The enantiomeric excess was >97% as measured by ^{1}H NMR of the urea derivative (mp 111–112 °C) formed from (*R*)-(+)-α-methylbenzyl isocyanate. This material was authenticated with the pure urea diastereoisomer originally isolated from the racemic amine.

Resolution of (±)-6b with (−)-Dibenzoyl-L-tartaric Acid. To the free amine **6b** (27.53 g, 0.193 mol) dissolved in methanol (60 mL) was added a solution of (−)-dibenzoyl-L-tartaric acid monohydrate (36.31 g, 0.096 mol) and methanol (50 mL). A colorless precipitate formed immediately. The mixture was stirred for 20 min, and the solid was collected by filtration. After four recrystallizations from methanol, 33.9 g (68%) of the pure dibenzoyl tartrate salt was obtained as colorless needles, mp 196–198 °C. The ^{1}H NMR spectrum of the urea derivative, formed from (*R*)-(+)-α-methylbenzyl isocyanate and the free amine from the dibenzoyltartrate salt, was used to determine the enantiomeric excess which was >97%.

Methyl (+)-3-(Benzoylamino)-4(*E*)-hexenoate [(+)-6c]. The amine was liberated from the salt with sodium carbonate and then reacted with benzoyl chloride and pyridine to give the *N*-benzoyl derivative **6c**. Crystallization from benzene–hexanes gave 3.21 g (83%) of pure **6c**: mp 89 °C; $[\alpha]^{23}_D$ +5.4° (*c* 10, methanol).

(+)-*lyxo*-3-(Benzoylamino)-2,3,6-trideoxyhexanoic Acid γ-Lactone (7a) and (−)-*xylo*-3-(Benzoylamino)-2,3,6-trideoxyhexanoic Acid γ-Lactone (8a). The optically active olefinic benzoate was hydroxylated in a manner analogous to that employed for the racemic compound. From **6c** (3.10 g, 12.5 mmol) there was obtained 1.70 g (55%) of the optically active *lyxo* lactone **7a** and 1.14 g (37%) of the optically active *xylo* lactone **8a**. Recrystallization (ethyl acetate–hexanes) gave colorless needles of *lyxo*-**7a**: mp 147 °C; $[\alpha]^{23}_D$ −16° (c 1, methanol). Recrystallization (ethyl acetate–hexanes) of *xylo*-**8a** gave colorless crystals: mp 170–173 °C; $[\alpha]^{23}_D$ −76° (*c* 1, methanol).

(+)-*lyxo*-3-(Benzoylamino)-2,3,6-trideoxyhexanoic Acid γ-Lactone 5-Acetate (7b) and (−)-*xylo*-3-(Benzoylamino)-2,3,6-trideoxyhexanoic Acid γ-Lactone 5-Acetate (8b). The individual optically active lactones **7a** and **8a** were acetylated as previously described for the racemic compounds. Acetylation of the *lyxo* lactone **7a** (1.29 g, 5.18 mmol) furnished 1.39 g (92%) of pure **7b**: mp 127–129 °C; $[\alpha]^{26}_D$ −8° (*c* 1, methanol). Acetylation of the *xylo* lactone **8a** (850 mg, 3.39 mmol) gave 0.94 g (95%) of pure **8b**: mp 160–162 °C; $[\alpha]^{26}_D$ −118° (*c* 1, methanol).

(+)-*lyxo*-3-(Benzoylamino)-2,3,6-trideoxyfuranohexose 5-Acetate (9). The chiral acetoxy lactone **7b** (1.25 g, 4.26 mmol) was reduced with DIBAL (12.78 mmol) in THF at −100 °C (ether–dry ice) as described for the racemic compound. Workup and chromatography (silica gel, 20 g, 2–4% MeOH–CH_2Cl_2) gave 730 mg (57%) of the acetoxy lactone **9**. Recrystallization from benzene–petroleum ether (30–65) gave colorless needles of **9**: mp 173–176 °C; $[\alpha]^{22}_D$ +30° (*c* 1, methanol).

L_s-(−)-*N*-Benzoyldaunosamine (L_s-1b). Ammonolysis of the lactol acetate **9** (320 mg, 1.09 mmol) in methanol at 0 °C for 2 h gave, after workup and recrystallization (acetone–hexanes), 244 mg (90%) of pure **1b** as colorless crystals: mp 151.5–153 °C (lit.[2] mp 154–156 °C; $[\alpha]^{26}_D$ −106° (ethanol) (lit.[2] $[\alpha]^{26}_D$ −107.5° (ethanol)). The TLC behavior and ^{1}H NMR spectrum were identical with those of an authentic sample. A mixture melting point determination was undepressed.

(−)-*xylo*-3-(Benzoylamino)-2,3,6-trideoxyfuranohexose 5-Acetate (10). Reduction of the *xylo* acetoxy lactone **8b** (680 mg, 231 mmol) was analogously performed to give 596 mg (78%) of **10**. A sample recrystallized from benzene–hexanes had the following properties: mp 168–170 °C; $[\alpha]^{26}_D$ −30° (*c* 1, methanol).

(+)-*xylo*-3-(Benzoylamino)-2,3,6-trideoxyhexanopyranose (11). Ammonolysis of the acetoxy lactone **10** (80 mg, 0.27 mmol) gave 60 mg (87%) of the benzamido hexose **11**. The recrystallized material (acetone–methanol–hexanes) had the following properties: mp 217–220 °C; $[\alpha]^{22}_D$ +84° (*c* 0.1, methanol).

Acknowledgment. We express our appreciation to Dr. S. Penco (Farmitalia, S.A.; Milan, Italy). This work was generously supported by the National Institutes of Health of the Department of Health, Education and Welfare (GM 26574).

Registry No. DL-**1b**, 75812-93-0; L-**1b**, 51996-44-2; **3**, 2004-70-8; **4**, 1189-71-5; (±)-**5**, 75812-84-9; (±)-**6a**, 75812-85-0; (±)-**6b**, 89889-13-4; (*S*)-**6b**·(−)-dibenzoyl-L-tartrate, 89921-33-5; (±)-**6c**, 89921-31-3; (+)-**6c**, 75812-86-1; DL-**7a**, 75812-87-2; L-**7a**, 82266-95-3; DL-**7b**, 75812-88-3; L-**7b**, 89889-15-6; DL-**8a**, 75812-90-7; DL-**8b**, 75812-91-8; D-**8b**, 89889-16-7; DL-**9**, 75812-89-4; L-**9**, 89889-17-8; DL-**10**, 75812-92-9; D-**10**, 89889-18-9; DL-**11**, 75812-94-1; D-**11**, 89889-19-0; (*R*)-**12**, 33375-06-3; (*SR*)-**13**, 89889-14-5; (*RR*)-**13**, 89908-11-2; D-**18a**, 75712-55-9; *p*-bromotartranilic acid, 17447-36-8; (−)-dibenzoyl-L-tartaric acid, 2743-38-6.

Intramolecular Diels–Alder Reactions of 1,2-Diazines: General Indoline Synthesis. Studies on the Preparation of the Central and Right-Hand Segments of CC-1065

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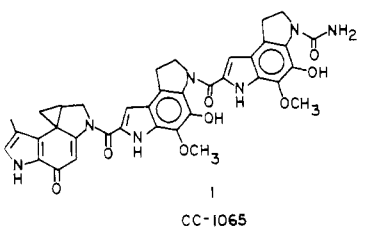
An investigation of the intramolecular Diels–Alder reaction of 1,2-diazines and the application of this cycloaddition to a general synthesis of indolines is described. The use of this cycloaddition in a short, regiospecific preparation of the 1,2-dihydro-3*H*-pyrrolo[3,2-*e*]indole skeleton, the structural subunit characteristic of the antitumor antibiotic CC-1065, is detailed.

CC-1065, an antitumor antibiotic[2-4] isolated from *Streptomyces zelensis*[3] and identified by X-ray crystallography,[4] is the most potent antitumor agent isolated to date. Preliminary studies indicate that CC-1065 binds



1
CC-1065

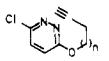
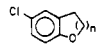
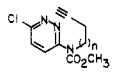
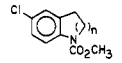
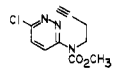
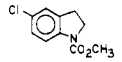
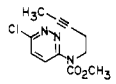
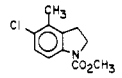
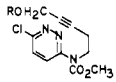
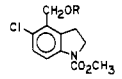
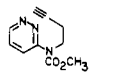
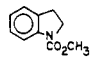
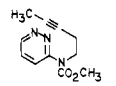
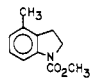
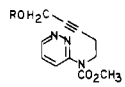
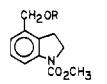
(1) (a) Searle Scholar Recipient, 1981–1984. National Institutes of Health Career Development Award Recipient, 1983–1988 (CA 00898). (b) National Institutes of Health Predoctoral Fellow, 1983–present (GM 07775).

