(pentane) 1747 cm^{-1} (C=O); ^{1}H NMR ($CDCl_3$) 1.02 (d, J_{HH} = 6.8 Hz, 9 H, CH_3CHSi), 1.03 (d, J_{HH} = 7.1 Hz, 9 H, CH_3CHSi), 1.08 (d, J_{HH} = 6.6 Hz, 9 H, CH_3CHSi), 1.09 (d, J_{HH} = 6.9 Hz, 9 H, CH_3CHSi), 1.16–1.31 (m, 6 H, CHSi), 3.65 and 3.66 (s, 3 H, OCH_3), 4.30 (AB system, J_{HAHB} = 3.9 Hz, 2 H, CH ring); ^{13}C NMR ($CDCl_3$) 11.54, 12.09 (s, CH_3CHSi), 17.80, 17.95, 18.37 (s, CH_3CHSi), 51.77, 51.81 (s, OCH_3), 61.55 (s, CH_A), 63.92 (s, CH_B), 142.75 (s, C=N ring), 170.44, 172.30 (s, C=O); ^{29}Si NMR ($CDCl_3$) +0.11, +9.39; mass spectrum, m/e 498 (M^+). Anal. Calcd for $C_{25}H_{50}N_2O_4Si_2$: C, 60.19; H, 10.10; N, 5.62. Found: C, 60.40; H, 10.21; N, 5.55.

33 and 34. A stoichiometric amount of *n*-BuLi (1.6 M in hexane) was added dropwise to a solution of nitrilimine **10a** (0.92 g, 2 mmol) in dry THF at −78 °C. After the mixture was warmed to room temperature the lithium salt **33** was characterized in solution: IR (THF) 1605 cm^{-1} (C=N); ^{31}P NMR (THF) +75.42. After slow hydrolysis and purification on silica gel (hexane/ether, 95/5, R_f = 0.67) **34** was isolated as a pale yellow oil (0.65 g, 63% yield): IR (pentane) 1530 cm^{-1} (C=N); ^{31}P NMR ($CDCl_3$) +68.57; ^{1}H NMR ($CDCl_3$) 0.94 (t, J_{HH} = 7.2 Hz, 3 H, CH_2CH_3), 1.06 (d, J_{HH} = 6.9 Hz, 18 H, CH_3CHSi), 1.26 (d, J_{HH} = 6.8 Hz, 12 H, CH_3CHN), 1.33 (d, J_{HH} = 6.8 Hz, 12 H, CH_3CHN), 1.60 (m, 2 H, CH_2), 2.55 (m, 2 H, CH_2), 3.85 (d sept, J_{PH} = 15.0 Hz, J_{HH} = 6.8 Hz, 4 H, CHN), 5.64 (s, 1 H, NH), CHSi and a CH_2 group from Bu were not observed; ^{13}C NMR ($CDCl_3$) 11.34 (s, CH_3CHSi), 13.89 (s, $CH_3(CH_2)_3$), 18.13 (s, CH_3CHSi), 23.40 (s, CH_2), 24.07, 24.11, 24.16, 24.18 (s, CH_3CHN), 26.79 (d, J_{PC} = 27.4 Hz, $CH_3(CH_2)_2CH_2$), 27.40 (s, CH_2CN), 47.22 (d, J_{PC} = 5.4 Hz, CH_3CHN), 146.58 (d, J_{PC} = 155.3 Hz, C=N); ^{29}Si NMR ($CDCl_3$) +6.71; mass spectrum, m/e 518 (M^+). Anal. Calcd for $C_{26}H_{59}N_4PSSi$: C, 60.18; H, 11.46; N, 10.80. Found: C, 60.35; H, 11.40; N, 10.70.

Intramolecular Diels–Alder Reactions of 1,2,4-Triazines. Synthesis of 2,3-Cyclopentenopyridines and 5,6,7,8-Tetrahydroquinolines

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2,3-Cyclopentenopyridines and 5,6,7,8-tetrahydroquinolines are prepared by intramolecular Diels–Alder reactions of appropriately substituted 1,2,4-triazines. Two general routes to the requisite triazine precursors are described.

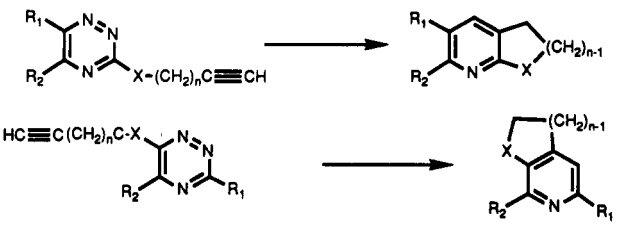
Introduction

Intramolecular inverse-electron-demand Diels–Alder reactions of 1,2,4-triazines constitute a versatile method for the preparation of a variety of functionalized, fused heterocycles.[2] Application of this method to the preparation of fused pyridines requires an alkyne or alkene (or their equivalents) as the dienophilic component which, when tethered to C-3 of the 1,2,4-triazine, leads to fused [2,3-*b*]pyridines following cycloaddition and nitrogen extrusion. The analogous reaction of C-6 tethered dienophiles gives fused [2,3-*c*]pyridines (Scheme I). Our previous efforts in this area employed heteroatoms (X = S, O, and N) to join the dienophile to the diene (1,2,4-triazine). Terminal acetylenes tethered through a carbon atom at position 3 (Scheme I, X = C) with n = 2 would afford 2,3-cycloalkenopyridines,[3] which are of interest as C-3′ quaternizing groups for cephalosporins; alternative synthetic approaches to these compounds have been reviewed.[4] The homologous 5,6,7,8-tetrahydroquinoline synthesis outlined in Scheme I (n = 3) is complimentary to the reduction of quinolines, which leads to the isomeric 1,2,3,4-tetrahydro derivatives through selective reduction of the electron-deficient pyridine ring.

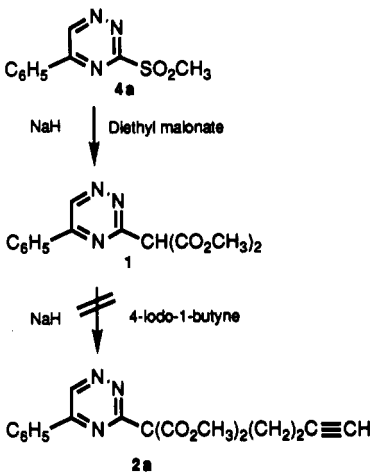
Results and Discussion

Displacement of methyl sulfinate from 3-(methylsulfonyl)-5,6-diphenyl-1,2,4-triazine with anions of active methylene compounds has been reported to occur readily.[5]

Scheme I



Scheme II



Alkylation of the anions of such displacement products (e.g., 1, Scheme II) with 4-iodo-1-butyne would provide access to a carbon-linked dienophilic substituent at C-3 of the 1,2,4-triazine ring. However, since attempts to carry out this alkylation of the displacement product prepared from 3-(methylsulfonyl)-5-phenyl-1,2,4-triazine (**4a**) proved

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(2) (a) Taylor, E. C. *Bull. Soc. Chim. Belg.* **1988**, *97*, 599. (b) Charushin, V. N.; Veldhuizen, B. V.; van der Plas, H. C. *Tetrahedron* **1989**, *20*, 6499 and references cited within.

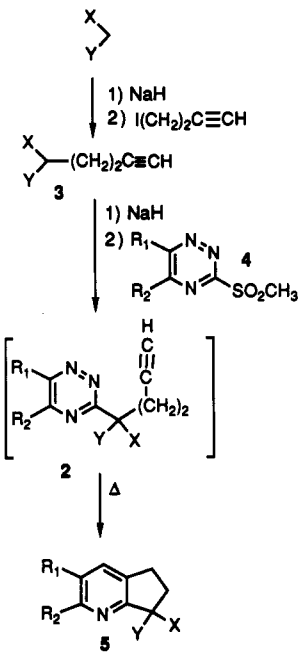
(3) For a preliminary report of some of this work, see: Taylor, E. C.; Macor, J. E. *Tetrahedron Lett.* **1986**, *27*, 2107.

