4π Participation of 1-Aza-1,3-butadienes in [4 + 2] Cycloaddition Reactions: Intramolecular Diels-Alder Reactions of α,β-Unsaturated N-Sulfonylimines

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The 4π participation of α,β-unsaturated *N*-sulfonylimines in intramolecular Diels-Alder reactions with *unactivated* dienophiles is detailed in studies which further extend the scope of the [4 + 2] cycloaddition reactions of this new class of 1-aza-1,3-butadienes. Similar to observations made in the intermolecular [4 + 2] cycloaddition reactions, a strong endo diastereoselectivity (>20:1) was observed to dominate in the cycloaddition reaction of **5b** versus **5a** and **5c**. This endo specific reaction may be attributed to the combination of a pronounced, stabilizing secondary orbital interaction and preferred cycloaddition through an anti-endo transition state in which the lone pair on nitrogen and the C-aryl bond of the dienophile lie trans periplanar to one another benefiting from stabilization analogous to the ground-state anomeric effect.

A limited number of substituted 1-aza-1,3-butadienes have been introduced that participate as productive 4π components of Diels-Alder reactions.[2-12] In recent studies, we have examined alternative approaches to promote their 4π participation in [4 + 2] cycloaddition reactions. In these studies, the complementary N1 substitution ($-SO_2R$) of an α,β-unsaturated imine with an electron-withdrawing substituent was shown to accentuate the inherent electron-deficient nature of the 1-aza-1,3-butadiene and accelerate its intermolecular reaction with electron-rich dienophiles in endo specific $LUMO_{diene}$-controlled Diels-Alder reactions (>20:1 endo/exo).[13-22] Further, the α,β-unsaturated *N*-sulfonylimines have been shown to constitute stable, nonbasic electron-deficient imine derivatives capable of simple preparation, isolation, and purification. Herein, we detail a study of the intramolecular[23] Diels-Alder reactions of *N*-sulfonyl α,β-unsaturated imines bearing *unactivated* dienophiles which further extend the scope of the [4 + 2] cycloaddition reactions of this new class of 1-aza-1,3-butadienes.

Preparation of Substrates. Five substrates **5a-e** were selected for study which possess a range of unactivated dienophiles tethered to the *N*-sulfonyl-1-aza-1,3-butadiene by a four-atom linker chain. Employing a protocol introduced in early studies,[16,21] Wittig reaction of **1** with aldehydes **2a-e** provided the THP ethers of the α,β-unsaturated oximes **3a-e** in excellent yields (83-94%), Scheme I and Table I. Deprotection of the THP ethers[24] followed by generation of the *O*-methanesulfinyl oximes in CH_2Cl_2 and subsequent in situ homolytic rearrangement[25] provided the α,β-unsaturated *N*-methanesulfonylimines **5a-e** in good yields, Table I.

Intramolecular [4 + 2] Cycloaddition Reactions. Each of the five substrates was found to undergo the intramolecular Diels-Alder reaction readily, and the substrates bearing terminal substitution on the unactivated tethered dienophile (**5b**, **5c**, and **5e**) qualitatively exhibited the greatest reactivity. Nonetheless, even the substrates lacking terminal substitution on the tethered alkene or alkyne (**5a** and **5d**) were found to participate in the intramolecular [4 + 2] cycloaddition reaction in good yield. Notably, substrate **5a**, like **5b-5e**, was observed to slowly undergo the intramolecular cyclization even at room temperature. In instances when the **5b** and **5c** preparative reaction mixtures were stirred at room temperature for longer than 11 h, the crude ^1H NMR of the reaction products indicated the presence of the [4 + 2] cycloadducts. Although no evidence for formation of the [4 + 2] cycloadducts was detected in the preparation of substrates **5a**, **5d**, and **5e**, the *N*-sulfonylimines were found to slowly

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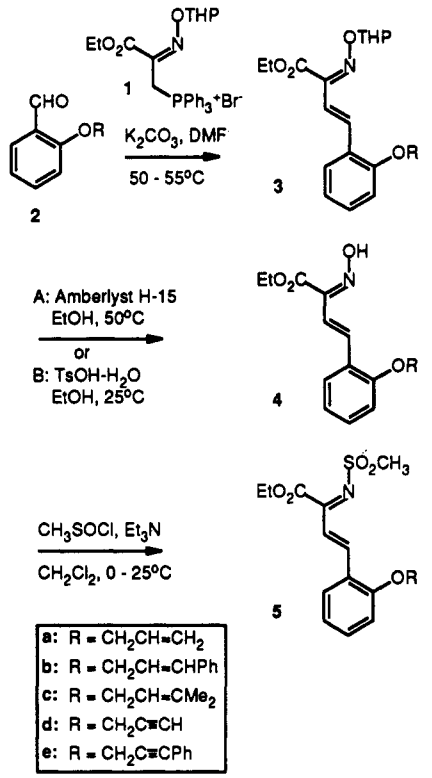
Table I

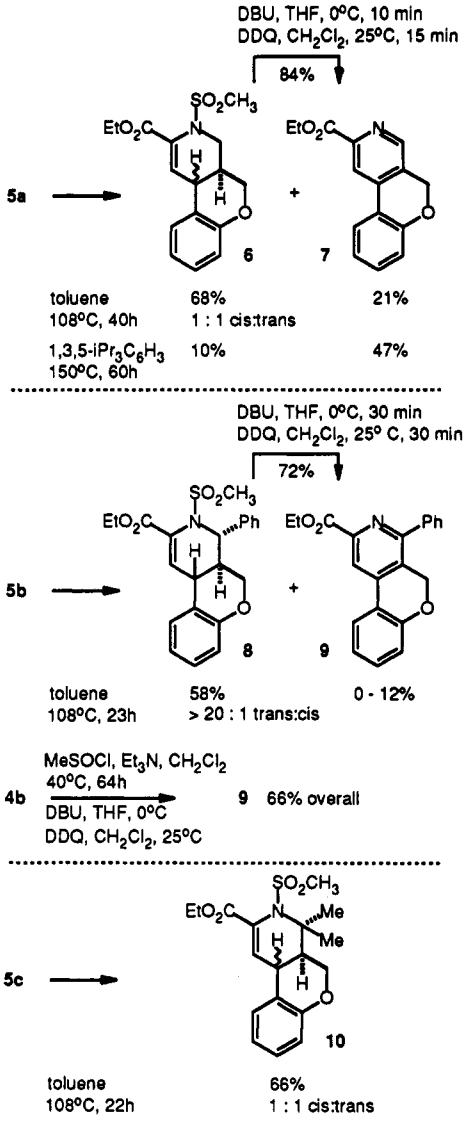
ıbstrate	reaction time (h)	3, % yield	method time (h)	4, % yield	5, % yield
a	84	83	A, 24	79	70
b	72	94	A, 36	72	86
c	72	92	B, 96	67	59
d	48	91	A, 13	97	59
e	48	94	A, 48	92	53

Scheme I



ınvert to the [4 + 2] cycloadducts at room temperature CH_2Cl_2 (^{1}H NMR). The only significant side reaction ɔserved under the thermal reaction conditions examined as hydrolysis of the *N*-sulfonylimine to the corresponding ɛtone by adventitious moisture. Provided adequate ɛecautions were taken to exclude water and oxygen from ıe reaction mixtures, the primary [4 + 2] cycloadducts **8**, and **10–12** or their subsequent elimination[26] and ɔmatization products **7** and **9** could be obtained in good elds, Schemes II and III. From a survey of representative ıermal reaction conditions, toluene at 108 °C (bath) was dged to provide the best conditions for clean and rapid ɛclization of the full range of alkene and alkyne substrates. ɛith the exception of substrate **5c** for which subsequent ɔmatization is not possible, the primary reaction prodɛts **6**, **8**, **11**, and **12** suffered partial aromatization under ıese conditions to provide **7** or **9**. For the alkyne ıbstrates **5d** and **5e**, this readily occurs through loss of ethanesulfinic acid under the thermal conditions alough the intermediate *N*-(methanesulfonyl)-1,4-dihy-

Scheme II



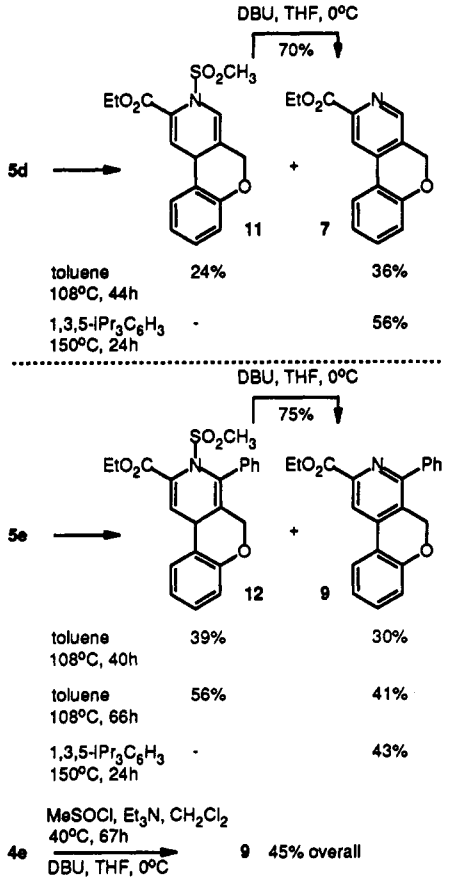
dropyridine primary cycloadducts proved surprisingly stable to isolation and characterization. Simple DBU treatment of isolated **11** and **12** (0 °C, THF) cleanly provided **7** and **9**, respectively. If the intramolecular cycloaddition reactions of **5d** and **5e** were conducted under more vigorous thermal conditions (150 °C), the aromatized products **7** and **9** could be isolated directly in high yield with little or no **11–12** being detected.

