Note

Overcoming the Usual Reactivity of *β*-Nitroenones: Synthesis of Polyfunctionalized Homoallylic Alcohols and Conjugated Nitrotriene Systems

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ABSTRACT: Herein, we report a new application of *β*-nitroenones as valuable building blocks for the preparation of polyfunctionalized homoallylic alcohols; they can be used as key precursors of conjugated nitrotriene systems. The synthesis of homoallylic alcohols was performed exploiting the chemoselective addition of metal allylating agents to the ketone moiety vs the nitroalkenyl group. The conversion of alcohols into nitrotrienes was achieved under Lewis-acid-promoted conditions. Both classes of compounds were obtained in good to excellent yields.
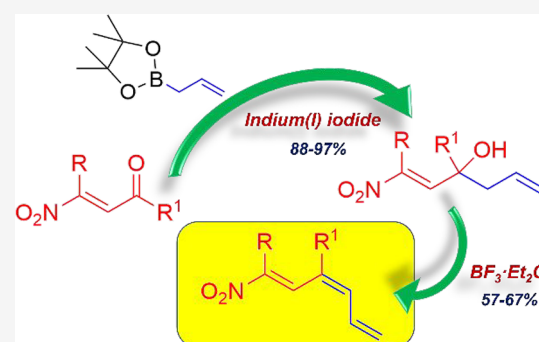
β-Nitroenones **1** represent a valuable class of nitroolefins characterized by the presence of nitro and ketone functionalities in the *α* and *β* positions to a double bond. The juxtaposition of these functionalities makes **1** highly reactive species toward a plethora of nucleophiles, and in particular, they chemoselectively react at position 2, behaving as excellent Michael acceptors (Figure 1). Over the years, the synthetic
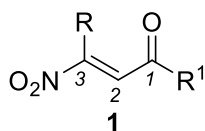

Figure 1. General structure of *β*-nitroenones **1**.

importance of these molecules was demonstrated by their usage for synthesizing heterocyclic systems such as pyrroles, furans, indoles,[1] and carbonyl derivatives.[2]

Following our ongoing research concerning the chemistry of *β*-nitroenones **1**, we have now discovered a peculiar reactivity of **1** when treated with metal allylating agents **2**. In fact, unlike the reactivity commonly observed with other nucleophilic species, compounds **2** exclusively react with the carbonyl group rather than the nitroalkene moiety, thus generating the corresponding homoallylic alcohols **3** (Scheme 1).

Homoallylic alcohols play a pivotal role as building blocks for the preparation of highly functionalized materials,[3] as well as key precursors for common frameworks of many natural products and bioactive compounds.[4] In this regard, due to the peculiar structure of **3**, in which the homoallylic alcohol
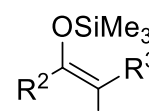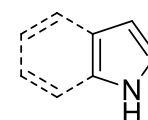
Scheme 1. Reactivity of *β*-Nitroenones 1
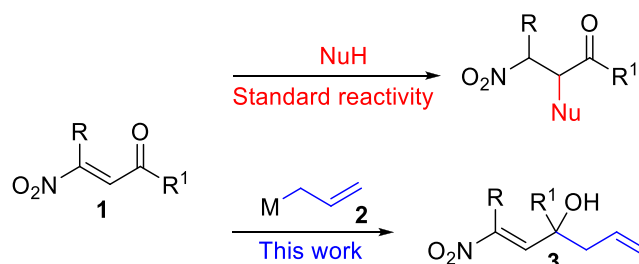
portion is connected to the nitroalkene system, we explored and successfully achieved the dehydration of **3** into the conjugated nitrotriene systems **4** (Scheme 2).

Scheme 2. Synthesis of Nitro-Functionalized Triene Systems 4
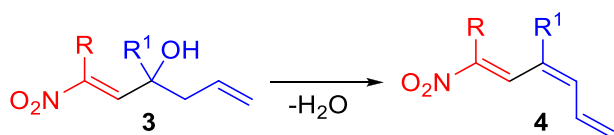
Although the chemistry of conjugated nitrodienes **5** has been largely studied (Figure 2),[5] very little information concerning
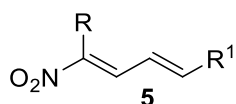

Figure 2. General structure of conjugated nitrodienes **5**.

their homologues **4** is available in the literature. This is probably due to the difficulty of preparing these compounds, whose synthesis often requires elaborate starting materials and/or severe reaction conditions.[6] In this context, our approach can be considered the first general and straightforward method to access conjugated nitrotrienes **4**.

First, we focused our attention on optimizing the allylation reaction. For this purpose, the conversion of **1a** into **3a** was selected as representative reaction, and a variety of allylating systems and reaction conditions were screened (Scheme 3).

Scheme 3. Test Reaction: Conversion of 1a into 3a

2a M= Bu$_3$Sn   **2c** M= (pinacol boronate)

2b M= Br   **2d** M= MgCl
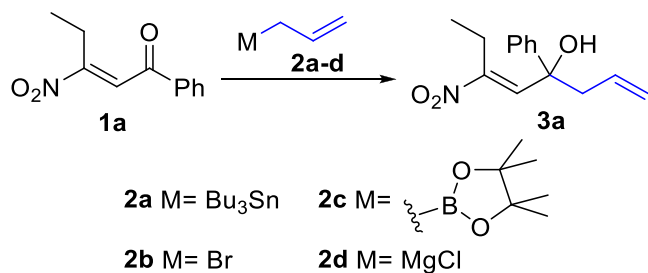
Based on the article of Kalita and Phukan relating to the allylation of chalcones,[7] we first attempted the conversion of **1a** into **3a** using allyltributylstannane **2a** in the presence of CuI (0.25 equiv) and DMF. The reaction gave a modest result, and **3a** was isolated in 56% yield. No improvement was observed by changing the solvent (Table 1, entries a−c). Successively, the growing use in the literature of indium as an efficient metal for promoting the Barbier reaction[8] spurred us to investigate the synthesis of **3a** starting from allyl bromide **2b** and **1a**. Once again, the product **3a** was isolated in a moderate yield of 58% and only in the presence of a significant excess of **2b** and indium (Table 1, entries d−g). Then, inspired by the Schneider and Kobayashi's paper,[9] we examined the allylation reaction of **1a** using the pinacolyl allylboronate **2c** in the presence of a catalytic amount of indium(I) iodide. To our delight, the reaction provided **3a** in 94% yield (Table 1, entry h). Extra catalytic systems based on indium species such as In/ InB$_3$ and In/InCl$_3$ were also screened. These systems are