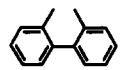
(4) Thummel, R. P. Carbocyclic Annelated Pyridines. In *Pyridine and Its Derivatives, Part 5*; Newkome, G. R., Ed.; Vol. 14 in the series *The Chemistry of Heterocyclic Compounds*; Weissberger, A., Taylor, E. C., Eds.; Wiley-Interscience: New York, 1984; pp 253–445.

(5) Konno, S.; Yokoyama, M.; Kaite, A.; Yomatsuta, I.; Ogawa, S.; Mitzugaki, M.; Yamanaka, H. *Chem. Pharm. Bull. Jpn.* **1982**, *30*, 152.

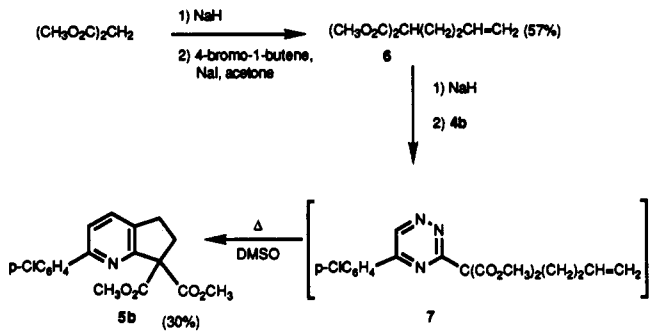
0022-3263/91/1956-1807$02.50/0

Scheme III



	R_1	R_2	X	Y	% Yield, 5 from 4
a)	-H	-Ph	$-CO_2CH_3$	$-CO_2CH_3$	41
b)	-H	-p-Cl-Ph	$-CO_2CH_3$	$-CO_2CH_3$	49
c)	-H	-p-Cl-Ph	$-CO_2Et$	$-COCH_3$	trace
d)	-H	-p-Cl-Ph	$-CO_2Et$	-CN	49
e)	-H	-p-Cl-Ph	-CN	-CN	80
f)			$-CO_2CH_3$	$-CO_2CH_3$	10

Scheme IV



fruitless, we therefore prepared the desired cycloaddition precursors **2** by incorporating the dienophilic sidechain into the active methylene compound prior to the displacement reaction (Scheme III). Reaction of the anions of a series of active methylene compounds with 4-iodo-1-butyne[6] yielded the alkynes **3**, which were then converted to their anions and treated with 3-(methylsulfonyl)-1,2,4-triazines (**4**)[7] to yield the desired Diels–Alder precursors **2**. Since isolation of the 3-(4-pentynyl)-1,2,4-triazines **2** was complicated by their propensity to undergo cyclization *at room temperature* to the cyclopentenopyridines **5**, the crude displacement reaction mixtures containing **2** were simply heated in tetrahydrofuran under reflux (66 °C) for a short period of time to complete cycloaddition. Integration of NMR spectra taken immediately after the displacement reaction gave the ratio of the unreacted alkyne **3** to the

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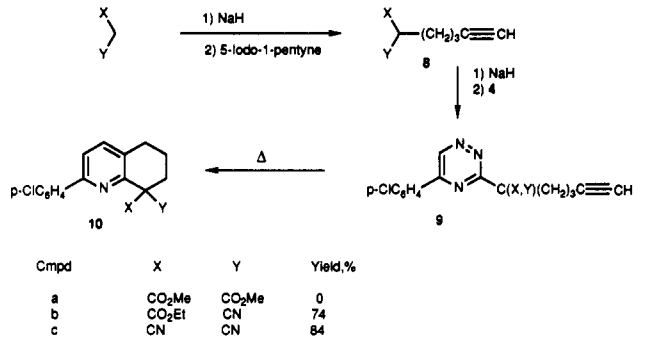
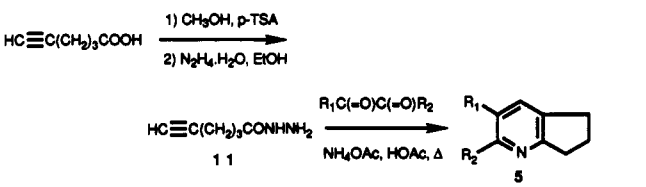
(7) Taylor, E. C.; Macor, J. E.; Pont, J. L. *Tetrahedron* **1987**, *43*, 5145.

Scheme V



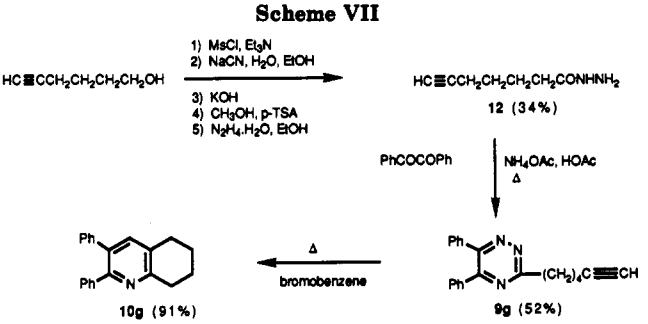
Cmpd	X	Y	Yield,%
a	CO_2Me	CO_2Me	0
b	CO_2Et	CN	74
c	CN	CN	84

Scheme VI



	R_1	R_2	Yield,%
5 g)	Ph	Ph	66
h)	Ph	H	18
i)	H	Ph	17

Scheme VII



intermediate triazine **2**, and comparison with the final isolated yields of **5** indicated that the cycloaddition reaction itself proceeded almost quantitatively; the overall yield of **5** from **4** was in effect the yield of the displacement reaction leading from **4** to **2**.

Use of an olefin as the dienophile was only briefly explored (Scheme IV). Synthesis of methyl 2-carbomethoxy-5-hexenoate (**6**) was achieved in a manner analogous to that employed for the preparation of the alkynes **3**. Reaction of the anion of **6** with 3-(methylsulfonyl)-5-(4′-chlorophenyl)-1,2,4-triazine (**4b**) gave **7**, which underwent intramolecular cyclization and in situ oxidation to yield **5b** (30%) when heated in DMSO. Since yields for this overall transformation utilizing an olefinic dienophile were significantly lower than with alkynyl dienophiles, no further work in this direction was pursued.

Synthesis of several 5-(4′-chlorophenyl)-3-(1,1-disubstituted-5-hexynyl)-1,2,4-triazines (**9**) (Scheme V) proceeded analogously to the 3-(5-pentynyl)-1,2,4-triazines (**2**). As expected, the rate of cycloaddition (**9** to **10**) was substantially slower due to the longer chain linking diene and dienophile. However, yields of products from these cyclizations were excellent, and this method represents a simple approach to 5,6,7,8-tetrahydroquinolines (**10**).

An alternate approach to cycloalkenopyridines based upon this 1,2,4-triazine Diels–Alder methodology was also explored (Schemes VI and VII). In this protocol, the dienophilic side chain is incorporated during construction of the 1,2,4-triazine nucleus. The requisite cycloaddition

precursors were prepared via a three-component condensation reaction involving a 1,2-dicarbonyl compound, an ω-alkynyl hydrazide, and a large excess of ammonium acetate.[8] 5-Hexynoic acid hydrazide (11) and 6-heptynoic acid hydrazide (12) were prepared in standard fashion from 5-hexyn-1-ol.[9] In the above condensations involving 5-hexynoic acid hydrazide (11), 1,2,4-triazines were not isolated under the usual condensation conditions (refluxing acetic acid); instead, these conditions led directly to the desired 2,3-cyclopentenopyridines (5) (Scheme VI). It should be noted that this approach suffers from lack of regioselectivity in the formation of the 1,2,4-triazines when unsymmetrical 1,2-dicarbonyl compounds are employed.

