Tetrahedron Vol. 43, No. 21, pp. 5145 to 5158, 1987
Printed in Great Britain.

0040-4020/87 $3.00+.00
Pergamon Journals Ltd.

INTRAMOLECULAR DIELS-ALDER REACTIONS OF 1,2,4-TRIAZINES. A GENERAL SYNTHESIS OF FURO[2,3-b]PYRIDINES, 2,3-DIHYDROPYRANO[2,3-b]PYRIDINES, AND PYRROLO[2,3-b]PYRIDINES[1]

EDWARD C. TAYLOR*, JOHN E. MACOR,[2] and JOSEPH L. PONT

Department of Chemistry, Princeton University
Princeton, New Jersey 08544, U.S.A.

(*Received in UK 5 August* 1987)

Abstract - Intramolecular inverse electron demand Diels-Alder reactions of 1,2,4-triazines have been effectively utilized for the synthesis of furo[2,3-b]pyridines, 2,3-dihydropyrano[2,3-b]pyridines, and 2,3-dihydropyrrolo-[2,3-b]pyridines.

Furo[2,3-b]pyridines, pyrrolo[2,3-b]pyridines, and 2,3-dihydropyrano[2,3-b]pyridines are structurally analogous to indoles and quinolines.[3] The furo[2,3-b]pyridine ring system makes up the backbone of the furo[2,3-b]pyridine alkaloids;[4] derivatives of this ring system have been claimed as potent herbicides and as integral components of cephalosporin derivatives.[5] Pyrrolo[2,3-b]pyridines (7-azaindoles) have been the target of extensive synthetic studies as a consequence of their potent pharmacological activity.[6] Nevertheless, there exists no general, common synthetic approach to these fused pyridine systems, which have been accessed in previous work in almost every case from preformed pyridines or preformed furans. This paper describes a synthetic strategy which commences with a common 1,2,4-triazine precursor, and constructs both the pyridine ring and the fused heterocyclic ring (furan, pyrrole or dihydropyran) through an intramolecular Diels-Alder reaction.[7,8] The nature of the ring fused to the pyridine ring is determined by the structure of the dienophilic sidechain tethered to the 3-position of the 1,2,4-triazine.

Scheme I summarizes our synthetic approach to the title compounds. The starting 3-methylthio-1,2,4-triazines (1) are available by an excellent procedure published by Paudler and Chen:[9] oxidation of (1) to the sulfone (2) was smoothly effected with two equivalents of m-chloroperbenzoic acid at room temperature. The resulting sulfones (2) must be handled with care, since they readily undergo displacement of methyl sulfinate by nucleophiles as weak as cyanide or water. Accordingly, their purification required strictly anhydrous conditions, especially in the case of the parent triazine (2a), where even use of normal (i.e. slightly hydrated) silica gel led to extensive hydrolysis. However, the high reactivity of (2) towards nucleophiles could be exploited in a facile synthesis of 3-(3-butynyloxy)-1,2,4-triazines (3), 3-(4-pentynyloxy)-1,2,4-triazines (6), and 3-(3-butynylamino)-1,2,4-triazines (8) by reaction at 0 °C with sodium 3-butynyl-1-oxide, sodium 4-

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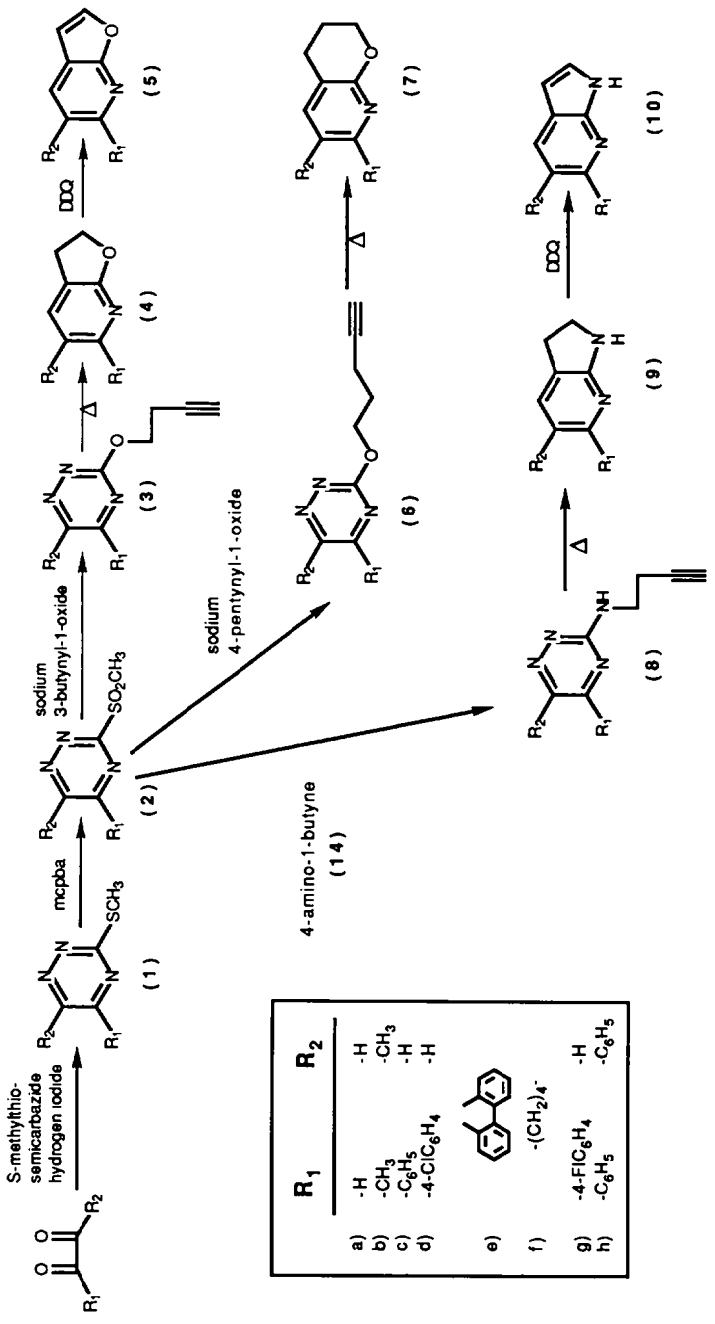
This paper is dedicated with all good wishes to my long-time friend and colleague, Prof. Hans Wynberg, on the occasion of his sixth-fifth birthday.

Scheme I


S-methylthio-semicarbazide hydrogen iodide
mcpba
sodium 3-butynyl-1-oxide
sodium 4-pentynyl-1-oxide
4-amino-1-butyne (14)
DDQ
DDQ
(1)
(2)
(3)
(4)
(5)
(6)
(7)
(8)
(9)
(10)
R1 R2
a) -H -H
b) -CH3 -CH3
c) -C6H5 -H
d) -4-ClC6H4 -H
e)
f) -(CH2)4-
g) -4-FlC6H4 -H
h) -C6H5 -C6H5

pentynyl-1-oxide, and 4-amino-1-butyne, respectively. [4-Amino-1-butyne (14) was prepared from 3-butyn-1-ol (11) (Scheme II) by conversion to the mesylate (12) with methanesulfonyl chloride/triethylamine, reaction of (12) with sodium azide in DMF to give the azide (13), and reaction of (13) with triphenylphosphine followed by hydrolysis of the resulting phosphinamine [39% from (12)]. In our hands, this method for the preparation of (14) proved to be preferable to an earlier method involving alkylation of sodium acetylide with 1-amino-2-bromoethane.[10]]

Although these nucleophilic displacement reactions generally proceeded smoothly, special note should be taken of the behavior of (2b) and (2f) (the only 5-alkyl-1,2,4-triazines tested) in their reactions with the above basic nucleophiles. From our work and the studies of others,[11] it is apparent that deprotonation of 5-alkyl-1,2,4-triazines can occur with bases as weak as amines. Thus, in the presence of strongly basic, hard nucleophiles (i.e. alkoxides), deprotonation competes with nucleophilic displacement, and the yield of the desired (displacement) product is low (compared to examples with 5-aryl substituents). This is evident in the low yielding formation of (3b) and (3f), and it is the reason why syntheses of (6b) and (6f) were not attempted. Less basic, softer nucleophiles (i.e. 4-amino-1-butyne) are not strong (hard) enough to react rapidly with the triazine (2b) in a nucleophilic displacement reaction, and an acid/base equilibrium is achieved with the 5-alkyl-1,2,4-triazine which inhibits the desired displacement reaction. For example, treatment of (2b) with 4-amino-1-butyne (14) resulted, over the course of one week, only in slow decomposition of the triazine and full protonation of the amine as seen by NMR spectroscopy.

Heating compounds (3) in refluxing chlorobenzene (132 °C) led via intramolecular cycloaddition, followed by the evolution of nitrogen, to the desired 2,3-dihydrofuro[2,3-b]pyridines (4) in good to excellent yields. The temperatures required for cyclization of the 3-(3-butynyloxy)-1,2,4-triazines (3) were more strenuous than those required for the analogous 3-(3-butynylthio)-1,2,4-triazines.[8f] This can be attributed to the greater electron donation into the pi system of the triazine diene by the alkoxy sidechain compared to an alkylthio sidechain; i.e., the LUMO of the more electron rich 3-(3-butynyloxy)-1,2,4-triazine is higher in energy than the LUMO of the corresponding 3-(3-butynyl-thio)-1,2,4-triazine, and the resulting $HOMO_{dienophile}/LUMO_{diene}$ energy separation (activation energy barrier) for the inverse electron demand Diels-Alder reaction of (3) is greater than in the case of the 3-(3-butynylthio)-1,2,4-triazines. Dehydrogenation of (4) using 2,3-dichloro-5,6-dicyano-1,4-benzoquinone (DDQ) gave the fully aromatic furo[2,3-b]pyridines (5) in moderate yields. Reaction of the parent 2,3-dihydrofuro[2,3-b]pyridine (4a) with DDQ led to decomposition with no product identification possible.