(2) Martin, D. G.; Hanka, L. J.; Neil, G. L. *Proc. Am. Assoc. Cancer Res.* **1978**, *19*, 99.

(3) (a) Hanka, L. J.; Dietz, A.; Gerpheide, S. A.; Kuentzel, S. L.; Martin, D. G. *J. Antibiot.* **1978**, *31*, 1211. (b) Martin, D. G.; Biles, C.; Gerpheide, S. A.; Hanka, L. J.; Krueger, W. C.; McGovren, J. P.; Mizsak, S. A.; Neil, G. L.; Steward, J. C.; Visser, J. *Ibid.* **1981**, *34*, 1119.

0022-3263/84/1949-2240$01.50/0

Table I. Intramolecular Diels–Alder Reactions of Alkyne 1,2-Diazines

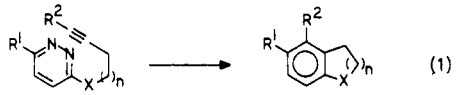
	1,2-diazine	conditions[a] temp, °C (time, h)	product[b]	yield[b]
3a–c		150–250 (6–24)		**9a**, n = 1, trace[c] **9b**, n = 2, 0% **9c**, n = 3, 0%
5b,c		150–250 (6–24)		**10b**, n = 2, 0% **10c**, n = 3, 0%
5a		200 (12) 230 (6) 230 (12)		**10a**, 64% (29%)[d] 82% (8%)[d] 91%
6a		200 (24) 230 (12) 230 (18)		**11a**, 17% (74%)[d] 62% (8%)[d] 85%
6d		230 (18)		**11d**, 72%, R = $SiMe_2$-t-Bu
8a		230 (12)		**12a**, 85%
8b		230 (6) 230 (12) 230 (18)		**12b**, 35% (60%)[d] 58% (37%)[d]- 77% (14%)[d]
8e		230 (18)		**12e**, 92%, R = $SiMe_2$-t-Bu

[a] All reactions were run in 1,3,5-triisopropylbenzene (TIPB, 0.1 M) under argon with exclusion of oxygen in sealed vessels. [b] All products exhibited the expected ^{1}H NMR, IR, and MS characteristics consistent with the assigned structure. Satisfactory C, H, N analysis or HRMS spectral information was obtained for each product. All yields are based on purified product isolated by chromatography (SiO_2). [c] Trace quantities of product could be isolated and the remainder of the material was recovered, unchanged 1,2-diazine. [d] The yield in parenthesis refers to recovered starting material.

to double-stranded DNA initially by a nonintercalative process[5] and subsequently forms a covalent linkage with DNA.[4a]

Herein we describe an investigation of the intramolecular Diels–Alder reaction of alkyne 1,2-diazines,[6] alkyne pyridazines, and the application of this cycloaddition to a general synthesis of substituted indolines including its use in a short, regiospecific preparation of the 1,2-dihydro-3*H*-pyrrolo[3,2-*e*]indole skeleton, the structural subunit characteristic of CC-1065.[7]

Table I details representative results of a study of the effects of the length of the alkyne side chain (n = 1, 2, 3), substitution (R^1 = H, Cl; R^2 = H, CH_3, CH_2OR), and heteroatom (X = O, NCO_2CH_3) on the intramolecular thermal cycloaddition of alkyne 1,2-diazines (eq 1). The



(1)

results of this study suggest that 1,2-diazine substitution ($R^1 \neq$ H) has little effect on the rate of cycloaddition, alkyne substitution ($R^2 \neq$ H) may noticeably slow the rate of [4 + 2] cycloaddition, and the appropriate choice of the length of the alkyne side chain (n = 1) and heteroatom (X = NCO_2CH_3) are the primary determinants in the success of the intramolecular Diels–Alder reaction of the alkyne 1,2-diazines. Unactivated 1,2-diazines do not participate in intermolecular [4 + 2] cycloaddition reactions with unactivated dienophiles[6] and it is the entropic assistance provided by the intramolecular Diels–Alder reaction which accounts for the success of the examples listed in Table I. 1,3,5-Triisopropylbenzene (TIPB, bp 232–236 °C)[8a] proved to be the most satisfactory solvent for the high-temperature Diels–Alder reactions (200–230 °C) listed in Table I and attempts to carry out the reactions at concentrations greater than 0.1 M in substrate resulted in diminished yields of product.[8b]

The preparation of the alkyne 1,2-diazines used in this study is detailed in Scheme I and, with the exception of **3a–c**, relied on the Mitsunobu alkylation[9] of the readily

(4) (a) Chidester, C. G.; Krueger, W. C.; Mizsak, S. A.; Duchamp, D. J.; Martin, D. G. *J. Am. Chem. Soc.* **1981**, *103*, 7629. (b) Martin, D. G.; Chidester, C. G.; Duchamp, D. J.; Mizsak, S. A. *J. Antibiot.* **1980**, *33*, 902.

(5) Baguley, B. C. *Mol. Cell. Biochem.* **1982**, *43*, 167.

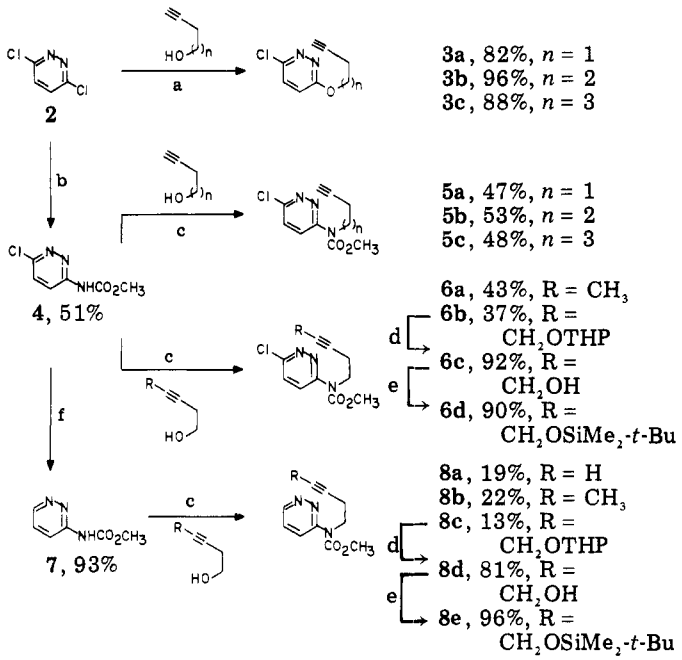
(6) (a) For prior examples of 1,2-diazines participating as the diene component in intramolecular Diels–Alder reactions, see: Jojima, T.; Takeshiba, H.; Konotsune, T. *Chem. Pharm. Bull.* **1972**, *20*, 2191. Jojima, T.; Takeshiba, H.; Kinoto, T. *Ibid.* **1976**, *24*, 1581, 1588; *Ibid.* **1980**, *28*, 198. (b) For a summary of the Diels–Alder reactions of 1,2-diazines, see: Boger, D. L. *Tetrahedron* **1983**, *39*, 2869.