Similarly, the alkene substrates **5a–5b** provided mixtures of the primary cycloadducts **6** and **8** along with the aromatized products **7** and **9** in toluene (108 °C). The aromatization which requires elimination of methanesulfinic acid[26] and subsequent (air) oxidation occurs less readily than that of the alkyne substrates, and accordingly less **7** and **9** were detected under the thermal (108 °C) reaction conditions. Increasing the reaction temperature increased the proportion of aromatized product generated under the thermal conditions (i.e., 21% **7** at 108 °C versus 47% at 150 °C), or a deliberate two-step aromatization sequence could be employed to convert **6** and **8** to **7** and **9**. Without serious effort at optimization, the mild treatment of **6** or **8** with DBU proved sufficient to eliminate methanesulfinic acid (0 °C, THF), and subsequent DDQ oxidation provided **7** and **9** in excellent overall conversions. Thus, the aromatization of the primary cycloadducts **6** and **8** proved substantially easier to accomplish than

(26) The unstable intermediate methanesulfinic acid elimination oduct from **6** was isolated and partially characterized.

(27) For DEPT ^{13}C NMR, e = even and o = odd number of attached otons. Flash chromatography was performed on 230–400-mesh silica l (SiO_2) and 60–100-mesh Florisil. Tetrahydrofuran (THF), ethyl ether t_2O), and benzene (C_6H_6) were distilled from sodium benzophenone tyl. Dichloromethane (CH_2Cl_2) was distilled from P_2O_5. Triethylamine t_3N) and *N*,*N*-dimethylformamide (DMF) were distilled from CaH_2. l extraction and chromatographic solvents, ethyl ether (Et_2O), dichlomethane (CH_2Cl_2), ethyl acetate (EtOAc), and hexane were distilled ior to use. All reactions requiring anhydrous conditions and/or an inert nosphere were performed under a positive pressure of Ar or N_2.

Scheme III



initially anticipated and provides ready access to condensed pyridines. Of additional note was the observation that the conversion of **4b** to **9** could be accomplished in high yield under mild conditions without the intermediate isolation and purification of **5b** or **8**. In this instance, crude **5b** derived from **4b** underwent efficient [4 + 2] cycloaddition in refluxing CH_2Cl_2 (64 h). Sequential mild treatment of the resulting product with DBU and DDQ provided **9** in good overall yield (66%) which reflects accurately the limiting efficiency of the conversion of **4b** to **5b**.

The stereochemical course of the intramolecular [4 + 2] cycloadditions of **5a–5c** proved especially interesting. The assignment of the cis (J(H-4/H-5) = 6–7 Hz) or trans (J(H-4/H-5) = 11–13 Hz) stereochemistry was derived unambiguously from the characteristic coupling constants and verified by 2D H^1–H^1 NOESY NMR. Substrates **5a** and **5c** provided the cycloadducts **6** and **10**, respectively, as 1:1 mixtures of cis and trans isomers indicating that cycloaddition through a syn or anti transition state is equally favorable and expectedly independent of the neutral terminal substitution (H versus Me) of the alkene. In contrast, substrate **5b** cleanly provided the trans cycloadduct **8** (>20:1 trans/cis). Consistent with observations made in studies of the intermolecular cycloaddition reactions in which near-exclusive endo addition (>20:1 endo/exo) was observed with electron-donating (–OR) and aryl dienophile substituents,[16,20–22] **5b** provided *trans*-**8** derived from cycloaddition through an anti-endo transition state in which the dienophile phenyl group lies endo to the azadiene, Figure 1. Thus, comparable to observations made in the study of the intermolecular cycloaddition reactions of α,β-unsaturated *N*-sulfonylimines, the intramolecular reaction of substrates like **5b** may exhibit a

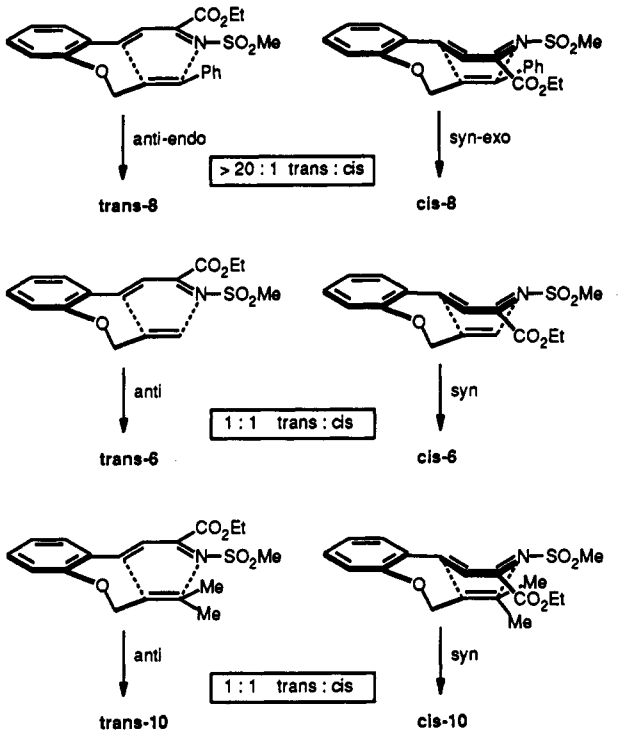


Figure 1.

strong and predictable endo diastereoselectivity attributable to a combination of stabilizing secondary orbital interactions and a transition-state anomeric effect with preferential cycloaddition through a transition state in which the azadiene N-1 lone pair and the C-aryl bond of the dienophile lie trans periplanar to one another.[16,21]

Experimental Section[27]

General Procedure for the Preparation of Aldehydes: 2-(2-Propenyloxy)benzaldehyde (2a). A solution of salicylaldehyde (3.21 g, 26.3 mmol, 1.0 equiv) in anhydrous THF (27 mL, 1.0 M) was treated with anhydrous K_2CO_3 (3.63 g, 26.3 mmol, 1.0 equiv). The slurry was stirred under N_2 for 5 min at 25 °C and was treated with allyl bromide (3.49 g, 28.9 mmol, 1.1 equiv). The reaction mixture was warmed at reflux for 48 h and allowed to cool to 25 °C. The mixture was diluted with H_2O (200 mL) and extracted with Et_2O (4 × 100 mL). The combined extracts were washed with H_2O (1 × 200 mL) and saturated aqueous NaCl (1 × 200 mL), dried (Na_2SO_4), and concentrated in vacuo. Flash chromatography (SiO_2, 5 × 15 cm, 10% EtOAc–hexanes) afforded **2a** (3.25 g, 4.26 g theoretical, 83%) as a pale yellow liquid: bp 75–76 °C (0.14 mmHg) (lit.[28] bp 142 °C (17 mmHg)); ^{1}H NMR ($CDCl_3$, 200 MHz, ppm) 10.42 (1 H, s, CHO), 7.71 (1 H, dd, J = 7.7, 1.8 Hz), 7.40 (1 H, dt, J = 7.4, 1.8 Hz), 6.87 (2 H, m), 5.95 (1 H, m, $OCH_2CH{=}CH_2$), 5.38 (1 H, dd, J = 17.3, 1.5 Hz, $CH{=}CH_tH_c$), 5.21 (1 H, dd, J = 10.5, 1.4 Hz, $CH{=}CH_tH_c$), 4.51 (2 H, dd, J = 3.1, 1.6 Hz, OCH_2); ^{13}C NMR ($CDCl_3$, 50 MHz, ppm) 189.4 (o, CHO), 160.8 (e), 135.9 (o), 132.2 (o, =CH), 128.0 (o), 124.8 (e), 120.5 (o), 117.6 (e, $=CH_2$), 112.6 (o), 68.6 (e, OCH_2); IR (neat) ν_{max} 3078, 2864, 2762, 1736, 1600, 1484, 1458, 1396, 1286, 1190, 1042, 996 cm^{-1}; EIHRMS m/e 162.0680 ($C_{10}H_{10}O_2$ requires 162.0680).

2-[(*E*)-(3-Phenyl-2-propenyl)oxy]benzaldehyde (2b): pale yellow solid; mp 49.5–51 °C (EtOAc–hexanes) (lit.[28] mp 51 °C); ^{1}H NMR ($CDCl_3$, 200 MHz, ppm) 10.58 (1 H, s, CHO), 7.85 (1 H, dd, J = 7.8, 1.9 Hz), 7.54 (1 H, dt, J = 7.2, 1.8 Hz), 7.24–7.44 (5 H, m), 7.02 (2 H, m), 6.77 (1 H, d, J = 16.0 Hz, $=CHPh$), 6.43 (1 H, dt, J = 16.0, 5.7 Hz, $CH_2CH{=}$), 4.84 (2 H, d, J = 5.7 Hz, OCH_2); ^{13}C NMR ($CDCl_3$, 50 MHz, ppm) 190.1 (o, CHO), 161.2

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(e), 136.2 (e), 136.0 (o), 133.7 (o), 128.8 (o), 128.6 (o), 128.3 (o), 126.7 (o), 125.3 (e), 123.5 (o), 121.0 (o), 113.0 (o), 69.1 (e, OCH_2); IR (KBr) ν_{max} 3028, 2944, 2862, 2756, 1794, 1598, 1480, 1456, 1376, 1286, 1236, 1156, 966 cm^{-1}; EIHRMS *m/e* 238.0994 ($C_{16}H_{14}O_2$ requires 238.0994).