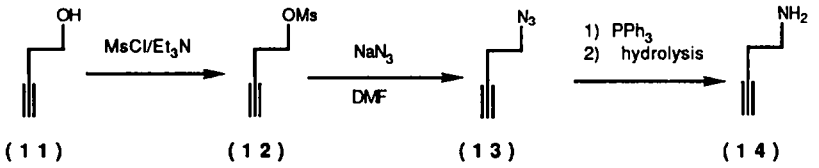
Homologation of the dienophilic sidechain in (3) gave access to the 2,3-dihydropyrano[2,3-b]pyridines (7) in good yields. The higher reaction temperature (200 °C) required to effect cyclization of (6) reflects the significant loss of entropic assistance associated with intramolecular reactions in which the tethered sidechain is lengthened from the ideal five atom sidechain in (3) to the longer six atom sidechain in (6).[12] The higher reaction temperatures required for Diels-Alder reactions of (6) not surprisingly resulted in substantially increased decomposition.

Heating the 3-(3-butynylamino)-1,2,4-triazines (8) in refluxing bromobenzene (156 °C) yielded the 2,3-dihydropyrrolo[2,3-b]pyridines (9). Here even higher reaction temperatures were required than in the cases of (3) or 3-(3-butynylthio)-1,2,4-triazines because of the greater electron donating ability of nitrogen vs. oxygen (vide supra). Yields were significantly lower when a substituent was present in the 6-position of the triazine ring, probably as a result of greater steric demands in the Diels-Alder reaction. Since, at the high temperatures required for cyclization of (8), decomposition begins to compete with the desired cyclization reaction, homologation of the sidechain in (8) was not attempted.

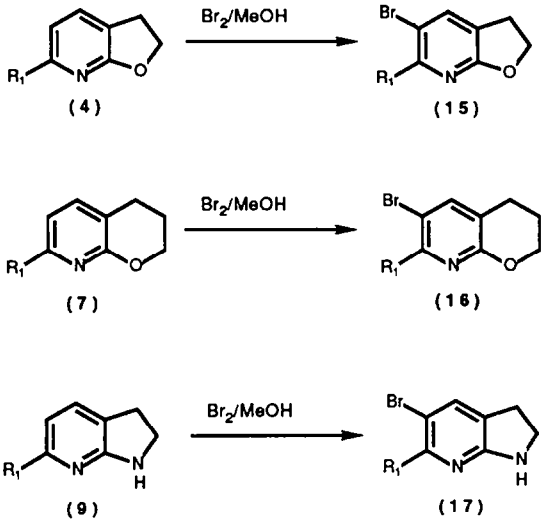
Aromatization of (9d) using DDQ [as previously described for (4)] proceeded smoothly at room temperature. Further examples of this straightforward reaction were not pursued.[13]

We are aware of only a single (low yielding) example of an intermolecular Diels-Alder reaction of a 6-alkoxy-1,2,4-triazine[14] and no examples of such reactions with 6- or 3-amino-1,2,4-triazines. These compounds are poor dienes in inverse electron demand Diels-Alder reactions

Scheme II



Scheme III



a, R_1 = H
d, R_1 = 4-ClC_6H_4

because the electron donation of the heteroatom substituent into the triazine ring raises the diene LUMO, thus diminishing the frontier orbital overlap between the triazine and the participat-ing dienophile. It is only through the "entropic assistance" inherent in the intramolecular reaction that this unfavorable electronic disposition is overcome.

Bromination of 2-alkoxy- or 2-aminopyridines to yield 2-alkoxy- or 2-amino-5-bromopyridines is well known.[15] Accordingly, it was found that bromination of (4d), (7a), (7d), (9a) and (9d) proceeded rapidly and selectively on the pyridine ring forming (15d), (16a), (16d), (17a) and (17d) respectively. These derivatives should be useful intermediates for further functionalization of these fused heterocycles (Scheme III).

Conclusion: Intramolecular Diels-Alder reactions of appropriately substituted 1,2,4-triazines have led to 2,3-dihydrofuro[2,3-b]pyridines, 2,3-dihydropyrano[2,3-b]pyridines, and 2,3-dihydropyrrolo[2,3-b]pyridines. Bromination of these compounds proceeded smoothly in the electron rich β-position of the pyridine ring yielding useful intermediates for further functionalization. Dehydrogenation of these 2,3-dihydrofuro[2,3-b]pyridines and 2,3-dihydropyrrolo[2,3-b]-pyridines has been accomplished using DDQ. Of particular note is the fact that neither heterocyclic ring found in the final fused pyridine systems 4, 7 or 9 exists in their monocyclic precursors.

EXPERIMENTAL

Melting points were determined on a Thomas-Hoover open capillary melting point apparatus and are uncorrected. Infrared spectra were obtained from a Perkin Elmer 1320 Infrared Spectrophotometer, and NMR spectra were obtained either on a JEOL FX-90Q (90 MHz) or on a Nicolet QE300 (300 MHz) spectrometer. Mass spectra were determined on a AEI MS-9 instrument, and elemental analyses were carried out by Eli Lilly & Co., Indianapolis, Indiana. Commercial reagents were utilized without further purification. General procedures listed here represent typical reaction procedures for the class of compounds described.

5-(4-Chlorophenyl)-3-methylthio-1,2,4-triazine (1d). To a stirred mixture of 4-chlorophenylglyoxal monohydrate (9.33 g, 50.00 mmol) and sodium bicarbonate (4.65 g, 55.35 mmol, 1.1 eq) in absolute ethanol (50 mL) at 0° C, a solution of S-methylthiosemicarbazide hydrogen iodide (11.65 g, 49.98 mmol, 1.00 eq) in water (50 mL) was added dropwise. The resulting effervescing mixture was stirred at 0 °C for 4.0 h and filtered to yield a yellow solid. This material was suspended in absolute ethanol (75 mL) and then filtered to yield 5-(4-chlorophenyl)-3-methylthio-1,2,4-triazine (11.00 g, 92.5%) as a pale yellow, crystalline solid: mp 160.0-163.0 °C; ^{1}H NMR (CDCl3) δ 9.35 (s, 1 H), 8.16-8.04 (m, 2 H), 7.60-7.47 (m, 2 H), 2.73 (s, 3 H). The spectral and physical properties of this solid were consistent with the spectral and physical properties previously reported for 5-(4-chlorophenyl)-3-methylthio-1,2,4-triazine.[16]

3-Methylthiophenanthro[9,10-e]-1,2,4-triazine (1e). To a stirred mixture of phenanthrenequinone (8.50 g, 40.82 mmol) and sodium bicarbonate (4.20 g, 50.0 mmol, 1.25 eq) in absolute ethanol (50 mL) at 0° C, a solution of S-methylthiosemicarbazide hydrogen iodide (9.60 g, 41.19 mmol, 1.04 eq) in water (70 mL) was addded dropwise over the course of 10 min. The resulting mixture was then vigorously stirred at 0 °C for 1 h, at room temperature for 4 h and was then filtered. The collected solid was dissolved in methylene chloride (200 mL), and the solution was passed through a silica gel filter (approx 250 g) followed by elution with methylene chloride (1 l). The combined methylene chloride filtrates were evaporated under reduced pressure to yield a brown solid (11 g) which was recrystallized from ethyl acetate to afford 3-methylthiophenanthro[9,10-e]-1,2,4-triazine (9.52 g, 84.1%) as a crystalline, yellow solid: mp 159.0-161.0 °C; IR (KBr) 1605, 1500, 1480, 1445, 1390, 1355 cm^{-1}; ^{1}H NMR (CDCl3) δ 9.13-9.02 (m, 1 H), 8.84-8.73 (m, 1 H), 8.26-8.15 (m, 2 H), 7.74-7.38 (m, 4 H), 2.77 (s, 3 H); ^{13}C NMR (CDCl3) δ 171.3, 142.8, 142.5, 133.9, 132.4, 132.1, 130.2, 130.0, 128.4, 127.7, 127.3, 126.3, 124.2, 122.8, 13.8.

Anal. Calcd for $C_{16}H_{11}N_3S$: C, 69.29; H, 4.00; N, 15.15; S, 11.56; Found: C, 69.36; H, 4.27; N, 15.01; S, 11.35.

3-Methylthio-5,6,7,8-tetrahydro-1,2,4-benzotriazine (1f). A solution of S-methylthiosemicarbazide hydrogen iodide (4.66 g, 19.99 mmol) in water (30 mL) was added dropwise to a stirred mixture of 1,2-cyclohexanedione (2.24 g, 19.98 mmol), sodium bicarbonate (2.00 g, 23.81 mmol, 1.2 eq), and absolute ethanol (20 mL). The resulting effervescing mixture was stirred at room temperature for 4.0 h. Ethanol was then removed by evaporation under reduced pressure, and the residual aqueous mixture was extracted with methylene chloride (3 x 25 mL). The combined methylene

chloride extracts were dried ($MgSO_4$) and evaporated under reduced pressure to yield a yellow solid (3.6 g). Column chromatography of this solid using silica gel (approx 100 g) and elution with 1:1 ether/petroleum ether afforded 3-methylthio-5,6,7,8-tetrahydro-1,2,4-benzotriazine (1.89 g, 52.2%) as a pale yellow solid: mp 102.0-104.0 °C; IR (KBr) 1520, 1500, 1460, 1425, 1410, 1285 cm^{-1}; ^1H NMR ($CDCl_3$) δ 3.06 (t, J=6.0 Hz, 2 H), 2.86 (t, J=6.0 Hz, 2 H), 2.63 (s, 3 H), 1.98-1.89 (m, 4 H); ^{13}C NMR ($CDCl_3$) δ 170.4, 158.8, 154.1, 31.3, 28.8, 21.9, 21.5, 13.6.

Anal. Calcd for $C_8H_{11}N_3S$: C, 53.01; H, 6.12; N, 23.18; S, 17.69; Found: C, 52.83; H, 5.84; N, 23.11; S, 17.89.

General Procedure for the Oxidation of 3-Methylthio-1,2,4-triazines (1) to 3-Methylsulfonyl-1,2,4-triazines (2). To a stirred solution of the 3-methylthio-1,2,4-triazine[9] (10.0 mmol) in anhydrous methylene chloride (40 mL) at 0 °C, m-chloroperbenzoic acid (80-85% tech solid, 4.40 g, 21.7 mmol max, 2.17 eq max) was added as a solid in small portions over the course of a few minutes. The resulting reaction mixture was stirred at r.t. with exclusion of moisture for 2-17 h, and then evaporated under reduced pressure. The residual solid was purified either by column chromatography using silica gel (approx 75 g, dried at 150 °C and 20 mm Hg overnight) and the appropriate solvent system or by trituration with ether (50 mL) and recrystallization (if necessary) to yield the desired 3-methylsulfonyl-1,2,4-triazine (2).

