this method was identical in every respect with the material prepared above.

Preparation of 6-Allyl-2,5-dihydroxy-3-methyl-1,4-benzoquinone (13). To a solution of 0.146 g (0.53 mmol) of benzobis(ethyloxazole) **11** and 0.278 g (1.62 mmol) of $CuCl_2 \cdot 2H_2O$ in 10 mL of absolute ethanol was added 2.7 mL of 4 N HCl. The resulting homogenous mixture was heated at reflux in air for 7 h, at which time no starting material could be detected by TLC (silica gel, 66:34 hexane/ethyl acetate). To the cooled solution was added 0.255 g (0.94 mmol) of $FeCl_3 \cdot 6H_2O$ This solution was brought to reflux for an additional 13 h. The resulting cooled, black solution was added to 50 mL of saturated aqueous EDTA solution, 15 mL of 4 N HCl, and 100 mL of $CHCl_3$. The mixture was shaken, the organic layer separated, and the aqueous layer extracted with chloroform (2 × 50 mL). The combined organic extracts were dried (Na_2SO_4), filtered, and concentrated in vacuo to afford 0.0975 g (94%) of the dihydroxyquinone **13** as a dark tan solid: mp 172–173 °C; IR (KBr) 3300 (s, br), 1610 (s), 1300 (s), 1190 (s), 760 (m) cm^{-1}; NMR ($CDCl_3$, 360 MHz) δ 1.94 (s, 3, CH_3), 3.20 (d, J = 6 Hz, 2, CH_2), 5.09 (m, 2, CH=CH_2), 5.84 (m, 1, C**H**=CH_2), 7.3 (s, 2, OH); UV ($CHCl_3$) 293 (log ϵ 4.33), 400 (log ϵ 2.52) nm; mass spectrum, m/e 194 (parent, 100), 193 (32), 179 (17), 83 (27), 55 (29). Anal. ($C_{10}H_{10}O_4$) C, H.

Preparation of 6-Allyl-2,5-dimethoxy-3-methyl-1,4-benzoquinone. To 0.101 g (0.52 mmol) of dihydroxyquinone **13** and 0.300 g (2.17 mmol) of anhydrous potassium carbonate was added 4 mL of dry acetone, followed immediately by the addition of 0.20 mL (2.10 mmol) of dimethyl sulfate. The resulting deep red inhomogeneous mixture was heated at reflux for 4 h. The solution was cooled, filtered, and concentrated in vacuo. The residual oil was extracted with small portions of Skellysolve (2 × 10 mL). This extract was concentrated in vacuo to afford a brown oil, which was purified by column chromatography (5 g, silica gel, 86:14 hexane/ethyl acetate) to yield 0.065 g (56%) of the dimethoxyquinone as a yellow oil: IR (neat) 3270 (w), 3300 (s), 2940 (s), 2840 (s), 1770 (s), 1730 (s), 1650 (vs, C=O), 1600 (vs), 1450 (s), 1375 (s), 1280 (s), 760 (m), cm^{-1}; NMR ($CDCl_3$, 60 MHz) δ 1.90 (m, 3, CH_3), 3.18 (d, J = 8 Hz, 2, CH_2CH=), 3.99 (s, 6, OCH_3), 4.9–5.3 (m, 2, CH=CH_2), 5.5–6.2 (m, 1, C**H**=CH_2). Anal. ($C_{12}H_{14}O_4$) C, H.

Reaction of 15 with DMF. The lithio compound **15** was formed by the standard procedure from the benzobisoxazole (100 mg, 0.324 mmol) and *n*-butyllithium (0.356 mmol) in THF (10 mL). Dry, argon-purged DMF (71.0 mg, 0.972 mmol, 0.075 mL) was added dropwise and the reaction stirred for 3.5 h at −78 °C. The reaction mixture was quenched at −78 °C by addition of 2 N HCl (4 mL) and allowed to warm to room temperature. The mixture was diluted with ether and the aqueous layer separated. The organic layer was washed with saturated aqueous NH_4Cl (twice) and saturated aqueous NaCl. The aqueous layers were back-extracted with ether, and the combined organic layers were dried over anhydrous $MgSO_4$. The ether layer was evaporated under reduced pressure to leave an amber oil (87 mg), which was purified by medium-pressure liquid chromatography (4:1 hexane/Et_2O increasing to 1:2 hexane/Et_2O) to give the desired aldehyde as a white solid: mp 201 °C; 49 mg (59% yield); NMR ($CDCl_3$) δ 1.5 (t, J = 6 Hz, 6, CH_2CH_3), 2.78 (s, 3, Ar CH_3), 3.05 (q, J = 6 Hz, 4, CH_2CH_3), 10.77 (s, 1, CHO); IR ($CDCl_3$) 1705 (C=O), 1605 (C=N) cm^{-1}. Anal. ($C_{14}H_{14}N_2O_3$) C, H, N.