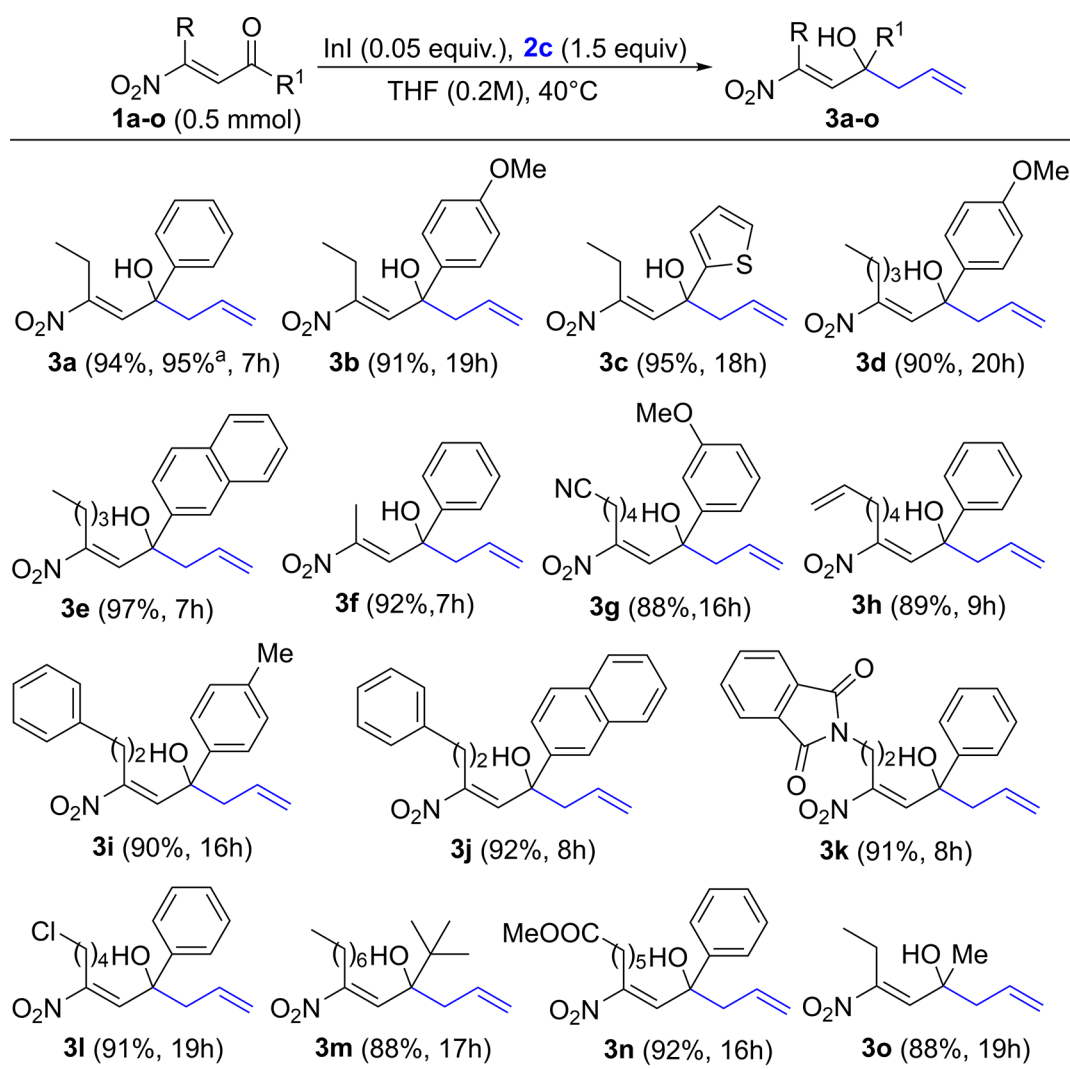### Table 1. Optimization Studies of the Allylation Reaction

entry	compound **2**	reaction conditions	yield[a] of **3a**
a	**2a** (1.2 equiv)	K$_2$CO$_3$ (1.2 equiv), CuI (0.25 equiv), DMF (0.7 M), 70 °C, 20 h	56%
b	**2a** (1.2 equiv)	K$_2$CO$_3$ (1.2 equiv), CuI (0.25 equiv), MeCN (0.7 M), 70 °C, 20 h	31%
c	**2a** (1.2 equiv)	K$_2$CO$_3$ (1.2 equiv), CuI (0.25 equiv), γ-valerolactone (0.7 M), 70 °C, 20 h	50%
d	**2b** (1.3 equiv)	In (1.5 equiv), EtOH (0.2 M), 0 °C, 7 h	21%
e	**2b** (2 equiv)	In (2 equiv), EtOH (0.2 M), 0 °C, 6 h	43%
f	**2b** (2 equiv)	In (2 equiv), EtOH (0.2 M), rt, 3 h	49%
g	**2b** (3 equiv)	In (2 equiv), EtOH (0.2 M), rt, 3 h	58%
h	**2c** (1.5 equiv)	InI (0.05 equiv), THF (0.2 M), 40 °C, 7 h	94%
i	**2c** (1.5 equiv)	In (0.20 equiv), InBr$_3$ (0.1 equiv), THF (0.2 M), 40 °C, 30 h	85%
j	**2c** (1.5 equiv)	In (0.20 equiv), InCl$_3$ (0.1 equiv), THF (0.2 M), 40 °C, 34 h	71%
k	**2d** (1.2 equiv)	THF (0.2 M), 0 °C, 20 h	

[a]Yield of the pure isolated product **3a**.

supposed to generate in situ the corresponding In(I) halides, which however were less effective than InI in terms of both yield and reaction time due to the lower thermodynamic stability, according to what was previously reported.[9] Finally, the reaction was attempted using allylmagnesium chloride **2d** without any appreciable result (Table 1, entry k).

Next, we explored both the substrate generality for the allylation of β-nitroenones **1a−o** with **2c** catalyzed by 5 mol % of indium(I) iodide and the scalability of our protocol exploring the conversion of **1a** into **2a** on 5 mmol scale. Pleasingly, both studies provided excellent results. In fact, it was seen that the reaction demonstrated good generality, affording the target homoallylic alcohols **3a−o** in very good yields (Figure 3), and the large-scale reaction provided **3a** in 95% yield (see SI).

Later, we investigated the use of nitroalkenyl alcohols **3** as valuable building blocks for the possible synthesis of conjugated nitrotriene systems **4**. This hitherto unknown class of nitro derivatives may open new scenarios in the synthesis of functionalized molecules exploiting the chemistry of trienes.[10] In order to find the best reaction conditions and following the available literature,[11] we initially explored the conversion of **3a** into **4a** using p-toluenesulfonic acid in toluene under reflux conditions, which however provided a complex mixture of inseparable compounds. Conversely, at room temperature, the reaction was completely ineffective. Then, we tested the dehydration reaction utilizing boron trifluoride diethyl etherate in dichloromethane (Table 2).[12] Under these conditions, at room temperature, we were able to isolate 43% of regioisomeric nitrotrienes **4a** and **5a** in a 75:25 ratio. After a careful screening of the reaction parameters, we obtained the best yield (67%) by working at −10 °C and in the presence of 1.5 equiv of BF$_3$·Et$_2$O. Noteworthy, the formation of the other regioisomer **5a** was limited to less than 10%. The increase of the observed regioselectivity at lower temperature is probably the result of better kinetic control in the formation of compounds **4**. Moreover, we attempted to convert **4a** into **5a** with the aim to obtain a single regioisomer. With this scope, the reaction was stirred at room temperature for 24 h; however, we observed extensive degradation of the product

Figure 3. Substrate scope demonstration: synthesis of homoallylic alcohols **3**.

Table 2. Optimization Studies of the Dehydration Reaction Using BF$_3$·Et$_2$O
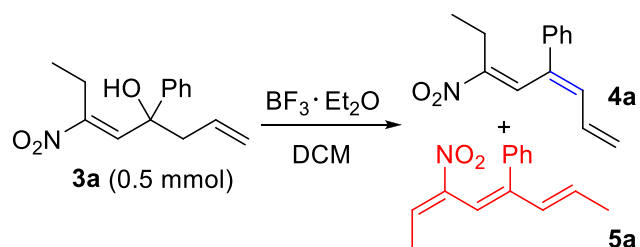
entry	BF$_3$·Et$_2$O (equiv)	reaction conditions	yield[a] of 4a + 5a (4a:5a)
a	1.2	rt, 2.5 h	43% (75:25)
b	1.2	0 °C, 2.5 h	49% (80:20)
c	1.5	0 °C, 2.5 h	54% (80:20)
d	1.5	−10 °C, 5 h	67% (90:10)
e	1.5	−20 °C, 24 h	traces
f	1.5	rt, 24 h	17% (75:25)
g	1.5	−10 °C, 5 h	69% (90:10)[b]

[a]Yield of sum of products **4a** and **5a**. [b]Reaction performed on 2 mmol scale.

without any change concerning the **4a:5a** regioisomeric ratio (Table 2, entry f).