3-Methylsulfonyl-1,2,4-triazine (2a). The reaction time was 2.0 h. The residual reaction solid was column chromatographed, with elution first with 1:1 ether/petroleum ether (to remove m-chlorobenzoic acid) and then with tetrahydrofuran to afford (2a) (90%) as a white, crystalline solid: mp 84.5-86.0 °C; IR (KBr) 1540, 1520, 1400, 1385, 1350-1310, 1135 cm^{-1}; ^1H NMR ($CDCl_3$) δ 9.54 (d, J=2.4 Hz, 1 H), 8.94 (d, J=2.4 Hz, 1 H), 3.52 (s, 3 H); ^{13}C NMR ($CDCl_3$) δ 167.3, 151.6, 150.6, 39.7.

Anal. Calcd for $C_4H_5N_3O_2S$: C, 30.18; H, 3.17; N, 26.40; S, 20.14; Found: C, 30.42; H, 2.90; N, 26.19; S, 19.85.

5,6-Dimethyl-3-methylsulfonyl-1,2,4-triazine (2b). The reaction time was 3.0 h. The residual reaction solid was column chromatographed with elution first with 1:1 ether/petroleum ether (to remove m-chlorobenzoic acid) and then with tetrahydrofuran to yield (2b) (98%) as a white, crystalline solid: mp 64.5-66.0 °C; IR (KBr) 1530, 1440, 1390, 1330-1310, 1135 cm^{-1}; ^1H NMR ($CDCl_3$) δ 3.44 (s, 3 H), 2.82 (s, 3 H), 2.72 (s, 3 H); ^{13}C NMR ($CDCl_3$) d 164.9, 162.0, 160.9, 39.6, 21.9, 19.7.

Anal. Calcd for $C_6H_9N_3O_2S$: C, 38.49; H, 4.85; N, 22.44; S, 17.13; Found: C, 38.69; H, 5.03; N, 22.20; S, 16.91.

3-Methylsulfonyl-5-phenyl-1,2,4-triazine (2c). The reaction time was 3.0 h. The residual reaction solid was suspended in boiling anhydrous ether, and the undissolved solid was collected by filtration and washed well with anhydrous ether to afford (2c) (71%) as a pale yellow, crystalline solid: mp 146.0-148.0 °C; IR (KBr) 1600, 1540, 1490, 1440, 1420, 1315, 1130 cm^{-1}; ^1H NMR ($CDCl_3$/DMSO-d_6 [6:1]) δ 10.03 (s, 1 H), 8.39-8.28 (m, 2 H), 7.73-7.53 (m, 3 H), 3.54 (s, 3 H); ^{13}C NMR ($CDCl_3$/DMSO-d_6 [6:1]) δ 165.9, 156.6, 147.5, 133.4, 130.8, 129.0, 127.8, 39.1.

Anal. Calcd for $C_{10}H_9N_3O_2S$: C, 51.05; H, 3.86; N, 17.86; S, 13.63; Found: C, 50.85; H, 3.92; N, 17.56; S, 13.36.

5-(4-Chlorophenyl)-3-methylsulfonyl-1,2,4-triazine (2d). The reaction time was 11 h. The residual reaction solid was suspended in anhydrous ether, and the undissolved solid was collected by filtration and recrystallized from methylene chloride/hexanes (1:1) to give (2d) (85%) as a pale yellow powder: mp 153.0-156.0 °C; IR (KBr) 1585, 1535, 1480, 1405, 1320, 1135 cm^{-1}; ^1H NMR (DMSO-d_6) δ 10.37 (s, 1 H), 8.54-8.41 (m, 2 H), 7.79-7.69 (m, 2 H), 3.61 (s, 3 H); ^{13}C NMR (DMSO-d_6) δ 165.8, 155.3, 148.3, 138.9, 129.9, 129.3, 128.8, 39.4.

Anal. Calcd for $C_{10}H_8ClN_3O_2S$: C, 44.53; H, 2.99; Cl, 13.14; N, 15.58; S, 11.89; Found: C, 44.25; H, 3.24; Cl, 13.29; N, 15.46; S, 11.63.

3-Methylsulfonylphenanthro[9,10-e]-1,2,4-triazine (2e). The reaction time was 17 h. The residual reaction solid was suspended in anhydrous ether, and the undissolved solid was collected by filtration to yield (2e) (95%) as a pale yellow solid: mp 252.5-253.5 °C; IR (KBr) 1600, 1515, 1500, 1480, 1450, 1360, 1325-1305, 1135 cm^{-1}; ^1H NMR ($CDCl_3$) δ 9.53-9.25 (m, 2 H), 8.64-8.54 (m, 2 H), 7.97-7.71 (m, 4 H), 3.67 (s, 3 H).

Anal. Calcd for $C_{16}H_{11}N_3O_2S$: C, 62.12; H, 3.58; N, 13.53; S, 10.36; Found: C, 62.39; H, 3.78; N, 13.26; S, 10.42.

3-Methylsulfonyl-5,6,7,8-tetrahydro-1,2,4-benzotriazine (2f). The reaction time was 3 h. The residual reaction solid was column chromatographed, with elultion first with ether (to remove m-chlorobenzoic acid) and then with 1:2 ether/tetrahydrofuran to yield (2f) (66%) as a pale yellow solid: mp 115.0-117.0 °C; IR (KBr) 1520, 1460, 1425, 1385, 1330-1310, 1125 cm^{-1}; ^1H NMR

($CDCl_3$) δ 3.44 (s, 3 H), 3.27 (t, J=5.8 Hz, 2 H), 3.12 (t, J=5.7 Hz, 2 H), 2.05-2.01 (m, 4 H); ^{13}C NMR ($CDCl_3$) δ 164.4, 162.5, 161.9, 39.6, 31.5, 29.6, 21.4, 21.0.

Anal. Calcd for $C_8H_{11}N_3O_2S$: C, 45.06; H, 5.20; N, 19.70; S, 15.04; Found: C, 44.85; H, 5.32; N, 19.45; S, 15.25.

5-(4-Fluorophenyl)-3-methylsulfonyl-1,2,4-triazine (2g). [from 5-(4-fluorophenyl)-3-methylthio-1,2,4-triazine[17]]. The reaction time was 3 h. The residual reaction solid was suspended in anhydrous ether, and the undissolved solid was collected by filtration to yield (2g) (93%) as a pale yellow solid: mp 146.0-147.5 °C (dec); IR (KBr) 1595, 1535, 1500, 1480, 1410 cm^{-1}; ^1H NMR ($CDCl_3$) δ 9.84 (s, 1 H), 8.38-8.34 (m, 2 H), 7.35-7.29 (m, 2 H), 3.56 (s, 3 H); HRMS Calcd for $C_{10}H_8FN_3O_2S$: 253.0321, Found: 253.0313 (-3.4 ppm deviation).

5,6-Diphenyl-3-methylsulfonyl-1,2,4-triazine (2h). The reaction time was 3 h. The residual reaction solid was stirred in anhydrous ether, and the undissolved solid was filtered to yield (2h) (92%) as a pale yellow solid: mp 131.5-133.5 °C (effervescent dec) (lit[18] mp 139.0-140.0 °C); IR (KBr) 1600, 1490, 1445, 1370 cm^{-1}; ^1H NMR ($CDCl_3$) δ 7.61-7.43 (m, 1 H), 3.55 (s, 3 H).

General Procedure for the Nucleophilic Displacement of Methyl Sulfinate from 3-Methylsulfonyl-1,2,4-triazines (2). To a stirred solution of the nucleophile (sodium 3-butynyl-1-oxide [6.50 mmol, 1.3 eq] and sodium 4-pentynyl-1-oxide [6.50 mmol, 1.3 eq] were prepared from the alcohol and NaH; 4-amino-1-butyne [13.00 mmol, 2.0 eq] was prepared as described below) in anhydrous tetrahydrofuran (20 mL) at 0 °C, the 3-methylsulfonyl-1,2,4-triazine (2) (5.00 mmol) was added as a solid all at once, and the resultant reaction mixture was stirred at r.t. with exclusion of moisture for 2-34 h. A saturated solution of sodium bicarbonate (20 mL) was then added, and the aqueous mixture was extracted with methylene chloride (3 x 20 mL). The combined methylene chloride extracts were dried ($MgSO_4$) and evaporated under reduced pressure. The residual oil or solid was then purified either by column chromatography using silica gel (approx 50 g) and the appropriate solvent system, or by trituration with ether and recrystallization (when indicated) to yield the desired 3-(3-butynyloxy)-1,2,4-triazine (3), 3-(4-pentynyloxy)-1,2,4-triazine (6), or 3-(3-butynylamino)-1,2,4-triazine (8).

3-(3-Butynyloxy)-1,2,4-triazine (3a). The nucleophile was sodium 3-butynyl-1-oxide, and the reaction time was 2 h. Chromatography of the residual oil with elution with ether afforded (3a) (86%) as a pale yellow oil; IR (neat) 3280, 2120, 1550, 1525, 1465, 1420 cm^{-1}; ^1H NMR ($CDCl_3$) δ 9.05 (d, J=2.2 Hz, 1 H), 8.53 (d, J=2.2 Hz, 1 H), 4.68 (t, J=7.0 Hz, 2 H), 2.82 (dt, J=2.6 and 7.0 Hz, 2 H), 2.10 (t, J=2.6 Hz, 1 H); ^{13}C NMR ($CDCl_3$) δ 165.0, 150.8, 144.9, 79.4, 70.1, 65.9, 18.8.

Anal. Calcd for $C_7H_7N_3O$: C, 56.37; H, 4.73; N, 28.17; Found: C, 56.32; H, 4.84; N, 27.91.

3-(3-Butynyloxy)-5,6-dimethyl-1,2,4-triazine (3b). The nucleophile was sodium 3-butynyl-1-oxide, and the reaction time was 2 h. Chromatography of the residual oil with ether elution afforded (3b) (45%) as a pale orange oil; IR (neat) 3280, 2120, 1555, 1525, 1460, 1425 cm^{-1}; ^1H NMR ($CDCl_3$) δ 4.62 (t, J=7.0 Hz, 2 H), 2.77 (dt, J=2.6 and 7.0 Hz, 2 H), 2.62 (s, 3 H), 2.51 (s, 3 H), 2.05 (t, J=2.6 Hz, 1 H); ^{13}C NMR ($CDCl_3$) δ 163.7, 161.6, 152.6, 79.7, 69.9, 65.6, 21.5, 18.9, 18.4.