Reactions of 15 with Aldehydes and Ketones. The lithio compound **15** was formed by the standard procedure from benzoxazole (100 mg, 0.324 mmol) and *n*-butyllithium (0.356 mmol) in THF (10 mL) at −78 °C. The aldehyde or ketone purified by the method suggested by Perrin[31] (0.356 mmol) was added dropwise, and the solution was allowed to warm to room temperature slowly and stirred overnight. The mixture was diluted with ether and washed with saturated, aqueous NH_4Cl (twice) and brine. The aqueous phases were back-extracted with ether and the combined organic layers dried over anhydrous magnesium sulfate. The organic layer was evaporated under reduced pressure and the residual oil purified by medium-pressure liquid chromatography (silica, 2:1 hexane/Et_2O).

(a) Propionaldehyde. Benzoxazole **9** (100 mg, 0.324 mmol), *n*-butyllithium (0.356 mmol), and propionaldehyde (20.6 mg, 0.026 mL, 0.356 mmol) reacted as above to give the desired alcohol as a colorless oil: 57 mg (61% yield); NMR ($CDCl_3$) δ 0.97 (t, J = 7 Hz, 3, CH_3), 1.43 (t, J = 7 Hz, 6, CH_3), 1.97 (q, J = 7 Hz, 2, $CH(OH)CH_2$), 2.67 (s, 3, Ar CH_3), 2.97 (q, J = 7 Hz, 4, CH_2CH_3), 4.18 (d, J = 9 Hz, 1, OH), 5.22 (m, 1, C**H**OH); IR (CCl_4) 3560 (OH), 1600 (C=N) cm^{-1}. Anal. ($C_{16}H_{20}N_2O_3$) C, H, N.

(b) Butyraldehyde. Benzoxazole **9** (100 mg, 0.324 mmol), *n*-butyllithium (0.356 mmol), and butyraldehyde (25.6 mg, 0.0314 mL, 0.356 mmol) reacted as above to yield the desired alcohol as a colorless oil: 58 mg (59% yield); NMR ($CDCl_3$) δ 0.93 (t, J = 6 Hz, 3, CH_3), 1.43 (t, J = 7 Hz, 6, CH_2CH_3), 1.10–2.27 (m, 4,

(31) D. D. Perrin, W. L. F. Armarego, D. R. Perrin, "Purification of Laboratory Chemicals", Pergamon, New York, 1966, p 350.

CH_2CH_2), 2.67 (s, 3, Ar CH_3), 2.97 (q, J = 7 Hz, 4, CH_2CH_3), 4.10 (d, J = 8 Hz, 1, OH), 5.35 (br, q, J = 8 Hz, 1, CHOH); IR (liquid film) 3400 (OH), 1595 (C=N) cm^{-1}. Anal. ($C_{17}H_{22}N_2O_3$) C, H, N.

(c) Benzaldehyde. Benzoxazole **9** (100 mg, 0.324 mmol), n-butyllithium (0.356 mmol), and benzaldehyde (37.7 mg, 0.036 mL, 0.356 mmol) reacted as above to yield the desired alcohol as a pale yellow solid (51 mg, 46%) which was purified by medium-pressure liquid chromatography using 1:1 hexane/ether as a solvent; NMR ($CDCl_3$) δ 1.40 (t, J = 7 Hz, 3, CH_3), 1.43 (t, J = 7 Hz, 3, CH_3), 2.67 (s, 3, Ar CH_3), 2.95 (q, J = 7 Hz, 4, CH_2), 5.25 (br, d, J = 8 Hz, 1, OH, position varied with concentration), 6.47 (br, d, J = 8 Hz, 1, CHOH), 7.17–7.63 (m, 5, Ar H); IR ($CDCl_3$) 3460 (OH), 1600 (C=N) cm^{-1}. Anal. ($C_{20}H_{20}N_2O_3$) C, H, N.