The reaction was also investigated using a different solvent such as 1,2-dichloroethane (DCE) and additional Lewis acids including AlCl$_3$, EtAlCl$_2$, BBr$_3$, and BF$_3$ and AlCl$_3$ supported on silica. The use of DCE instead of DCM as well as the use of aluminum trichloride led to a notable drop of the efficiency, giving **4a** in 32% (5 h, −10 °C) and 22% (8 h, rt) yield, respectively. The reaction promoted by BBr$_3$ at −10 °C for 6 h led to **4a** in just 41% conversion, while warming to room temperature resulted in complete degradation of the expected product. Finally, use of ethylaluminum dichloride and the heterogeneous BF$_3$ and AlCl$_3$ was completely ineffective.

We also repeated the reaction starting from 2 mmol of **3a** to demonstrate the larger scale viability of the protocol. Even under these conditions the process was very efficient; in fact, the regioisomeric mixture of **4a** and **5a** (90:10) was isolated in 69% yield (see SI), a value comparable to that obtained on a smaller scale (Table 2, entry g).

With the aim to establish the configuration of the newly generated double bond, we performed NOESY experiments on the isomer **4a**. These studies highlighted a strong cross-peak signal between the proton at C-2 and that at C-5, thus

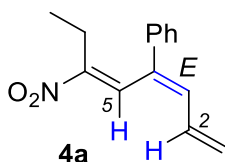confirming the 3E geometry for the prevailing regioisomer **4a** (Figure 4).

Figure 4. NOESY experiment concerning the isomer **4a**.

The formation of the *E* diastereomer can be explained considering the initial generation of the carbocation **A**, which potentially can assume conformation **B** or **C** to give the *Z* or *E* configuration, respectively. In particular, the higher stability of **C**, in which the steric hindrance and electronic repulsion between the alkyl and the phenyl groups is minimized, over the **B** conformer leads exclusively to the *E* double-bond geometry (Scheme 4).

Finally, we applied the optimized reaction conditions to a variety homoallylic alcohols **3**. In all cases, products **4** were obtained in satisfactory yields, albeit around 10% of the **5** isomer was always detected except for compound **4i** which was obtained as a single regioisomer (Figure 5). The dehydration was also attempted on alkyl derivative **3m**, bearing a 4-*tert*-butyl group, which however was unreactive under the reaction conditions, presumably because of the reduced stability of the carbocationic intermediate.

In conclusion, we disclosed a new significant reactivity of β-nitroenones in combination with allylating agents which enables one to prepare a series of polyfunctionalized homoallylic alcohols in excellent yields, demonstrating once again the utility of β-nitroenones as pivotal starting materials in organic synthesis. The usefulness of the obtained allylated derivatives has been demonstrated by their stereoselective conversion into functionalized nitrotrienes under mild conditions.

■ EXPERIMENTAL SECTION

General Remarks. ^{1}H NMR analyses were recorded at 400 MHz on a Varian Mercury Plus 400. ^{13}C NMR analyses were recorded at 100 MHz. IR spectra were recorded with a PerkinElmer FTIR spectrometer Spectrum Two UATR. Microanalyses were performed with a CHNS-O analyzer model EA 1108 from Fisons Instruments. GS-MS analyses were obtained on a Hewlett-Packard GC/MS 6890N that works with the EI technique (70 eV). Compounds **1a**−**o** were prepared starting from alkyl- and arylglyoxals and nitro compounds by following reported procedures;[14] **1a** was a known compound,[2b] while compounds **1b**−**o** were new compounds. Allyltributyltin **2a** was purchased from Sigma-Aldrich (code 271411) and used as received. Allyl bromide **2b** was purchased from Sigma-Aldrich (code A29585) and used as received. Allylboronic acid pinacol ester **2c** was purchased from Sigma-Aldrich (code 324647) and used as received. Allylmagnesium chloride **2d** was purchased from Sigma-Aldrich (code 225908) and used as received. Boron trifluoride diethyl etherate was purchased from Sigma-Aldrich (code 216607) and used as received. Tetrahydrofuran was purchased from Sigma-Aldrich (code 87368) and distilled over sodium before usage. Dichloromethane (stabilized with amylene) was purchased from Carlo Erba (code 463314) and used as received. Indium(I) iodide was prepared according to the literature.[13] Heating for synthesizing compounds **3a**−**o** was accomplished by means of a heating magnetic stirrer equipped with an aluminum heating block. Configuration assignment of compound **4a** was made with additional information from the NOESY experiment.

General Procedure for the Preparation of Compounds 3. An oven-dried round-bottom flask with a magnetic stir bar, maintained under inert atmosphere, was charged with the appropriate β-nitroenones **1** (0.5 mmol), dry THF (2.5 mL), InI (0.025 mmol, 6 mg), and the allylboronic acid pinacol ester **2c** (0.75 mmol, 141 μL). The resulting mixture was vigorously stirred at 40 °C for the appropriate time (see Figure 3), diluted with dichloromethane (20 mL), and treated with a saturated aqueous solution of NaHCO$_3$ (10 mL). After phase separation, the aqueous phase was extracted with dichloromethane (2 × 20 mL), and the combined organic layers were dried with dry Na$_2$SO$_4$. Finally, the solution was filtered and concentrated in vacuo to give the crude products **3**, which were purified by flash column chromatography (hexane/ethyl acetate).

(E)-6-Nitro-4-phenylocta-1,5-dien-4-ol 3a. Flash chromatography on silica gel using hexane/EtOAc = 95:5 as eluent yielded **3a** (116 mg, 94% yield) as a pale yellow oil. IR (cm^{-1}, neat): 703, 924, 1334, 1520, 1634, 3392. ^{1}H NMR (400 MHz, CDCl$_3$) δ: 7.47−7.42 (m,