Anal. Calcd for $C_9H_{11}N_3O$: C, 61.00; H, 6.26; N, 23.71; Found: C, 60.89; H, 6.19; N, 23.71.

3-(3-Butynyloxy)-5-phenyl-1,2,4-triazine (3c). The nucleophile was sodium 3-butynyl-1-oxide, and the reaction time was 1 h. The residual solid was triturated in ether (5 mL), and the undissolved solid was filtered to yield (3c) (67%) as a white, crystalline solid: mp 105.0-106.5 °C; IR (KBr) 3220, 2115, 1590, 1540, 1515, 1465, 1445, 1430 cm^{-1}; ^1H NMR ($CDCl_3$) δ 9.43 (s, 1 H), 8.22-8.08 (m, 2 H), 7.68-7.47 (m, 3 H), 4.73 (t, J=7.0 Hz, 2 H), 2.83 (dt, J=2.6 and 7.0 Hz, 2 H), 2.09 (t, J=2.6 Hz, 1 H); ^{13}C NMR ($CDCl_3$) δ 164.9, 157.7, 141.5, 132.9, 132.6, 129.2, 127.7, 79.7, 70.2, 66.0, 19.0.

Anal. Calcd for $C_{13}H_{11}N_3O$: C, 69.32; H, 4.92; N, 18.66; Found: C, 69.05; H, 5.05; N, 18.66.

3-(3-Butynyloxy)-5-(4-chlorophenyl)-1,2,4-triazine (3d). The nucleophile was sodium 3-butynyl-1-oxide, and the reaction time was 2 h. The residual solid was triturated in ether (5 mL), and the undissolved solid was filtered to yield (3d) (78%) as a white, crystalline solid: mp 145.5-147.0 °C; IR (KBr) 3220, 2110, 1585, 1535, 1500, 1435, 1400 cm^{-1}; ^1H NMR ($CDCl_3$) δ 9.41 (s, 1 H), 8.20-8.04 (m, 2 H), 7.60-7.44 (m, 2 H), 4.74 (t, J=7.0 Hz, 2 H), 2.84 (dt, J=2.6 and 7.0 Hz, 2 H), 2.06 (t, J=2.6 Hz, 1 H); ^{13}C NMR ($CDCl_3$) δ 166.3, 156.9, 141.3, 139.4, 131.8, 129.8, 129.1, 79.8, 70.3, 66.4, 19.3.

Anal. Calcd for $C_{13}H_{10}ClN_3O$: C, 60.12; H, 3.88; Cl, 13.65; N, 16.18; Found: C, 60.26; H, 3.68; Cl, 13.61; N, 16.16.

3-(3-Butynyloxy)phenanthro[9,10-e]-1,2,4-triazine (3e). The nucleophile was sodium 3-butynyl-1-oxide, and the reaction time was 34 h. The residual solid was triturated in ether (5 mL), and the undissolved solid was filtered to yield (3e) (89%) as a pale yellow powder: mp 193.0-195.0 °C; IR (KBr) 3240, 2120, 1605, 1505, 1495, 1470, 1445, 1430 cm^{-1}; ^1H NMR ($CDCl_3$) δ 9.34-9.04 (m, 2 H), 8.54-8.46 (m 2 H), 7.95-7.59 (m, 4 H), 4.87 (t, J=7.0 Hz, 2 H), 2.94 (dt, J=2.6 and 7.0 Hz, 2 H), 2.11 (t, J=2.6 Hz, 1 H).

Anal. Calcd for $C_{19}H_{13}N_3O$: C, 76.24; H, 4.38; N, 14.04; Found: C, 76.46; H, 4.46; N, 13.77.

3-(4-Pentynyloxy)-1,2,4-triazine (6a). The nucleophile was sodium 4-pentynyl-1-oxide, and the reaction time was 2 h. Chromatography of the residual oil with elution with 1:4 ether/petroleum ether afforded (6a) (42%) as a clear, colorless liquid; IR (neat) 3290, 2120, 1550, 1530, 1520, 1470, 1430 cm^{-1}; ^1H NMR ($CDCl_3$) δ 9.04 (d, J=2.4 Hz, 1 H), 8.54 (d, J=2.2 Hz, 1 H), 4.67 (t, J=6.2 Hz, 2 H), 2.57-2.38 (m, 2 H), 2.26-1.96 (m, 3 H); ^{13}C NMR ($CDCl_3$) δ 165.2, 150.4, 144.5, 82.6, 68.8, 66.8, 27.4, 14.7.

Anal. Calcd for $C_8H_9N_3O$: C, 58.88; H, 5.56; N, 25.75; Found: C, 58.58; H, 5.52; N, 25.35.

3-(4-Pentynyloxy)-5-phenyl-1,2,4-triazine (6c). The nucleophile was sodium 4-pentynyl-1-oxide, and the reaction time was 1 h. Chromatography of the residual solid followed by elution with 2:3 ether/petroleum ether afforded (6c) (52%) as a pale yellow solid: mp 85.5-88.0 °C; IR (KBr) 3240, 2110, 1600, 1540-1510, 1495, 1460, 1430 cm^{-1}; ^1H NMR ($CDCl_3$) δ 9.41 (s, 1 H), 8.22-8.11 (m, 2 H), 7.60-7.45 (m, 3 H), 4.72 (t, J=6.2 Hz, 2 H), 2.56-2.00 (m, 4 H), 2.01 (t, J=2.6 Hz, 1 H); ^{13}C NMR ($CDCl_3$) δ 165.4, 157.6, 141.2, 133.3, 132.3, 129.1, 127.7, 83.0, 68.9, 66.9, 27.8, 15.1.

Anal. Calcd for $C_{14}H_{13}N_3O$: C, 70.27; H, 5.48; N, 17.56; Found: C, 70.00; H, 5.55; N, 17.62.

5-(4-Chlorophenyl)-3-(4-pentynyloxy)-1,2,4-triazine (6d). The nucleophile was sodium 4-pentynyl-1-oxide, and the reaction time was 1 h. Chromatography of the residual oil with elution with 1:1 ethyl acetate/petroleum ether afforded (6d) (78%) as a pale yellow, crystalline solid: mp 106.0-109.0 °C; IR (KBr) 3220-3200, 2120, 1590, 1540, 1505-1490, 1435, 1400 cm^{-1}; ^1H NMR ($CDCl_3$) δ 9.39 (s, 1 H), 8.21-8.05 (m, 2 H), 7.63-7.44 (m, 2 H), 4.73 (t, J=6.3 Hz, 2 H), 2.59-2.05 (m, 4 H), 2.00 (t, J=2.6 Hz, 1 H); ^{13}C NMR ($CDCl_3$) δ 165.5, 156.6, 141.0, 139.2, 131.9, 129.7, 129.1, 83.0, 69.0, 67.2, 28.0, 15.2; HRMS ([M+]=$C_{14}H_{12}ClN_3O$) Calculated for ([M^+] - H) (molecular ion unavailable due to immediate loss of acetylenic proton in the mass spectrometer) 272.05889; Found 272.05889 +/- 0.0030.

3-(4-Pentynyloxy)phenanthro[9,10-e]-1,2,4-triazine (6e). The nucleophile was sodium 4-pentynyl-1-oxide, and the reaction time was 6 h. The residual solid was triturated in anhydrous ether to yield (6e) (79%) as a pale yellow solid: mp 137.0-140.0 °C (with effervescence); IR (KBr) 3250, 2120, 1610, 1570, 1515, 1490, 1435 cm^{-1}; ^1H NMR ($CDCl_3$) δ 9.25-8.90 (m, 2 H), 8.59-8.33 (m, 2 H), 7.90-7.50 (m, 4 H), 4.82 (t, J=6.0 Hz, 2 H), 2.58-2.45 (m, 2 H), 2.40-2.16 (m 2 H), 2.04 (t, J=2.6 Hz, 1 H); ^{13}C NMR ($CDCl_3$) δ 164.1, 145.0, 142.9, 134.2, 132.5, 129.8, 129.7, 128.6, 127.8, 127.7, 127.4, 126.6, 124.1, 123.0, 122.8, 83.2, 69.2, 67.1, 27.9, 15.3.

Anal. Calcd for $C_{20}H_{15}N_3O$: C, 76.66; H, 4.83; N, 13.41; Found: C, 76.45; H, 5.00; N, 13.24.

3-(3-Butynyl-1-amino)-1,2,4-triazine (8a). The nucleophile was 4-amino-1-butyne, and the reaction time was 24 h. The residual solid was triturated with ether to yield (8a) (64%) as a yellow solid: mp 104.0-105.0 °C; IR (KBr) 3240, 3150, 1520, 1455 cm^{-1}; ^1H NMR ($CDCl_3$) δ 8.61 (d, J=2.5 Hz, 1 H), 8.17 (d, J=2.2 Hz, 1 H), 5.75 (bm, 1 H), 3.72 (q, J=6.0 Hz, 2 H), 2.59 (dt, J=6.5 and 2.7 Hz, 2 H), 2.06 (t, J=2.3 Hz, 1 H); HRMS Calcd for $C_7H_8N_4$ 148.0749; Found 148.0743 (-4.0 ppm deviation).

3-(3-Butynyl-1-amino)-5-phenyl-1,2,4-triazine (8c). The nucleophile was 4-amino-1-butyne, and the reaction time was 24 h. The residual solid was triturated with ether and then recrystallized from ethyl acetate to yield (8c) (80%) as yellow needles: mp 130.5-131.5 °C; IR (KBr) 3220, 3190, 1590, 1560, 1520 cm^{-1}; ^1H NMR ($CDCl_3$) δ 9.10 (s, 1 H), 8.14-8.11 (m, 2 H), 7.63-7.53 (m, 3 H), 5.69 (bm, 1 H), 3.82 (q, J=6.4 Hz, 2 H), 2.65 (dt, J= 6.5 and 2.7 Hz, 2 H), 2.09 (t, J=2.6 Hz, 1 H).

Anal. Calcd for $C_{13}H_{12}N_4$: C, 69.62; H, 5.39; N, 24.98; Found: C, 69.25; H, 5.18; N, 24.66.