(7) Synthetic studies on CC-1065: (a) Preparation of the left-hand segment of CC-1065: Wierenga, W. *J. Am. Chem. Soc.* **1981**, *103*, 5621. Wierenga, W.; Griffin, J.; Warpehoski, M. A. *Tetrahedron Lett.* **1983**, *24*, 2437. (b) Preparation of the central and right-hand segment of CC-1065: Komoto, N.; Enomoto, Y.; Miyagaki, M.; Tanaka, Y.; Nitanai, K.; Umezawa, H. *Agric. Biol. Chem.* **1979**, *43*, 555. Komoto, N.; Enomoto, Y.; Tanaka, Y.; Nitanai, K.; Umezawa, H. *Ibid.* **1979**, *43*, 559. (c) Studies on the preparation of the monomer units of CC-1065: Magnus, P.; Or, Y.-S. *J. Chem. Soc., Chem. Commun.* **1983**, 26. Kraus, G. A.; Yue, S. *Ibid.* **1983**, 1198. Sundberg, R. J.; Nishiguchi, T. *Tetrahedron Lett.* **1983**, *24*, 4773. (d) Derivatives of the identical central and right-hand segments of CC-1065 have been previously isolated and characterized as phosphodiesterase inhibitors-I and -II (PDE-I and PDE-II), inhibitors of 3′,5′-cAMP phosphodiesterase: Enomoto, Y.; Furutani, Y.; Naganawa, H.; Hamada, M.; Takeuchi, T.; Umezawa, H. *Agric. Biol. Chem.* **1978**, *42*, 1331. Nakamura, H.; Enomoto, Y.; Takeuchi, T.; Umezawa, H.; Iitaka, Y. *Ibid.* **1978**, *42*, 1337.

(8) (a) Available from Aldrich Chemical Company. (b) Cyclization of **6b** (200 °C, 1 h) was unsuccessful resulting in acetal cleavage to afford **6c**. Diels–Alder reaction of **6c** was precluded by its insolubility in TIPB. Careful exclusion of oxygen from the reaction vessel and the use of carefully purified alkyne 1,2-diazine noticeably affected the mass recovery and appearance of the Diels–Alder reactions.

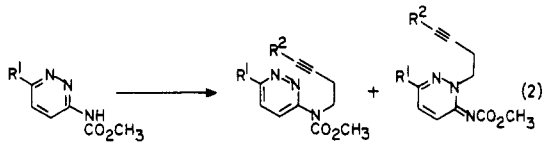
(9) Mitsunobu, O.; Wada, M.; Sano, T. *J. Am. Chem. Soc.* **1972**, *94*, 679.

Scheme I[a]



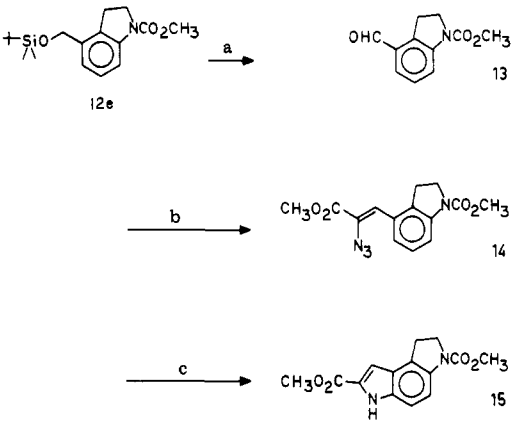
[a] a, NaH, THF, 25 °C; b, concentrated NH_4OH,[12] then $ClCO_2Me$, THF, K_2CO_3, 25 °C; c, Ph_3P, DEAD,[9] THF, 25 °C; d, PPTS,[13] EtOH; e, $ClSiMe_2$-*t*-Bu, imidazole, DMF;[14] f, H_2, Pd/C, EtOH.[15]

available *N*-carbomethoxy-3-amino-1,2-diazines.[10] Attempts to use other methods of direct N-alkylation were unsuccessful.[11] In each case, N-alkylation under the Mitsunobu conditions proceeded to give a 2:1 to 1:2 mixture of desired product **5**, **6**, or **8** and the corresponding pyridazine N-alkylation product (eq 2). Similar observations have been described previously.[10] The low yields recorded in Scheme I for **8a–c** reflect the difficulty in separating these two types of alkylation products and are not representative of the true conversion.



The implementation of this work in a short, regiospecific preparation of the 1,2-dihydro-3*H*-pyrrolo[3,2-*e*]indole skeleton characteristic of the central and right-hand segments of CC-1065 is detailed in Scheme II. Deprotection[14] of **12e** followed by mild oxidation afforded *N*-carbomethoxyindoline-4-carboxaldehyde (**13**), a key intermediate in a number of synthetic approaches to the ergot alkaloids.[16]

Scheme II[a]



[a] a, $(n\text{-Bu})_4NF$, THF, then MnO_2, CH_2Cl_2, 91%; b, $NaOCH_3$, CH_3OH, $N_3CH_2CO_2CH_3$, −23 to 0 °C; c, 140 °C, xylene, 30 min, 52% from **13**.

Condensation of methyl azidoacetate[17b] with **13** followed by mild thermolysis[17] afforded **15**.

Application of this work in the preparation of the monomer units of CC-1065 is in progress.

Experimental Section

Proton nuclear magnetic resonance spectra (^1H NMR) and carbon nuclear magnetic resonance spectra (^{13}C NMR) were recorded on a Varian FT-80A spectrometer and chemical shifts are reported in parts per million (ppm) relative to internal tetramethylsilane (0.00 ppm). Infrared spectra (IR) were recorded on an IBM FTIR 32 as KBr pellets (for solids) or thin films (liquids). Melting points were determined on a Thomas-Hoover capillary melting point apparatus and are uncorrected. Electron-impact mass spectra (EIMS), chemical-ionization mass spectra (CIMS), and high-resolution mass spectra (HRMS) were recorded on a Varian CH-5 or Ribermag R10-10 spectrometer by Charles Judson and Robert Drake. Microanalyses were performed by Tho I. Nguyen on a Hewlett-Packard Model 185 CHN analyzer at the University of Kansas. Medium-pressure liquid chromatography (MPLC) was performed on Merck silica gel 60 (230–400 mesh).[18] Preparative centrifugal thin-layer chromatography (PCTLC)[19] was performed on a Harrison Model 7924 Chromatotron (Harrison Research, Palo Alto, CA) using Merck silica gel 60 PF_{254} containing $CaSO_4 \cdot {}^1/_2H_2O$ binder. Dry solvents were distilled under nitrogen and stored over activated 3-Å molecular sieves (300–325 °C, 24 h). Tetrahydrofuran (THF) was distilled from sodium benzophenone ketyl. Ethanol (EtOH) and methanol (MeOH) were distilled from magnesium turnings. *N,N*-Dimethylformamide (DMF) was distilled from calcium oxide. Xylene, benzene, and 1,3,5-triisopropylbenzene (TIPB) were distilled from calcium hydride. Methylene chloride (CH_2Cl_2) was distilled from phosphorus pentoxide. All extraction and chromatographic solvents, ethyl acetate (EtOAc), ether (Et_2O), hexane, pentane, methylene chloride, and chloroform ($CHCl_3$), were distilled before use. 3-Butynol,[20a] 4-pentyn-1-ol,[20b] 5-hexyn-1-ol,[20c] and 3-pentyn-1-ol[20b] were used as received from commercial sources.

All reactions requiring anhydrous conditions and/or an inert atmosphere were performed under a positive pressure of argon. All Diels–Alder reactions were performed in cleaned ($K_2S_2O_8$/H_2SO_4), dry 3-mL Kontes vials with Teflon-coated cap liners under argon unless otherwise noted and were heated in either a silicone

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(11) Efforts to alkylate derivatives of 3-chloro-6-amino-1,2-diazine (*N*-carbomethoxy and *N*-benzyl) under standard conditions (NaH, THF/DMF, 25 °C, 1–24 h) with simple alkylating agents including ethyl iodide proceeded uneventfully. Attempts to utilize homopropargylic alkylating agents (e.g., 3-pentynyl iodide, 3-pentynol tosylate) resulted only in consumption of the alkylating agent with no evidence of N-alkylation.

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oil bath (temperature ≤ 200 °C) or a sand bath (temperature > 200 °C). Reaction temperatures are uncorrected and were maintained to within ±5 °C of the stated temperatures.