Scheme 4. Possible Explanation for the Formation of the *E* Diastereomer 4a
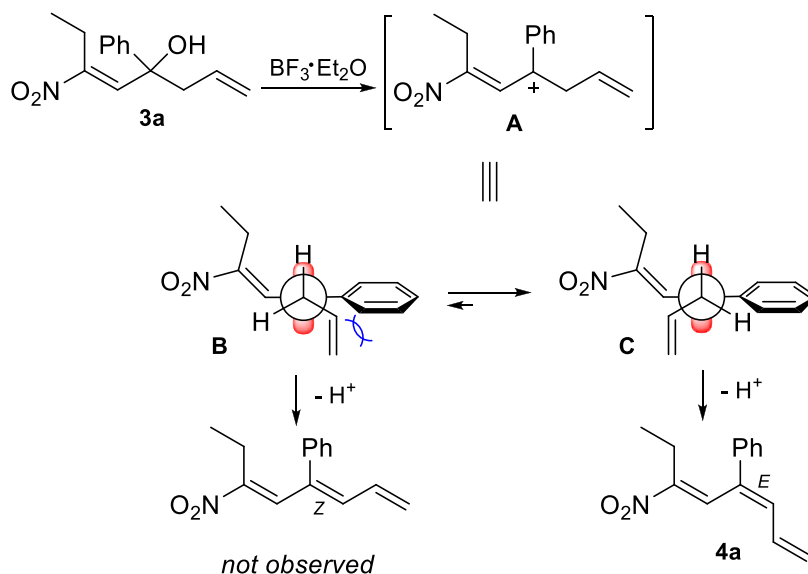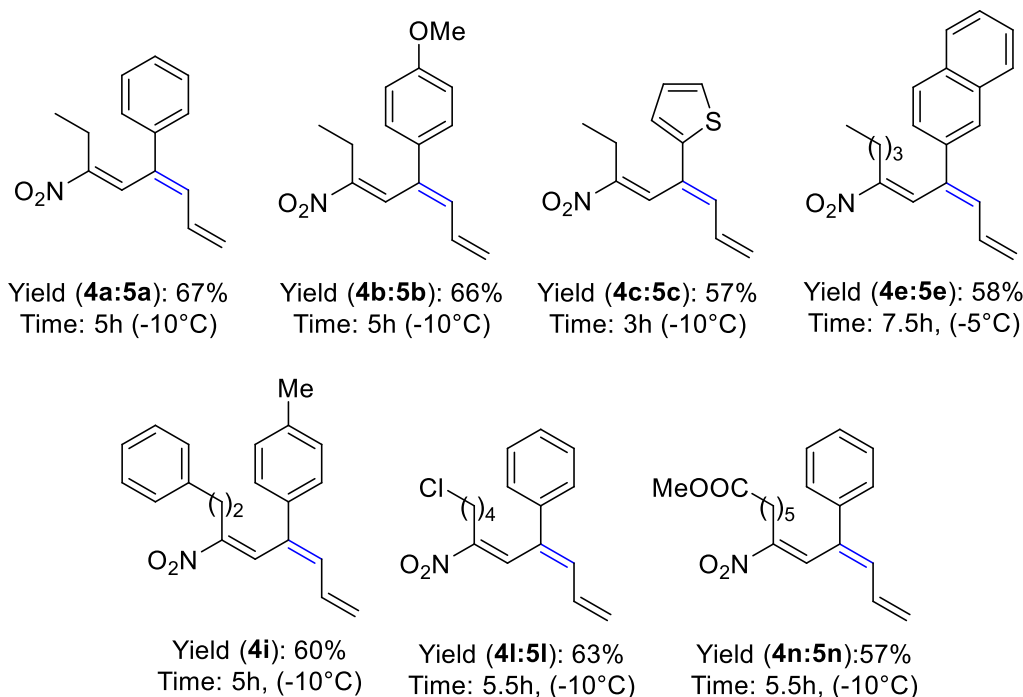
Figure 5. Synthesis of conjugated nitrotriene systems **4**.

2H), 7.40−7.34 (m, 3H), 7.31−7.25 (m, 1H), 5.73−5.60 (m, 1H), 5.32−5.24 (m, 2H), 2.78 (d, 2H, J = 7.7 Hz), 2.76 (q, 2H, J = 7.4 Hz), 2.50 (br s, 1H), 0.92 (t, 3H, J = 7.3 Hz). $^{13}C\{^1H\}$ NMR (100 MHz, CDCl$_3$) δ: 155.8, 144.3, 138.3, 131.7, 128.9, 127.9, 125.3, 122.3, 74.5, 49.1, 20.8, 12.5. GC-MS (70 eV): m/z 206 (59), 159 (100), 131 (12), 105 (37), 77 (32). Anal. Calcd for C$_{14}$H$_{17}$NO$_3$ (247.29): C, 68.00; H, 6.93; N, 5.66. Found: C, 68.05; H, 6.96; N, 5.69.

*(E)-4-(4-Methoxyphenyl)-6-nitroocta-1,5-dien-4-ol **3b**.* Flash chromatography on silica gel using hexane/EtOAc = 95:5 as eluent yielded **3b** (126 mg, 91% yield) as a pale yellow oil. IR (cm^{-1}, neat): 832, 926, 1034, 1176, 1248, 1334, 1513, 1608, 3464. ^{1}H NMR (400 MHz, CDCl$_3$) δ: 7.38−7.32 (m, 3H), 6.89 (d, 2H, J = 8.9 Hz), 5.74−5.60 (m, 1H), 5.29 (s, 1H), 5.27−5.23 (m, 1H), 3.81 (s, 3H), 2.81−2.71 (m, 4H), 2.38 (br s, 1H), 0.95 (t, 3H, J = 7.3 Hz). $^{13}C\{^1H\}$ NMR (100 MHz, CDCl$_3$) δ: 159.2, 155.4, 138.3, 136.2, 131.9, 126.6, 122.1, 114.2, 74.3, 55.6, 48.9, 20.7, 12.6. GC-MS (70 eV): m/z 236 (73), 189 (100), 135 (42), 81 (15), 77 (13). Anal. Calcd for C$_{15}$H$_{19}$NO$_4$ (277.32): C, 64.97; H, 6.91; N, 5.05. Found: C, 65.02; H, 6.94; N, 5.02.

*(E)-6-Nitro-4-(thiophen-2-yl)octa-1,5-dien-4-ol **3c**.* Flash chromatography on silica gel using hexane/EtOAc = 95:5 as eluent yielded **3c** (120 mg, 95% yield) as a pale yellow oil. IR (cm^{-1}, neat): 709, 931, 1331, 1434, 1525, 1609, 3528. ^{1}H NMR (400 MHz, CDCl$_3$) δ: 7.27 (dd, 1H, J = 4.4, 1.9 Hz), 7.24 (s, 1H), 7.00−6.96 (m, 2H), 5.82−5.68 (m, 1H), 5.33−5.31 (m, 1H), 5.30−5.26 (m, 1H), 2.92−2.76 (m, 4H), 2.65 (br s, 1H), 1.04 (t, 3H, J = 7.3 Hz). $^{13}C\{^1H\}$ NMR (100 MHz, CDCl$_3$) δ: 155.3, 148.7, 136.8, 131.4, 127.4, 125.6, 124.0, 122.5, 73.9, 49.2, 20.7, 12.9. GC-MS (70 eV): m/z 212 (61), 165 (100), 111 (47), 81 (19), 39 (17). Anal. Calcd for C$_{12}$H$_{15}$NO$_3$S (253.32): C, 56.90; H, 5.97; N, 5.53; S, 12.66. Found: C, 56.93; H, 6.00; N, 5.56; S, 12.70.

*(E)-4-(4-Methoxyphenyl)-6-nitrodeca-1,5-dien-4-ol **3d**.* Flash chromatography on silica gel using hexane/EtOAc = 95:5 as eluent yielded **3d** (137 mg, 90% yield) as a pale yellow oil. IR (cm^{-1}, neat): 739, 833, 920, 1035, 1177, 1252, 1334, 1508, 1607, 3539. ^{1}H NMR (400 MHz, CDCl$_3$) δ: 7.35 (d, 2H, J = 8.9 Hz), 7.33 (s, 1H), 6.89 (d, 2H, J = 8.9 Hz), 5.73−5.61 (m, 1H), 5.29 (s, 1H), 5.27−5.23 (m, 1H), 3.81 (s, 3H), 2.78−2.70 (m, 4H), 2.37 (br s, 1H), 1.39−1.15 (m, 4H), 0.83 (t, 3H, J = 7.1 Hz). $^{13}C\{^1H\}$ NMR (100 MHz, CDCl$_3$) δ: 159.2, 154.5, 138.4, 136.3, 131.9, 126.6, 122.1, 114.1, 74.3, 55.5,

48.9, 26.9, 30.2, 22.9, 13.9. GC-MS (70 eV): m/z 264 (67), 243 (12), 217 (100), 175 (13), 135 (91), 77 (21). Anal. Calcd for C$_{17}$H$_{23}$NO$_4$ (305.37): C, 66.86; H, 7.59; N, 4.56. Found: C, 66.91; H, 7.63; N, 4.59.