Use of 6-heptynoic acid hydrazide (12) in this three-component reaction should lead ultimately to 5,6,7,8-tetrahydroquinolines (10, Scheme VII). Thus, condensation of benzil, 6-heptynoic acid hydrazide (12) and excess ammonium acetate in refluxing acetic acid provided the intermediate alkynyl-substituted 1,2,4-triazine (**9g**) in 52% yield. Intramolecular cycloaddition leading to 2,3-diphenyl-5,6,7,8-tetrahydroquinoline (**10g**) required heating in refluxing bromobenzene (155 °C), but proceeded in 91% yield.

In conclusion, intramolecular Diels–Alder reactions of 3-(ω-alkynyl)-1,2,4-triazines leads to 2,3-cyclopentenopyridines and 5,6,7,8-tetrahydroquinolines. This methodology can be viewed as complementary to *inter*molecular Diels–Alder reactions of 1,2,4-triazines with cyclopentenyl- and cyclohexenylenamines.[10]

Experimental Section

Methyl 1-Carbomethoxy-1-(5-phenyl-3-triazinyl)acetate (1). Solid 3-(methylsulfonyl)-5-phenyl-1,2,4-triazine (**4a**) (0.70 g, 2.98 mmol) was added all at once with stirring to a 0 °C solution of sodium hydride (60% dispersion in mineral oil, 0.163 g, 4.07 mmol, 1.4 equiv) and dimethyl malonate (0.45 mL, 3.94 mmol, 1.3 equiv) in anhydrous tetrahydrofuran (15 mL). The resulting deep red solution was stirred at 0 °C with exclusion of moisture for 30 min. Water (pH 4, 10 mL) was added, and the aqueous mixture was extracted with ether (3 × 10 mL). The ether extracts were combined, dried ($MgSO_4$), and evaporated under reduced pressure to yield an oil (1.2 g), which was chromatographed on silica gel (ca. 40 g). Elution with 1:2 ether/petroleum ether yielded 1 (0.26 g, 0.91 mmol, 30%) as a pale orange oil: IR (neat) 1740, 1600, 1540, 1500, 1430 cm^{-1}; ^1H NMR ($CDCl_3$) δ 9.65 (s, 1 H), 8.23–8.10 (m, 2 H), 7.65–7.50 (m, 3 H), 5.37 (s, 1 H), 3.85 (s, 6 H); ^{13}C NMR ($CDCl_3$) δ 166.1, 162.8, 155.5, 144.9, 132.7, 129.3, 128.6, 127.7, 59.8, 53.3; LRMS (*m/z*, relative intensity) 287 (M^+, 11), 256 (15), 103 (39), 102 (100), 76 (28); HRMS calcd for $C_{14}H_{13}N_3O_4$ 287.0906, found 287.0893 ± 0.0029.

General Procedure for the Synthesis of 3. 4-Iodo-1-butyne[6] (1.00 mL, 1.80 g, 10.0 mmol) was added to a stirred mixture of the active methylene compound (10.0 mmol) and sodium hydride (60% dispersion in mineral oil, 0.44 g, 1.1 equiv) in anhydrous tetrahydrofuran (20 mL) at room temperature, and this mixture was heated at reflux (66 °C) under nitrogen for 48 h. A saturated solution of sodium bicarbonate (10 mL) was then added to the reaction mixture, which was extracted with ether (3 × 20 mL). The ether extracts were combined, dried ($MgSO_4$), and evaporated under reduced pressure. The residual oil was purified either by distillation or by column chromatography using silica gel (ca. 40 g) and elution with the appropriate eluent to afford **3**.

Methyl 2-Carbomethoxy-5-hexynoate (3a). The active methylene compound employed was dimethyl malonate; vacuum distillation of the reaction residue yielded **3a** (70%) as a clear, colorless liquid: bp 84.0–87.0 °C (0.6 mmHg); IR (neat) 3280, 2115, 1740, 1430, 1340, 1240 cm^{-1}; ^1H NMR ($CDCl_3$) δ 3.75 (s, 6 H), 3.62 (t, *J* = 7.5 Hz, 1 H), 2.31–2.08 (m, 4 H), 2.02 (t, *J* = 2.6 Hz, 1 H); ^{13}C NMR ($CDCl_3$) δ 169.3, 82.1, 69.6, 52.4, 50.1, 27.4, 16.3. Anal. Calcd for $C_9H_{12}O_4$: C, 58.69; H, 6.57. Found: C, 58.40; H, 6.64.

Ethyl 2-Acetyl-5-hexynoate (3c). The active methylene compound employed was ethyl acetoacetate; chromatography of the residual reaction oil and elution with 1:9 ether/petroleum ether yielded **3c** (47%) as a clear, colorless liquid: IR (neat) 3290, 2120, 1740, 1715, 1645, 1445, 1360, 1250–1230 cm^{-1}; ^1H NMR ($CDCl_3$) δ 4.21 (q, *J* = 7.0 Hz, 2 H), 3.71 (t, *J* = 6.6 Hz, 1 H), 2.34–1.95 (m, 4 H), 2.27 (s, 3 H), 2.01 (t, *J* = 2.6 Hz, 1 H), 1.28 (t, *J* = 7.0 Hz, 3 H); ^{13}C NMR ($CDCl_3$) δ 201.9, 169.1, 82.5, 69.5, 61.2, 58.1, 28.9, 26.5, 16.3, 13.9. Anal. Calcd for $C_{10}H_{14}O_3$: C, 65.91; H, 7.74. Found: C, 65.66; H, 7.78.

Ethyl 2-Cyano-5-hexynoate (3d). The active methylene compound employed was ethyl cyanoacetate; chromatography of the residual reaction oil and elution with 1:4 ether/petroleum ether yielded **3d** (54%) as a clear, colorless liquid: IR (neat) 3290, 2250, 2120, 1740, 1445, 1370 cm^{-1}; ^1H NMR ($CDCl_3$) δ 4.28 (q, *J* = 7.0 Hz, 2 H), 3.76 (t, *J* = 7.0 Hz, 1 H), 2.55–2.02 (m, 4 H), 2.08 (t, *J* = 2.6 Hz, 1 H), 1.33 (t, *J* = 7.0 Hz, 3 H). Anal. Calcd for $C_9H_{11}NO_2$: C, 65.44; H, 6.71; N, 8.48. Found: C, 65.64; N, 6.47; N, 8.21.

2-Cyano-5-hexynenitrile (3e). The active methylene compound employed was malononitrile; chromatography of the residual reaction oil and elution with 1:4 ether/petroleum ether yielded **3e** (48%) as a white, crystalline solid: mp 69.0–70.5 °C; IR (KBr) 3300, 2260, 2125, 1450, 1435 cm^{-1}; ^1H NMR ($CDCl_3$) δ 3.98 (t, *J* = 7.7 Hz, 1 H), 2.55–2.47 (m, 2 H), 2.25–2.16 (m, 2 H), 2.10 (t, *J* = 2.6 Hz, 1 H); ^{13}C NMR ($CDCl_3$) δ 112.1, 79.2, 72.3, 29.7, 21.2, 15.9. Anal. Calcd for $C_7H_6N_2$: C, 71.17; H, 5.12; N, 23.71. Found: C, 70.98; H, 5.33; N, 23.63.

General Procedure for the Synthesis of 2,3-Cyclopentenopyridines (5) from 3-(Methylsulfonyl)-1,2,4-triazines (4). The solid 3-(methylsulfonyl)-1,2,4-triazine (**4**,[7] 4.00 mmol) was added all at once with stirring to a 0 °C solution of sodium hydride (60% dispersion in mineral oil, 0.18 g, 4.5 mmol, 1.1 equiv) and **3** (4.4 mol, 1.1 equiv) in anhydrous tetrahydrofuran. The resulting reaction mixture was stirred at room temperature under nitrogen for 2 h and then heated at reflux (66 °C) under nitrogen for 8–48 h, depending on the substrate. A saturated solution of sodium bicarbonate was added to the reaction mixture, which was extracted with methylene chloride (3 × 10 mL). The methylene chloride extracts were combined, dried ($MgSO_4$), and evaporated under reduced pressure, and the residual solid/oil was chromatographed using silica gel (ca. 40 g). Elution with the appropriate solvent system afforded **5**.