Preparation of 6-(Alkynyloxy)-3-chloro-1,2-diazines. 6-(3-Butynyloxy)-3-chloro-1,2-diazine (3a). 3-Butyn-1-ol[20a] (0.99 g, 14.1 mmol) was added (5 min) to a slurry of sodium hydride (0.8 g of 50% oil dispersion, 16.7 mmol) in 10 mL of THF at 0 °C. The solution was stirred 10 min at 0 °C before 3,6-dichloro-1,2-diazine[20a] (**2**, 2.0 g, 13.4 mmol) was added and the resulting solution was allowed to warm to 25 °C. After 2 h at 25 °C, the reaction mixture was treated with 50 mL of aqueous saturated ammonium chloride and extracted with methylene chloride (100 mL). The organic phase was washed with water (50 mL), dried ($MgSO_4$), and concentrated in vacuo. Chromatography (SiO_2, 5 × 20 cm, 50% ether–pentane) afforded 2.0 g (2.45 g theory, 82%) of **3a**: mp 74–75 °C (hexane, white crystals); ^1H NMR ($CDCl_3$, ppm) 7.35 (d, 1 H, J = 9 Hz, H-4), 6.95 (d, 1 H, J = 9 Hz, H-5), 4.58 (t, 2 H, J = 7 Hz, OCH_2), 2.73 (td, 2 H, J = 7, 3 Hz, $CH_2C{\equiv}C$), 2.03 (t, 1 H, J = 3 Hz, $C{\equiv}CH$); IR (KBr) ν_{max} 3281, 3063, 2969, 1592, 1435, 1383, 1312, 1150, 1017, 704, 642 cm^{-1}; EIMS, m/e (relative intensity) 182/184 (M^+, 2/1), 147 (20), 130/132 (base/35), 119 (8), 102/104 (18/6).

Anal. Calcd for $C_8H_7N_2OCl$: C, 52.62; H, 3.86; N, 15.34. Found: C, 53.00; H, 4.20; N, 15.18.

3-Chloro-6-(4-pentynyloxy)-1,2-diazine (3b). When the procedure for the preparation of **3a** was followed, 4-pentyn-1-ol[20b] (1.2 g, 14.3 mmol), sodium hydride (0.8 g of 50% oil dispersion, 16.7 mmol), and **2** (2.0 g, 13.4 mmol) afforded 2.53 g (2.63 g theory, 96%) of **3b**: mp 71.5–73 °C (hexane, white crystals); ^1H NMR ($CDCl_3$, ppm) 7.35 (d, 1 H, J = 9 Hz, H-4), 6.90 (d, 1 H, J = 9 Hz, H-5), 4.58 (t, 2 H, J = 7 Hz, OCH_2), 2.5–1.7 (m, 5 H, $CH_2CH_2C{\equiv}CH$); IR (KBr) ν_{max} 3306, 3063, 2952, 1590, 1470, 1379, 1308, 1032, 841, 646 cm^{-1}; EIMS, m/e (relative intensity) 197/199 (M + 1, 2/1), 168/170 (16/6), 161 (28), 130/132 (45/18), 102/104 (12/4).

Anal. Calcd for $C_9H_9N_2OCl$: C, 54.97; H, 4.61; N, 14.25. Found: C, 54.80; H, 4.63; N, 14.30.

3-Chloro-6-(5-hexynyloxy)-1,2-diazine (3c). When the procedure for the preparation of **3a** was followed, 5-hexyn-1-ol[20c] (1.4 g, 14.3 mmol), sodium hydride (0.8 g of 50% oil dispersion, 16.7 mmol), and **2** (2.0 g, 13.4 mmol) afforded 2.48 g (2.8 g theory, 88%) of **3c**: mp 31–32.5 °C (hexane, white plates); ^1H NMR ($CDCl_3$, ppm) 7.35 (d, 1 H, J = 9 Hz, H-4), 6.90 (d, 1 H, J = 9 Hz, H-5), 4.50 (t, 2 H, J = 7 Hz, OCH_2), 2.4–1.5 (m, 7 H, $(CH_2)_3C{\equiv}C$); IR (KBr) ν_{max} 3303, 2953, 1588, 1428, 1383, 1304, 1138, 839, 700 cm^{-1}; EIMS, m/e (relative intensity) 211/213 (M + 1, 3/1), 181/183 (6/2), 131/133 (60/28), 130/132 (32/14), 102/104 (14/5), 79 (base).

Anal. Calcd for $C_{10}H_{11}N_2OCl$: C, 57.02; H, 5.26; N, 13.30. Found: C, 57.40; H, 5.30; N, 13.20.

6-(*N*-Carbomethoxyamino)-3-chloro-1,2-diazine (4). A mixture of 3,6-dichloro-1,2-diazine[20a] (**2**, 20 g, 0.134 mol) and 125 mL of concentrated ammonium hydroxide was warmed at 130 °C for 12 h in a sealed, stainless steel tube. The tube was cooled to 0 °C, the contents filtered, and the resulting solid washed with water. Drying in vacuo afforded 13.0 g (17.4 g theory, 75%) of 3-amino-6-chloro-1,2-diazine.[12] A slurry of 3-amino-6-chloro-1,2-diazine (13.0 g, 0.1 mol) and potassium carbonate (27 g, 0.2 mol) in 500 mL of THF was treated with methyl chloroformate (19 g, 0.2 mol) and the resulting mixture was stirred at room temperature for 18 h. The THF was removed in vacuo and the residue was partitioned between 500 mL of ethyl acetate and 500 mL of water. The aqueous phase was extracted with ethyl acetate (3 × 150 mL) and the combined organic extracts were dried (Na_2SO_4) and concentrated in vacuo. The yellow solid was triturated with 75 mL of methylene chloride and filtered to afford 11.5 g of **4** as a white, crystalline solid. The filtrate was evaporated in vacuo and the residue triturated with 25 mL of methylene chloride to afford an additional 1.3 g of **4**. The combined weight was 12.8 g (18.8 g theory, 68%) of **4**: mp 182–184 °C; ^1H NMR ($CDCl_3$, ppm) 8.28 (d, 1 H, J = 9 Hz, H-5), 8.2–7.8 (br s, 1 H, NH), 7.48 (d, 1 H, J = 9 Hz, H-4), 3.84 (s, 3 H, OCH_3); IR (KBr) ν_{max} 3200, 3006, 2957, 1798, 1723, 1603, 1536, 1412, 1256, 1142, 1111 cm^{-1}, EIMS, m/e (relative intensity) 187/189 (M^+, 61/21), 172/174 (8/3), 156/158 (14/5), 129/131 (81/26), 116/118 (16/6), 73/75 (base/34).

Anal. Calcd for $C_6H_6N_3O_2Cl$: C, 38.42; H, 3.22; N, 22.40. Found: C, 38.30; H, 3.37; N, 22.05.

General Procedure for the Preparation of 6-(*N*-Carbomethoxy-*N*-alkynylamino)-3-chloro-1,2-diazines.[9] 6-[*N*-Carbomethoxy-*N*-(3-butynyl)amino]-3-chloro-1,2-diazine (5a). A stirred solution of triphenylphosphine (7.5 g, 28.6 mmol, 1.2 equiv), 3-butyn-1-ol[20a] (2.0 g, 28.5 mmol, 1.2 equiv), and **4** (4.5 g, 24.0 mmol) in 50 mL of dry THF at 0–5 °C was treated dropwise (1 h) with a solution of diethyl azodicarboxylate (5.0 g, 28.7 mmol, 1.2 equiv) in 15 mL of dry THF. The resulting yellow solution was allowed to warm to 25 °C and was stirred for 24 h. The THF was removed in vacuo and the residue triturated with 30/20 mL (2×) of ether with filtration to remove dicarboethoxyhydrazine and triphenylphosphine oxide. MPLC (SiO_2, 15 × 1000 mm, 45% ether–hexane eluant) afforded 2.7 g (5.75 g theory, 47%) of **5a**: mp 82.5–84 °C (hexane, light yellow plates); ^1H NMR ($CDCl_3$, ppm) 8.05 (d, 1 H, J = 9 Hz, H-5), 7.37 (d, 1 H, J = 9 Hz, H-4), 4.30 (t, 2 H, J = 7 Hz, NCH_2), 3.85 (s, 3 H, OCH_3), 2.65 (td, 2 H, J = 7, 3 Hz, $CH_2C{\equiv}C$), 1.91 (t, 1 H, J = 3 Hz, $C{\equiv}CH$); IR (KBr) ν_{max} 3305, 3094, 1727, 1418, 1291, 1200, 1105, 1053, 639 cm^{-1}; EIMS, m/e (relative intensity) 240/242 (M + 1, 18/6), 204 (94), 187/189 (43/15), 156/158 (base/38), 144 (28), 129/131 (64/22).

Anal. Calcd for $C_{10}H_{10}N_3O_2Cl$: C, 50.12; H, 4.21; N, 17.53. Found: C, 50.30; H, 4.30; N, 17.60.