3-(3-Butynyl-1-amino)-5-(4-chlorophenyl)-1,2,4-triazine (8d). The nucleophile was 4-amino-1-butyne, and the reaction time was 24 h. The residual solid was triturated with ether and then recrystallized from ethyl acetate to yield (8d) (96%) as yellow needles: mp 137.5-138.0 °C; IR (KBr) 3220, 1595, 1530, 1470, 1440 cm^{-1}; ^1H NMR ($CDCl_3$) δ 9.04 (s, 1 H), 8.04 (d, J=9.0 Hz, 2 H), 7.50 (d, J=9.0 Hz, 2 H), 5.75 (bm, 1 H), 3.78 (q, J=6.4 Hz, 2 H), 2.61 (dt, J=7.5 and 2.7 Hz, 2 H), 2.05 (t, J=2.6 Hz, 1 H).

Anal. Calcd for $C_{13}H_{11}ClN_4$: C, 60.35; H, 4.29; Cl, 13.70; N, 21.66; Found: C, 60.11; H, 4.25; Cl, 13.91; N, 21.37.

3-(3-Butynyl-1-amino)phenanthro[9,10-e]-1,2,4-triazine (8e). The nucleophile was 4-amino-1-butyne, the reaction solvent was DMF, and the reaction time was 36 h. The residual reaction solid was triturated with methylene chloride and then recrystallized from ethyl acetate to yield (8e) (90%) as yellow needles: mp 220.0-222.0 °C (dec); IR (KBr) 3220, 1590, 1560, 1520, 1470, 1430 cm^{-1}; ^1H NMR ($CDCl_3$) δ 9.26-9.23 (m, 1 H), 9.10-9.07 (m, 1 H), 8.56-8.48 (m, 2 H), 7.86-7.80 (m, 1 H), 7.74-7.65 (m, 3 H), 6.05 (bm, 1 H), 3.92 (q, J=6.4 Hz, 2 H), 2.72 (dt, J=6.6 and 2.7 Hz, 2 H), 2.09 (t, J=2.9 Hz, 1 H).

Anal. Calcd for $C_{19}H_{14}N_4$: C, 76.49; H, 4.73; N, 18.78; Found: C, 76.24; H, 4.86; N, 18.58.

3-(3-Butynyl-1-amino)-5-(4-fluorophenyl)-1,2,4-triazine (8g). The nucleophile was 4-amino-1-butyne, and the reaction time was 24 h. The residual solid was triturated with ether and then recrystallized from ethyl acetate to yield (8g) (78%) as yellow needles: mp 144.0-145.0 °C (effervescent dec); IR (KBr) 3280, 3220, 1600, 1585, 1530, 1510, 1470 cm^{-1}; ^1H NMR ($CDCl_3$) δ 9.04 (s, 1 H), 8.15-8.10 (m, 2 H), 7.27-7.19 (m, 2 H), 5.85 (bm, 1 H), 3.79 (q, J=6.4 Hz, 2 H), 2.63 (dt, J=6.5 and 2.7 Hz, 2 H), 2.07 (t, J=2.7 Hz, 1 H).

Anal. Calcd for $C_{13}H_{11}FN_4$: C, 64.45; H, 4.58; F, 7.84; N, 23.13; Found: C, 64.71; H, 4.61; F, 8.00; N, 23.41.

3-(3-Butynyl-1-amino)-5,6-diphenyl-1,2,4-triazine (8h). The nucleophile was 4-amino-1-butyne, and the reaction time was 24 h. The residual reaction solid was triturated with ether and then recrystallized from ethyl acetate to yield (8h) (97%) as yellow needles: mp 131.0-132.0 °C; IR (KBr) 3280, 3230, 1600, 1520, 1470, 1430 cm^{-1}; ^1H NMR ($CDCl_3$) δ 7.52-7.26 (m, 10 H), 5.85 (bm, 1 H), 3.79 (q, J=6.6 Hz, 2 H), 2.62 (dt, J=6.4 and 2.6 Hz, 2 H), 2.04 (t, J=2.6 Hz, 1 H).

Anal. Calcd for $C_{19}H_{16}N_4$: C, 75.98; H, 5.37; N, 18.65; Found: C, 75.69; H, 5.22; N, 18.71.

General Procedure for the Intramolecular Diels-Alder Reaction of 3-(3-Butynyloxy)-1,2,4-triazines (3) to 2,3-Dihydrofuro[2,3-b]pyridines (4). A solution of the 3-(3-butynyloxy)-1,2,4-triazine (3) (3.00 mmol) in anhydrous chlorobenzene (or bromobenzene) (10 mL) was heated at reflux (132 °C for chlorobenzene, 156 °C for bromobenzene) under nitrogen for 10-53 hours, depending on the substrate. The reaction course was followed by tlc. The resulting reaction solution was then evaporated under reduced pressure and the residual solid or oil was purified either by a silica gel (approx 25 g) filtration with elution with the appropriate solvent(s) or by trituration with ether to yield the desired 2,3-dihydrofuro[2,3-b]pyridine (4).

2,3-Dihydrofuro[2,3-b]pyridine (4a). The reaction solvent was chlorobenzene, and reaction time was 10 h. The residual oil was purified by silica gel filtration, eluting first with petroleum ether (75 mL) and then with ether (125 mL). The ether filtrate was evaporated under reduced pressure to yield (4a) (80%) as a clear, pale yellow oil; IR (neat) 1595, 1480, 1455, 1420 cm^{-1}; ^1H NMR ($CDCl_3$) δ 7.95 (br d, J=5.1 Hz, 1 H), 7.45 (dd, J=1.5 and 7.3 Hz, 1 H), 6.75 (dd, J=5.1 Hz and 7.3 Hz, 1 H), 4.58 (t, J=8.6 Hz, 2 H), 3.22 (t, J=8.6 Hz, 2 H); ^{13}C NMR ($CDCl_3$) δ 168.3, 146.1, 133.2, 119.3, 116.1, 68.5, 27.7.

Anal. Calcd for C_7H_7NO: C, 69.40; H, 5.82; N, 11.56; Found: C, 69.12; H, 5.87; N, 11.47.

2,3-Dihydro-5,6-dimethylfuro[2,3-b]pyridine (4b). The reaction solvent was chlorobenzene, and reaction time was 53 h. The residual reaction oil was purified by silica gel filtration with elution with ether (100 mL). This ether eluate was evaporated under reduced pressure to yield (4b) (100%) as a white, crystalline solid: mp 68.0-70.5 °C; IR (KBr) 1600, 1585, 1475, 1430, 1400 cm^{-1}; ^1H NMR ($CDCl_3$) δ 7.19 (s, 1 H), 4.54 (t, J=8.6 Hz, 2 H), 3.15 (t, J=8.6 Hz, 2 H), 2.35 (s, 3 H), 2.16 (s, 3 H); ^{13}C NMR ($CDCl_3$) δ 166.3, 153.1, 135.1, 122.8, 116.0, 68.7, 27.8, 21.9, 18.2; LRMS, m/z (relative intensity) 150 (11), 149 (100, M+), 148 (38), 134 (18), 120 (23), 119 (13), 104 (19), 79 (19), 77 (17); HRMS Calcd for $C_9H_{11}NO$ 149.0841; Found 149.0836 +/- 0.0015.

Anal. Calcd for $C_9H_{11}NO$: C, 72.46; H, 7.43; N, 9.39; Found: C, 72.58; H, 7.71; N, 9.16.

2,3-Dihydro-6-phenylfuro[2,3-b]pyridine (4c). The reaction solvent was chlorobenzene, and reaction time was 16.5 h. The residual reaction solid was purified by silica gel filtration, eluting first with petroleum ether (50 mL) and then with 1:1 ether/petroleum ether (200 mL). The ether/petroleum ether eluate was evaporated under reduced pressure to yield (4c) (95%) as a white, crystalline solid: mp 84.5-86.0 °C; IR (KBr) 1595, 1570, 1480, 1425 cm^{-1}; ^1H NMR ($CDCl_3$) δ 8.03-7.92 (m, 2 H), 7.52-7.30 (m, 4 H), 7.21 (d, J=7.7 Hz, 1 H), 4.60 (t, J=8.7 Hz, 2 H), 3.20 (t, J=8.5 Hz, 2 H); ^{13}C NMR ($CDCl_3$) δ 168.6, 155.0, 138.9, 133.8, 128.5, 128.4, 126.6, 117.9, 112.9, 68.9, 27.8.

Anal. Calcd for $C_{13}H_{11}NO$: C, 79.16; H, 5.62; N, 7.10; Found: C, 79.11; H, 5.61; N, 6.96.

6-(4-Chlorophenyl)-2,3-dihydrofuro[2,3-b]pyridine (4d). The reaction solvent was chlorobenzene, and the reaction time was 16 h. The residual reaction solid was purified by silica gel filtration with elution with methylene chloride (100 mL). The methylene chloride eluate was evaporated under reduced pressure to yield (4d) (90%) as a white, crystalline solid: mp 119.5-121.5 °C; IR

(KBr) 1590, 1560, 1490, 1470, 1445, 1425, 1400 cm^{-1}; ^1H NMR ($CDCl_3$) δ 7.90 (d, J=8.6 Hz, 2 H), 7.46 (d, J=7.5 Hz, 1 H), 7.35 (d, J=8.6 Hz, 2 H), 7.16 (d, J=7.5 Hz, 1 H), 4.62 (t, J=8.8 Hz, 2 H), 3.21 (t, J=8.8 Hz, 2 H); ^{13}C NMR ($CDCl_3$) δ 168.8, 153.9, 137.6, 134.6, 133.8, 128.6, 127.9, 118.3, 112.8, 69.0, 27.9.

Anal. Calcd for $C_{13}H_{10}ClNO$: C, 67.40; H, 4.35; Cl, 15.30; N, 6.05; Found: C, 67.62; H, 4.41; Cl, 15.12; N, 6.36.

2,3-Dihydrophenanthro[9,10-e]furo[2,3-b]pyridine (4e). The reaction solvent was bromobenzene, and the reaction time was 50 h. The resulting reaction solution was passed through a silica gel filter followed by elution with methylene chloride (150 mL). The methylene chloride filtrate was concentrated to approximately 3 mL via under reduced pressure, and anhydrous ether (20 mL) was added to this solution. The resulting triturated solid was filtered to yield (4e) (69%) as a pale yellow, crystalline solid: mp 188.0-190.0 °C; IR (KBr) 1630, 1610, 1590, 1500, 1475, 1445, 1435 cm^{-1}; ^1H NMR ($CDCl_3$) δ 9.28-9.10 (m, 1 H), 8.62-8.44 (m, 2 H), 8.40 (s, 1 H), 8.33-8.15 (m, 1 H), 7.75-7.48 (m, 4 H), 4.66 (t, J=8.4 Hz, 2 H), 3.29 (t, J=8.4 Hz, 2 H); ^{13}C NMR ($CDCl_3$) δ 167.7, 145.1, 131.3, 130.7, 129.2, 128.8, 128.4, 128.2, 127.0, 126.4, 125.7, 123.4, 122.3, 120.3, 119.6, 69.3, 28.2.