*(E)-4-(Naphthalen-2-yl)-6-nitrodeca-1,5-dien-4-ol **3e**.* Flash chromatography on silica gel using hexane/EtOAc = 95:5 as eluent yielded **3e** (158 mg, 97% yield) as a pale yellow oil. IR (cm^{-1}, neat): 748, 823, 1331, 1426, 1517, 1607, 1635, 3062, 3545. ^{1}H NMR (400 MHz, CDCl$_3$) δ: 7.94 (d, 1H, J = 1.8 Hz), 7.88−7.81 (m, 3H), 7.54−7.48 (m, 3H), 7.47 (s, 1H), 5.74−5.62 (m, 1H), 5.35−5.27 (m, 2H), 2.88 (d, 2H, J = 7.3 Hz), 2.74 (dd, 2H, J = 8.3, 7.0 Hz), 2.54 (br s, 1H), 1.08−1.37 (m, 4H), 0.74 (t, 3H, J = 7.2 Hz). $^{13}C\{^1H\}$ NMR (100 MHz, CDCl$_3$) δ: 155.2, 141.5, 137.9, 133.3, 132.8, 131.7, 128.8, 128.4, 127.8, 126.8, 126.6, 124.1, 123.5, 122.4, 74.6, 49.0, 30.0, 27.0, 22.8, 13.8. GC-MS (70 eV): m/z 278 (15), 263 (64), 237 (17), 207 (17), 155 (100), 127 (76), 77 (12). Anal. Calcd for C$_{20}$H$_{23}$NO$_3$ (325.41): C, 73.82; H, 7.12; N, 4.30. Found: C, 73.78; H, 7.09; N, 4.27.

*(E)-6-Nitro-4-phenylhepta-1,5-dien-4-ol **3f**.* Flash chromatography on silica gel using hexane/EtOAc = 95:5 as eluent yielded **3f** (107 mg, 92% yield). IR (cm^{-1}, neat): 698, 724, 987, 1326, 1519, 1608, 1640, 3062, 3537. ^{1}H NMR (400 MHz, CDCl$_3$) δ: 7.47−7.45 (m, 2H), 7.44 (s, 1H), 7.40−7.35 (m, 2H), 7.32−7.27 (m, 1H), 5.74−5.61 (m, 1H), 5.33−5.24 (m, 2H), 2.79 (d, 2H, J = 7.4 Hz), 2.46 (br s, 1H), 2.24 (s, 3H). $^{13}C\{^1H\}$ NMR (100 MHz, CDCl$_3$) δ: 150.3, 143.8, 138.3, 131.5, 128.7, 127.7, 125.1, 122.0, 74.2, 48.7, 13.6. GC-MS (70 eV): m/z 192 (60), 145 (100), 105 (29), 77 (31), 67 (32). Anal. Calcd for C$_{13}$H$_{15}$NO$_3$ (233.27): C, 66.94; H, 6.48; N, 6.00. Found: C, 66.99; H, 6.52; N, 5.97.

*(E)-8-Hydroxy-8-(3-methoxyphenyl)-6-nitroundeca-6,10-diene-nitrile **3g**.* Flash chromatography on silica gel using hexane/EtOAc = 95:5 as eluent yielded **3g** (145 mg, 88% yield) as a pale yellow oil. IR (cm^{-1}, neat): 698, 1042, 1247, 1328, 1432, 1520, 1583, 1600, 1640, 2249, 3460. ^{1}H NMR (400 MHz, CDCl$_3$) δ: 7.40 (s, 1H), 7.30 (t, 1H, J = 7.9 Hz), 7.03−6.96 (m, 2H), 6.87−6.81 (m, 1H), 5.70−5.57 (m, 1H), 5.32 (d, 1H, J = 1.0 Hz), 5.30−5.26 (m, 1H), 3.82 (s, 3H), 2.86−2.69 (m, 4H), 2.52 (br s, 1H), 2.27 (t, 2H, J = 7.2 Hz),1.65−1.34 (m, 4H). $^{13}C\{^1H\}$ NMR (100 MHz, CDCl$_3$) δ: 159.9, 152.9, 145.5, 138.9, 131.2, 129.9, 122.4, 119.5, 117.4, 112.5, 111.4, 74.2, 55.3, 48.7, 26.9, 26.0, 25.0, 16.7. GC-MS (70 eV): m/z 284 (25), 268 (93), 229 (30), 187 (16), 135 (100), 107 (27), 77 (34). Anal. Calcd

for C$_{18}$H$_{22}$N$_2$O$_4$ (330.38): C, 65.44; H, 6.71; N, 8.48. Found: C, 65.49; H, 6.74; N, 8.51.

(E)-6-Nitro-4-phenyldodeca-1,5,11-trien-4-ol 3h. Flash chromatography on silica gel using hexane/EtOAc = 95:5 as eluent yielded **3h** (134 mg, 89% yield) as a pale yellow oil. IR (cm^{-1}, neat): 699, 912, 994, 1331, 1521, 1640, 3540. ^{1}H NMR (400 MHz, CDCl$_3$) δ: 7.47−7.42 (m, 2H), 7.40−7.34 (m, 3H), 7.32−7.26 (m, 1H), 5.80−5.59 (m, 2H), 5.30 (d, 1H, J = 0.8 Hz), 5.28−5.24 (m, 1H), 5.00−4.88 (m, 2H), 2.78 (d, 2H, J = 7.3 Hz), 2.76−2.70 (m, 2H), 2.41 (br s, 1H), 1.96 (q, 2H, J = 6.9 Hz), 1.14−1.12 (m, 4H). ^{13}C{^{1}H} NMR (100 MHz, CDCl$_3$) δ: 154.4, 144.0, 138.5, 138.1, 131.5, 128.6, 127.7, 125.1, 122.1, 114.5, 74.2, 48.8, 33.3, 28.6, 27.2, 26.8. GC-MS (70 eV): m/z 260 (7), 213 (11), 186 (18), 105 (100), 91 (10), 77 (26), 41 (14). Anal. Calcd for C$_{18}$H$_{23}$NO$_3$ (301.39): C, 71.73; H, 7.69; N, 4.65. Found: C, 71.77; H, 7.73; N, 4.62.