(d) Acetone. Benzoxazole **9** (100 mg, 0.324 mmol), n-butyllithium (0.356 mmol), and acetone (20.6 mg, 0.026 mL, 0.356 mmol) reacted as above to yield the desired carbinol as a white solid: 70 mg (74% yield); mp 144–146 °C; NMR ($CDCl_3$) δ 1.47 (t, J = 8 Hz, 6, CH_2CH_3), 1.85 (s, 6, CCH_3), 2.70 (s, 3, Ar CH_3), 3.00 (q, J = 8 Hz, 4, CH_2CH_3), 6.2 (s, 1, OH); IR ($CDCl_3$) 3440 (OH), 1600 (C=N) cm^{-1}. Anal. ($C_{16}H_{20}N_2O_3$) C, H, N.

(e) Pentan-3-one. Benzoxazole **9** (100 mg, 0.324 mmol), n-butyllithium (0.356 mmol), and pentan-3-one (30.6 mg, 0.0375 mL, 0.356 mmol) reacted as above to yield the desired carbinol as a white solid: 46 mg (45% yield); mp 121–124 °C; NMR ($CDCl_3$) δ 0.78 (t, J = 8 Hz, 6, CH_3), 1.45 (t, J = 7 Hz, 6, CH_3), 2.10 (m, 4, CH_2), 2.70 (s, 3, Ar CH_3), 2.98 (q, 4, J = 7 Hz, CH_2), 6.50 (s, 1, OH); IR ($CDCl_3$) 3440 (OH), 1600 (C=N) cm^{-1}. Anal. ($C_{18}H_{24}N_2O_3$) C, H, N.

(f) Acetophenone. Benzoxazole **9** (100 mg, 0.324 mmol), n-butyllithium (0.356 mmol), and acetophenone (42.7 mg, 0.041 mL, 0.356 mmol) reacted as described above to produce the desired carbinol: 58 mg (51% yield); mp 78 °C; NMR ($CDCl_3$) δ 1.43 (t, J = 7 Hz, 6, CH_3), 2.23 (s, 3, CCH_3), 2.68 (s, 3, Ar CH_3), 2.78–3.16 (m, 4, CH_2), 6.80 (s, 1, OH), 7.13–7.57 (m, 5, Ar H); IR ($CDCl_3$) 3460 (OH), 1600 (C=N) cm^{-1}. Anal. ($C_{21}H_{22}N_2O_3$) C, H, N.

Reaction of 15 with CO_2. The lithio intermediate **15** was formed by the standard procedure from benzobis(oxazole) **9** (150 mg, 0.485 mmol) and n-butyllithium (0.534 mmol) in THF (15 mL). Solid CO_2 (freshly crushed, approximately 100 mg) was added, and the reaction went from yellow to red immediately. The mixture was allowed to warm to room temperature over a period of 1 h and then warmed at 55 °C overnight. The reaction mixture was diluted with ether and washed with saturated aqueous NH_4Cl (twice) and saturated brine. The combined NH_4Cl phases were acidified with HCl and extracted twice with ether. These ether layers were washed with brine and dried over anhydrous magnesium sulfate. The ether layer was reduced in volume to yield a pale yellow solid: 75.8 mg (57% yield); NMR ($CDCl_3$) δ 1.52 (t, J = 7 Hz, 6, CH_3), 2.77 (s, 3, Ar CH_3), 3.10 (q, J = 7 Hz, 4, CH_2), 11.8 (br, s, 1, CO_2H); IR ($CDCl_3$) 3200 (OH), 1750 (C=O), 1600 (C=N) cm^{-1}. Anal. ($C_{12}H_{14}N_2O_4$) C, H, N.

Reaction of 15 with Methyl Iodide. The lithio intermediate **15** was formed by the standard procedure from benzobis(oxazole) **9** (100 mg, 0.324 mmol) and n-butyllithium in THF (10 mL). Methyl iodide (130 mg, 0.061 mL, 0.981 mmol) was added and the reaction allowed to warm slowly to room temperature and stirred overnight. The mixture was diluted with ether (15 mL) and washed with saturated aqueous NH_4Cl (2 × 20 mL) and brine (20 mL). The aqueous washings were back-extracted with ether, dried over $MgSO_4$, and evaporated under reduced pressure to leave an off-white solid (88.4 mg). This was purified twice by medium-pressure liquid chromatography to give the desired compound as a white solid: 55.1 mg (69% yield); mp 127–129 °C; NMR ($CDCl_3$) δ 1.47 (t, J = 6 Hz, 6, CH_3), 2.70 (s, 6, Ar CH_3), 2.98 (q, J = 6 Hz, 4, CH_2); IR ($CDCl_3$) 1600 (C=N) cm^{-1}. Anal. ($C_{16}H_{20}N_2O_2$) C, H, N.