Anal. Calcd for $C_{19}H_{13}NO$: C, 84.11; H, 4.83; N, 5.16; Found: C, 84.05; H, 4.93; N, 5.36.

2,3,5,6,7,8-Hexahydrofuro[2,3-b]quinoline (4f). To a stirred solution of 3-butyn-1-ol (0.35 mL, 4.62 mmol, 1.3 eq) and sodium hydride (60% oil, 0.18 g, 4.50 mmol, 1.26 eq) in anhydrous tetrahydrofuran at r.t., 3-methylsulfonyl-5,6,7,8-tetrahydro-1,3,4-benzotriazine (0.76 g, 3.56 mmol) was added as a solid all at once. The resulting black reaction mixture was stirred at r.t. with exclusion of moisture for 1 h. A saturated solution of sodium bicarbonate (20 mL) was then added to the reaction mixture, and this aqueous mixture was extracted with ether (4 x 25 mL). The ether extracts were combined, dried ($MgSO_4$), and evaporated under reduced pressure to yield a dark brown oil. Column chromatography of this oil using silica gel (approx 40 g) and elution with 1:1 ether/petroleum ether yielded 3-(3-butynyloxy)-5,6,7,8-tetrahydro-1,3,4-benzotriazine (0.27 g, 37%) as a clear, colorless liquid; IR (neat) 3300, 2120, 1545, 1525, 1465, 1430 cm^{-1}; ^1H NMR ($CDCl_3$) δ 4.61 (t, J=7.0 Hz, 2 H), 3.08 (t, J=6.1 Hz, 2 H), 2.90 (t, J=6.1 Hz, 2 H), 2.77 (dt, J=2.6 and 7.1 Hz, 2 H), 2.05 (t, J=2.6 Hz, 1 H), 1.98-1.91 (m, 4 H). This liquid was then dissolved in chlorobenzene (3 mL), and this solution was heated at reflux under nitrogen for 47 h. The resulting reaction solution was evaporated under reduced pressure, and the residual oil was chromatographed using silica gel (approx 40 g). Elution with 1:1 ether/petroleum ether yielded 2,3,5,6,7,8-hexahydrofuro[2,3-b]quinoline (0.22 g, 95% for the cyclization, 35% overall) as a clear, colorless liquid; IR (neat) 1620, 1590, 1480, 1450-1400 cm^{-1}; ^1H NMR ($CDCl_3$) δ 7.13 (s, 1 H), 4.53 (t, J=8.5 Hz, 2 H), 3.14 (t, J=8.5 Hz, 2 H), 2.76 (t, J=6.1 Hz, 2 H), 2.62 (t, J=6.0 Hz, 2 H), 1.85-1.71 (m, 4 H); ^{13}C NMR ($CDCl_3$) δ 166.0, 153.0, 134.4, 123.7, 116.3, 68.5, 31.8, 27.9, 27.5, 22.7, 22.7.

Anal. Calcd for $C_{11}H_{13}NO$: C, 75.40; H, 7.48; N, 7.99; Found: C, 75.11; H, 7.19; N, 8.11.

General Procedure for the Intramolecular Diels-Alder Reaction of 3-[3-Butynyl-1-amino]-1,2,4-triazines (8) to 2,3-Dihydropyrrolo[2,3-b]pyridines (9). A stirred suspension of the 3-(3-butynyl-1-amino)-1,2,4-triazine (8) (2.00 mmol) in bromobenzene (unless otherwise noted) was heated to reflux (156 °C) under nitrogen for 24-50 h; the reaction was followed to completion by tlc. After cooling to r.t., the reaction mixture was filtered through a silica gel pad (approx 20 g), eluting first with hexanes and then with 1% methanol/methylene chloride. The methylene chloride eluates were then evaporated under reduced pressure to afford the crude 2,3-dihydropyrrolo[2,3-b]pyridine (9) which was further purified as described below.

2,3-Dihydropyrrolo[2,3-b]pyridine (9a). The crude product was purified by preparative tlc (20x20 cm plate, 1500 micron thickness), eluting with 1:1 hexanes/ethyl acetate to afford (9a) (48%) as a tan solid which was obtained as orange crystals upon recrystallization from 1:2 ether/petroleum ether: mp 78.5-79.5 °C; IR (KBr) 1580, 1490, 1420 cm^{-1}; ^1H NMR ($CDCl_3$) δ 7.80 (d, J=3.0 Hz, 1 H), 7.26-7.21 (m, 1 H), 6.50-6.46 (m, 1 H), 5.28 (bs, 1 H), 3.59 (t, J=9.0 Hz, 2 H), 3.03 (t, J=9.0 Hz, 2 H).

Anal. Calcd for $C_7H_8N_2$: C, 69.98; H, 6.71; N, 23.31; Found: C, 69.69; H, 6.88; N, 23.11.

Compound (9a) could also be obtained (68%) by heating (8a) for 6 days in refluxing chlorobenzene (132 °C). The spectral and physical properties of this material were identical with those described above.

2,3-Dihydro-6-phenylpyrrolo[2,3-b]pyridine (9c). The crude product was purified by column chromatography followed by elution with 4:1 hexanes/ethyl acetate to afford (9c) (44%) as a tan solid which was obtained as white plates upon recrystallization from benzene: mp 167.0-168.0 °C; IR (KBr) 1610, 1590, 1490, 1420 cm^{-1}; ^1H NMR ($CDCl_3$) δ 7.89-7.86 (m, 2 H), 7.45-7.31 (m, 4 H), 6.96 (d, J=7.4 Hz, 1 H), 4.85 (bs, 1 H), 3.65 (t, J=8.3 Hz, 2 H), 3.09 (t, J=8.6 Hz, 2 H).

Anal. Calcd for $C_{13}H_{12}N_2$: C, 79.56; H, 6.16; N, 14.27; Found: C, 79.12; H, 6.41; N, 13.92.

6-(4-Chlorophenyl)-2,3-dihydropyrrolo[2,3-b]pyridine (9d). The crude product was triturated with ether to afford (9d) (61%) as an off-white solid: mp 168.0-169.0 °C; IR (KBr) 1610, 1585, 1490, 1420 cm^{-1}; ^1H NMR ($CDCl_3$) δ 7.82 (d, J=8.8 Hz, 2 H), 7.43-7.31 (m, 3 H), 6.89 (d, J=7.5 Hz, 1 H), 4.83 (bs, 1 H), 3.62 (t, J=8.1 Hz, 2 H), 3.06 (t, J=7.9 Hz, 2 H).

Anal. Calcd. for $C_{13}H_{11}ClN_2$: C, 67.68; H, 4.81; Cl, 15.37; N, 12.14; Found: C, 67.47; H, 4.55; Cl, 15.09; N, 12.03.

2,3-Dihydrophenanthro[9,10-e]pyrrolo[2,3-b]pyridine (9e). The reaction solvent was triisopropylbenzene (232 °C), and the reaction time was 7 h. The reaction mixture was filtered through a silica gel pad (approx 20 g) (elution first with hexanes and then with 1% methanol/methylene chloride). The methylene chloride eluates were evaporated under reduced pressure to afford a gummy yellow-red solid. Purification of this material by preparative tlc (20x20 cm plate, 1500 micron thickness; elution with 1:1 hexanes/ethyl acetate) afforded a trace amount of crude (9e) as a gummy yellow solid; ^1H NMR ($CDCl_3$) δ 9.11 (t, J=6.0 Hz, 1 H), 8.63 (m, 3 H), 8.36-8.32 (m, 2 H), 7.71-7.55 (m, 3 H), 5.40 (bs, 1 H), 3.78 (t, J=6.0 Hz, 2 H), 3.26 (t, J=6.0 Hz, 2 H). HRMS Calcd for $C_{19}H_{14}N_2$: 270.1157: Found: 270.1140 (-6.1 ppm deviation).

6-(4-Fluorophenyl)-2,3-dihydropyrrolo[2,3-b]pyridine (9g). The crude product was purified by column chromatography, with elution with 1:1 hexanes/ethyl acetate, to afford (9g) (66%) as a tan solid which was obtained as beige needles upon recrystallization from benzene/hexanes: mp 161.5-162.0 °C; IR (KBr) 1590, 1495, 1425 cm^{-1}; ^1H NMR ($CDCl_3$) δ 7.88-7.84 (m, 2 H), 7.31 (d, J=7.4 Hz, 1 H), 7.13-7.07 (m, 2 H), 6.90 (d, J=7.7 Hz, 1 H), 4.83 (bs, 1 H), 3.64 (t, J=8.3 Hz, 2 H), 3.09 (t, J=8.3 Hz, 2 H).

Anal. Calcd for $C_{13}H_{11}FN_2$: C, 72.88; H, 5.17; F, 8.87; N, 13.08; Found: C, 73.04; H, 5.15; F, 8.68; N, 13.28.

2,3-Dihydro-5,6-diphenylpyrrolo[2,3-b]pyridine (9h). The crude product was purified by column chromatography (elution with 5:1 hexanes/ethyl acetate) followed by preparative tlc (20x20 cm plate, 1500 micron thickness, elution with 1:1 hexanes/ethyl acetate) to afford (9h) (20%) as a light tan solid: mp 202.0-204.0 °C; IR (KBr) 1620, 1580, 1510, 1490, 1470, 1445, 1410 cm^{-1}; ^1H NMR ($CDCl_3$) δ 7.32 (s, 1 H), 7.27-7.13 (m, 10 H), 4.85 (bs, 1 H), 3.55 (t, J=7.9 Hz, 2 H), 3.12 (t, J=7.7 Hz, 2 H); HRMS Calcd for $C_{19}H_{16}N_2$: 272.1313; Found 272.1310 (-1.1 ppm deviation).