(E)-6-Nitro-8-phenyl-4-(p-tolyl)octa-1,5-dien-4-ol 3i. Flash chromatography on silica gel using hexane/EtOAc = 95:5 as eluent yielded **3i** (152 mg, 90% yield) as a pale yellow oil. IR (cm^{-1}, neat): 699, 733, 1326, 1453, 1521, 1603, 1640, 3540. ^{1}H NMR (400 MHz, CDCl$_3$) δ: 7.46 (s, 1H), 7.34−7.29 (m, 4H), 7.26−7.18 (m, 3H), 7.17−7.12 (m, 2H), 5.65−5.54 (m, 1H), 5.27−5.20 (m, 2H), 3.20−3.06 (m, 2H), 2.79−2.60 (m, 4H), 2.38 (s, 3H), 2.05 (br s, 1H). ^{13}C{^{1}H} NMR (100 MHz, CDCl$_3$) δ: 152.5, 140.8, 140.7, 139.5, 137.5, 131.5, 129.4, 128.7, 128.5, 126.3, 125.0, 121.6, 74.4, 48.5, 33.9, 29.1, 21.0. GC-MS (70 eV): m/z 290 (19), 275 (48), 248 (9), 199 (12), 119 (100), 91 (82), 65 (24). Anal. Calcd for C$_{21}$H$_{23}$NO$_3$ (337.42): C, 74.75; H, 6.87; N, 4.15. Found: C, 74.79; H, 6.90; N, 4.12.

(E)-4-(Naphthalen-2-yl)-6-nitro-8-phenylocta-1,5-dien-4-ol 3j. Flash chromatography on silica gel using hexane/EtOAc = 95:5 as eluent yielded **3j** (172 mg, 92% yield) as a pale yellow oil. IR (cm^{-1}, neat): 476, 734, 748, 1326, 1521, 1600, 1639, 3027, 3537. ^{1}H NMR (400 MHz, CDCl$_3$) δ: 7.94−7.85 (m, 4H), 7.59 (s, 1H), 7.58−7.52 (m, 2H), 7.50 (dd, 1H, J = 8.7, 1.9 Hz), 7.29−7.17 (m, 3H), 7.06 (d, 2H, J = 7.0 Hz), 5.67−5.56 (m, 1H), 5.33−5.22 (m, 2H), 3.21−3.07 (m, 2H), 2.87−2.69 (m, 3H), 2.65−2.55 (m, 1H), 2.20 (br s, 1H). ^{13}C{^{1}H} NMR (100 MHz, CDCl$_3$) δ: 152.9, 141.0, 140.6, 139.2, 133.1, 132.6, 131.3, 128.7, 128.6, 128.5, 128.2, 127.6, 126.6, 126.4, 126.3, 123.9, 123.2, 122.0, 74.5, 48.5, 33.8, 29.1. GC-MS (70 eV): m/z 326 (34), 311 (34), 284 (59), 207 (29), 155 (100), 127 (90), 91 (34), 77 (17). Anal. Calcd for C$_{24}$H$_{23}$NO$_3$ (373.45): C, 77.19; H, 6.21; N, 3.75. Found: C, 77.24; H, 6.18; N, 3.78.

(E)-2-(5-Hydroxy-3-nitro-5-phenylocta-3,7-dien-1-yl)isoindoline-1,3-dione 3k. Flash chromatography on silica gel using hexane/EtOAc = 95:5 as eluent yielded **3k** (179 mg, 91% yield) as a pale yellow solid. Mp: 134−176 °C. IR (cm^{-1}, neat): 701, 716, 935, 1331, 1398, 1517, 1703, 1770, 3073, 3513. ^{1}H NMR (400 MHz, CDCl$_3$) δ: 7.80−7.77 (m, 2H), 7.72−7.68 (m, 2H), 7.50 (s, 1H), 7.28−7.11 (m, 5H), 5.49−5.37 (m, 1H), 5.08 (dd, 1H, J = 10.2, 1.8 Hz), 4.94 (dd, 1H, J = 17.1, 1.6 Hz), 3.99−3.84 (m, 2H), 3.28−3.22 (m, 2H), 2.74 (dd, 1H, J = 13.7, 6.5 Hz), 2.67 (br s, 1H), 2.51 (dd, 1H, J = 13.8, 8.2 Hz). ^{13}C{^{1}H} NMR (100 MHz, CDCl$_3$) δ: 168.5, 149.4, 143.4, 141.2, 134.1, 132.4, 131.3, 128.9, 127.9, 125.0, 123.5, 122.2, 74.8, 48.5, 36.0, 26.5. GC-MS (70 eV): m/z 345 (35), 330 (38), 183 (99), 171 (47), 160 (65), 105 (100), 77 (80). Anal. Calcd for C$_{22}$H$_{20}$N$_2$O$_5$ (392.41): C, 67.34; H, 5.14; N, 7.14. Found: C, 67.38; H, 5.17; N, 7.11.

(E)-10-Chloro-6-nitro-4-phenyldeca-1,5-dien-4-ol 3l. Flash chromatography on silica gel using hexane/EtOAc = 95:5 as eluent yielded **3l** (141 mg, 91% yield) as a yellow oil. IR (cm^{-1}, neat): 699, 1331, 1520, 3537. ^{1}H NMR (400 MHz, CDCl$_3$) δ: 7.47−7.35 (m, 5H), 7.32−7.27 (m, 1H), 5.72−5.59 (m, 1H), 5.33−5.25 (m, 2H), 3.44 (dt, 2H, J = 6.8, 0.8 Hz), 2.81−2.74 (m, 4H), 2.47 (br s, 1H), 1.73−1.63 (m, 2H), 1.60−1.46 (m, 1H), 1.44−1.31 (m, 1H). ^{13}C{^{1}H} NMR (100 MHz, CDCl$_3$) δ: 153.5, 143.9, 138.7, 131.3, 128.7, 127.8, 125.0, 122.3, 74.3, 48.7, 44.4, 32.2, 26.1, 25.2. GC-MS (70 eV): m/z 268 (43), 221 (81), 105 (100), 77 (54), 41 (17). Anal. Calcd for C$_{16}$H$_{20}$ClNO$_3$ (309.79): C, 62.03; H, 6.51; N, 4.52. Found: C, 62.08; H, 6.48; N, 4.55.

(E)-4-(tert-Butyl)-6-nitrotrideca-1,5-dien-4-ol 3m. Flash chromatography on silica gel using hexane/EtOAc = 95:5 as eluent yielded **3m** (131 mg, 88% yield) as a yellow oil. IR (cm^{-1}, neat): 1329, 1522,

3558. ^{1}H NMR (400 MHz, CDCl$_3$) δ: 7.10 (s, 1H), 5.80−5.69 (m, 1H), 5.27 (d, 1H, J = 10.1 Hz), 5.23 (d, 1H, J = 17.0 Hz), 3.06−2.98 (m, 1H), 2.84−2.76 (m, 1H), 2.61 (dd, 1H, J = 13.5, 5.5 Hz), 2.34 (dd, 1H, J = 13.6, 9.4 Hz), 1.80 (br s, 1H), 1.56−1.47 (m, 1H), 1.43−1.21 (m, 9H), 1.04 (s, 9H), 0.90 (t, 3H, J = 7.0 Hz). ^{13}C{^{1}H} NMR (100 MHz, CDCl$_3$) δ: 154.6, 136.7, 133.2, 121.0, 78.8, 41.3, 39.2, 31.7, 29.6, 28.9, 28.6, 26.4, 25.4, 22.6, 14.0. GC-MS (70 eV): m/z 256 (24), 209 (30), 139 (15), 109 (14), 95 (18), 81 (25), 69 (100), 57 (90), 41 (74). Anal. Calcd for C$_{17}$H$_{31}$NO$_3$ (297.44): C, 68.65; H, 10.51; N, 4.71. Found: C, 68.60; H, 10.54; N, 4.74.