2-[(3-Methyl-2-butenyl)oxy]benzaldehyde (2c): yellow liquid; bp 172–174 °C (3.7 mmHg); ^1H NMR ($CDCl_3$, 200 MHz, ppm)[29] 10.51 (1 H, s, CHO), 7.83 (1 H, dd, *J* = 7.9, 1.8 Hz), 7.51 (1 H, dt, *J* = 8.1, 1.9 Hz), 7.02 (2 H, t, *J* = 8.0 Hz), 5.50 (1 H, t, *J* = 6.6 Hz, CH=), 4.63 (2 H, d, *J* = 6.7 Hz, OCH_2), 1.81 (3 H, s, CH_3), 1.76 (3 H, s, CH_3); ^{13}C NMR ($CDCl_3$, 50 MHz, ppm) 190.2 (o, CHO), 161.5 (e), 138.8 (e), 135.9 (o), 128.3 (o), 125.2 (e), 120.6 (o), 119.1 (o), 113.0 (o), 65.4 (e, OCH_2), 25.6 (o, CH_3), 18.0 (o, CH_3); IR (neat) ν_{max} 3036, 2934, 2916, 2862, 2758, 1688, 1598, 1480, 1286, 1162, 1042, 992 cm^{-1}; EIHRMS *m/e* 190.0994 ($C_{12}H_{14}O_2$ requires 190.0994).

2-[(2-Propynyl)oxy]benzaldehyde (2d): white solid; mp 60–61 °C (EtOAc–hexanes) (lit.[30] mp 66–68 °C (petroleum ether)); ^1H NMR ($CDCl_3$, 200 MHz, ppm) 10.39 (1 H, s, CHO), 7.74 (1 H, dd, *J* = 7.7, 1.8 Hz), 7.48 (1 H, dt, *J* = 7.2, 1.8 Hz), 6.99 (2 H, m), 4.73 (2 H, d, *J* = 2.4 Hz, OCH_2), 2.56 (1 H, t, *J* = 2.4 Hz, ≡CH); ^{13}C NMR ($CDCl_3$, 50 MHz, ppm) 189.5 (o, CHO), 159.7 (e), 135.7 (o), 128.3 (o), 125.3 (e), 121.5 (o), 113.1 (o), 77.5 (e, C≡CH), 76.4 (e, OCH_2), 56.0 (o, C≡CH); IR (KBr) ν_{max} 3270, 3224, 2872, 2766, 2118, 1684, 1600, 1484, 1460, 1374, 1288, 1194, 1044, 956 cm^{-1}; EIHRMS *m/e* 160.0523 ($C_{10}H_8O_2$ requires 160.0524).

2-[(3-Phenyl-2-propynyl)oxy]benzaldehyde (2e): pale yellow solid; mp 82.5–84 °C (EtOAc–hexanes); ^1H NMR ($CDCl_3$, 200 MHz, ppm)[11,31] 10.51 (1 H, s, CHO), 7.87 (1 H, dd, *J* = 7.7, 1.8 Hz), 7.57 (1 H, dt, *J* = 7.6, 1.8 Hz), 7.40 (2 H, m), 7.32 (3 H, m), 7.19 (1 H, d, *J* = 8.4 Hz), 7.09 (1 H, t, *J* = 7.6 Hz), 5.04 (2 H, s, OCH_2); ^{13}C NMR ($CDCl_3$, 50 MHz, ppm) 190.0 (o, CHO), 160.3 (e), 135.9 (o), 131.9 (o), 129.0 (o), 128.6 (o), 128.5 (o), 125.6 (e), 122.0 (e), 121.6 (o), 113.5 (o), 88.1 (e, PhC≡C), 82.9 (e, PhC≡*C*), 57.2 (e, OCH_2); IR (KBr) ν_{max} 3074, 3034, 2962, 2934, 2238, 1680, 1662, 1597, 1488, 1480, 1462, 1374, 1286, 1166, 1106, 1044, 996 cm^{-1}; EIHRMS *m/e* 236.0837 ($C_{16}H_{12}O_2$ requires 236.0837).

General Procedure for the Wittig Reaction of 1 with Aldehydes 2a–e: Ethyl (*E*)-4-[2-(2′-Propenyloxy)phenyl]-2-[(2-tetrahydropyranyloxy)imino]-3-butenoate (3a). A stirred suspension of **1** (8.12 g, 14.6 mmol, 1.1 equiv) in anhydrous DMF (67 mL, 0.2 M) was treated with anhydrous K_2CO_3 (2.02 g, 14.6 mmol, 1.1 equiv). The slurry was stirred under N_2 for 5 min at 25 °C and was treated with **2a** (2.15 g, 13.3 mmol, 1.0 equiv). The reaction mixture was stirred at 50 °C for 86 h and then diluted with H_2O (100 mL) and extracted with Et_2O (4 × 100 mL). The combined organic extracts were washed with H_2O (1 × 100 mL) and saturated aqueous NaCl (1 × 100 mL), dried (Na_2SO_4), and concentrated in vacuo. Flash chromatography (SiO_2, 4 × 23 cm, 21% EtOAc–hexanes) afforded **3a** (3.98 g, 4.78 g theoretical, 83%) as a colorless viscous oil: ^1H NMR ($CDCl_3$, 200 MHz, ppm) 7.92 (1 H, d, *J* = 16.9 Hz, C4-H), 7.54 (1 H, d, *J* = 7.7 Hz), 7.29 (1 H, d, *J* = 16.9 Hz, C3-H), 7.21 (1 H, m), 6.93 (1 H, t, *J* = 7.6 Hz), 6.84 (1 H, d, *J* = 8.4 Hz), 6.01 (1 H, m, OCH_2CH=CH_2), 5.47 (1 H, m, OCHO), 5.39 (1 H, dd, *J* = 17.3, 1.5 Hz, CH=CH_tH_c), 5.23 (1 H, dd, *J* = 10.5, 1.4 Hz, CH=CH_tH_c), 4.54 (2 H, dd, *J* = 5.1, 1.8 Hz, OCH_2CH=CH_2), 4.33 (2 H, q, *J* = 7.3 Hz, $CO_2CH_2CH_3$), 3.90 (1 H, m, $OCHHCH_2$), 3.63 (1 H, m, $OCHHCH_2$), 1.85 (2 H, m, $O_2CHCH_2CH_2$), 1.60 (4 H, m, CH_2CH_2), 1.34 (3 H, t, *J* = 7.1 Hz, CH_3); ^{13}C NMR ($CDCl_3$, 50 MHz, ppm) 163.9 (e, C=O), 156.9 (e), 150.0 (e, C=N), 135.6 (o), 133.0 (o, C4), 130.6 (o), 127.6 (o), 125.4 (e), 120.9 (o), 117.5 (e, $=CH_2$), 114.2 (o, C3), 112.4 (o), 101.7 (o, OCHO), 68.9 (e, OCH_2CH=), 62.4 (e, $CO_2CH_2CH_3$), 61.7 (e, OCH_2CH_2), 28.3 (e, O_2CHCH_2), 24.8 (e, OCH_2CH_2), 19.0 (e, $CH_2CH_2CH_2$), 13.8 (o, CH_3); IR (neat) ν_{max} 2946, 1722, 1598, 1486, 1456, 1265, 1246, 1176, 1042, 1018, 954 cm^{-1}; CIHRMS (2-methylpropane) *m/e* 360.1811 (M + H^+, $C_{20}H_{25}NO_5$ requires 360.1811).

Ethyl (*E*)-4-[2(*E*)-[(3′-phenyl-2′-propenyl)oxy]phenyl]-2-[(2-tetrahydropyranyloxy)imino]-3-butenoate (3b): yellow oil; ^1H NMR ($CDCl_3$, 200 MHz, ppm) 8.04 (1 H, d, *J* = 16.9 Hz, C4-H), 7.61 (1 H, dd, *J* = 7.6, 1.5 Hz), 7.23–7.41 (7 H, m PhH, ArH, C3-H), 6.97 (2 H, m), 6.76 (1 H, d, *J* = 16.0 Hz, =*CH*Ph), 6.41 (1 H, dt, *J* = 16.0, 5.6 Hz, OCH_2CH=), 5.49 (1 H, t, *J* = 2.8 Hz, OCHO), 4.73 (2 H, dd, *J* = 5.6, 1.3 Hz, OCH_2CH=), 4.35 (2 H, q, *J* = 7.2 Hz, $CO_2CH_2CH_3$), 3.87 (1 H, m, $OCHHCH_2$), 3.61 (1 H, m, $OCHHCH_2$), 1.82 (2 H, m, O_2CHCH_2), 1.56 (4 H, m, CH_2CH_2), 1.34 (3 H, t, *J* = 7.1 Hz, CH_3); ^{13}C NMR ($CDCl_3$, 50 MHz, ppm) 163.7 (e, C=O), 157.1 (e), 149.9 (e, C=N), 136.4 (e), 135.7 (o), 133.0 (o), 139.7 (o, C4), 128.6 (o), 128.0 (o), 127.5 (o), 126.6 (o), 125.6 (e), 124.1 (o), 121.0 (o), 114.2 (o), 112.5 (o, C3), 101.8 (o, OCHO), 68.9 (e, OCH_2CH=), 62.6 (e, $CO_2CH_2CH_3$), 61.8 (e, OCH_2CH_2), 28.4 (e, O_2CHCH_2), 24.8 (e, OCH_2CH_2), 19.1 (e, $CH_2CH_2CH_2$), 13.8 (o, CH_3); IR (neat) ν_{max} 2946, 2870, 1718, 1612, 1598, 1486, 1452, 1374, 1244, 1176, 1116, 1042, 956 cm^{-1}; EIHRMS *m/e* 435.2046 ($C_{26}H_{29}NO_5$ requires 435.2046).