6-[*N*-Carbomethoxy-*N*-(4-pentynyl)amino]-3-chloro-1,2-diazine (5b): 53%; mp 61.5–62.5 °C (hexane, colorless needles); ^1H NMR ($CDCl_3$, ppm) 8.10 (d, 1 H, J = 9 Hz, H-5), 7.42 (d, 1 H, J = 9 Hz, H-4), 4.24 (t, 2 H, J = 7 Hz, NCH_2), 3.86 (s, 3 H, OCH_3), 2.4–1.7 (m, 5 H, $CH_2CH_2C{\equiv}CH$); IR (KBr) ν_{max} 3297, 2957, 1721, 1437, 1416, 1273, 1190, 1105, 839, 770 cm^{-1}; EIMS, m/e (relative intensity) 254/256 (M + 1, 12/4), 218 (12), 214/216 (18/6), 194/196 (base/34), 156/158 (46/22), 142/144 (42/16), 129/131 (24/11).

Anal. Calcd for $C_{11}H_{12}N_3O_2Cl$: C, 52.08; H, 4.77; N, 16.56. Found: C, 52.40; H, 4.93; N, 16.30.

6-[*N*-Carbomethoxy-*N*-(5-hexynyl)amino]-3-chloro-1,2-diazine (5c): 48%; mp 62.5–63.5 °C (hexane, white needles); ^1H NMR ($CDCl_3$, ppm) 8.08 (d, 1 H, J = 9 Hz, H-5), 7.41 (d, 1 H, J = 9 Hz, H-4), 4.17 (t, 2 H, J = 7 Hz, NCH_2), 3.86 (s, 3 H, OCH_3), 2.4–1.4 (m, 7 H, $(CH_2)_3C{\equiv}CH$); IR (KBr) ν_{max} 3299, 2953, 1721, 1439, 1416, 1266, 1177, 1154, 1107 cm^{-1}; EIMS, m/e (relative intensity) 268/270 (M + 1, 12/3), 208/210 (57/20), 156/158 (87/30), 142/144 (21/9), 129/131 (51/16).

Anal. Calcd for $C_{12}H_{14}N_3O_2Cl$: C, 53.84; H, 5.27; N, 15.70. Found: C, 53.68; H, 5.38; N, 15.60.

6-[*N*-Carbomethoxy-*N*-(3-pentynyl)amino]-3-chloro-1,2-diazine (6a): 43%; mp 74–75.5 °C (hexane, light yellow needles); ^1H NMR ($CDCl_3$, ppm) 8.07 (d, 1 H, J = 9 Hz, H-5), 7.42 (d, 1 H, J = 9 Hz, H-4), 4.27 (t, 2 H, J = 7 Hz, NCH_2), 3.85 (s, 3 H, OCH_3), 2.57 (m, 2 H, $CH_2C{\equiv}C$), 1.69 (t, 3 H, J = 2.5 Hz, CH_3); IR (KBr) ν_{max} 3145, 3097, 2954, 2919, 1727, 1420, 1291, 1200, 1105, 1053 cm^{-1}; EIMS, m/e (relative intensity) 254/256 (M + 1, 10/3), 238/240 (10/3), 226/228 (8/3), 218 (base), 194/196 (12/4), 187/189 (25/10), 156/158 (89/41), 129/131 (49/19).

Anal. Calcd for $C_{11}H_{12}N_3O_2Cl$: C, 52.08; H, 4.77; N, 16.56. Found: C, 51.91; H, 5.00; N, 16.30.

6-[*N*-Carbomethoxy-*N*-[5-(tetrahydro-2-pyranyloxy)-3-pentynyl]amino]-3-chloro-1,2-diazine (6b). As described in the procedure for the preparation of **5a**, a solution of triphenylphosphine (1.68 g, 6.4 mmol, 1.2 equiv), 5-(tetrahydro-2-pyranyloxy)-3-pentyn-1-ol[21] (1.2 g, 6.4 mmol, 1.2 equiv), and **4** (1.0 g, 5.3 mmol) in 20 mL of dry THF was treated with diethyl azodicarboxylate (1.1 g, 6.4 mmol, 1.2 equiv). MPLC (SiO_2, 15 × 1000 mm, 40% ether–hexane eluant) afforded 695 mg (1.87 g theory, 37%) of **6b** as a white solid: mp 49–52 °C; ^1H NMR ($CDCl_3$, ppm) 8.08 (d, 1 H, J = 9 Hz, H-5), 7.41 (d, 1 H, J = 9 Hz, H-4), 4.71 (m, 1 H, OCHO), 4.31 (t, 2 H, J = 7 Hz, NCH_2), 4.17 (m, 2 H, $C{\equiv}CCH_2O$), 3.86 (s, 3 H, OCH_3), 3.7–3.4 (m, 2 H, CH_2CH_2O), 2.69 (tt, 2 H, J = 7, 2 Hz, $C{\equiv}CCH_2$), 1.8–1.5 (br m, 6 H, $(CH_2)_3$); IR (KBr) ν_{max} 3027, 2950, 1723, 1416, 1202, 1105, 1022 cm^{-1}; CIMS(NH_3) m/e (relative intensity) 354/356 (M + 1, 5/2), 270/272 (base/36), 253/255 (8/3), 218 (16), 156/158 (6/3), 85 (11).

6-[*N*-Carbomethoxy-*N*-(5-hydroxy-3-pentynyl)amino]-3-chloro-1,2-diazine (6c). Pyridinium *p*-toluenesulfonate[13] (35 mg, 0.14 mmol) was added to a solution of **6b** (300 mg, 0.85 mmol)

in 7.0 mL of dry ethanol and the reaction mixture was warmed at 55 °C under nitrogen for 3 h. Removal of the solvent in vacuo, chromatography (SiO_2, 5 × 70 mm plug, ethyl acetate eluant), and PCTLC (1 mm SiO_2, 50% ethyl acetate–hexane) afforded 211 mg (229 mg theory, 92%) of **6c** as a white solid: mp 65–66 °C; ^1H NMR ($CDCl_3$, ppm) 8.09 (d, 1 H, J = 9 Hz, H-5), 7.43 (d, 1 H, J = 9 Hz, H-4), 4.31 (t, 2 H, J = 7 Hz, NCH_2), 4.16 (br s, 2 H, CH_2O), 3.87 (s, 3 H, OCH_3), 2.69 (tt, 2 H, J = 7, 2 Hz, $CH_2C{\equiv}C$); IR (KBr) ν_{max} 3270, 3154, 2954, 1715, 1435, 1414, 1385, 1260, 1211, 1136 cm^{-1}; EIMS, m/e (relative intensity) 270/272 (M + 1, 2/1), 252/254 (42/13), 234 (59), 174 (30), 156/158 (base/40), 129/131 (47/17).

6-[*N*-Carbomethoxy-*N*-(5-((*tert*-butyldimethylsilyl)oxy)-3-pentynyl)amino]-3-chloro-1,2-diazine (6d). Compound **6c** (27 mg, 0.1 mmol) was added to a solution of *tert*-butyldimethylsilyl chloride (18 mg, 0.12 mmol) and imidazole (17 mg, 0.25 mmol) in 0.1 mL of dry DMF at 25 °C and the reaction solution was stirred at room temperature for 3 h. PCTLC (1 mm SiO_2, 30% ether–hexane) afforded 34 mg (38 mg theory, 90%) of **6d**: mp 89–90 °C (hexane, colorless plates); ^1H NMR ($CDCl_3$, ppm) 8.08 (d, 1 H, J = 9 Hz, H-5), 7.41 (d, 1 H, J = 9 Hz, H-4), 4.4–4.1 (m, 4 H, NCH_2 and $C{\equiv}CCH_2O$), 3.85 (s, 3 H, OCH_3), 2.67 (m, 2 H, $CH_2C{\equiv}C$), 0.89 (s, 9 H, $SiCMe_3$), 0.09 (s, 6 H, $SiMe_2$); IR (KBr) ν_{max} 3146, 3094, 2953, 2861, 1727, 1441, 1366, 1291, 1202, 1082, 837 cm^{-1}; CIMS (NH_3), m/e (relative intensity) 384/386 (M + 1, base/39), 326/328 (30/11), 292/294 (12/4), 252/254 (10/3), 156/158 (9/5), 109 (7), 106 (9); HRMS, m/e 383.1440; $C_{17}H_{26}N_3O_3SiCl$ requires 383.1430.