2,3-(1,1-Dicarbomethoxycyclopenteno)-6-phenylpyridine (5a). 3-(Methylsulfonyl)-5-phenyl-1,2,4-triazine (**4a**) and **3a** were used; the reaction time was 9.5 h; the eluent was 1:4 ether/petroleum ether. Compound **5a** (41%) was obtained as a white crystalline solid: mp 129.0–130.5 °C; IR (KBr) 1740–1720, 1585, 1560, 1495, 1445, 1430 cm^{-1}; ^1H NMR ($CDCl_3$) δ 8.04–7.93 (m, 2 H), 7.57 (s, 2 H), 7.50–7.35 (m, 3 H), 3.78 (s, 6 H), 3.10–2.73 (m, 4 H); ^{13}C NMR ($CDCl_3$) δ 170.3, 160.0, 156.6, 139.5, 135.7, 133.0, 128.6, 128.5, 126.9, 119.6, 66.4, 52.5, 34.0, 28.2. Anal. Calcd for $C_{18}H_{17}NO_4$: C, 69.44; H, 5.50; N, 4.50. Found: C, 69.59; H, 5.54; N, 4.44.

6-(4′-Chlorophenyl)-2,3-(1,1-dicarbomethoxycyclopenteno)pyridine (5b) (Method A). 5-(4′-Chlorophenyl)-3-(methylsulfonyl)-1,2,4-triazine (**4b**) and 3a were used; the reaction time was 9 h; the eluent was 1:3 ether/petroleum ether. Compound **5b** (49%) was obtained as a white, crystalline solid: mp 149.5–150.0 °C; IR (KBr) 1755–1720, 1580, 1560, 1490, 1445, 1410, 1385, 1300 cm^{-1}; ^1H NMR ($CDCl_3$) δ 7.93 (d, *J* = 8.6 Hz, 2 H), 7.57 (s, 2 H), 7.38 (d, *J* = 8.6 Hz, 2 H), 3.80 (s, 6 H), 3.11–2.72 (m, 4 H); ^{13}C NMR ($CDCl_3$) δ 170.4, 160.2, 155.5, 137.9, 136.2, 135.0, 133.3, 128.8, 128.4, 119.6, 66.4, 52.7, 34.1, 28.3. Anal. Calcd for $C_{18}H_{16}ClNO_4$: C, 62.52; H, 4.66; Cl, 10.25; N, 4.05. Found: C, 62.49; H, 4.90; Cl, 10.41; N, 3.80.

6-(4′-Chlorophenyl)-2,3-(1-carbethoxy-1-cyanocyclopenteno)pyridine (5d). 5-(4′-Chlorophenyl)-3-(methyl-

(8) Atkinson, C. M.; Cossy, H. D. *J. Chem. Soc.* **1962**, 1805.
(9) Available from Farchan Laboratories.
(10) (a) Boger, D. L.; Panek, J. S. *J. Org. Chem.* **1981**, *46*, 2179. (b) Boger, D. L.; Panek, J. S.; Meier, M. M. *J. Org. Chem.* **1982**, *47*, 895. (c) Boger, D. L. *Chem. Rev.* **1986**, *86*, 781 and references cited therein. (d) Boger, D. L. *Tetrahedron* **1983**, *39*, 2869 and references cited therein. (e) Taylor, E. C.; Macor, J. E. *Tetrahedron Lett.* **1985**, *26*, 2415. (f) Taylor, E. C.; McDaniel, K. F.; Warner, J. C. *Tetrahedron Lett.* **1987**, *28*, 1977. (g) Taylor, E. C.; Macor, J. E. *J. Org. Chem.* **1989**, *54*, 4984.
(11) Earl, R. A.; Vollhardt, K. P. C. *J. Org. Chem.* **1984**, *49*, 4786.

sulfonyl)-1,2,4-triazine (**4b**) and **3d** were used; the reaction time was 8 h; the eluent was 1:1 methylene chloride/hexanes. Compound **5d** (49%) was obtained as a white, crystalline solid: mp 138.0–140.5 °C; IR (KBr) 2255, 1735, 1590, 1560, 1495, 1450, 1415, 1385, 1370 cm^{-1}; ^1H NMR ($CDCl_3$) δ 8.00–7.89 (m, 2 H), 7.62 (s, 2 H), 7.44–7.32 (m, 2 H), 4.29 (q, J = 7.0 Hz, 2 H), 3.25–3.02 (m, 2 H), 2.96–2.65 (m, 2 H), 1.31 (t, J = 7.0 Hz, 3 H); ^{13}C NMR ($CDCl_3$) δ 167.3, 158.2, 156.1, 136.8, 135.3, 135.2, 134.2, 128.8, 128.1, 120.3, 118.1, 63.1, 54.1, 35.6, 28.5, 13.9. Anal. Calcd for $C_{18}H_{15}ClN_2O_2$: C, 66.16; H, 4.63; Cl, 10.85; N, 8.57. Found: C, 65.91; H, 4.86; Cl, 11.11; N, 8.53.

6-(4′-Chlorophenyl)-2,3-(1,1-dicyanocyclopenteno)pyridine (5e). 5-(4′-Chlorophenyl)-3-(methylsulfonyl)-1,2,4-triazine (**4b**) and **3e** were used, and the reaction time was 18 h. The resulting reaction solution was evaporated under reduced pressure, and the residual solid was triturated with anhydrous ether (15 mL). The undissolved solid was collected by filtration, redissolved in methylene chloride, and passed through a silica gel filter (ca. 30 g) followed by elution with methylene chloride (150 mL). The filtrate was evaporated under reduced pressure to yield **5e** (80%) as a white, crystalline solid: mp 211.0–212.0 °C; IR (KBr) 2250, 1590, 1580, 1560, 1490, 1450, 1410, 1380, 1300 cm^{-1}; ^1H NMR ($CDCl_3$) δ 7.99–7.94 (m, 2 H), 7.71 (s, 2 H), 7.42–7.38 (m, 2 H), 3.19 (t, J = 7.0 Hz, 2 H), 2.95 (t, J = 7.1 Hz, 2 H); ^{13}C NMR ($CDCl_3$) δ 157.2, 154.3, 135.9, 135.0, 134.1, 129.0, 128.3, 121.6, 114.3, 40.4, 37.7, 28.0. Anal. Calcd for $C_{16}H_{10}ClN_3$: C, 68.70; H, 3.60; Cl, 12.67; N, 15.02. Found: C, 68.88; H, 3.76; Cl, 12.90; N, 15.00.