Ethyl (*E*)-4-[2-[(3′-methyl-2′-butenyl)oxy]phenyl]-2-[(2-tetrahydropyranyloxy)imino]-3-butenoate (3c): yellow oil; ^1H NMR ($CDCl_3$, 200 MHz, ppm) 7.91 (1 H, d, *J* = 16.9 Hz, C4-H), 7.54 (1 H, d, *J* = 7.7 Hz), 7.27 (1 H, d, *J* = 16.9 Hz, C3-H), 7.24 (1 H, m), 6.89 (2 H, m), 5.47 (2 H, m, OCHO, OCH_2CH=), 4.53 (2 H, d, *J* = 6.3 Hz, OCH_2CH=), 4.34 (2 H, q, *J* = 7.2 Hz, $CO_2CH_2CH_3$), 3.86 (1 H, m, $OCHHCH_2$), 3.67 (1 H, m, $OCHHCH_2$), 1.85 (2 H, m, O_2CHCH_2), 1.74 (3 H, s, CH_3), 1.70 (3 H, s, CH_3), 1.61 (4 H, m, CH_2CH_2), 1.35 (3 H, t, *J* = 7.1 Hz, $CO_2CH_2CH_3$); ^{13}C NMR ($CDCl_3$, 50 MHz, ppm) 163.6 (e, C=O), 157.3 (e), 150.0 (e, C=N), 137.9 (e), 135.9 (o), 131.0 (o, C4), 127.4 (o), 125.4 (e), 120.6 (o), 119.7 (o), 114.0 (o, C3), 112.4 (o), 101.7 (o, OCHO), 65.2 (e, OCH_2CH=), 62.4 (e, $CO_2CH_2CH_3$), 61.6 (e, OCH_2CH_2), 28.3 (e, O_2CHCH_2), 25.4 (o, CH_3), 24.8 (e, OCH_2CH_2), 19.0 (e, $CH_2CH_2CH_2$), 17.8 (o, CH_3), 13.5 (o, $CO_2CH_2CH_3$); IR (neat) ν_{max} 2944, 2872, 1726, 1614, 1598, 1487, 1456, 1322, 1296, 1204, 1160, 1076, 1042, 954 cm^{-1}; CIHRMS (2-methylpropane) *m/e* 388.2128 (M + H^+, $C_{22}H_{29}NO_5$ requires 388.2124).

Ethyl (*E*)-4-[2-(2′-propynyloxy)phenyl]-2-[(2-tetrahydropyranyloxy)imino]-3-butenoate (3d): white solid; mp 80–81 °C (EtOAc–hexanes); ^1H NMR ($CDCl_3$, 200 MHz, ppm) 7.93 (1 H, d, *J* = 16.9 Hz, C4-H), 7.59 (1 H, dd, *J* = 8.4, 1.8 Hz), 7.28 (1 H, dt, *J* = 8.3, 1.4 Hz), 7.23 (1 H, d, *J* = 16.5 Hz, C3-H), 6.95 (2 H, m), 5.48 (1 H, t, *J* = 2.9 Hz, OCHO), 4.69 (2 H, d, *J* = 2.3 Hz, OCH_2C≡), 4.34 (2 H, q, *J* = 7.0 Hz, $CO_2CH_2CH_3$), 3.85 (1 H, m, $OCHHCH_2$), 3.65 (1 H, m, $OCHHCH_2$), 2.50 (1 H, t, *J* = 2.2 Hz, ≡CH), 1.85 (2 H, m, O_2CHCH_2), 1.60 (4 H, m, CH_2CH_2), 1.34 (3 H, t, *J* = 6.9 Hz, CH_3); ^{13}C NMR ($CDCl_3$, 50 MHz, ppm) 163.5 (e, C=O), 155.7 (e), 149.6 (e, C=N), 135.1 (o), 130.5 (o, C4), 127.1 (o), 125.7 (e), 121.6 (o), 114.2 (o, C3), 112.6 (o), 101.7 (o, OCHO), 78.0 (e, PhC≡), 75.7 (e, OCH_2C≡), 62.4 (e, $CO_2CH_2CH_3$), 61.6 (e, OCH_2CH_2), 55.9 (o, ≡CH), 28.3 (e, O_2CHCH_2), 24.7 (e, OCH_2CH_2), 18.9 (e, $CH_2CH_2CH_2$), 13.7 (o, CH_3); IR (KBr) ν_{max} 3300, 2944, 2864, 2122, 1726, 1614, 1598, 1578, 1480, 1458, 1392, 1354, 1298, 1258, 1172, 1050, 1019, 946 cm^{-1}; CIHRMS (2-methylpropane) *m/e* 358.1654 (M + H^+, $C_{20}H_{23}NO_5$ requires 358.1654).

Ethyl (*E*)-4-[2-[(3′-phenyl-2′-propynyl)oxy]phenyl]-2-[(2-tetrahydropyranyloxy)imino]-3-butenoate (3e): yellow oil; ^1H NMR ($CDCl_3$, 200 MHz, ppm) 8.01 (1 H, d, *J* = 16.9 Hz, C4-H), 7.62 (1 H, d, *J* = 7.7 Hz), 7.39 (2 H, m, ArH, C3-H), 7.30 (5 H, m), 7.09 (1 H, d, *J* = 8.3 Hz), 7.02 (1 H, t, *J* = 7.7 Hz), 5.51 (1 H, t, *J* = 3.3 Hz, OCHO), 4.96 (2 H, s, OCH_2C≡), 4.36 (2 H, q, *J* = 7.2 Hz, $CO_2CH_2CH_3$), 3.88 (1 H, m, $OCHHCH_2$), 3.64 (1 H, m, $OCHHCH_2$), 1.87 (2 H, m, $O_2CHCH_2CH_2$), 1.62 (4 H, m, CH_2CH_2), 1.37 (3 H, t, *J* = 7.2 Hz, CH_3); ^{13}C NMR ($CDCl_3$, 50 MHz, ppm), 163.7 (e, C=O), 156.2 (e), 149.9 (e, C=N), 135.5 (o), 131.9 (o), 130.7 (o, C4), 128.8 (o), 128.4 (o), 127.3 (o), 126.1 (e), 122.3 (e), 121.7 (o), 114.4 (o, C3), 113.1 (o), 101.9 (o, OCHO), 87.4 (e, PhC≡), 83.6 (e, ≡CCH_2O), 62.6 (c, $CO_2CH_2CH_3$), 61.9 (e, OCH_2CH_2), 57.1 (e, OCH_2C≡), 28.4 (e, O_2CHCH_2), 24.9 (e, OCH_2CH_2), 19.1 (e, $CH_2CH_2CH_2$), 13.9 (o, CH_3); IR (neat) ν_{max} 2948, 2872, 2244, 1726, 1598, 1578, 1488, 1372, 1322, 1298, 1258, 1176, 1040, 1018, 998 cm^{-1}; CIHRMS (2-methylpropane) *m/e* 434.1967 (M + H^+, $C_{26}H_{27}NO_5$ requires 434.1967).

General Procedure for Deprotection of the Oxime Tetrahydropyranyl Ethers 3a–e. Method A: Ethyl (*E*)-2-(Hydroxyimino)-4-[2-(2′-propenyloxy)phenyl]-3-but-

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enoate (4a). A solution of **3a** (765 mg, 2.13 mmol, 1.0 equiv) in anhydrous EtOH (14.2 ml, 0.15 M) was treated with catalytic Amberlyst H-15 (64 mg, 300 mg catalyst/10 mmol substrate) and warmed at 60 °C for 26.5 h. The reaction mixture was filtered to remove the Amberlyst H-15, and the filtrate was concentrated in vacuo. Flash chromatography (SiO_2, 2.5 × 9.0 cm, 30% EtOAc–hexanes) afforded **4a** (465 mg, 586 mg theoretical, 79%) as a pale yellow solid: mp 100–101 °C (EtOAc–hexanes); ^{1}H NMR ($CDCl_3$, 200 MHz, ppm) 9.84 (1 H, bs, NOH), 8.16 (1 H, d, J = 16.9 Hz, C4-H), 7.60 (1 H, dd, J = 7.7, 1.3 Hz), 7.32 (1 H, d, J = 16.9 Hz, C3-H), 7.23 (1 H, m), 6.97 (1 H, t, J = 7.7 Hz), 6.88 (1 H, d, J = 8.4 Hz), 6.14 (1 H, m, OCH_2CH=CH_2), 5.44 (1 H, dd, J = 17.3, 1.6 Hz, CH=CH_tH_c), 5.28 (1 H, dd, J = 10.5, 1.5 Hz, CH=CH_tH_c), 4.58 (2 H, dd, J = 5.0, 1.5 Hz, OCH_2CH=CH_2), 4.36 (2 H, q, J = 7.1 Hz, $CO_2CH_2CH_3$), 1.39 (3 H, t, J = 7.2 Hz, CH_3); ^{13}C NMR ($CDCl_3$, 50 MHz, ppm) 163.3 (e, C=O), 157.1 (e), 147.5 (e, C=N), 135.7 (o), 133.1 (o, C4), 130.6 (o), 127.5 (o), 125.8 (e), 121.0 (o), 117.4 (e, $=CH_2$), 113.5 (o, C3), 112.5 (o), 69.0 (e, OCH_2CH=), 61.7 (e, $CO_2CH_2CH_3$), 13.8 (o, CH_3); IR (KBr) ν_{max} 3208, 2982, 2912, 1732, 1606, 1594, 1490, 1454, 1386, 1284, 1116, 1036, 1002, 988 cm^{-1}; EIHRMS m/e 275.1158 ($C_{15}H_{17}NO_4$ requires 275.1158).