General Procedure for the Dehydrogenation of 2,3-Dihydrofuro[2,3-b]pyridines (4) to Furo[2,3-b]pyridines (5). A solution of the 2,3-dihydrofuro[2,3-b]pyridine (4) (2.00 mmol) and 2,3-dichloro-5,6-dicyano-1,4-benzoquinone (1.02 g, 4.5 mmol, 2.25 eq) in anhydrous dioxane (10 mL) was heated at reflux (101 °C) with exclusion of moisture for 6-24 h. A saturated solution of sodium bicarbonate (10 mL) was then added, and this aqueous mixture was extracted with methylene chloride (3 x 10 mL). The methylene chloride extracts were combined, dried ($MgSO_4$), and evaporated under reduced pressure. Column chromatography of the residual oil using silica gel (approx 40 g) and elution with the appropriate solvent system afforded the desired furo[2,3-b]pyridine (5).

5,6-Dimethylfuro[2,3-b]pyridine (5b). The reaction time was 21 h. Chromatography of the residual reaction oil, eluting with 1:2 ether/petroleum ether, yielded (5b) (49%) as a light blue liquid which crystallized below room temperature; IR (neat) 3120, 1610, 1585, 1525, 1470, 1450, 1405 cm^{-1}; ^1H NMR ($CDCl_3$) δ 7.59 (s, 1 H), 7.56 (d, J=2.6 Hz, 1 H), 6.63 (d, J=2.6 Hz, 1 H), 2.54 (s, 3 H), 2.31 (s, 3 H); ^{13}C NMR ($CDCl_3$) δ 160.6, 152.1, 143.6, 130.5, 126.7, 116.8, 105.2, 22.3, 18.8.

Anal. Calcd for C_9H_9NO: C, 73.45; H, 6.16; N, 9.52; Found: C, 73.20; H, 6.18; N, 9.26.

6-Phenylfuro[2,3-b]pyridine (5c). The reaction time was 6 h. Chromatography of the residual reaction oil (elution with 1:1 ether/petroleum ether) yielded (5c) (53%; 63% based on recovered starting material) as a white, crystalline solid: mp 62.5-64.5° C; IR (KBr) 1585, 1570, 1515, 1455, 1435, 1395 cm^{-1}; ^1H NMR ($CDCl_3$) δ 8.10-7.89 (m, 2 H), 8.08 (d, J=7.9 Hz, 1 H), 7.68 (d, J=2.4 Hz, 1 H), 7.67 (d, J=7.9 Hz, 1 H), 7.53-7.40 (m, 3 H), 6.74 (d, J=2.4 Hz, 1 H); ^{13}C NMR ($CDCl_3$) δ 162.5, 153.0, 144.9, 139.2, 130.5, 128.7, 127.1, 127.1, 117.8, 116.2, 105.8.

Anal. Calcd for $C_{13}H_9NO$: C, 79.98; H, 4.65; N, 7.17; Found: C, 79.78; H, 4.85; N, 6.96.

6-(4-Chlorophenyl)furo[2,3-b]pyridine (5d). The reaction time was 24 h. Chromatography of the residual reaction oil (elution with 1:4 ether/petroleum ether) yielded (5d) (R_f=0.6 in ether) (72%) as a white, crystalline solid: mp 85.5-87.0 °C; IR (KBr) 1590, 1520, 1490, 1455, 1410, 1395 cm^{-1}; ^1H NMR ($CDCl_3$) δ 8.08-7.92 (m, 2 H), 7.94 (d, J=7.9 Hz, 1 H), 7.70 (d, J=2.4 Hz, 1 H), 7.62 (d, J=7.9 Hz, 1 H), 7.48-7.33 (m, 2 H), 6.76 (d, J=2.4 Hz, 1 H); ^{13}C NMR ($CDCl_3$) δ 162.4, 151.6, 145.2, 137.7, 135.1, 130.6, 128.9, 128.4, 118.2, 116.0, 105.9.

Anal. Calcd for $C_{13}H_8ClNO$: C, 67.99; H, 3.51; Cl, 15.44; N, 6.09; Found: C, 68.12; H, 3.73; Cl, 15.25; N, 6.25.

Phenanthro[9,10-e]furo[2,3-b]pyridine (5e). The reaction time was 9 h. Chromatography of the residual reaction oil with elution with methylene chloride yielded (5e) (67%) as a white powder: mp 161.5-163.0 °C; IR (KBr) 1610, 1590, 1530, 1500, 1485, 1435, 1390 cm^{-1}; ^1H NMR ($CDCl_3$) δ 9.36-9.21 (m, 1 H), 8.87 (s, 1 H), 8.60-8.33 (m, 3 H), 7.78-7.48 (m, 5 H), 6.83 (d, J=2.6 Hz, 1 H); ^{13}C NMR ($CDCl_3$) δ 161.4, 146.1, 143.1, 131.3, 131.0, 129.2, 128.6, 127.3, 127.1, 125.8, 124.6, 123.4, 123.0, 122.5, 122.0, 119.0, 106.0; HRMS Calcd for $C_{19}H_{11}NO$: 269.08386; Found 269.08386 +/- 0.0050.

6-(4-Chlorophenyl)pyrrolo[2,3-b]pyridine (10d). A suspension of (9d) (0.066 g, 0.29 mmol) and 2,3-dichloro-5,6-dicyano-1,4-benzoquinone (0.069 g, 0.30 mmol) in p-dioxane (4 mL) was stirred at r.t. for 15 min under nitrogen. The reaction mixture was then filtered through a silica gel pad (approx 10 g), eluting with 1:1 hexanes/ethyl acetate (80 mL). The eluates were evaporated under reduced pressure to afford a brown solid. Purification of this material by column chromatography using silica gel (approx 10 g) and eluting with1:1 hexanes/ethyl acetate afforded (10d) (0.030 g, 45%) as a pale tan solid: mp 228.0-230.0 °C (dec); ^1H NMR ($CDCl_3$) δ 9.91 (bs, 1 H), 8.07 (d, J=8.2 Hz, 1 H), 7.97 (d, J=8.5 Hz, 2 H), 7.54 (d, J=8.2 Hz, 1 H), 7.49 (d, J=8.5 Hz, 2 H), 7.32 (d, J=3.4 Hz, 1 H), 6.56 (d, J=3.4 Hz, 1 H). HRMS Calcd for $C_{13}H_9N_2Cl$: 228.0454; Found: 228.0455 (0.5 ppm deviation).

General Procedure for the Intramolecular Diels-Alder Reaction of 3-(4-Pentynyloxy)-1,2,4-triazines (6) to 2,3-Dihydropyrano[2,3-b]pyridines (7). A solution of the 3-(4-pentynyloxy)-1,2,4-triazine (6) (2.00 mmol) in either bromobenzene or triisopropylbenzene (3 mL) was heated between 156-210 °C under nitrogen for 5-48 h depending on reaction solvent and substrate. The resulting reaction solution was chomatographed using silica gel (approx 40 g) with elution with the appropriate solvent system to yield the desired 2,3-dihydropyrano[2,3-b]pyridine (7).

2,3-Dihydropyrano[2,3-b]pyridine (7a). Compound (6a) was heated at 200° C in triisopropylbenzene for 5 h. The reaction solution was chromatographed with elution first with 1:4 ether/petroleum ether (to remove triisopropylbenzene) and then with 1:1 ether/petroleum ether to yield (7a) (61%) as a pale yellow liquid; IR (neat) 1595, 1575, 1470, 1440-1420 cm^{-1}; ^1H NMR ($CDCl_3$) δ 8.06 (dd, J=4.8 and 2.0 Hz, 1 H), 7.36 (dd, J=7.5 and 2.0 Hz, 1 H), 6.81 (dd, J=7.5 and 4.8 Hz, 1 H), 4.33 (t, J=5.1 Hz, 2 H), 2.79 (t, J=6.2 Hz, 2 H), 2.12-1.86 (m, 2 H); ^{13}C NMR ($CDCl_3$) δ 161.3, 146.2, 138.3, 117.1, 116.8, 66.9, 24.7, 21.7.

Anal. Calcd for C_8H_9NO: C, 71.09; H, 6.71; N, 10.36; Found: C, 70.84; H, 6.51; N, 10.09.

2,3-Dihydro-7-phenylpyrano[2,3-b]pyridine (7c). Compound (6c) was heated at 200-210 °C in triisopropylbenzene for 5 h. The reaction solution was then chromatographed (elution with 1:2 ether/petroleum ether) to yield (7c) (81%) as a pale yellow, crystalline solid: mp 68.5-70.0 °C; IR (KBr) 1595, 1580, 1560, 1490, 1470, 1460-1430, 1410 cm^{-1}; ^1H NMR ($CDCl_3$) δ 8.06-7.93 (m, 2 H), 7.49-7.29 (m, 5 H), 4.33 (t, J=5.3 Hz, 2 H), 2.75 (t, J=6.4 Hz, 2 H), 2.09-1.83 (m, 2 H); ^{13}C NMR ($CDCl_3$) δ 160.9, 154.4, 139.1, 132.3, 128.4, 128.2, 126.6, 115.6, 113.4, 67.0, 24.6, 21.9.

Anal. Calcd for $C_{14}H_{13}NO$: C, 79.60; H, 6.20; N, 6.63; Found: C, 79.48; H, 6.27; N, 6.38.

7-(4-Chlorophenyl)-2,3-dihydropyrano[2,3-b]pyridine (7d). Compound (6d) was heated in refluxing bromobenzene (156 °C) for 48 h. The reaction solution was chromatographed (elution with 1:1 methylene chloride/hexanes) to afford (7d) (68%) as a white, crystalline solid: mp 147.0-148.5 °C; IR (KBr) 1590, 1580, 1560, 1490, 1470, 1450, 1415 cm^{-1}; ^1H NMR ($CDCl_3$) δ 7.98-7.85 (m, 2 H), 7.46-7.28 (m, 4 H), 4.37 (t, J=5.3 Hz, 2 H), 2.81 (t, J=6.6 Hz, 2 H), 2.15-1.92 (m, 2 H); ^{13}C NMR ($CDCl_3$) δ 161.0, 153.0, 139.2, 137.3, 134.6, 128.5, 127.9, 116.1, 113.2, 67.2, 24.7, 21.9.

Anal. Calcd for $C_{14}H_{12}ClNO$: C, 68.44; H, 4.92; Cl, 14.43; N, 5.70; Found: 68.67; H, 5.04; Cl, 14.67; N, 5.51.