Reaction of π-(2-Methylallyl)nickel Bromide with 9. A mixture of π-(2-methylallyl)nickel bromide (967 mg, 2.49 mmol) and benzobis(oxazole) **9** (200 mg, 0.647 mmol) in dry argon-purged DMF was stirred at 45 °C for 8 days under an argon atmosphere. The reaction was then poured in water (60 mL) and extracted with ether (3 × 150 mL). The combined ether layers were washed with saturated aqueous Na_2CO_3 (3 × 150 mL) and dried over $MgSO_4$. After filtration, the organic layer was reduced in volume to leave a red oil (195 mg). This product was purified by medium-pressure liquid chromatography (4:1 hexane/Et_2O, silica) to give a viscous oil 42 mg (23% yield); NMR ($CDCl_3$) δ 1.40 (t, J = 7 Hz, 6, CH_2CH_3), 1.77 (br, s, 3, CCH_3), 2.63 (s, 3, Ar CH_3), 2.95 (q, J = 7 Hz, 4, CH_2CH_3), 3.77 (br, s, 2, Ar CH_2), 4.60–4.70 (br, d, 2, CCH_2); IR (neat) 3040 (C=CH_2), 1650 (C=CH_2), 1600 (C=N), 885 (C=CH_2) cm^{-1}.

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Registry No. **1**, 81534-82-9; **2**, 81534-83-0; **3**, 81534-84-1; **4**, 81534-85-2; **5**, 43036-73-3; **6**, 81553-79-9; **7**, 81534-86-3; **8**, 81534-87-4; **9**, 81534-88-5; **10**, 81534-89-6; **11**, 81534-90-9; **12**, 81534-91-0; **13**, 81534-92-1; **14**, 81534-93-2; **15**, 81534-94-3; bromanilic acid, 4370-59-6; bromanil, 488-48-2; 2,5-diamino-3,6-dibromoquinone, 27344-26-9; 2,5-dibromo-3,5-dipropionamidohydroquinone, 81534-95-4; 6-allyl-2,5-dimethoxy-3-methyl-1,4-benzoquinone, 81534-96-5; dimethyl formamide, 68-12-2; 2,6-diethyl-8-methylbenzo[1,2-*d*:4,5-*d*']bis(oxazole)-4-carboxaldehyde, 81534-97-6; propionaldehyde, 123-38-6; 1-(2,6-diethyl-8-methylbenzo[1,2-*d*:4,5-*d*']bis(oxazol)-4-yl)-1-propanol, 81534-98-7; butyraldehyde, 123-72-8; 1-(2,6-diethyl-8-methylbenzo-[1,2-*d*:4,5-*d*']bis(oxazol)-4-yl)-1-butanol, 81534-99-8; benzaldehyde, 100-52-7; α-(2,6-diethyl-8-methylbenzo[1,2-*d*:4,5-*d*']bis(oxazol)-4-yl)benzyl alcohol, 81535-00-4; acetone, 67-64-1; 1-(2,6-diethyl-8-methylbenzo[1,2-*d*:4,5-*d*']bis(oxazol)-4-yl)-1-methylethanol, 81535-01-5; pentan-3-one, 96-22-0; 1-(2,6-diethyl-8-methylbenzo[1,2-*d*:4,5-*d*']bis(oxazol)-4-yl)-1-ethyl-1-propanol, 81535-02-6; acetophenone, 98-86-2; α-(2,6-diethyl-8-methylbenzo[1,2-*d*:4,5-*d*']bis(oxazol)-4-yl)-α-methylbenzyl alcohol, 81553-80-2; carbon dioxide, 463-79-6; 2,6-diethyl-8-methylbenzo[1,2-*d*:4,5-*d*']bis(oxazole)-4-carboxylic acid, 81535-03-7; methyl iodide, 74-88-4; 2,6-diethyl-4,8-dimethylbenzo-[1,2-*d*:4,5-*d*']bis(oxazole), 81535-04-8; π-(2-methylallyl)nickel bromide, 12300-62-8; 2,6-diethyl-8-methyl-4-(2-methyl-2-propenyl)benzo-[1,2-*d*:4,5-*d*']bis(oxazole), 81535-05-9; propionyl chloride, 79-03-8; acetic acid, 64-19-7; propionic acid, 79-09-4; isobutyric acid, 79-31-2; benzoic acid, 65-85-0; trifluoroacetic acid, 76-05-1; acetamide, 60-35-5; benzamide, 55-21-0.