3-(*N*-Carbomethoxyamino)-1,2-diazine (7). A slurry of **4** (8.0 g, 42.6 mmol), sodium hydroxide (1.8 g, 45 mmol), and 10% Pd/C (1.0 g) in 200 mL of absolute ethanol was shaken under 3 atm of hydrogen until hydrogen absorption halted (ca 1 h).[15] The solution was filtered through Celite and the filtrate was concentrated in vacuo. Chromatography (SiO_2, 5 × 20 cm plug, ethyl acetate eluant) afforded 6.0 g (6.5 g theory, 93%) of **7** as a white, crystalline solid: mp 112.5–115 °C; ^1H NMR ($CDCl_3$, ppm) 8.90 (dd, 1 H, J = 5, 1.5 Hz, H-6), 8.6–8.2 (br, 1 H, NH), 8.28 (dd, 1 H, J = 9, 1.5 Hz, H-4), 7.47 (dd, 1 H, 9, 5 Hz, H-5), 3.84 (s, 3 H, OCH_3); IR (KBr) ν_{max} 3442, 3013, 2967, 1734, 1584, 1541, 1449, 1250, 1161, 1071 cm^{-1}; EIMS, m/e (relative intensity) 153 (M^+, 78), 138 (6), 122 (22), 95 (base).

General Procedure for the Preparation of 3-[*N*-Carbomethoxy-*N*-(3-alkynyl)amino]-1,2-diazines. 3-[*N*-Carbomethoxy-*N*-(3-butynyl)amino]-1,2-diazine (8a). As described in the procedure for the preparation of **5a**, a solution of triphenylphosphine (2.05 g, 7.8 mmol, 1.2 equiv), 3-butyn-1-ol[20a] (0.55 g, 7.8 mmol, 1.2 equiv), and **7** (1.0 g, 6.5 mmol) in 20 mL of dry THF was treated with diethyl azodicarboxylate (1.36 g, 7.8 mmol, 1.2 equiv). MPLC (SiO_2, 15 × 1000 mm, 40% ethyl acetate–hexane eluant) afforded a 1:2 mixture of **8a**:1,2-diazine N-alkylated material. These were partially separated by repetitive MPLC (3×, SiO_2, 15 × 1000 mm, 2% methanol–chloroform eluant) to afford 260 mg (1.34 g theory, 19%) of pure **8a** as a colorless solid: mp 59.5–60.5 °C (hexane, white needles); ^1H NMR ($CDCl_3$, ppm) 8.93 (dd, 1 H, J = 5, 1.5 Hz, H-6), 8.05 (dd, 1 H, J = 9, 1.5 Hz, H-4), 7.41 (dd, 1 H, J = 9, 5 Hz, H-5), 4.36 (t, 2 H, J = 7 Hz, NCH_2), 3.86 (s, 3 H, OCH_3), 2.69 (td, 2 H, J = 7, 3 Hz, $CH_2C{\equiv}C$); IR (KBr) ν_{max} 3254, 2960, 1719, 1582, 1439, 1406, 1213, 1196, 1073 cm^{-1}; EIMS, m/e (relative intensity) 205 (M^+, 19), 178 (9), 166 (9), 153 (51), 146 (50), 122 (base), 95 (49).

Anal. Calcd for $C_{10}H_{11}N_3O_2$: C, 58.53; H, 5.40; N, 20.48. Found: C, 58.89; H, 5.58; N, 20.80.

3-[*N*-Carbomethoxy-*N*-(3-pentynyl)amino]-1,2-diazine (8b): 22%; mp 54–55.5 °C (hexane, white needles); ^1H NMR ($CDCl_3$, ppm) 8.92 (dd, 1 H, J = 5, 1.5 Hz, H-6), 8.02 (dd, 1 H, J = 9, 1.5 Hz, H-4), 7.40 (dd, 1 H, J = 9, 5 Hz, H-5), 4.30 (t, 2 H, J = 7 Hz, NCH_2), 3.84 (s, 3 H, OCH_3), 2.62 (m, 2 H, $CH_2C{\equiv}C$), 1.69 (t, 3 H, J = 2.5 Hz, $C{\equiv}CCH_3$); IR (KBr) ν_{max} 2959, 2923, 1723, 1437, 1404, 1294, 1213, 1192 cm^{-1}; EIMS, m/e (relative intensity) 219 (M^+, 24), 204 (18), 192 (13), 160 (28), 153 (31), 132 (19), 122 (base), 95 (53).

Anal. Calcd for $C_{11}H_{13}N_3O_2$: C, 60.26; H, 5.98; N, 19.17. Found: C, 60.58; H, 6.04; N, 19.00.

3-[*N*-Carbomethoxy-*N*-(5-hydroxy-3-pentynyl)amino]-1,2-diazine (8d). As described in the procedure for the preparation of **8a**, a solution of triphenylphosphine (2.06 g, 7.85 mmol, 1.2 equiv), 5-(tetrahydro-2-pyranyloxy)-3-pentyn-1-ol[21] (1.2 g, 6.54 mmol, 1.0 equiv), and **7** (1.0 g, 6.54 mmol) in 15 mL of dry THF was treated with diethyl azodicarboxylate (1.38 g, 7.85 mmol, 1.2 equiv). MPLC (SiO_2, 15 × 1000 mm, 70% ethyl acetate–hexane eluant) and repetitive MPLC (3×, SiO_2, 15 × 1000 mm, 2% methanol–hexane eluant) afforded 260 mg (2.09 g theory, 13%) of **8c** as a light yellow oil.

A solution of **8c** (260 mg, 0.81 mmol) in 8 mL of absolute ethanol was treated with pyridinium *p*-toluenesulfonate[13] (50 mg, 0.2 mmol) and the resulting solution was warmed at 60 °C under nitrogen for 3 h. PCTLC (1 mm SiO_2, ether) afforded 154 mg (191 mg theory, 81%) of **8d**: ^1H NMR ($CDCl_3$, ppm) 8.92 (dd, 1 H, J = 5, 1.5 Hz, H-6), 8.04 (dd, 1 H, J = 9, 1.5 Hz, H-4), 7.41 (dd, 1 H, J = 9, 5 Hz, H-5), 4.35 (t, 2 H, J = 7 Hz, NCH_2), 4.2–4.0 (m, 2 H, $C{\equiv}CCH_2O$), 3.86 (s, 3 H, OCH_3), 2.71 (tt, 2 H, J = 7, 2 Hz, $C{\equiv}CCH_2$); IR (KBr) ν_{max} 3422, 3279, 2955, 1721, 1439, 1406, 1291, 1217, 1073 cm^{-1}; EIMS, m/e (relative intensity) 235 (M^+, 3), 218 (76), 204 (8), 193 (11), 166 (9), 158 (16), 153 (20), 122 (base).

3-[*N*-Carbomethoxy-*N*-(5-((*tert*-butyldimethylsilyl)oxy)-3-pentynyl)amino]-1,2-diazine (8e). A solution of *tert*-butyldimethylsilyl chloride (210 mg, 1.39 mmol, 1.2 equiv) and imidazole (200 mg, 2.95 mmol, 2.5 equiv) in 1 mL of dry DMF was added to **8d** (270 mg, 1.15 mmol) and the reaction mixture was stirred at 25 °C for 4 h. Ether (15 mL) was added and the solution was washed with water (2 × 10 mL), dried (K_2CO_3), and concentrated in vacuo. PCTLC (1 mm SiO_2, ether) afforded 385 mg (402 theory, 96%) of **8e** as a colorless oil: ^1H NMR ($CDCl_3$, ppm) 8.92 (dd, 1 H, J = 5, 1.5 Hz, H-6), 8.03 (dd, 1 H, J = 9, 1.5 Hz, H-4), 7.40 (dd, 1 H, J = 9, 5 Hz, H-5), 4.33 (t, 2 H, J = 7 Hz, NCH_2), 4.23 (t, 2 H, J = 2 Hz, $C{\equiv}CCH_2O$), 3.85 (s, 3 H, OCH_3), 2.69 (tt, 2 H, J = 7, 2 Hz, $C{\equiv}CCH_2$), 0.89 (s, 9 H, $SiCMe_3$), 0.09 (s, 6 H, $SiMe_2$); IR (film) ν_{max} 2955, 2930, 2857, 1723, 1439, 1377, 1252, 1211, 1072, 839 cm^{-1}; EIMS, m/e (relative intensity) 349 (M^+, 1), 334 (3), 292 (61), 260 (5), 234 (13), 218 (37), 158 (19), 122 (42), 109 (29), 89 (base); HRMS, m/e 349.1825; $C_{17}H_{27}N_3O_3Si$ requires 349.1820.