2,3-Dihydrophenanthro[9,10-e]pyrano[2,3-b]pyridine (7e). Compound (6e) was heated at 200 °C in triisopropylbenzene for 22 h. The reaction solution was chromatographed (elution first with 1:3 methylene chloride/hexanes (to remove triisopropylbenzene) and then with methylene chloride) to yield (7e) (20%) as a pale yellow, crystalline solid: mp 157.0-159.0 °C; IR (KBr) 1615, 1610, 1575, 1535, 1480, 1430, 1410 cm^{-1}; ^1H NMR ($CDCl_3$) δ 9.22-9.10 (m, 1 H), 8.56-8.42 (m, 2 H), 8.32 (s, 1 H), 8.28-8.20 (m, 1 H), 7.72-7.56 (m, 2 H), 7.56-7.40 (m, 2 H), 4.41 (t, J=5.2 Hz, 2 H), 2.90 (t, J=6.4 Hz, 2 H), 2.07-1.99 (m, 2 H); ^{13}C NMR ($CDCl_3$) δ 159.9, 144.0, 133.5, 131.2, 130.2, 128.6, 128.3, 127.0, 126.5, 125.4, 123.2, 122.4, 122.4, 119.8, 117.6, 67.6, 25.4, 22.0.

Anal. Calcd for $C_{20}H_{15}NO$: C, 84.14; H, 5.30; N, 4.91; Found: C, 83.93; H, 5.21; N, 4.69.

General Procedure for the Bromination of 2,3-Dihydrofuro[2,3-b]pyridines (4), 2,3-Dihydropyrano[2,3-b]pyridines (7), and 2,3-Dihydropyrrolo[2,3-b]pyridines (9). To a stirred mixture of the 2,3-dihydrofuro[2,3-b]pyridine (4), 2,3-dihydropyrano[2,3-b]pyridine (7), or 2,3-

dihydropyrrolo[2,3-b]pyridine (9) (1.00 mmol) and sodium bicarbonate (0.21 g, 2.50 mmol, 2.5 eq) in absolute methanol (5 mL) at r.t., bromine (0.055 ml, 1.07 mmol, 1.1 eq) was added dropwise. The bromine was quickly absorbed in an exothermic reaction. The resulting reaction mixture was stirred at r.t. with exclusion of moisture for 1 h. A saturated solution of sodium bicarbonate (10 mL) was then added, and the solution was extracted with methylene chloride (3 x 10 mL). The methylene chloride extracts were combined, dried ($MgSO_4$), and evaporated under reduced pressure. The residual oil or solid was purified via silica gel (approx 30 g) chromatography, eluting with the appropriate solvent system, to yield the desired 5-bromo-2,3-dihydrofuro[2,3-b]pyridine (15), 6-bromo-2,3-dihydropyrano[2,3-b]pyridine (16), or 5-bromo-2,3-dihydropyrrolo[2,3-b]pyridine (17).

5-Bromo-6-(4-chlorophenyl)-2,3-dihydrofuro[2,3-b]pyridine (15d). The residual solid was chromatographed (elution with methylene chloride) to yield (15d) (93%) as a white, cyrstalline solid: mp 108.0-111.0 °C; IR (KBr) 1605, 1595, 1575, 1560, 1490, 1475, 1440, 1425-1390 cm^{-1}; ^1H NMR ($CDCl_3$) δ 7.67 (s, 1 H), 7.61 (d, J=8.4 Hz, 2 H), 7.37 (d, J=8.4 Hz, 2 H), 4.66 (t, J=8.6 Hz, 2 H), 3.26 (t, J=8.6 Hz, 2 H); ^{13}C NMR ($CDCl_3$) δ 167.7, 153.7, 138.4, 138.1, 134.6, 130.9, 127.9, 121.0, 109.8, 69.7, 27.8.

Anal. Calcd for $C_{13}H_9BrClNO$: C, 50.27; H, 2.92; Br, 25.73; Cl, 11.42; N, 4.51; Found: C, 50.31; H, 2.97; Br, 26.00; Cl, 11.57; N, 4.45.

6-Bromo-2,3-dihydropyrano[2,3-b]pyridine (16a). The residual oil was chromatographed on a preparative tlc plate (20x20 cm, 1500 micron; elution with ethyl acetate) to yield (16a) (26% ; 61% based on recovered starting material) as a clear, pale yellow liquid; IR (neat) 1560, 1470, 1445, 1425, 1405 cm^{-1}; ^1H NMR ($CDCl_3$) δ 8.10 (br d, 1 H), 7.49 (d, J=2.4 Hz, 1 H), 4.34 (t, J=5.3 Hz, 2 H), 2.80 (t, J=6.2 Hz, 2 H), 2.12-1.87 (m, 2 H); HRMS Calcd for C_8H_8BrNO: 212.9780; Found 212.9780 +/- 0.0030.

6-Bromo-7-(4-chlorophenyl)-2,3-dihydropyrano[2,3-b]pyridine (16d). The residual solid was chromatographed (elution with 1:1 methylene chloride/hexanes) to yield (16d) (84%) as a white, fluffy solid: mp 126.0-128.0 °C; IR (KBr) 1590, 1570, 1545, 1490, 1470, 1445, 1420 cm^{-1}; ^1H NMR ($CDCl_3$) δ 7.69-7.60 (m, 2 H), 7.63 (s, 1 H), 7.41-7.31 (m, 2 H), 4.35 (t, J=5.3 Hz, 2 H), 2.81 (t, J=6.6 Hz, 2 H), 2.14-1.88 (m, 2 H); ^{13}C NMR ($CDCl_3$) δ 159.8, 153.1, 143.2, 137.6, 134.5, 130.8, 127.9, 118.1, 109.7, 67.4, 24.4, 21.5.

Anal. Calcd for $C_{14}H_{11}BrClNO$: C, 51.80; H, 3.42; Br, 24.62; Cl, 10.92; N, 4.31; Found: C, 51.57; H, 3.55; Br, 24.79; Cl, 11.11; N, 4.34.

5-Bromo-2,3-dihydropyrrolo[2,3-b]pyridine (17a). The residual reaction solid was purified by preparative tlc (20x20 cm plate, 1500 micron thickness, elution with 1:1 methylene chloride/ethyl acetate) to yield (17a) (40%) as a white solid: mp 182.0-184.0 °C (dec); IR (KBr) 1620, 1575, 1500, 1480, 1420 cm^{-1}; ^1H NMR ($CDCl_3$) δ 7.83 (s, 1 H), 7.30 (s, 1 H), 4.58 (bs, 1 H), 3.64 (t, J=8.3 Hz, 2 H), 3.06 (t, J=8.6 Hz, 2 H).

Anal. Calcd for $C_7H_7BrN_2$: C, 42.24; H, 3.55; N, 14.07; Br, 40.14; Found: C, 41.99; H, 3.60; N, 13.82; Br, 40.36.

5-Bromo-6-(4-chlorophenyl)-2,3-dihydropyrrolo[2,3-b]pyridine (17d). The residual reaction solid was purified by preparative tlc (20x20 cm plate, 1500 micron thickness, elution with 1:1 hexanes/ethyl acetate) to yield (17d) (75%) as a white solid: mp 212.0-214.0 °C (dec); IR (KBr) 1615, 1590, 1550, 1410 cm^{-1}; ^1H NMR ($CDCl_3$) δ 7.53 (d, J=8.7 Hz, 2 H), 7.45 (s, 1 H), 7.38 (d, J=8.4 Hz, 2 H), 4.80 (s, 1 H), 3.65 (t, J=8.3 Hz, 2 H), 3.11 (t, J=8.2 Hz, 2 H).

Anal. Calcd for $C_{13}H_{10}BrClN_2$: C, 50.43; H, 3.26; N, 9.05; Br, 25.81; Cl, 11.45; Found: C, 50.18; H, 3.17; N, 8.97; Br, 25.67; Cl, 11.57.

3-Butynyl-1-methanesulfonate (12). A stirred solution of 3-butyn-1-ol (25.00 g, 0.357 mol) and triethylamine (38.26 g, 0.378 mol) in anhydrous ether (400 mL) at 0 °C under nitrogen was treated slowly with methanesulfonyl chloride (42.90 g, 0.375 mol). After 4 h, water (100 mL) was added to the reaction mixture. The organic layer was separated and washed with water (60 mL), dried ($MgSO_4$), and evaporated under reduced pressure to afford 51.91 g (98%) of 3-butynyl-1-methanesulfonate (12) as a deep golden oil; IR (neat) 3280, 1710, 1415, 1350 cm^{-1}; ^1H NMR ($CDCl_3$) δ 4.30 (t, J=6.6 Hz, 2 H), 3.07 (s, 3 H), 2.70 (dt, J=6.4 and 2.4 Hz, 2 H), 2.12 (t, J=2.6 Hz, 1 H).

The spectral and physical properties of this oil were identical with those reported.[19]

4-Amino-1-butyne (14). A stirred suspension of (12) (104.03 g, 0.703 mol) and sodium azide (120.90 g, 1.86 mol) in anhydrous DMF (500 mL) under nitrogen was heated to no greater than 67 °C for 3.5 h. The reaction mixture was then cooled to r.t. and water (200 mL) was added to bring excess sodium azide into solution. The mixture was then extracted with ether (2 x 200 mL). The ether extracts were combined, washed with water (2 x 200 mL), and dried ($MgSO_4$). To this ethereal solution of 4-azido-1-butyne (13) at 0 °C was added triphenylphosphine (184.37

g, 0.703 mol) all at once. Effervescence commenced immediately. After 1.5 h, water (50 mL) was added to the reaction mixture to hydrolyze the intermediate phosphinimine. Triphenylphosphine oxide precipitated from the mixture at once. After 15 h, the mixture was vacuum filtered and washed with cold n-pentane. The filtrate was evaporated under reduced pressure to a volume of 100 mL and then distilled at atmospheric pressure to afford 18.73 g (39%) of (14) as a clear liquid, bp 94-95 °C (lit[10] bp 99 °C); IR (neat) 3370, 3300, 2120, 1600, 1515, 1495, 1450, 1425, 1380 cm^{-1}; ^1H NMR ($CDCl_3$) δ 2.83 (t, J=6.2 Hz, 2 H), 2.35 (dt, J=5.5 and 2.6 Hz, 2 H), 2.06 (t, J=2.3 Hz, 1 H), 1.66 (bs, 2 H).

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