2,3-(1,1-Dicarbomethoxycyclopenteno)phenanthreno-[9,10-*e*]pyridine (5f). To a stirred solution of sodium hydride in anhydrous tetrahydrofuran (10 mL) at room temperature was added solid 3-(methylsulfonyl)phenanthreno[9,10-*e*]-1,2,4-triazine (**4f**) (0.62 g, 2.00 mmol) all at once with stirring to a 0 °C solution of sodium hydride (60% dispersion in mineral oil, 0.080 g, 2.00 mmol) and methyl 2-carbomethoxy-5-hexynoate (**3a**) (0.37 g, 2.01 mmol) in anhydrous tetrahydrofuran. The resulting mixture was heated at reflux (66 °C) under nitrogen for 48 h. A saturated solution of sodium bicarbonate (10 mL) was added to the reaction mixture, and this aqueous mixture was extracted with methylene chloride (3 × 25 mL). The methylene chloride extracts were combined, dried ($MgSO_4$), and evaporated under reduced pressure. The residual solid/oil mixture (0.8 g) was triturated in anhydrous ether, and the undissolved solid was collected by filtration to give recovered 3-(methylsulfonyl)phenanthreno[9,10-*e*]-1,2,4-triazine (0.23 g, 0.74 mmol, 37% recovered). The filtrate was evaporated under reduced pressure, and the residual oil was chromatographed using silica gel (ca. 40 g). Elution with methylene chloride first gave unreacted methyl 2-carbomethoxy-5-hexynoate (0.18 g, 0.98 mmol, 49% recovered); further elution yielded 3-(1,1-dicarbomethoxy-4-pentynyl)phenanthreno[9,10-*e*]-1,2,4-triazine (**2f**) (0.095 g, 0.25 mmol, 12% actual, 18% based on recovered sulfone): ^1H NMR ($CDCl_3$) δ 9.40–9.24 (m, 1 H), 9.10–8.96 (m, 1 H), 8.47–8.37 (m, 2 H), 7.88–7.65 (m, 4 H), 3.90 (s, 6 H), 3.10–2.90 (m, 2 H), 2.74–2.50 (m, 2 H), 1.95 (t, J = 2.6 Hz, 1 H). This solid was dissolved in anhydrous dioxane (2 mL), and the solution was heated at reflux (101 °C) under nitrogen for 24.0 h. The reaction solution was then passed through a silica gel filter (ca. 30 g) followed by elution with methylene chloride (100 mL). The eluate was evaporated under reduced pressure to yield 2,3-(1,1-dicarbomethoxycyclopenteno)phenanthreno[9,10-*e*]pyridine (**5f**) (0.080 g, 0.21 mmol, 10% overall, 84% for the cycloaddition reaction) as an off-white powder: mp 191.0–194.0 °C; IR (KBr) 1750, 1730, 1605, 1575, 1495, 1475, 1450, 1435, 1400 cm^{-1}; ^1H NMR ($CDCl_3$) δ 9.35–9.32 (m, 1 H), 8.65 (s, 1 H), 8.59–8.45 (m, 3 H), 7.70–7.55 (m, 4 H), 3.82 (s, 6 H), 3.18 (t, J = 7.1 Hz, 2 H), 2.95 (t, J = 7.1 Hz, 2 H); ^{13}C NMR ($CDCl_3$) δ 170.5, 159.4, 146.0, 135.9, 131.1, 130.9, 129.9, 128.7, 128.5, 127.7, 127.3, 127.2, 126.9, 125.8, 124.1, 123.4, 123.3, 122.3, 66.3, 53.1, 34.3, 28.5; HRMS calcd for $C_{24}H_{19}NO_4$ 386.1391, found 386.1391 ± 0.0050.

6-(4′-Chlorophenyl)-2,3-(1,1-dicarbomethoxycyclopenteno)pyridine (5b) (Method B). Solid 5-(4′-chlorophenyl)-3-(methylsulfonyl)-1,2,4-triazine (**4b**, 1.07 g, 3.97 mmol) was added all at once with stirring to a 0 °C solution of sodium hydride (0.160 g, 60% dispersion in mineral oil, 4.00 mmol) and methyl 2-carbomethoxy-5-hexenoate (**6**) (0.75 g, 4.02 mmol) in anhydrous tetrahydrofuran (15 mL). The resulting mixture was stirred at room temperature with exclusion of water for 2.0 h. A saturated solution of sodium bicarbonate (10 mL) was added to the reaction mixture, which was then extracted with methylene chloride (2 × 20 mL). The combined methylene chloride extracts were combined, dried ($MgSO_4$), and evaporated under reduced pressure, and the residual solid/oil mixture was dissolved in a solution of tetrahydrofuran and DMSO (10 mL/2 mL). This solution was heated at reflux (66 °C) with exclusion of water for 18 h. The resulting mixture was concentrated via evaporation under reduced pressure, and the residual solid/oil mixture was chromatographed using silica gel (ca. 40 g). Elution with 1:1 methylene chloride/hexanes yielded **5b** (0.41 g, 1.19 mmol, 30%) as a white, crystalline solid (mp 145.0–147.0 °C) whose physical and spectral properties were identical with those of the product obtained by method A.

Methyl 2-Carbomethoxy-5-hexenoate (6). To a stirred mixture of dimethyl malonate (2.28 mL, 19.95 mmol) and sodium hydride (60% dispersion in mineral oil, 0.80 g, 20.00 mmol) in anhydrous tetrahydrofuran at room temperature was added 4-iodo-1-butene (2.03 mL, 20.27 mmol, 1.0 equiv) all at once, and the resulting mixture was then heated at reflux under nitrogen for 43 h. A saturated solution of sodium bicarbonate (25 mL) was added to the reaction mixture, which was then extracted with ether (2 × 50 mL). The combined extracts were combined, dried ($MgSO_4$), and evaporated under reduced pressure. Chromatography of the residual liquid using silica gel (ca. 100 g) followed by elution with 1:4 ether/petroleum ether gave **6** (2.13 g, 11.44 mmol, 57%) as a clear, colorless liquid: IR (neat) 1750, 1640, 1435, 1350–1150 cm^{-1}; ^1H NMR ($CDCl_3$) δ 5.99–5.56 (m, 1 H), 5.13–4.94 (m, 2 H), 3.73 (s, 6 H), 3.40 (t, J = 7.3 Hz, 1 H), 2.20–1.92 (m, 4 H); ^{13}C NMR ($CDCl_3$) δ 169.5, 136.8, 115.7, 52.1, 51.0, 31.2, 28.0. Anal. Calcd for $C_9H_{14}O_4$: C, 58.05; H, 7.58. Found: C, 57.76; H, 7.61.

General Procedure for the Synthesis of 8. 5-Iodo-1-pentyne[6] (2.13 g, 11.0 mmol, 1.1 equiv) was added to a stirred mixture of the active methylene compound (10.0 mmol) and sodium hydride (60% dispersion in mineral oil, 0.44 g, 1.1 equiv) in anhydrous tetrahydrofuran (20 mL) at room temperature, and this mixture was heated at reflux (66 °C) under nitrogen for 72 h. A saturated solution of sodium bicarbonate (10 mL) was then added to the reaction mixture, which was extracted with ether (3 × 20 mL). The combined ether extracts were combined, dried ($MgSO_4$), and evaporated under reduced pressure, and the residual oil purified by column chromatography using silica gel (ca. 40 g). Elution with the appropriate eluent gave **8**.

Methyl 2-Carbomethoxy-6-heptynoate (8a). The active methylene compound employed was dimethyl malonate; chromatography of the residual reaction oil followed by elution with 1:4 ether/petroleum ether yielded **8a** (63%) as a clear, colorless liquid: IR (neat) 2120, 1740, 1440, 1300–1150 cm^{-1}; ^1H NMR ($CDCl_3$) δ 3.64 (s, 6 H), 3.30 (t, J = 7.5 Hz, 1 H), 2.15–2.10 (m, 2 H), 1.95–1.90 (m, 2 H), 1.88 (t, J = 2.7 Hz, 1 H), 1.51–1.41 (m, 2 H); ^{13}C NMR ($CDCl_3$) δ 169.5, 83.3, 69.0, 52.4, 51.1, 27.8, 26.0, 18.0. Anal. Calcd for $C_{10}H_{14}O_4$: C, 60.59; H, 7.12. Found: C, 60.69; H, 7.05.

Ethyl 2-Cyano-6-heptynoate (8d). The active methylene compound employed was ethyl cyanoacetate; chromatography of the residual reaction oil followed by elution with 1:4 ether/petroleum ether yielded **8d** (49%) as a clear, colorless liquid: IR (neat) 2250, 2120, 1740, 1455, 1370 cm^{-1}; ^1H NMR ($CDCl_3$) δ 4.16 (q, J = 7.2 Hz, 2 H), 3.49 (t, J = 7.0 Hz, 1 H), 2.21–2.12 (m, 2 H), 2.02–1.90 (m, 3 H), 1.67–1.60 (m, 2 H), 1.22 (t, J = 7/0 Hz, 3 H); ^{13}C NMR ($CDCl_3$) δ 165.9, 116.3, 82.6, 69.6, 62.8, 37.1, 28.6, 25.3, 17.7, 13.9. Anal. Calcd for $C_{10}H_{13}NO_2$: C, 67.02; H, 7.31; N, 7.82. Found: C, 67.25; H, 7.05; N, 7.62.