General Procedure for Alkyne 1,2-Diazine Diels–Alder Reactions. *N*-Carbomethoxy-5-chloroindoline (10a). Compound **5a** (49.5 mg, 0.206 mmol) was weighed into a dry 3-mL Kontes vial. The vial was evacuated and refilled with argon (3×) and 2.0 mL of argon-saturated 1,3,5-triisopropylbenzene (TIPB) was added with an argon-flushed syringe under an argon atmosphere. The reaction vial was sealed, warmed (ca. 100 °C) to affect solution and then warmed to 230 °C for 12 h. After the vessel was cooled to room temperature, the reaction mixture was placed on a silica gel column (5 × 70 mm, hexane), eluted with hexane to remove TIPB, and further eluted with ether to remove the reaction products. The ether effluent was concentrated in vacuo. PCTLC (1 mm SiO_2, 30% ether–hexane) afforded 39.8 mg (43.6 g theory, 91%) of **10a**: mp 100.5–101.5 °C (hexane, white needles); ^1H NMR ($CDCl_3$, ppm), 7.7–7.5 (br, 1 H, H-7), 7.2–6.95 (m, 2 H, H-4 and H-6), 4.03 (t, 2 H, J = 9 Hz, NCH_2), 3.83 (s, 3 H, OCH_3), 3.09 (t, 2 H, J = 9 Hz, $ArCH_2$); ^{13}C NMR ($CDCl_3$, ppm, multiplicity in SFORD ^{13}C NMR) 153.4 (s), 140.9 (s), 132.8 (s), 127.2 (d), 127.15 (s), 124.7 (d), 115.4 (d), 52.5 (q), 47.5 (t), 27.0 (t); IR (KBr) ν_{max} 3120, 2955, 1711, 1601, 1487, 1446, 1397, 1337, 1138, 1073, 833 cm^{-1}; EIMS, m/e (relative intensity) 211/213 (M^+, base/34), 166/168 (27/7), 152/154 (22/7), 131 (35), 117 (81), 89 (45).

Anal. Calcd for $C_{10}H_{10}NO_2Cl$: C, 56.75; H, 4.76; N, 6.62. Found: C, 57.10; H, 4.78; N, 6.40.

***N*-Carbomethoxy-5-chloro-4-methylindoline (11a).** A solution of **6a** (20.2 mg, 0.08 mmol) in 0.8 mL of TIPB was warmed at 230 °C for 18 h. PCTLC (1 mm SiO_2, 35% ether–hexane) afforded 15.3 mg (18.0 mg theory, 85%) of **11a**: mp 140–141 °C (hexane, white needles); ^1H NMR ($CDCl_3$, ppm) 7.7–7.4 (br, 1 H, H-7), 7.15 (d, 1 H, J = 8 Hz, H-6), 4.04 (t, 2 H, J = 9 Hz, NCH_2), 3.82 (s, 3 H, OCH_3), 3.03 (t, 2 H, J = 9 Hz, $ArCH_2$), 2.24 (s, 3 H, $ArCH_3$); IR (KBr) ν_{max} 2957, 1703, 1474, 1445, 1383, 1337, 1144 cm^{-1}; EIMS, m/e (relative intensity) 225/227 (M^+, base/34), 180/182 (11/4), 166/168 (15/5), 145 (26), 131 (72), 103 (19), 77 (32); HRMS, m/e 225.0557; $C_{11}H_{12}NO_2Cl$ requires 225.0556.

***N*-Carbomethoxy-5-chloro-4-(((*tert*-butyldimethylsilyl)oxy)methyl)indoline (11d).** A solution of **6d** (40.4 mg, 0.105

(21) Mimaki, K.; Masunari, M.; Nakaminami, G.; Nakagawa, M. *Bull. Chem. Soc. Jpn.* **1972**, *45*, 2620.

mmol) in 1.05 mL of TIPB was warmed at 230 °C for 18 h. PCTLC (1 mm SiO_2, 5–50% ether–hexane gradient) afforded 26.9 mg (37.4 mg theory, 72%) of **11d**: mp 84–85.5 °C (hexane, white needles); ^1H NMR ($CDCl_3$, ppm) 7.8–7.3 (br, 1 H, H-7), 7.15 (d, 1 H, J = 8 Hz, H-6), 4.79 (s, 2 H, $ArCH_2O$), 4.04 (t, 2 H, J = 9 Hz, NCH_2), 3.83 (s, 3 H, OCH_3), 3.22 (t, 2 H, J = 9 Hz, $ArCH_2$), 0.90 (s, 9 H, $SiCMe_3$), 0.09 (s, 6 H, $SiMe_2$); IR (KBr) ν_{max} 2957, 2857, 1703, 1474, 1387, 1146, 1065, 837 cm^{-1}; EIMS, m/e (relative intensity) 355/357 (M^+, 4/1.5), 298/300 (52/23), 222/224 (base/53), 188/190 (13/4), 164/166 (10/4), 144 (11), 130 (18).

Anal. Calcd for $C_{17}H_{26}NO_3ClSi$: C, 57.37; H, 7.36; N, 3.94. Found: C, 57.48; H, 7.55; N, 4.33.

***N*-Carbomethoxyindoline (12a).** A solution of **8a** (39.2 mg, 0.191 mmol) in 1.9 mL of TIPB was warmed at 230 °C for 12 h. PCTLC (1 mm SiO_2, 5–50% ether–hexane gradient) afforded 28.9 mg (33.8 theory, 85%) of **12a** as a yellow oil identical by ^1H NMR and IR with authentic material: mp 72.5–73.5 °C (hexane, white plates); ^1H NMR ($CDCl_3$, ppm) 7.9–7.6 (br, 1 H, H-7), 7.2–6.8 (m, 3 H, H-4, 5, and 6), 4.01 (t, 2 H, J = 9 Hz, NCH_2), 3.83 (s, 3 H, OCH_3), 3.10 (t, 2 H, J = 9 Hz, $ArCH_2$); IR (film) ν_{max} 2955, 1715, 1489, 1443, 1395, 1335, 1318, 1192, 1138 cm^{-1}; EIMS, m/e (relative intensity) 177 (M^+, base), 162 (11), 132 (33), 118 (62), 91 (75); HRMS, m/e 177.0780; $C_{10}H_{11}NO_2$ requires 177.0789.

***N*-Carbomethoxy-4-methylindoline (12b).** A solution of **8b** (37.6 mg, 0.17 mmol) in 1.7 mL of TIPB was warmed at 230 °C for 18 h. PCTLC (1 mm SiO_2, 5–50% ether–hexane gradient) afforded 5.1 mg of recovered **8b** (14%) and 25.3 mg (32.8 mg theory, 77%) of **12b**: mp 67.5–68.5 °C (hexane, light yellow needles); ^1H NMR ($CDCl_3$, ppm) 7.7–7.4 (br s, 1 H, H-7), 7.2–6.6 (m, 2 H, H-5 and 6), 4.02 (t, 2 H, J = 9 Hz, NCH_2), 3.82 (s, 3 H, OCH_3), 2.99 (t, 2 H, J = 9 Hz, $ArCH_2$), 2.21 (s, 3 H, $ArCH_3$); IR (KBr) ν_{max} 2957, 2919, 1709, 1487, 1474, 1395, 1316, 1136, 779 cm^{-1}; EIMS, m/e (relative intensity) 191 (M^+, base), 146 (26), 132 (66), 117 (56), 105 (31), 77 (50).

Anal. Calcd for $C_{11}H_{13}NO_2$: C, 69.09; H, 6.85; N, 7.32. Found: C, 68.97; H, 7.00; N, 7.50.