Methyl (E)-9-Hydroxy-7-nitro-9-phenyldodeca-7,11-dienoate 3n. Flash chromatography on silica gel using hexane/EtOAc = 95:5 as eluent yielded **3n** (160 mg, 92% yield) as a pale yellow oil. IR (cm^{-1}, neat): 699, 1331, 1520, 1732, 3484. ^{1}H NMR (400 MHz, CDCl$_3$) δ: 7.46−7.24 (m, 6H), 5.72−5.58 (m, 1H), 5.31−5.23 (m, 2H), 3.65 (s, 3H), 2.78 (d, 2H, J = 7.3 Hz), 2.73 (dd, 2H, J = 8.5, 6.0 Hz), 2.57 (br s, 1H), 2.23 (t, 2H, J = 7.5 Hz), 1.59−1.47 (m, 2H), 1.43−1.11 (m, 4H). ^{13}C{^{1}H} NMR (100 MHz, CDCl$_3$) δ: 174.2, 154.2, 144.0, 138.3, 131.5, 128.6, 127.7, 125.1, 122.0, 74.3, 51.5, 48.8, 33.8, 28.7, 27.2, 26.6, 24.3. GC-MS (70 eV): m/z 300 (6), 285 (13), 199 (22), 197 (18), 105 (100), 77 (41). Anal. Calcd for C$_{19}$H$_{25}$NO$_5$ (347.41): C, 65.69; H, 7.25; N, 4.03. Found: C, 65.73; H, 7.28; N, 4.07.

(E)-4-Methyl-6-nitroocta-1,5-dien-4-ol 3o. Flash chromatography on silica gel using hexane/EtOAc = 90:10 as eluent yielded **3o** (81 mg, 88% yield) as a pale yellow oil. IR (cm^{-1}, neat): 735, 921, 1334, 1457, 1519, 1641, 3533. ^{1}H NMR (400 MHz, CDCl$_3$) δ: 7.03 (s, 1H), 5.89−5.76 (m, 1H), 5.33−5.19 (m, 2H), 2.95 (dq, 2H, J = 7.3, 1.7 Hz), 2.52−2.46 (m, 1H), 2.42−2.35 (m, 1H), 1.94 (br s, 1H), 1.45 (s, 3H), 1.13 (t, 3H, J = 7.3 Hz). ^{13}C{^{1}H} NMR (100 MHz, CDCl$_3$) δ: 154.6, 138.4, 132.0, 121.1, 71.7, 47.8, 28.4, 20.1, 13.2. GC-MS (70 eV): m/z 144 (45), 97 (100), 43 (58). Anal. Calcd for C$_9$H$_{15}$NO$_3$ (185.22): C, 58.36; H, 8.16; N, 7.56. Found: C, 58.40; H, 8.19; N, 7.58.

General Procedure for the Preparation of Compounds 4. BF$_3$·Et$_2$O (0.75 mmol, 93 μL) was added dropwise at −10 °C to a stirred solution of the appropriate homoallylic alcohol **3** (0.5 mmol) in dichloromethane (5 mL). The reaction was stirred at the same temperature (−5 °C for compound **3e**) for the appropriate time (see Figure 4), diluted with dichloromethane (10 mL), and treated with a saturated aqueous solution of NaHCO$_3$ (10 mL). After phase separation, the aqueous phase was extracted with dichloromethane (2 × 20 mL), and the combined organic layers were dried with dry Na$_2$SO$_4$. Finally, the solution was filtered and concentrated in vacuo to give the crude regioisomeric products **4** and **5**, which were purified by flash column chromatography (hexane/ethyl acetate).

((3E,5E)-6-Nitroocta-1,3,5-trien-4-yl)benzene 4a (Major Regioisomer). Flash chromatography on silica gel using hexane/EtOAc = 98:2 as eluent yielded a 90:10 mixture of **4a** and **5a** (77 mg, 67% yield) as a pale yellow oil. Major regioisomer **4a**. IR (cm^{-1}, neat): 695, 760, 1333, 1520, 1632. ^{1}H NMR (400 MHz, CDCl$_3$) δ: 7.81 (s, 1H), 7.44−7.29 (m, 5H), 6.73−6.48 (m, 2H), 5.51 (d, 1H, J = 16.4 Hz), 5.39 (d, 1H, J = 9.9 Hz), 2.42 (q, 2H, J = 7.4 Hz), 0.96 (t, 3H, J = 7.4 Hz). ^{13}C{^{1}H} NMR (100 MHz, CDCl$_3$) δ: 155.7, 138.8, 133.8, 133.1, 132.7, 130.1, 128.5, 128.4, 126.7, 122.0, 21.1, 11.5. GC-MS (70 eV): m/z 229 ([M$^+$], 63), 168 (100), 152 (59), 128 (32), 115 (36), 91 (29), 77 (24). Anal. Calcd for C$_{14}$H$_{15}$NO$_2$ (229.28): C, 73.34; H, 6.59; N, 6.11. Found: C, 73.38; H, 6.63; N, 6.14.

1-Methoxy-4-((3E,5E)-6-nitroocta-1,3,5-trien-4-yl)benzene 4b (Major Regioisomer). Flash chromatography on silica gel using hexane/EtOAc = 98:2 as eluent yielded a 90:10 mixture of **4b** and **5b** (86 mg, 66% yield) as a pale yellow oil. Major regioisomer **4b**. IR (cm^{-1}, neat): 832, 1030, 1175, 1244, 1333, 1511, 1604. ^{1}H NMR (400 MHz, CDCl$_3$) δ: 7.76 (s, 1H), 7.28 (d, 2H, J = 8.9 Hz), 6.89 (d, 2H, J = 8.9 Hz), 6.63−6.44 (m, 2H), 5.45 (dd, 1H, J = 16.0, 1.4 Hz), 5.33 (dd, 1H, J = 9.5, 1.3 Hz), 3.82 (s, 3H), 2.43 (q, 2H, J = 7.4 Hz), 0.97 (t, 3H, J = 7.4 Hz). ^{13}C{^{1}H} NMR (100 MHz, CDCl$_3$) δ: 160.0, 155.8, 133.5, 131.3, 131.1, 130.7, 128.7, 128.1, 121.3, 114.4, 55.6, 21.4, 11.8. GC-MS (70 eV): m/z 259 ([M$^+$], 84), 215 (51), 198 (100), 183 (47), 65 (27), 153 (31), 128 (24), 115 (26). Anal. Calcd

for C$_{15}$H$_{17}$NO$_3$ (259.31): C, 69.48; H, 6.61; N, 5.40. Found: C, 69.52; H, 6.57; N, 5.42.

2-((3E,5E)-6-Nitroocta-1,3,5-trien-4-yl)thiophene 4c (Major Regioisomer). Flash chromatography on silica gel using hexane/EtOAc = 98:2 as eluent yielded a 90:10 mixture of **4c** and **5c** (67 mg, 57% yield) as a pale yellow oil. Major regioisomer **4c**. IR (cm^{-1}, neat): 694, 828, 909, 1329, 1523, 1612, 1656. ^{1}H NMR (400 MHz, CDCl$_3$) δ: 7.65 (s, 1H), 7.25 (dd, 1H, *J* = 3.9, 0.8 Hz), 7.01−6.97 (m, 1H), 6.94 (dd, 1H, *J* = 3.6, 1.0 Hz), 6.68 (d, 1H, *J* = 11.6 Hz), 6.47−6.33 (m, 1H), 5.48 (dd, 1H, *J* = 16.7, 0.7 Hz), 5.33 (dd, 1H, *J* = 10.1, 0.7 Hz), 2.53 (q, 2H, *J* = 7.4 Hz), 1.05 (t, 3H, *J* = 7.4 Hz). ^{13}C{^{1}H} NMR (100 MHz, CDCl$_3$) δ: 156.4, 142.2, 132.8, 131.2, 129.3, 129.0, 127.8, 125.6, 125.5, 121.4, 21.2, 11.8. GC-MS (70 eV): *m/z* 235 ([M$^+$], 76), 174 (100), 147 (26), 128 (35), 115 (33), 97 (24), 77 (19). Anal. Calcd for C$_{12}$H$_{13}$NO$_2$S (235.30): C, 61.25; H, 5.57; N, 5.95; S, 13.63. Found: C, 61.29; H, 5.60; N, 5.98; S, 13.67.