Method B: Ethyl (*E*)-2-(Hydroxyimino)-4-[2-[(3′-methyl-2′-butenyl)oxy]phenyl]-3-butenoate (4c). A solution of **3c** (2.16 g, 5.57 mmol, 1.0 equiv) in anhydrous EtOH (28 mL, 0.2 M) was treated with 20 mol % p-TsOH–H_2O (212 mg, 1.1 mmol) and stirred at 25 °C for 4 d. The reaction mixture was concentrated in vacuo. Flash chromatography (SiO_2, 4 × 10 cm, 30% EtOAc–hexanes) afforded **4c** (1.14 g, 1.69 g theoretical, 67%) as a yellow solid: mp 103–104 °C (EtOAc–hexanes); ^{1}H NMR ($CDCl_3$, 400 MHz, ppm) 10.4 (1 H, bs, NOH), 8.1 (1 H, d, J = 16.9 Hz, C4-H), 7.59 (1 H, dd, J = 7.7, 1.5 Hz), 7.33 (1 H, d, J = 16.9 Hz, C3-H), 7.27 (1 H, t, J = 8.3 Hz), 6.94 (1 H, t, J = 7.6 Hz), 6.88 (1 H, d, J = 7.7 Hz), 5.50 (1 H, dt, J = 6.5, 1.4 Hz, $OCHCH$=), 4.57 (2 H, d, J = 6.5 Hz, OCH_2CH=), 4.37 (2 H, q, J = 7.2 Hz, CO_2CH_2-CH_3), 1.77 (3 H, s, CH_3), 1.73 (3 H, s, CH_3), 1.40 (3 H, t, J = 7.1 Hz, $CO_2CH_2CH_3$); ^{13}C NMR ($CDCl_3$, 50 MHz, ppm) 163.4 (e, C=O), 157.5 (e), 147.8 (e, C=N), 137.8 (e), 135.9 (o), 130.6 (o, C4), 127.7 (o), 125.8 (e), 120.8 (o), 119.9 (o), 113.4 (o, C3), 112.6 (o), 65.4 (e, OCH_2CH=), 61.7 (e, $CO_2CH_2CH_3$), 25.6 (o, CH_3), 18.1 (o, CH_3), 13.8 (o, $CH_2CH_2CH_3$); IR (KBr) ν_{max} 3213, 2984, 2933, 1724, 1596, 1490, 1453, 1411, 1386, 1296, 1233, 1169, 1102, 1019, 982 cm^{-1}; FABHRMS (NBA) m/e 304.1549 (M + H$^+$, $C_{17}H_{21}$-NO_4 requires 304.1549).

Ethyl (*E*)-2-(hydroxyimino)-4-[2(*E*)-[(3′-phenyl-2′-propenyl)oxy]phenyl]-3-butenoate (4b): white solid; mp 157–158 °C (EtOAc–hexanes); ^{1}H NMR ($CDCl_3$, 200 MHz, ppm) 9.39 (1 H, bs, NOH), 8.21 (1 H, d, J = 16.8 Hz, C4-H), 7.63 (1 H, d, J = 7.7 Hz), 7.41–7.46 (2 H, m, ArH, C3-H), 7.26–7.37 (5 H, m), 6.98 (2 H, m), 6.82 (1 H, d, J = 16.2 Hz, =CHPh), 6.43 (1 H, dt, J = 16.1, 5.2 Hz, OCH_2CH=), 4.78 (2 H, d, J = 5.2 Hz, OCH_2-CH=), 4.34 (2 H, q, J = 7.3 Hz, $CO_2CH_2CH_3$), 1.36 (3 H, t, J = 7.2 Hz, CH_3); ^{13}C NMR ($CDCl_3$, 50 MHz, ppm) 163.4 (e, C=O), 157.2 (e), 148.0 (e, C=N), 136.7 (e), 135.7 (o), 132.7 (o), 130.8 (o, C4), 128.7 (o), 128.0 (o), 127.6 (o), 127.0 (o), 125.9 (e), 124.3 (o), 121.2 (o), 113.5 (o), 112.7 (o, C3), 68.9 (e, OCH_2CH=), 61.8 (e, $CO_2CH_2CH_3$), 13.9 (o, CH_3); IR (KBr) ν_{max} 3224, 3060, 2980, 2904, 1724, 1618, 1598, 1486, 1454, 1412, 1386, 1330, 1246, 1164, 1110, 1016, 986 cm^{-1}; CIHRMS (2-methylpropane) m/e 352.1553 (M + H$^+$, $C_{21}H_{21}NO_4$ requires 352.1549).

Ethyl (*E*)-2-(hydroxyimino)-4-[2-(2′-propynyloxy)phenyl]-3-butenoate (4d): yellow solid; mp 139–140 °C (EtOAc–hexanes); ^{1}H NMR ($CDCl_3$, 200 MHz, ppm) 9.56 (1 H, bs, NOH), 8.11 (1 H, d, J = 16.9 Hz, C4-H), 7.62 (1 H, d, J = 7.3 Hz), 7.26–7.37 (2 H, m, ArH, C3-H), 7.04 (2 H, m), 4.76 (2 H, d, J = 1.9 Hz, OCH_2C≡), 4.38 (2 H, q, J = 7.0 Hz, $COCH_2CH_3$), 2.50 (1 H, s, C≡CH), 1.41 (3 H, t, J = 7.1 Hz, CH_3); ^{13}C NMR ($CDCl_3$, 50 MHz, ppm) 163.4 (e, C=O), 156.0 (e), 147.9 (e, C=N), 135.3 (o), 130.6 (o), 127.5 (o), 126.2 (e), 121.9 (o), 113.7 (o, C3), 112.9 (o), 78.4 (e, CH_2C≡), 75.8 (o, OCH_2C≡), 61.8 (e, $CO_2CH_2CH_3$), 56.2 (o, ≡CH), 13.9 (o, CH_3); IR (KBr) ν_{max} 3250, 3122, 2980, 2966, 2116, 1728, 1612, 1598, 1578, 1484, 1428, 1386, 1296, 1252, 1166, 1120, 1038, 986 cm^{-1}; EIHRMS m/e 273.0998 ($C_{15}H_{15}NO_4$ requires 273.1001).

Ethyl (*E*)-2-(hydroxyimino)-4-[2-[(3′-phenyl-2′-propynyl)oxy]phenyl]-3-butenoate (4e): yellow solid; mp 115–116 °C (EtOAc–hexanes); ^{1}H NMR ($CDCl_3$, 200 MHz, ppm) 10.1 (1 H, bs, NOH), 8.20 (1 H, d, J = 16.9 Hz, C4-H), 7.66 (1 H, d, J = 7.6 Hz), 7.26–7.46 (7 H, m, ArH, C3-H, PhH), 7.12 (1 H, d, J = 8.1 Hz), 7.03 (1 H, t, J = 7.6 Hz), 4.99 (2 H, s, OCH_2C≡), 4.36 (2 H, q, J = 7.2 Hz, $CO_2CH_2CH_3$), 1.40 (3 H, t, J = 7.2 Hz, CH_3); ^{13}C NMR ($CDCl_3$, 50 MHz, ppm) 163.3 (e, C=O), 156.3 (e), 147.5 (e, C=N), 135.5 (o), 131.9 (o), 130.6 (o, C4), 128.8 (o), 128.4 (o), 127.4 (o), 126.2 (e), 122.3 (e), 121.7 (o), 113.6 (o, C3), 113.1 (o), 87.4 (e, C≡CPh), 83.8 (e, OCH_2C≡C), 61.8 (e, $CO_2CH_2CH_3$), 57.1 (e, OCH_2C≡), 13.9 (o, CH_3); IR (KBr) ν_{max} 3168, 3000, 2972, 2240, 1738, 1598, 1486, 1420, 1366, 1298, 1254, 1202, 1174, 1148, 1106, 988 cm^{-1}; EIHRMS m/e 349.1309 ($C_{21}H_{19}NO_4$ requires 349.1314).

General Procedure for the Preparation of *N*-(Methylsulfonyl)-1-aza-1,3-butadienes: Ethyl (*E*)-2-[(Methylsulfonyl)imino]-4-[2-(2′-propenyloxy)phenyl]-3-butenoate (5a). A solution of **4a** (197 mg, 0.72 mmol, 1.0 equiv) in anhydrous CH_2Cl_2 (7.2 mL, 0.1 M) was cooled to 0 °C under N_2 and treated sequentially with Et_3N (145 mg, 200 μL, 1.43 mmol, 2.0 equiv) and methanesulfinyl chloride (141 mg, 97 μL, 1.43 mmol, 2.0 equiv). The reaction mixture was stirred at 0 °C for 30 min, allowed to warm to 25 °C, and further stirred at 25 °C for an additional 30 min. The resulting reaction mixture was concentrated in vacuo. Flash chromatography (SiO_2, 2.0 × 8.0 cm, 25% EtOAc–hexanes) afforded **5a** (169 mg, 242 mg theoretical, 70%) as a yellow oil: ^{1}H NMR ($CDCl_3$, 400 MHz, ppm) 7.84 (1 H, d, J = 16.8 Hz, C4-H), 7.53 (1 H, d, J = 7.2 Hz), 7.38 (1 H, t, J = 7.2 Hz), 6.97 (1 H, t, J = 7.2 Hz), 6.92 (1 H, d, J = 16.9 Hz, C3-H), 6.89 (1 H, d, J = 8.7 Hz), 6.04 (1 H, m, OCH_2CH=CH_2), 5.39 (1 H, dd, J = 17.3, 1.6 Hz, CH=CH_tH_c), 5.29 (1 H, dd, J = 10.5, 1.5 Hz, CH=CH_tH_c), 4.58 (2 H, d, J = 4.5 Hz, OCH_2CH=CH_2), 4.43 (2 H, q, J = 7.2 Hz, $CO_2CH_2CH_3$), 3.10 (3 H, s, SO_2CH_3), 1.40 (3 H, t, J = 7.2 Hz, $CO_2CH_2CH_3$); IR (neat) ν_{max} 3016, 2986, 2936, 1738, 1599, 1557, 1486, 1454, 1317, 1246, 1179, 1147, 1012, 966 cm^{-1}; FABHRMS (NBA-CsI) m/e 470.0038 (M + Cs$^+$, $C_{16}H_{19}NO_5S$ requires 470.0038).