***N*-Carbomethoxy-4-(((*tert*-butyldimethylsilyl)oxy)-methyl)indoline (12e).** A solution of **8e** (257 mg, 0.735 mmol) in 10 mL of TIPB in a 20-mL resealable glass tube equipped with a threaded Teflon stopper was warmed at 230 °C for 18 h. PCTLC (1 mm SiO_2, 0–50% ether–hexane gradient) afforded 217 mg (236 mg theory, 92%) of **12e** as a white solid: mp 87–89 °C; ^1H NMR ($CDCl_3$, ppm) 7.7–7.5 (br, 1 H, H-7), 7.25–6.75 (m, 2 H, H-5 and H-6), 4.64 (s, 3 H, $ArCH_2O$), 4.03 (t, 2 H, J = 9 Hz, NCH_2), 3.83 (s, 3 H, OCH_3), 3.04 (t, 2 H, J = 9 Hz, $ArCH_2$), 0.93 (s, 9 H, $SiCMe_3$), 0.09 (s, 6 H, $SiMe_2$); IR (KBr) ν_{max} 2955, 2928, 2857, 1707, 1480, 1399, 1138, 1113, 857, 837, 777 cm^{-1}, EIMS, m/e (relative intensity) 321 (M^+, 7), 264 (28), 234 (7), 188 (base), 130 (25); HRMS, m/e 321.1759; $C_{17}H_{27}NO_3Si$ requires 321.1759.

***N*-Carbomethoxyindoline-4-carboxaldehyde (13).** A solution of **12e** (142 mg, 0.44 mmol) in 1.0 mL of THF was added to a solution of tetra-*n*-butylammonium fluoride (235 mg, 0.90 mmol, 2.0 equiv) in 1.2 mL of THF and the resulting solution was stirred at 25 °C for 40 min. The solvent was removed in vacuo and chromatography (SiO_2, 5 × 70 mm, ether eluant) afforded 83 mg (91 mg theory, 91%) of *N*-carbomethoxy-4-(hydroxymethyl)-indoline (**12d**)[22] as a white solid: ^1H NMR ($CDCl_3$, ppm) 7.7–7.4 (br, 1 H, H-7), 7.2–6.8 (m, 2 H, H-5 and H-6), 4.64 (br s, 2 H, $ArCH_2O$), 4.04 (t, 2 H, J = 9 Hz, NCH_2), 3.83 (s, 3 H, OCH_3), 3.12 (t, 2 H, J = 9 Hz, $ArCH_2$); IR (KBr) ν_{max} 3422, 3274, 2959, 1709, 1470, 1395, 1316, 1140, 760 cm^{-1}; EIMS, m/e (relative intensity) 207 (M^+, base), 189 (78), 174 (27), 144 (75), 130 (71), 118 (33).

Manganese dioxide (800 mg) was added to a solution of **12d** (82 mg, 0.4 mmol) in 6 mL of dry methylene chloride and the resulting slurry was stirred for 24 h at 25 °C. The reaction mixture was filtered through Celite, the solid washed well with THF, and the combined filtrate concentrated in vacuo to afford 81 mg (81 mg theory, 100%) of **13** as a white solid: mp 105–108 °C; ^1H NMR ($CDCl_3$, ppm) 10.07 (s, 1 H, CHO), 8.1–7.7 (br, 1 H, H-7), 7.35 (m, 2 H, H-5 and H-6), 3.99 (t, 2 H, J = 9 Hz, NCH_2), 3.85 (s, 3 H, OCH_3), 3.48 (t, 2 H, J = 9 Hz, $ArCH_2$); IR (KBr) ν_{max} 2959, 2748 (w), 2708 (w), 1692, 1470, 1395, 1321, 1138 cm^{-1}; EIMS, m/e (relative intensity) 205 (M^+, base), 188 (13), 176 (24), 144 (22), 118 (57), 91 (56); HRMS, m/e 205.0721; $C_{11}H_{11}NO_3$ requires 205.0739.

***N*-Carbomethoxy-5-carbomethoxypyrrolo[3,2-*e*]indoline (15).** A solution of **13** (30.3 mg, 0.147 mmol) and methyl azidoacetate[17a] (0.14 g, 1.2 mmol, 8 equiv) in 0.3 mL of dry benzene was added dropwise (15 min) to a solution of sodium methoxide (1.2 mmol, 8 equiv) in 0.75 mL of dry methanol cooled to −23 °C and the resulting solution was stirred at 0 °C (30 min). The reaction mixture was partitioned between 15 mL of ethyl acetate (0 °C) and 10 mL of water (0 °C). The aqueous layer was extracted with ethyl acetate (4 × 20 mL) and the combined organic extracts were dried (K_2CO_3). Concentration in vacuo afforded 36.7 mg (44.4 mg theory, 83%) of crude **14** as an unstable, white solid: ^1H NMR ($CDCl_3$, ppm) 7.9–7.5 (br m, 2 H, aromatic), 7.3–7.0 (m, 1 H, aromatic), 6.85 (s, 1 H, C=CH), 3.8–4.1 (m, 2 H, NCH_2), 3.91 (s, 3 H, CCO_2CH_3), 3.84 (s, 3 H, NCO_2CH_3), 3.16 (t, 2 H, J = 9 Hz, $ArCH_2$); IR (KBr) ν_{max} 2957, 2124, 1715, 1466, 1393, 1321, 1140, 1092 cm^{-1}; EIMS, m/e (relative intensity) 302 (M^+, 6), 274 (26), 242 (56), 215 (17), 188 (13), 183 (11), 169 (15), 155 (57), 130 (26).

A solution of **14** (34.5 mg, 0.114 mmol) in 10 mL of xylene was warmed at reflux for 30 min using a condenser open to the atmosphere. Removal of the xylene in vacuo and PCTLC (1 mm SiO_2, 10–30% ethyl acetate in hexane gradient) afforded 19.8 mg (31.3 mg theory, 52% from **13**) of **15**: ^1H NMR ($CDCl_3$, ppm) 8.9–8.7 (br, 1 H, NH), 8.2–7.7 (br, 1 H, H-7), 7.4–7.0 (m, 2 H, aromatic), 4.15 (t, 2 H, J = 9 Hz, NCH_2), 3.94 (s, 3 H, CCO_2CH_3), 3.85 (s, 3 H, NCO_2CH_3), 3.29 (t, 2 H, J = 9 Hz, $ArCH_2$); ^{13}C NMR (Me_2SO-d_6, ppm, multiplicity in SFORD ^{13}C NMR) 161.5 (s), 152.9 (s), 135.4 (s), 134.6 (s), 127.9 (s), 123.8 (s), 121.9 (s), 113.1 (d), 110.8 (d), 105.2 (d), 52.1 (q), 51.7 (q), 47.5 (t), 26.1 (t); IR (KBr) ν_{max} 3322, 2953, 1701, 1686, 1456, 1374, 1329, 1258 cm^{-1}; EIMS, m/e (relative intensity) 274 (M^+, 67), 242 (base), 183 (8), 155 (31), 128 (27), 101 (16); HRMS, m/e 274.0950; $C_{14}H_{14}N_2O_4$ requires 274.0953.

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Registry No. **1**, 69866-21-3; **2**, 141-30-0; **3a**, 89875-43-4; **3b**, 89875-18-3; **3c**, 89875-19-4; **4**, 89875-20-7; **5a**, 89875-21-8; **5b**, 89875-22-9; **5c**, 89875-23-0; **6a**, 89875-24-1; **6b**, 89875-25-2; **6c**, 89875-26-3; **6d**, 89875-27-4; **7**, 89875-28-5; **8a**, 89875-29-6; **8b**, 89875-30-9; **8c**, 89875-31-0; **8d**, 89875-32-1; **8e**, 89875-33-2; **10a**, 89875-34-3; **11a**, 89875-35-4; **11d**, 89875-36-5; **12a**, 89875-37-6; **12b**, 89875-38-7; **12d**, 89875-39-8; **12e**, 89875-40-1; **13**, 89875-41-2; **14**, 89875-42-3; **15**, 89889-12-3; $CH{\equiv}C(CH_2)_2OH$, 927-74-2; $CH{\equiv}C(CH_2)_3OH$, 5390-04-5; $CH{\equiv}C(CH_2)_4OH$, 928-90-5; ClC(O)OMe, 79-22-1; $CH_3C{\equiv}C(CH_2)_2OH$, 10229-10-4; $THPOCH_2C{\equiv}C(CH_2)OH$, 38996-32-6; $N_3CH_2C(O)OMe$, 1816-92-8; 3-amino-6-chloro-1,2-diazine, 5469-69-2.

(22) *N*-Carbomethoxy-4-(hydroxymethyl)indoline was also prepared from *N*-carbomethoxy-5-chloro-4-(((*tert*-butyldimethylsilyl)oxy)-methyl)indoline (**11d**) by the following sequence: (a) HOAc:H_2O:THF (3:1:1), 25 °C, 90%; (b) 1 atm H_2, 10% Pd/C, CH_3OH–NaOH, 25 °C, 97%.