2-Cyano-6-heptynenitrile (8e). The active methylene compound employed was malononitrile; chromatography of the residual reaction oil followed by elution with 1:4 ether/petroleum ether yielded **8e** (63%) as a clear, colorless liquid: IR (neat) 2260, 2120, 1455, 1435, 1320 cm^{-1}; ^1H NMR ($CDCl_3$) δ 3.88 (t, J = 6.6 Hz, 1 H), 2.43–2.22 (m, 2 H), 2.19–2.05 (m, 2 H), 2.08 (t, J = 2.6 Hz, 1 H), 1.97–1.64 (m, 2 H); ^{13}C NMR ($CDCl_3$) δ 112.4, 81.8, 70.0, 29.5, 24.8, 22.1, 17.1. Anal. Calcd for $C_8H_8N_2$: C, 72.70: H, 6.10; N, 21.20. Found: C, 73.07; H, 6.20; N, 20.94.

5-(4′-Chlorophenyl)-3-(1,1-dicyano-5-hexynyl)-1,2,4-triazine (9e). To a stirred solution of **8e** (0.48 g, 3.63 mol, 1.1 equiv) and sodium hydride (60% dispersion in mineral oil, 0.145 g, 3.6 mmol,

1.1 equiv) in anhydrous tetrahydrofuran (15 mL) at room temperature, 5-(4'-chlorophenyl)-3-(methylsulfonyl)-1,2,4-triazine (**4b**) (0.92 g, 3.41 mmol) was added as a solid all at once. The resulting reaction mixture was stirred at room temperature under nitrogen for 1.5 h, a saturated solution of sodium bicarbonate was added, and the mixture was extracted with methylene chloride (3 × 10 mL). The combined methylene chloride extracts were dried ($MgSO_4$) and evaporated under reduced pressure, and the residual yellow solid was chromatographed using silica gel (ca. 40 g). Elution with 1:1 methylene chloride/hexanes gave 0.77 g (80%) of **9e** as a pale yellow, crystalline solid: mp 136.0–137.5 °C (with effervescence); IR (KBr) 2260, 2225, 1590, 1540, 1490, 1455, 1430, 1400, 1315 cm^{-1}; ^1H NMR ($CDCl_3$) δ 9.74 (s, 1 H), 8.20–8.16 (m, 2 H), 7.56–7.52 (m, 2 H), 2.68–2.63 (m, 2 H), 2.31 (dt, J = 6.7 and 2.7 Hz, 2 H), 1.97–1.87 (m, 2 H), 1.95 (t, J = 2.7 Hz, 1 H); ^{13}C NMR ($CDCl_3$) δ 161.4, 155.5, 147.2, 144.9, 140.8, 131.3, 128.5, 112.8, 81.6, 71.2, 44.6, 38.5, 24.3, 17.6. Anal. Calcd for $C_{17}H_{12}ClN_3$: C, 63.46; H, 3.76; N, 21.77. Found: C, 63.17; H, 3.74; N, 21.76.

8-Carbethoxy-2-(4-chlorophenyl)-8-cyano-5,6,7,8-tetrahydroquinoline (10d). To a stirred solution of ethyl 2-cyano-6-heptynoate (**8d**) (0.42 g, 2.34 mmol, 1.1 equiv) and sodium hydride (60% oil, 0.090 g, 2.25 mmol, 1.0 equiv) in anhydrous tetrahydrofuran (10 mL) at room temperature was added 5-(4-chlorophenyl)-3-(methylsulfonyl)-1,2,4-triazine (**4b**) (0.59 g, 2.19 mmol). The reaction mixture was stirred at room temperature with exclusion of moisture for 12 h, a saturated solution of sodium bicarbonate (10 mL) was added, and the mixture was extracted with methylene chloride (2 × 20 mL). The combined methylene chloride extracts were dried ($MgSO_4$) and evaporated under reduced pressure to give an oily residue, which was chromatographed using silica gel (ca. 40 g). Elution with 1:1 methylene chloride/hexanes yielded crude 3-(1-carbethoxy-1-cyano-5-hexynyl)-5-(4-chlorophenyl)-1,2,4-triazine (**9d**) (0.29 g, 0.79 mmol, 36% crude) as a yellow oil: ^1H NMR ($CDCl_3$) δ 9.70 (s, 1 H), 8.25–8.12 (m, 2 H), 7.62–7.52 (m, 2 H), 4.35 (q, J = 7.3 Hz, 2 H), 2.80–2.62 (m, 2 H), 2.40–2.25 (m, 2 H), 1.98 (t, J = 2.6 Hz, 1 H), 2.00–1.55 (m, 2 H), 1.30 (t, J = 7.3 Hz, 3 H). A solution of this crude oil in chlorobenzene (5 mL) was heated at reflux (132 °C) under nitrogen for 36 h, at which time TLC showed only a single, new spot at R_f = 0.45 (methylene chloride). The reaction solution was then filtered through a silica gel plug (ca. 30 g), which was eluted with methylene chloride (150 mL). The filtrate was evaporated under reduced pressure to yield **10d** (0.20 g, 0.59 mmol, 74% for the cycloaddition reaction, 27% overall) as a pale yellow solid: mp 119.0–120.5 °C; IR (KBr) 2240, 1735, 1590, 1575, 1550, 1490, 1455, 1410, 1375 cm^{-1}; ^1H NMR ($CDCl_3$) δ 7.92–7.88 (m, 2 H), 7.57 (d, J = 8.1 Hz, 1 H), 7.47 (d, J = 8.2 Hz, 1 H), 7.37–7.33 (m, 2 H), 4.36–4.25 (m, 2 H), 2.84 (t, J = 6.3 Hz, 2 H), 2.54–2.44 (m, 2 H), 2.08–1.99 (m, 2 H), 1.29 (t, J = 7.1 Hz, 3 H); ^{13}C NMR ($CDCl_3$) δ 168.6, 154.0, 149.4, 138.9, 136.5, 135.2, 130.7, 128.8, 128.0, 120.0, 119.3, 63.0, 51.6, 32.8, 27.3, 19.0, 14.1. Anal. Calcd for $C_{19}H_{17}ClN_2O_2$: C, 66.96; H, 5.03; Cl, 10.40; N, 8.22. Found: C, 66.84; H, 5.12; Cl, 10.66; N, 8.39.

2-(4-Chlorophenyl)-8,8-dicyano-5,6,7,8-tetrahydroquinoline (10e). A solution of 5-(4-chlorophenyl)-3-(1,1-dicyano-5-hexynyl)-1,2,4-triazine (**9e**) (0.59 g, 1.83 mmol) in anhydrous dioxane (5 mL) was heated at reflux (101 °C) under nitrogen for 168 h, by which time no starting material remained as judged by TLC (a new spot at R_f = 0.6 in methylene chloride was the only spot detected). The reaction solution was chromatographed over silica gel (ca. 40 g); elution with 1:1 methylene chloride/hexanes gave **10e** (0.45 g, 1.53 mmol, 84%) as a fluffy white, microcrystalline solid: mp 185.5–186.5 °C; IR (KBr) 2250, 1595, 1570, 1550, 1495, 1460, 1430, 1410, cm^{-1}; ^1H NMR ($CDCl_3$) δ 8.01–7.96 (m, 2 H), 7.68 (d, J = 8.2 Hz, 1 H), 7.55 (d, J = 8.2 Hz, 1 H), 7.42–7.37 (m, 2 H), 2.87 (t, J = 6.4 Hz, 2 H), 2.64–2.60 (m, 2 H), 2.15–2.07 (m, 2 H); ^{13}C NMR ($CDCl_3$) δ 155.0, 145.2, 139.5, 135.8, 135.7, 130.2, 129.0, 128.1, 121.2, 115.6, 39.1, 33.9, 26.7, 18.9. Anal. Calcd for $C_{17}H_{12}ClN_3$: C, 69.51; H, 4.12; Cl, 12.07; N, 14.30. Found: C, 69.47; H, 3.78; Cl, 12.25; N, 14.24.