Ethyl (*E*)-2-[(methylsulfonyl)imino]-4-[2(*E*)-[(3′-phenyl-2′-propenyl)oxy]phenyl]-3-butenoate (5b): yellow oil; ^{1}H NMR ($CDCl_3$, 400 MHz, ppm) 7.89 (1 H, d, J = 16.4 Hz, C4-H), 7.57 (1 H, d, J = 7.6 Hz), 7.26–7.40 (6 H, m), 6.99 (3 H, m, ArH, C3-H), 6.74 (1 H, d, J = 16.1 Hz, =CHPh), 6.37 (1 H, m, OCH_2CH=), 4.77 (2 H, d, J = 5.6 Hz, OCH_2CH=), 4.39 (2 H, q, J = 7.3 Hz, $CO_2CH_2CH_3$), 3.12 (3 H, s, SO_2CH_3), 1.32 (3 H, t, J = 7.1 Hz, $CO_2CH_2CH_3$); IR (neat) ν_{max} 3031, 2982, 2933, 1737, 1598, 1567, 1484, 1450, 1370, 1316, 1245, 1146, 966 cm^{-1}; FABHRMS (NBA-CsI), m/e 546.0351 (M + Cs$^+$, $C_{22}H_{23}NO_5S$ requires 546.0351).

Ethyl (*E*)-4-[2-[(3′-methyl-2′-butenyl)oxy]phenyl]-2-[(methylsulfonyl)imino]-3-butenoate (5c): yellow oil; ^{1}H NMR ($CDCl_3$, 400 MHz, ppm) 7.84 (1 H, d, J = 16.8 Hz, C4-H), 7.54 (1 H, d, J = 7.6 Hz), 7.39 (1 H, dt, J = 7.5, 1.7 Hz), 6.97 (1 H, t, J = 7.5 Hz), 6.95 (1 H, d, J = 17.0 Hz, C3-H), 6.91 (1 H, d, J = 7.8 Hz), 5.45 (1 H, m, OCH_2CH_2), 4.57 (2 H, d, J = 6.6 Hz, OCH_2CH=), 4.46 (2 H, q, J = 7.2 Hz, $CO_2CH_2CH_3$), 3.13 (3 H, s, SO_2CH_3), 1.78 (3 H, s, CH_3), 1.73 (3 H, s, CH_3), 1.42 (3 H, t, J = 7.2 Hz, $CO_2CH_2CH_3$); IR (neat) ν_{max} 2976, 2925, 1735, 1599, 1559, 1484, 1453, 1312, 1242, 1146, 971 cm^{-1}; FABHRMS (NBA-CsI) m/e 498.0355 (M + Cs$^+$, $C_{18}H_{23}NO_5S$ requires 498.0351).

Ethyl (*E*)-2-[(methylsulfonyl)imino]-4-[2-(2′-propynyloxy)phenyl]-3-butenoate (5d): yellow oil; ^{1}H NMR ($CDCl_3$, 400 MHz, ppm) 7.82 (1 H, d, J = 16.3 Hz, C4-H), 7.57 (1 H, d, J = 7.8 Hz), 7.43 (1 H, dt, J = 7.9, 1.7 Hz), 7.04 (2 H, t, J = 7.6 Hz), 6.94 (1 H, d, J = 16.3 Hz, C3-H), 4.77 (2 H, d, J = 2.1 Hz, OCH_2C≡CH), 4.47 (2 H, q, J = 7.1 Hz, $CO_2CH_2CH_3$), 3.13 (3 H, s, SO_2CH_3), 2.54 (1 H, t, J = 2.2 Hz, OCH_2C≡CH), 1.43 (3 H, t, J = 7.1 Hz, $CO_2CH_2CH_3$); IR (neat) ν_{max} 3277, 2986, 2925, 2122, 1732, 1600, 1557, 1485, 1461, 1370, 1311, 1135, 1018, 967 cm^{-1}; FABHRMS (NBA-CsI) m/e 467.9882 (M + Cs$^+$, $C_{16}H_{17}NO_5S$ requires 467.9882).

Ethyl (*E*)-2-[(methylsulfonyl)imino]-4-[2-[(3′-phenyl-2′-propynyl)oxy]phenyl]-3-butenoate (5e): yellow oil; ^{1}H NMR ($CDCl_3$, 400 MHz, ppm) 7.86 (1 H, d, J = 16.6 Hz, C4-H), 7.57 (1 H, d, J = 7.3 Hz), 7.41–7.47 (3 H, m), 7.30–7.35 (3 H, m), 7.13 (1 H, d, J = 8.1 Hz), 7.04 (1 H, t, J = 7.5 Hz), 6.97 (1 H, d, J = 16.5 Hz, C3-H), 4.99 (2 H, s, OCH_2C≡CPh), 4.44 (2 H, q, J = 7.2 Hz, $CO_2CH_2CH_3$), 3.13 (3 H, s, SO_2CH_3), 1.39 (3 H, t, J = 7.2 Hz, $CO_2CH_2CH_3$); IR (neat) ν_{max} 2957, 2951, 2870, 2254, 1737, 1599,

1568, 1490, 1371, 1321, 1225, 1149, 1016, 966 cm^{-1}: FABHRMS (NBA-CsI) *m/e* 544.0195 (M + Cs$^+$, $C_{22}H_{21}NO_5S$ requires 544.1095).

General Procedure for the Intramolecular Diels–Alder Reactions of α,β-Unsaturated *N*-Sulfonylimines. A solution of **5a** (133 mg, 0.39 mmol) in anhydrous toluene (2.0 mL, 0.15 M) was placed in a Kontes vial. The reaction vessel was purged with N_2, sealed, and placed in an oil bath (108 °C) for 40 h. After 40 h, TLC showed the presence of three new products. The reaction mixture was allowed to cool to 25 °C, transferred to a round-bottom flask, and concentrated in vacuo. Examination of the crude ^{1}H NMR (400 MHz) showed a 1:1 mixture of cis/trans isomers. Flash chromatography (SiO_2, 1.5 × 11 cm, 25% EtOAc–hexanes) afforded **6** (90.6 mg, 133 mg theoretical, 68%, 1:1 (cis/trans)) and **7** (21.0 mg, 100 mg theoretical, 21%).

(4a*R,10b*R**)-2-(Ethoxycarbonyl)-3-(methylsulfonyl)-3,4,4a,10b-tetrahydro-5*H*-[1]benzopyrano[3,4-*c*]pyridine (6-*cis*)**: yellow solid; mp 130–131 °C (Et_2O–hexanes); ^{1}H NMR ($CDCl_3$, 400 MHz, ppm), 7.29 (1 H, d, *J* = 7.7 Hz, ArH), 7.13 (1 H, dt, *J* = 8.1, 1.1 Hz, ArH), 6.86 (1 H, dt, *J* = 7.6, 1.1 Hz, ArH), 6.84 (1 H, d, *J* = 8.1, 1.1 Hz, ArH), 6.51 (1 H, d, *J* = 3.9 Hz, C1-H), 4.26 (2 H, dq, *J* = 7.2, 1.3 Hz, CO_2CHHCH_3), 4.23 (1 H, dd, *J* = 11.5, 2.9 Hz, C5-H_eH_a), 4.11 (1 H, dd, *J* = 11.6, 5.9 Hz, C5-H_eH_a), 3.77 (1 H, dd, *J* = 13.5, 3.1 Hz, C4-H_eH_a), 3.72 (1 H, dd, *J* = 6.7, 4.0 Hz, C10b-H), 3.56 (1 H, dd, *J* = 13.5, 8.0 Hz, C4-H_eH_a), 3.25 (3 H, s, CO_2CH_3), 2.51 (1 H, m, C4a-H), 1.32 (3 H, t, *J* = 7.2 Hz, $CO_2CH_2CH_3$); ^{13}C NMR ($CDCl_3$, 100 MHz, ppm) 163.9 (e, C=O), 153.9 (e, =CN), 130.0 (e), 129.1 (o), 127.9 (o), 125.9 (o), 121.4 (o), 121.3 (e) 117.6 (o), 66.3 (e, OCH_2), 61.8 (e, $CO_2CH_2CH_3$), 45.9 (e, NCH_2), 42.4 (o, SO_2CH_3), 32.7 (o, C10b), 31.7 (o, C4a), 14.1 (o, $CO_2CH_2CH_3$); IR (neat) ν_{max} 2976, 2925, 2875, 1720, 1629, 1574, 1464, 1453, 1323, 1222, 1137, 1047 cm^{-1}; FABHRMS (NBA-CsI) *m/e* 470.0030 (M + Cs$^+$, $C_{16}H_{19}NO_5S$ requires 470.0038).

(4a*R,10b*S**)-2-(Ethoxycarbonyl)-3-(methylsulfonyl)-3,4,4a,10b-tetrahydro-5*H*-[1]benzopyrano[3,4-*c*]pyridine (6-*trans*)**: yellow oil; ^{1}H NMR ($CDCl_3$, 400 MHz, ppm) 7.26 (1 H, d, *J* = 7.7 Hz, ArH), 7.16 (1 H, t, *J* = 7.5 Hz, ArH), 6.93 (1 H, dt, *J* = 7.4, 1.0 Hz, ArH), 6.83 (1 H, dd, *J* = 8.2, 1.0 Hz, ArH), 6.74 (1 H, d, *J* = 2.9 Hz, C1-H), 4.43 (1 H, dd, *J* = 10.3, 3.8 Hz, C5-H_eH_a), 4.31 (2 H, q, *J* = 7.2 Hz, $CO_2CH_2CH_3$), 3.93 (2 H, m, C4-H_eH_a, C5-H_eH_a), 3.46 (1 H, dd, *J* = 11.4, 2.8 Hz, C10b-H), 3.26 (1 H, dd, *J* = 11.7, 6.5 Hz, C4-H_eH_a), 3.25 (3 H, s, SO_2CH_3), 2.31 (1 H, m, *J* = 11.4 Hz, C4a-H), 1.36 (3 H, t, *J* = 7.2 Hz, $CO_2CH_2CH_3$); ^{13}C NMR ($CDCl_3$, 100 MHz, ppm) 163.9 (e, C=O), 153.8 (e, =CN), 132.4 (e), 128.3 (o), 125.6 (o), 124.4 (o), 121.4 (e), 120.7 (o), 116.9 (o), 67.9 (e, OCH_2), 61.7 (e, $CO_2CH_2CH_3$), 46.6 (e, NCH_2), 41.4 (o, SO_2CH_3), 36.7 (o, CH), 36.3 (o, CH), 14.1 (o, $CO_2CH_2CH_3$); IR (neat) ν_{max} 2986, 2936, 1725, 1624, 1570, 1489, 1453, 1333, 1228, 1147, 1047, 1012 cm^{-1}; FABHRMS (NBA-CsI) *m/e* 470.0041 (M + Cs$^+$, $C_{16}H_{19}NO_5S$ requires 470.0038).