2-((3E,5E)-6-Nitrodeca-1,3,5-trien-4-yl)naphthalene 4e (Major Regioisomer). Flash chromatography on silica gel using hexane/EtOAc = 98:2 as eluent yielded a 90:10 mixture of **4e** and **5e** (89 mg, 58% yield) as a pale yellow oil. Major regioisomer **4e**. IR (cm^{-1}, neat): 464, 751, 812, 1325, 1430, 1467, 1519, 3054. ^{1}H NMR (400 MHz, CDCl$_3$) δ: 7.96 (s, 1H), 7.89−7.83 (m, 3H), 7.76 (d, 1H, *J* = 1.4 Hz), 7.58−7.49 (m, 3H), 6.84 (d, 1H, *J* = 11.0 Hz), 6.70−6.58 (m, 1H), 5.58 (d, 1H, *J* = 16.7 Hz), 5.45 (d, 1H, *J* = 10.1 Hz), 2.45−2.38 (m, 2H), 1.42−1.33 (m, 2H), 1.15−1.05 (m, 2H), 0.70 (t, 3H, *J* = 7.3 Hz). ^{13}C{^{1}H} NMR (100 MHz, CDCl$_3$) δ: 154.9, 136.0, 133.6, 133.3, 133.2, 133.1, 130.5, 128.8, 128.5, 128.2, 127.6, 126.7, 126.5, 126.1, 124.2, 122.2, 29.1, 27.4, 22.3, 13.4. GC-MS (70 eV): *m/z* 307 ([M$^+$], 50), 264 (37), 218 (100), 202 (92), 165 (14), 41 (14). Anal. Calcd for C$_{20}$H$_{21}$NO$_2$ (307.39): C, 78.15; H, 6.89; N, 4.56. Found: C, 78.19; H, 6.92; N, 4.59.

1-Methyl-4-((3E,5E)-6-nitro-8-phenylocta-1,3,5-trien-4-yl)-benzene 4i. Flash chromatography on silica gel using hexane/EtOAc = 98:2 as eluent yielded **4i** (96 mg, 60% yield) as a pale yellow oil. IR (cm^{-1}, neat): 699, 821, 915, 1330, 1520, 3025. ^{1}H NMR (400 MHz, CDCl$_3$) δ: 7.89 (s, 1H), 7.29−7.07 (m, 7H), 6.93−6.89 (m, 2H), 6.62−6.45 (m, 2H), 5.47 (dd, 1H, *J* = 16.0, 1.7 Hz), 5.37 (dd, 1H, *J* = 9.4, 1.6 Hz), 2.66 (s, 4H), 2.37 (s, 3H). ^{13}C{^{1}H} NMR (100 MHz, CDCl$_3$) δ: 153.1, 140.1, 138.4, 136.0, 133.6, 133.0, 132.9, 131.8, 129.5, 128.4, 128.3, 126.8, 126.3, 122.0, 33.0, 29.9, 21.2. GC-MS (70 eV): *m/z* 319 ([M$^+$], 7), 227 (100), 182 (92), 165 (50), 152 (17), 91 (58). Anal. Calcd for C$_{21}$H$_{21}$NO$_2$ (319.40): C, 78.97; H, 6.63; N, 4.39. Found: C, 79.01; H, 6.60; N, 4.42.

((3E,5E)-10-Chloro-6-nitrodeca-1,3,5-trien-4-yl)benzene 4l (Major Regioisomer). Flash chromatography on silica gel using hexane/EtOAc = 98:2 as eluent yielded a 90:10 mixture of **4l** and **5l** (92 mg, 63% yield) as a pale yellow oil. Major regioisomer **4l**. IR (cm^{-1}, neat): 700, 1326, 1519, 1640. ^{1}H NMR (400 MHz, CDCl$_3$) δ: 7.93 (s, 1H), 7.43−7.27 (m, 5H), 6.70−6.51 (m, 2H), 5.52 (dd, 1H, *J* = 15.9, 1.5 Hz), 5.42 (dd, 1H, *J* = 9.4, 1.5 Hz), 3.34 (t, 2H, *J* = 6.2 Hz), 2.40−2.34 (m, 2H), 1.62−1.44 (m, 4H). ^{13}C{^{1}H} NMR (100 MHz, CDCl$_3$) δ: 153.7, 138.8, 133.7, 133.6, 132.8, 131.0, 128.9, 128.5, 126.8, 122.6, 44.1, 32.0, 26.9, 24.4. GC-MS (70 eV): *m/z* 291 (29), 214 (43), 168 (100), 167 (70), 165 (53), 153 (32), 152 (59), 115 (22), 91 (20), 41 (21). Anal. Calcd for C$_{16}$H$_{18}$ClNO$_2$ (291.77): C, 65.86; H, 6.22; N, 4.80. Found: C, 65.91; H, 6.19; N, 4.83.

Methyl (7E,9E)-7-Nitro-9-phenyldodeca-7,9,11-trienoate 4n (Major Regioisomer). Flash chromatography on silica gel using hexane/EtOAc = 98:2 as eluent yielded a 90:10 mixture of **4n** and **5n** (94 mg, 57% yield) as a yellow oil. Major regioisomer **4n** IR (cm^{-1}, neat): 697, 732, 1331, 1521, 1734. ^{1}H NMR (400 MHz, CDCl$_3$) δ: 7.87 (s, 1H), 7.40−7.27 (m, 5H), 6.68−6.49 (m, 2H), 5.50 (dd, 1H, *J* = 16.3, 1.5 Hz), 5.39 (dd, 1H, *J* = 9.8, 1.5 Hz), 3.63 (s, 3H), 2.37−2.31 (m, 2H), 2.16 (t, 2H, *J* = 7.5 Hz), 1.49−1.30 (m, 4H), 1.15−1.04 (m, 2H). ^{13}C{^{1}H} NMR (100 MHz, CDCl$_3$) δ: 174.0, 154.2, 138.8, 133.7, 133.2, 132.9, 130.7, 128.8, 128.4, 126.8, 122.3, 51.5, 33.7, 28.7, 27.4, 26.6, 24.2. GC-MS (70 eV): *m/z* 294 (10), 220 (81), 210 (80), 168 (100), 167 (94), 115 (40), 87 (41), 55 (35). Anal. Calcd for C$_{19}$H$_{23}$NO$_4$ (329.40): C, 69.28; H, 7.04; N, 4.25. Found: C, 69.33; H, 7.07; N, 4.21.

ASSOCIATED CONTENT

Data Availability Statement

The data underlying this study are available in the published article and its online Supporting Information.

Ⓢ Supporting Information

The Supporting Information is available free of charge at https://pubs.acs.org/doi/10.1021/acs.joc.2c02669.

Full characterization of compounds **1**; copies of ^{1}H NMR and ^{13}C{1H} NMR spectra for compounds **1**, **3**, and **4** (PDF)

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Notes

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