5-Hexynoic Acid Hydrazide (11). A solution of 5-hexynoic acid (3.00 g, 26.7 mmol) and *p*-toluenesulfonic acid (0.035 g) in methylene chloride (10 mL) and methanol (3 mL) was heated at reflux for 26 h. Saturated aqueous bicarbonate (25 mL) was added, and the organic layer was separated. The aqueous layer was extracted with methylene chloride (25 mL), and the combined methylene chloride extracts were washed with brine (50 mL), dried ($MgSO_4$), and evaporated under reduced pressure to give methyl 5-hexynoate (2.87 g, 22.7 mmol, 85%) as a yellow liquid: IR (neat) 2110, 1735, 1435, 1370, 1315 cm^{-1}; ^1H NMR ($CDCl_3$) δ 3.68 (s, 3 H), 2.46 (t, J = 7.1 Hz, 2 H), 2.27 (dt, J = 5.9 and 2.6 Hz, 2 H), 1.97 (t, J = 2.6 Hz, 1 H), 1.87 (m, 2 H).

A mixture of the crude ester (1.25 g, 9.92 mmol) and hydrazine hydrate (0.74 g, 14.8 mmol, 1.5 equiv) in ethanol (2 mL) was heated at reflux for 17 h, and the resulting solution was evaporated under reduced pressure. The residual white solid was washed with petroleum ether and recrystallized from isopropyl ether/methylene chloride to give **11** (1.00 g, 7.94 mmol, 80%, 68% from 5-hexynoic acid) as a colorless, crystalline solid: mp 72.0–74.0 °C; IR (KBr) 1640, 1515, 1450, 1430, 1415 cm^{-1}; ^1H NMR ($CDCl_3$) δ 6.96 (br s, 1 H), 3.93 (br s, 2 H), 2.39–2.19 (m, 4 H), 1.99 (t, J = 2.6 Hz, 1 H), 1.90 (m, 2 H). Anal. Calcd for $C_6H_{10}N_2O$: C, 57.12; H, 7.99; N, 22.20. Found: C, 57.04; H, 8.23; N, 21.96.

6-Heptynoic acid hydrazide (12) was prepared by a five-step process (Scheme VII) without full characterization of the intermediates. To a solution of 5-hexyn-1-ol (10.41 g, 106.1 mmol) and triethylamine (14.39 g, 142.2 mmol, 1.3 equiv) in methylene chloride (100 mL) stirred at −78 °C under nitrogen was added over 1 h a solution of methanesulfonyl chloride (14.58 g, 127.3 mmol, 1.2 equiv) in methylene chloride (100 mL). The stirred reaction mixture was allowed to warm to room temperature overnight and then was washed with water (100 mL), 1 N sulfuric acid (2 × 60 mL), and water again (2 × 100 mL), dried ($MgSO_4$), and evaporated under reduced pressure to yield 5-hexynyl methanesulfonate (17.53 g, 99.7 mmol, 94% crude) as a light yellow oil: IR (neat) 2115, 1350 cm^{-1}; ^1H NMR ($CDCl_3$) δ 4.27 (t, J = 5.8 Hz, 2 H), 3.01 (s, 3 H), 2.26 (dd, J = 7.1 and 2.7 Hz, 2 H), 1.98 (t, J = 2.7 Hz, 1 H), 1.83–1.65 (m, 4 H). The spectral and physical data for this compound agreed with those previously reported for this compound.[12]

To a stirred solution of crude 5-hexynyl methanesulfonate (17.53 g, 99.7 mmol) in 80% aqueous ethanol (120 mL) was added potassium cyanide (11.69 g, 179.5 mmol, 1.8 equiv), and the mixture was heated at reflux for 46 h. Water (100 mL) was added, and the mixture was extracted with ether (3 × 100 mL). The combined ether extracts were washed with water (100 mL) followed by brine (100 mL), dried over $MgSO_4$, and filtered through a column of Florisil. Evaporation of the filtrate under reduced pressure gave crude 6-cyano-1-hexyne (7.48 g, 69.8 mmol, 70%) as a yellow liquid: IR (neat) 3290, 2245, 2115, 1455 cm^{-1}; ^1H NMR ($CDCl_3$) δ 2.48–2.18 (m, 4 H), 1.99 (t, J = 2.6 Hz, 1 H), 1.91–1.68 (m, 4 H).

A mixture of crude 6-cyano-1-hexyne (7.48 g, 69.8 mmol) and potassium hydroxide (8.33 g, 148.5 mmol, 2.1 equiv) in water (75 mL) was heated at reflux for 6.5 h, cooled, and extracted with ether (100 mL), and the aqueous layer was acidified with concentrated HCl to pH 6. A yellow oil separated which was extracted with ether (75 mL). The aqueous layer was further acidified to pH 1, whereupon an additional quantity of oil separated which was extracted with ether (75 mL). The combined ether extracts from the acidic aqueous layer were dried ($MgSO_4$) and evaporated under reduced pressure to yield crude 6-heptynoic acid (6.70 g, 53.1 mmol, 76%) as a colorless oil: IR (neat) 3600–2500, 2115, 1710, 1455 cm^{-1}; ^1H NMR ($CDCl_3$) δ 10.82 (br s, 1 H), 2.47–2.14 (m, 4 H), 1.96 (t, J = 2.6 Hz, 1 H), 1.87–1.48 (m, 4 H).

A solution of crude 6-heptynoic acid (6.70 g, 53.1 mmol) and *p*-toluenesulfonic acid (100 mg) in methylene chloride (35 mL) and methanol (10 mL) was heated at reflux for 23 h. The resulting solution was washed with saturated sodium bicarbonate (50 mL), and the aqueous layer was extracted with methylene chloride (50 mL). The combined organic layers were dried ($MgSO_4$) and evaporated under reduced pressure to afford crude methyl 6-heptynoate (6.25 g, 44.6 mmol, 84%) as a pale yellow liquid. This material was characterized by IR spectroscopy and found to be uncontaminated by starting carboxylic acid: IR (neat) 2110, 1730, 1435 cm^{-1}.

A solution of crude methyl 6-heptynoate (6.25 g, 44.6 mmol) and hydrazine hydrate (3.13 g, 62.5 mmol, 1.40 eq) in ethanol (20

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mL) was heated at reflux for 20 h. Evaporation of the solvent under reduced pressure gave a yellow oil which was triturated with isopropyl ether, and the precipitated white solid was recrystallized from methylene chloride/isopropyl ether to give 6-heptynoic acid hydrazide (**12**) (5.00 g, 35.67 mmol, 80% for the last step, 34% overall starting from 5-hexyn-1-ol) as shiny white plates: mp 56.0–58.0 °C; IR (KBr) 2100, 1625, 1530, 1455 cm^{-1}; ^1H NMR ($CDCl_3$) δ 7.05 (br s, 1 H), 3.80 (br s, 2 H), 2.23–2.13 (m, 4 H), 1.96 (t, J = 2.6 Hz, 1 H), 1.80–1.55 (m, 4 H). Anal. Calcd for $C_7H_{12}N_2O$: C, 59.98; H, 8.63; N, 19.98. Found: C, 60.27; H, 8.42; N, 19.75.

5,6-Diphenyl-3-(5-hexynyl)-1,2,4-triazine (9g). A solution of 6-heptynoic acid hydrazide (**12**) (1.25 g, 8.93 mmol), benzil (1.89 g, 9.00 mmol), and ammonium acetate (11.4 g, 148 mmol, 16 equiv) in glacial acetic acid (20 mL) was heated at reflux for 5 h (116 °C). The resulting dark red solution was poured into water (100 mL), and the aqueous mixture was extracted with methylene chloride (2 × 100 mL). The combined methylene chloride extracts were extracted with water (150 mL) followed by a saturated solution of sodium bicarbonate (150 mL), dried ($MgSO_4$), and evaporated under reduced pressure to yield an amber oil (2.5 g). Chromatography of this oil using silica gel (60 g), eluting with 15% ether/petroleum ether, gave **9g** (1.45 g, 4.64 mmol, 52%) as a yellow solid, mp 72.0–74.0 °C; IR (KBr) 2110, 1600, 1500, 1440 cm^{-1}; ^1H NMR ($CDCl_3$) δ 7.60–7.26 (m, 10 H), 3.24 (t, J = 7.5 Hz, 2 H), 2.32–1.71 (m, 7 H), including 1.95 (t, J = 2.6 Hz, 1 H); LRMS m/z (relative intensity) 313 (M^+, 12), 178 (100). Anal. Calcd for $C_{21}H_{19}N_3$: C, 80.48; H, 6.11; N, 13.41. Found: C, 80.36; H, 5.96; N, 13.32.