2-(Ethoxycarbonyl)-5*H*-[1]benzopyrano[3,4-*c*]pyridine (7): yellow solid; mp 96–97 °C (Et_2O–hexanes); ^{1}H NMR ($CDCl_3$, 400 MHz, ppm) 8.53 (1 H, s, C4-H), 8.38 (1 H, s, C1-H), 7.83 (1 H, dd, *J* = 7.8, 1.6 Hz, ArH), 7.37 (1 H, dt, *J* = 8.1, 1.6 Hz, ArH), 7.12 (1 H, dt, *J* = 7.7, 1.1 Hz, ArH), 7.02 (1 H, dd, *J* = 8.1, 1.1 Hz, ArH), 5.22 (2 H, s, OCH_2), 4.50 (2 H, q, *J* = 7.1 Hz, $CO_2CH_2CH_3$), 1.47 (3 H, t, *J* = 7.1 Hz, $CO_2CH_2CH_3$); ^{13}C NMR ($CDCl_3$, 100 MHz, ppm) 165.2 (e, C=O), 155.6 (e, C=N), 148.7 (e), 145.9 (o), 138.9 (e), 132.4 (o), 128.9 (e), 124.4 (o), 122.7 (o), 119.9 (e), 117.9 (o), 117.5 (o), 65.7 (e, OCH_2), 62.1 (e, $CO_2CH_2CH_3$), 14.4 (o, $CO_2CH_2CH_3$); IR (neat) ν_{max} 3056, 2976, 1735, 1716, 1600, 1589, 1455, 1409, 1295, 1242, 1117, 1014 cm^{-1}; FABHRMS (NBA-CsI) *m/e* 387.9938 (M + Cs$^+$, $C_{15}H_{13}NO_3$ requires 387.9950).

(4a*S,10b*S**)-2-(Ethoxycarbonyl)-3-(methylsulfonyl)-4-phenyl-3,4,4a,10b-tetrahydro-5*H*-[1]benzopyrano[3,4-*c*]pyridine (8-*trans*)**: yellow oil; ^{1}H NMR ($CDCl_3$, 400 MHz, ppm) 7.35–7.46 (6 H, m, ArH), 7.17 (1 H, t, *J* = 7.4 Hz, ArH), 7.00 (1 H, t, *J* = 7.4 Hz, ArH), 6.93 (1 H, d, *J* = 3.6 Hz, C1-H), 6.80 (1 H, d, *J* = 7.3 Hz, ArH), 4.90 (1 H, d, *J* = 11.3 Hz, C4-H), 4.34 (2 H, m, CO_2CHHCH_3), 4.03 (2 H, m, OCH_eH_a), 3.67 (1 H, dd, *J* = 11.5, 3.6 Hz, C10b-H), 2.65 (3 H, s, SO_2CH_3), 2.27 (1 H, dddd, *J* = 11.4, 11.3, 9.7, 4.6 Hz, C4a-H), 1.38 (3 H, t, *J* = 7.1 Hz, $CO_2CH_2CH_3$); ^{13}C NMR ($CDCl_3$, 100 MHz, ppm) 163.9 (e, C=O), 154.1 (e, =CN), 138.9 (e), 133.7 (e), 131.9 (o), 129.2 (o), 128.8 (o), 128.5 (o), 127.6 (o), 127.4 (o), 121.4 (o), 121.1 (e), 117.0 (o), 66.9 (e, OCH_2), 62.3 (o, NCH), 61.9 (e, $CO_2CH_2CH_3$), 48.0 (o, C10b), 42.4 (o, SO_2CH_3), 35.8 (o, C4a), 14.2 (o, $CO_2CH_2CH_3$); IR (neat) ν_{max} 3066, 3026, 2976, 2925, 1725, 1630, 1489, 1452, 1348, 1309, 1232, 1156, 997 cm^{-1}; FABHRMS (NBA-CsI) *m/e* 546.0351 (M + Cs$^+$, $C_{22}H_{23}NO_5S$ requires 546.0351).

2-(Ethoxycarbonyl)-4-phenyl-5*H*-[1]benzopyrano[3,4-*c*]pyridine (9): yellow solid; mp 128–129 °C (Et_2O–hexanes); ^{1}H NMR ($CDCl_3$, 400 MHz, ppm) 8.36 (1 H, s, C1-H), 7.88 (1 H, dd, *J* = 7.8, 1.6 Hz, ArH), 7.46–7.52 (5 H, m, ArH), 7.37 (1 H, dt, *J* = 8.2, 1.6 Hz, ArH), 7.15 (1 H, dt, *J* = 7.6, 1.1 Hz, ArH), 7.01 (1 H, dd, *J* = 8.2 Hz, 1.1 Hz, ArH), 5.23 (2 H, s, OCH_2), 4.50 (2 H, q, *J* = 7.1 Hz, $CO_2CH_2CH_3$), 1.45 (3 H, t, *J* = 7.1 Hz, $CO_2CH_2CH_3$); ^{13}C NMR ($CDCl_3$, 100 MHz, ppm) 165.4 (e, C=O), 156.3 (e, C=N), 155.5 (e), 147.0 (e), 139.8 (e), 138.0 (e), 132.1 (o), 129.1 (o), 128.5 (o), 127.1 (e), 124.5 (o), 122.7 (o), 120.7 (e), 117.6 (o), 116.6 (o), 65.6 (e, OCH_2), 62.0 (e, $CO_2CH_2CH_3$), 14.4 (o, $CO_2CH_2CH_3$); IR (neat) ν_{max} 3066, 2981, 2925, 1742, 1716, 1589, 1553, 1406, 1370, 1304, 1232, 1119, 1015 cm^{-1}; FABHRMS (NBA-CsI) *m/e* 464.0263 (M + Cs$^+$, $C_{21}H_{17}NO_3$ requires 464.0263).

(4a*S,10b*R**)-4,4-Dimethyl-2-(ethoxycarbonyl)-3-(methylsulfonyl)-3,4,4a,10b-tetrahydro-5*H*-[1]benzopyrano[3,4-*c*]pyridine (10-*cis*)**: yellow solid; mp 150–151 °C (Et_2O–hexanes); ^{1}H NMR ($CDCl_3$, 400 MHz, ppm) 7.26 (1 H, d, *J* = 6.4 Hz, ArH), 7.13 (1 H, dt, *J* = 7.7, 1.6 Hz, ArH), 6.94 (1 H, dt, *J* = 7.5, 1.2 Hz, ArH), 6.84 (1 H, dd, *J* = 8.2, 1.1 Hz, ArH), 6.32 (1 H, dd, *J* = 3.3, 0.7 Hz, C1-H), 4.46 (1 H, ddd, *J* = 11.6, 3.4, 1.4 Hz, C5-H_eH_a), 4.24 (2 H, m, CO_2CHHCH_3), 3.79 (1 H, dd, *J* = 11.5, 9.9 Hz, C5-H_eH_a), 3.65 (1 H, dd, *J* = 6.5, 3.2, Hz, C10b-H), 3.29 (3 H, s, SO_2CH_3), 2.14 (1 H, ddd, *J* = 9.9, 6.5, 3.4 Hz, C4a-H), 1.76 (3 H, s, CH_3), 1.50 (3 H, s, CH_3), 1.31 (3 H, t, *J* = 7.1 Hz, $CO_2CH_2CH_3$); ^{13}C NMR ($CDCl_3$, 100 MHz, ppm) 164.8 (e, C=O), 154.7 (e, =CN), 130.8 (e), 129.2 (o), 128.0 (o), 124.7 (o), 121.1 (o), 120.9 (e), 117.2 (o), 65.3 (e, OCH_2), 61.6 (e, $CO_2CH_2CH_3$), 59.7 (e, $C(CH_3)_2$), 45.0 (o, C10b), 40.8 (o, SO_2CH_3), 33.3 (o, C4a), 27.3 (o, CH_3), 24.9 (o, CH_3), 14.1 (o, $CO_2CH_2CH_3$); IR (neat) ν_{max} 2986, 2925, 1724, 1585, 1490, 1338, 1275, 1229, 1146, 1018 cm^{-1}; FABHRMS (NBA) *m/e* 366.1388 (M + H$^+$, $C_{18}H_{23}NO_5S$ requires 366.1375).

(4a*S,10b*S**)-4,4-Dimethyl-2-(ethoxycarbonyl)-3-(methylsulfonyl)-3,4,4a,10b-tetrahydro-5*H*-[1]benzopyrano[3,4-*c*]pyridine (10-*trans*)**: orange oil; ^{1}H NMR ($CDCl_3$, 400 MHz, ppm) 7.27 (1 H, dd, *J* = 6.6, 1.1 Hz, ArH), 7.15 (1 H, dt, *J* = 7.5, 1.5 Hz, ArH), 6.91 (1 H, dt, *J* = 7.5, 1.1 Hz, ArH), 6.83 (1 H, d, *J* = 3.0 Hz, C1-H), 6.82 (1 H, dd, *J* = 6.4, 1.1 Hz, ArH), 4.42 (1 H, dd, *J* = 10.1, 4.0 Hz, C5-H_eH_a), 4.31 (2 H, dq, *J* = 7.1, 1.2 Hz, CO_2CHHCH_3), 3.88 (1 H, dd, *J* = 11.5, 10.1 Hz, C5-H_eH_a), 3.48 (1 H, dd, *J* = 11.7, 2.9 Hz, C10b-H), 3.28 (3 H, s, SO_2CH_3), 2.43 (1 H, dt, *J* = 11.6, 3.9 Hz, C4a-H), 1.79 (3 H, s, CH_3), 1.37 (3 H, t, *J* = 7.1 Hz, $CO_2CH_2CH_3$), 1.30 (3 H, s, CH_3); ^{13}C NMR ($CDCl_3$, 100 MHz, ppm) 164.9 (e, C=O), 154.6 (e, =CN), 132.7 (e), 128.2 (o), 125.5 (o), 123.9 (o), 122.5 (e), 120.5 (o), 116.7 (o), 67.6 (e, OCH_2), 61.6 (e, $CO_2CH_2CH_3$), 60.6 (e, $C(CH_3)_2$), 45.1 (o, C10b), 43.9 (o, SO_2CH_3), 35.2 (o, C4a), 25.1 (o, CH_3), 22.6 (o, CH_3), 14.1 (o, $CO_2CH_2CH_3$); IR (neat) ν_{max} 2986, 2933, 1725, 1582, 1489, 1454, 1322, 1237, 1141, 1043 cm^{-1}; FABHRMS (NBA) *m/e* 366.1380 (M + H$^+$, $C_{18}H_{23}NO_5S$ requires 366.1375).