6-Phenyl-2,3-cyclopentenopyridine (5i) and 5-Phenyl-2,3-cyclopentenopyridine (5h). To a stirred solution of 5-hexynoic acid hydrazide (**11**) (0.75 g, 6.0 mmol) and phenylglyoxal (0.90 g, 6.0 mmol, 1.0 equiv) in glacial acetic acid (15 mL) was added ammonium acetate (7.5 g, 97 mmol, 16 equiv), and the resulting mixture was heated at reflux (ca. 118 °C) for 5 h. The dark orange-red solution was then poured into water (50 mL), and the mixture was extracted with methylene chloride (2 × 50 mL). The combined extracts were dried ($MgSO_4$) and evaporated under reduced pressure, and the residue was chromatographed over a column of silica gel (ca. 30 g). Elution with a 25–33% ether/petroleum ether gradient gave 6-phenyl-2,3-cyclopentenopyridine (**5i**) (R_f = 0.40, methylene chloride) (0.20 g, 1.0 mmol, 17%) as a yellow solid: mp 82.0–83.0 °C (lit.[13] mp 79 °C or 80 °C); IR (KBr) 1580, 1565, 1440, 1425 cm^{-1}; ^1H NMR ($CDCl_3$) δ 8.00–7.86 (m, 2 H), 7.60–7.25 (m, 5 H), 3.09 (t, J = 7.6 Hz, 2 H), 2.96 (t, J = 7.6 Hz, 2 H), 2.32–1.93 (m, 2 H); LRMS m/z (relative intensity) 195 (M^+, 100), 115 (14), 91 (14).

(13) Gill, N. S.; James, B. K.; Lions, F.; Potts, K. T. *J. Am. Chem. Soc.* **1952**, *74*, 4923.

Evaporation of a second fraction (R_f = 0.15, methylene chloride) gave 5-phenyl-2,3-cyclopentenopyridine (**5h**) (0.21 g, 1.1 mmol, 18%) as an orange solid: mp 92.0–93.0 °C; IR (KBr) 1620, 1595, 1460, 1445, 1385 cm^{-1}; ^1H NMR ($CDCl_3$) δ 8.56 (br m, 1 H), 7.67–7.32 (m, 6 H), 3.14–2.90 (m, 4 H), 2.33–1.99 (m, 2 H); LRMS m/z (relative intensity) 195 (M^+, 100), 115 (4), 91 (3). Anal. Calcd for $C_{14}H_{13}N$: C, 86.12; H, 6.71; N, 7.17. Found: C, 85.92; H, 6.91; N, 7.26.

5,6-Diphenyl-2,3-cyclopentenopyridine (5g). To a solution of **11** (0.85 g, 6.8 mmol) and benzil (1.42 g, 6.8 mmol) in glacial acetic acid (15 mL) was added ammonium acetate (8.5 g, 110 mmol, 16 equiv), and the resulting mixture was heated at reflux for 4 h. Cooling and scratching induced the separation of a pale orange precipitate. Water (50 mL) was added, and the separated solid was removed by suction filtration and washed well with water. Drying in vacuo gave a tan solid (1.50 g), which was recrystallized from isopropyl ether to yield **5g** (1.24 g, 4.6 mmol, 68%) as golden needles: mp 161.0–163.0 °C; IR (KBr) 1595, 1545, 1490, 1445, 1420 cm^{-1}; ^1H NMR ($CDCl_3$) δ 7.53 (s, 1 H), 7.33–7.14 (m, 10 H), 3.21–2.94 (m, 4 H), 2.27–2.11 (m, 2 H); LRMS m/z (relative intensity) 271 (M^+, 55), 270 (100), 165 (6), 135 (7). Anal. Calcd for $C_{20}H_{17}N$: C, 88.52; H, 6.31; N, 5.16. Found: C, 88.24; H, 6.53; N, 5.15.

2,3-Diphenyl-5,6,7,8-tetrahydroquinoline (10g). A solution of 5,6-diphenyl-3-(5-hexynyl)-1,2,4-triazine (**9g**) (0.75 g, 2.4 mmol) in bromobenzene (3 mL) was heated at reflux (156 °C) with exclusion of moisture for 20 h. The reaction mixture was chromatographed over a column of silica gel (20 g); elution with 15% ether/petroleum ether gave **10g** (0.62 g, 2.2 mmol, 91%) as a white solid: mp 109.0–111.0 °C; IR (KBr) 1600, 1590, 1575, 1540, 1490, 1445, 1415, 1405 cm^{-1}; ^1H NMR ($CDCl_3$) δ 7.40 (s, 1 H), 7.28–7.15 (m, 10 H), 3.10–2.79 (m, 4 H), 2.00–1.84 (m, 4 H); LRMS m/z (relative intensity) 285 (M^+, 100), 256 (7), 123 (7). Anal. Calcd for $C_{21}H_{19}N$: C, 88.38; H, 6.71; N, 4.91. Found: C, 88.32; H, 6.81; N, 4.71.

Registry No. **1**, 130905-53-2; **2f**, 130905-54-3; **3a**, 106814-27-1; **3c**, 42809-56-3; **3d**, 106814-28-2; **3e**, 106814-29-3; **4a**, 83413-00-7; **4b**, 105783-78-6; **4f**, 106814-26-0; **5a**, 106814-31-7; **5b**, 106814-32-8; **5d**, 106814-34-0; **5e**, 106814-35-1; **5f**, 106814-33-9; **5g**, 126005-06-9; **5h**, 101161-85-7; **5i**, 56396-63-5; **6**, 74090-14-5; **8a**, 130905-55-4; **8d**, 91012-16-7; **8e**, 106814-30-6; **9d**, 106814-37-3; **9e**, 106814-36-2; **9g**, 130905-56-5; **10d**, 106814-39-5; **10e**, 106814-38-4; **10g**, 82132-58-9; **11**, 4230-19-7; **12**, 130905-57-6; $HC{:}C(CH{=}2)_3COOH$, 53293-00-8; $HC{:}C(CH_2)_3COOMe$, 77758-51-1; dimethyl malonate, 108-59-8; ethyl acetoacetate, 141-97-9; ethyl cyanoacetate, 105-56-6; malonitrile, 109-77-3; 4-iodo-1-butyne, 43001-25-8; 4-iodo-1-butene, 7766-51-0; 5-iodo-1-pentyne, 2468-55-5; 5-hexyn-1-ol, 928-90-5; 5-hexynyl methanesulfonate, 79496-61-0; 6-cyano-1-hexyne, 15295-69-9; 6-heptynoic acid, 30964-00-2; methyl 6-heptynoate, 56909-02-5; benzil, 134-81-6; phenylglyoxal, 1074-12-0.

Pteridines. 54. A Novel Synthetic Approach to C-6 Carbon Substituted Pterins via Intermolecular 1,3-Dipolar Cycloaddition Reactions[1]

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A number of 5-[(hydroxyimino)methyl]pyrazines and 6-[(hydroxyimino)methyl]pterins were converted to their respective nitrile oxides in the presence of dipolarophiles to give side-chain isoxazoles and isoxazolines as potential intermediates for the construction of multifunctional C-6 pterin substituents.

In earlier papers in this series we have described a variety of novel and unequivocal synthetic routes to 6-carbon-substituted pteridine derivatives, since most biologically significant pterins and chemotherapeutically useful pteridine derivatives are of this type (e.g., biopterin, folic acid, methotrexate, 10-deazafolic acid, the molybde-

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