(10b*R)-2-(Ethoxycarbonyl)-3-(methylsulfonyl)-3,10b-dihydro-5*H*-[1]benzopyrano[3,4-*c*]pyridine (11)**: gold oil; ^{1}H NMR ($CDCl_3$, 400 MHz, ppm) 8.49 (1 H, s, C4-H), 7.27 (1 H, d, *J* = 7.6 Hz, ArH), 7.15 (1 H, t, *J* = 7.3 Hz, ArH), 6.94 (1 H, t, *J* = 7.6 Hz, ArH), 6.82 (1 H, d, *J* = 8.1 Hz, ArH), 6.73 (1 H, d, *J* = 3.4 Hz, C1-H), 5.21 (2 H, s, OCH_2), 4.49 (2 H, q, *J* = 7.1 Hz, $CO_2CH_2CH_3$), 3.45 (1 H, d, *J* = 3.3 Hz, C10b-H), 3.24 (3 H, s, SO_2CH_3), 1.36 (3 H, t, *J* = 7.2 Hz, $CO_2CH_2CH_3$); ^{13}C NMR ($CDCl_3$, 100 MHz, ppm) 164.0 (e, C=O), 154.2 (e, =CN), 138.9 (e), 132.3 (e), 128.1 (o), 124.9 (o), 124.2 (o), 123.5 (o, NCH), 121.0 (e), 120.5 (o), 116.9 (o), 67.4 (e, OCH_2), 61.6 (e, $CO_2CH_2CH_3$), 41.3 (o, SO_2CH_3), 36.7 (o, C10b), 14.0 (o, $CO_2CH_2CH_3$); IR (neat) ν_{max} 2977, 2922, 1723, 1613, 1560, 1487, 1323, 1147, 1044, 997 cm^{-1}; FABHRMS (NBA-CsI) *m/e* 467.9882 (M + Cs$^+$, $C_{16}H_{19}NO_5S$ requires 467.9880).

(10b*R)-2-(Ethoxycarbonyl)-3-(methylsulfonyl)-4-phenyl-3,10b-dihydro-5*H*-[1]benzopyrano[3,4-*c*]pyridine (12)**: yellow oil: ^{1}H NMR ($CDCl_3$, 400 MHz, ppm) 7.32–7.44 (6 H, m, PhH, ArH), 7.19 (1 H, t, *J* = 7.6 Hz, ArH), 6.99 (1 H, t, *J* = 7.5 Hz, ArH), 6.95 (1 H, d, *J* = 3.4 Hz, C1-H), 6.81 (1 H, d, *J* = 7.4 Hz, ArH), 5.19 (2 H, s, OCH_2), 4.37 (2 H, q, *J* = 7.1 Hz, CO_2CH_2-

CH_3), 3.76 (1 H, d, J = 3.3 Hz, C10b-H), 3.17 (3 H, s, SO_2CH_3), 1.43 (3 H, t, J = 7.2 Hz, $CO_2CH_2CH_3$); ^{13}C NMR ($CDCl_3$, 100 MHz, ppm) 165.1 (e, C=O) 154.4 (e, =CN), 137.8 (e), 133.2 (e), 131.8 (o), 129.1 (o), 128.8 (o), 128.2 (o), 127.7 (o), 127.4 (o), 121.2 (o), 121.1 (e), 120.9 (e), 117.0 (o), 66.7 (e, OCH_2), 61.9 (e, $CO_2CH_2CH_3$), 47.8 (o, C10b), 41.7 (o, SO_2CH_3), 14.3 (o, $CO_2CH_2CH_3$); IR (neat) ν_{max} 3024, 2977, 1722, 1613, 1567, 1463, 1382, 1212, 1156, 984 cm^{-1}; FABHRMS (NBA-CsI) m/e 544.0192 ($M + Cs^+$, $C_{22}H_{21}NO_5S$ requires 544.0195).

2-(Ethoxycarbonyl)-5*H*-[1]benzopyrano[3,4-*c*]pyridine (7). From 6. A solution of **6** (19.7 mg, 58.4 μmol, 1.0 equiv) in anhydrous THF (584 μL, 0.1 M) was cooled to 0 °C under N_2 and treated with DBU (13.3 mg, 13.1 μL, 87.6 μmol, 1.5 equiv). The reaction mixture was stirred at 0 °C for 10 min whereupon TLC confirmed the disappearance of **6**. Concentration of the reaction mixture in vacuo afforded an orange residue. The residue was dissolved in CH_2Cl_2 (584 μL) and treated with DDQ (15.9 mg, 70.1 μmol, 1.2 equiv) at 25 °C, and the reaction mixture was stirred at 25 °C for 15 min. Flash chromatography (SiO_2, 1 × 9 cm, 50% EtOAc–hexanes) afforded **7** (12.4 mg, 14.8 mg theoretical, 84% for two steps).

From 11. A solution of **11** (6.1 mg, 18.2 μmol, 1.0 equiv) in anhydrous THF (182 μL, 0.1 M) was cooled to 0 °C under N_2 and treated with DBU (3.6 mg, 3.5 μL, 23.6 μmol, 1.3 equiv). The reaction mixture was stirred at 0 °C for 15 min whereupon TLC confirmed the disappearance of **11**. Flash chromatography (SiO_2, 1 × 3 cm, 35% EtOAc–hexanes) afforded **7** (3.2 mg, 4.5 mg theoretical, 70%).

2-(Ethoxycarbonyl)-4-phenyl-5*H*-[1]benzopyrano[3,4-*c*]pyridine (9). From 8. A solution of **8** (13.4 mg, 32.4 μmol, 1.0 equiv) in anhydrous THF (324 μL, 0.1 M) was cooled to 0 °C under N_2 and treated with DBU (9.9 mg, 9.7 μL, 64.8 μmol, 2.0 equiv). The reaction mixture was stirred at 0 °C (30 min) whereupon TLC confirmed the disappearance of **8**. Concentration of the reaction mixture in vacuo afforded an orange residue. The residue was dissolved in CH_2Cl_2 (324 μL), treated with DDQ (8.8 mg, 38.9 μmol, 1.2 equiv) at 25 °C and stirred at 25 °C for 30 min. Flash chromatography (SiO_2, 1 × 4 cm, 15% EtOAc–hexanes) afforded **9** (7.7 mg, 10.7 mg theoretical, 72% for 2 steps).

From 12. A solution of **12** (23.2 mg, 56.4 μmol, 1.0 equiv) in anhydrous THF (564 μL, 0.1 M) was cooled to 0 °C under N_2 and treated with DBU (12.9 mg, 12.6 μL, 84.6 μmol, 1.5 equiv). The reaction was stirred at 0 °C for 20 min. Flash chromatography (SiO_2, 1 × 6 cm, 15% EtOAc–hexanes) afforded **9** (14.0 mg, 18.7 mg theoretical, 75%).

From 4b: A solution of crude **5b** generated from **4b** (10.2 mg, 24.7 μmol, 1.0 equiv) in anhydrous CH_2Cl_2 (247 μL, 0.1 M) was warmed at reflux for 64 h. The reaction mixture was cooled to 25 °C and concentrated in vacuo to afford a yellow oil. This oil was dissolved in anhydrous THF, cooled to 0 °C, and treated with DBU (7.5 mg, 7.4 μL, 49.4 μmol, 2.0 equiv). The reaction mixture was stirred at 0 °C for 30 min and concentrated in vacuo to give an orange residue. This residue was dissolved in CH_2Cl_2 (247 μL), treated with DDQ (6.7 mg, 29.6 μmol, 1.2 equiv) at 25 °C and stirred for 15 min. Flash chromatography (SiO_2, 1 × 4 cm, 10% EtOAc-hexanes) afforded **9** (5.4 mg, 8.2 mg theoretical, 66% for 3 steps).

From 4e: A solution of crude **5e** generated from **4e** (7.0 mg, 17.0 μmol, 1.0 equiv) in anhydrous CH_2Cl_2 (170 μL, 0.1 M) was warmed at reflux for 67 h. The reaction mixture was cooled to 25 °C and concentrated in vacuo to afford an orange oil. This oil was dissolved in anhydrous THF (170 μL), cooled to 0 °C, and treated with DBU (3.4 mg, 3.3 μL, 22.1 μmol, 1.3 equiv). The reaction mixture was stirred at 0 °C for 20 min. Flash chromatography (SiO_2, 1 × 3 cm, 20% EtOAc-hexanes) afforded **9** (2.5 mg, 5.6 mg theoretical, 45% for 2 steps).

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Supplementary Material Available: ^{13}C NMR spectra of **3a–e**, **4a–e**, and **6–12** and ^1H NMR spectra of **5a–e** (24 pages). This material is contained in libraries on microfiche, immediately follows this article in the microfilm version of the journal, and can be ordered from the ACS; see any current masthead page for ordering information.