JOC The Journal of Organic Chemistry

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One-Pot Synthesis of 5-Amino-2,5-dihydro-1-benzoxepines: Access to Pharmacologically Active Heterocyclic Scaffolds

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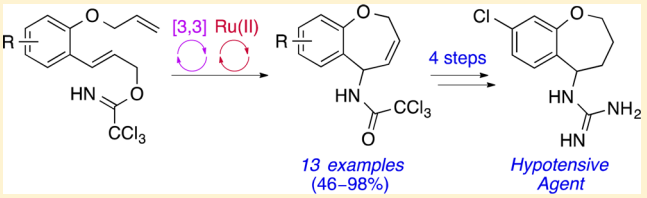
Supporting Information

ABSTRACT: A one-pot multibond-forming process involving a thermally mediated Overman rearrangement and a ring closing metathesis reaction of allylic trichloroacetimidates bearing a 2-allyloxyaryl group has been developed for the synthesis of 5-amino-substituted 2,5-dihydro-1-benzoxepines. Chemoselective reduction and functionalization of these compounds allowed access to a range of pharmacologically active 5-amino-2,3,4,5-tetrahydro-1-benzoxepine scaffolds.



INTRODUCTION

Dihydrobenzo[*b*]oxepines are an important class of seven-membered heterocyclic compound found as a key constituent in a variety of natural products and biologically active substances.[1−3] In particular, 2,5-dihydro-1-benzoxepines such as radulanin A (**1**)[4] and heliannuol B[5] were isolated from liverwort and sunflowers, respectively, while 2,3-dihydro-1-benzoxepines including pterulone (**2**) have been recovered from various fungi and shown to possess antibiotic activity (Figure 1).[1,3]

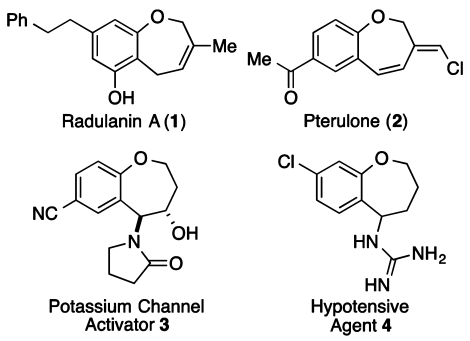
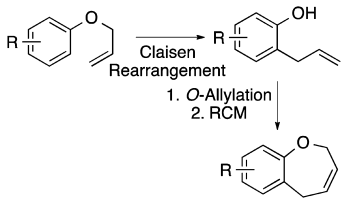


Figure 1. Structures of dihydro-1-benzoxepine natural products (**1** and **2**) and biologically active amino-substituted 2,3,4,5-tetrahydro-1-benzoxepines (**3** and **4**).

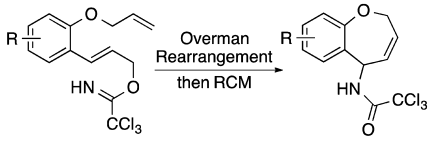
As a result of their biological significance and interesting structures, various methods for the preparation of these compounds have been reported. 2,3-Dihydro-1-benzoxepines have been synthesized by metal catalyzed formation of the oxepine ring using suitably derived phenol ethers and alkynes[6,7] and also via a Wittig homologation of 2-(chloromethyl)-2*H*-chromen-2-ol derivatives.[8] A variety of methods have also been reported for the preparation of 2,5-dihydro-1-benzoxepines.[9−13] These include a general approach involving the Claisen rearrangement of allyl phenyl ethers followed by *O*-allylation and a ring closing metathesis (RCM) reaction (Scheme 1a).[11] This particular strategy has been utilized for the total synthesis of a number of 2,5-dihydro-1-benzoxepine-containing natural products.[2,12,13]

Scheme 1. 3,3-Sigmatropic Rearrangement and RCM Routes to 2,5-Dihydro-1-benzoxepines

a) Typical Stepwise Approach for the Synthesis of 2,5-Dihydro-1-benzoxepines - Refs 2, 11 & 13



b) One-Pot Synthesis of 5-Amino-Substituted 2,5-Dihydro-1-benzoxepines - This Work



Building on the general strategy of using sigmatropic rearrangements in combination with RCM reactions for the synthesis of medium-sized heterocycles (Scheme 1a) and our previous work on the development of one-pot multistep reactions,[14−16] we were interested in developing an approach for the synthesis of 5-amino-2,5-dihydro-1-benzoxepines (Scheme 1b). Previous one-pot methods developed by our group for the preparation of seven-membered ring systems have encountered issues during the metathesis step, such as the formation of dimeric products,[14a] and the requirement of

Received: March 14, 2015
Published: April 7, 2015

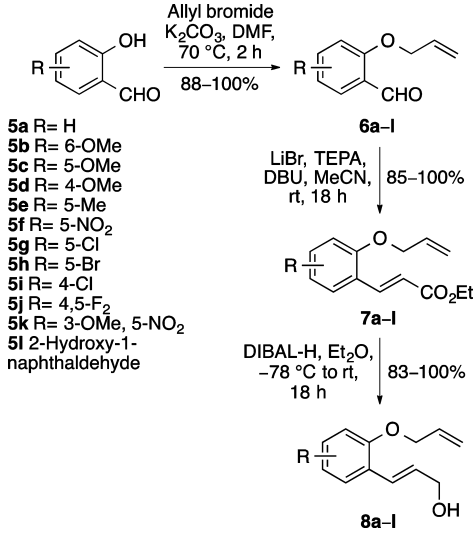
DOI: 10.1021/acs.joc.5b00583
J. Org. Chem. 2015, 80, 4683−4696

forcing conditions to form the seven-membered ring in good yields.[15a] In this current study, we wished to investigate whether more rigid alkene derived allylic alcohols bearing an aromatic ring would prove to be more suitable substrates for such a process, yielding a library of 5-amino-2,5-dihydro-1-benzoxepines. Subsequent oxidation or chemoselective reduction of the alkene moiety of these targets would then allow access to functionalized 5-amino-2,3,4,5-tetrahydro-1-benzoxepines that are present in a wide range of pharmacologically active compounds (e.g., **3** and **4**, Figure 1).[17−20] We now report an efficient synthesis of 5-amino-2,5-dihydrobenzoxepines from commercially available salicylaldehydes using a one-pot multibond-forming process for introduction of the amine functionality and consecutive formation of the oxepine ring. As well as demonstrating the general scope of this strategy, we also explore the synthetic utility of 5-amino-2,5-dihydro-1-benzoxepines for the preparation of 2,3,4,5-tetrahydro-1-benzoxepine targets.

RESULTS AND DISCUSSION

The study began with the development of a general approach for the synthesis of (*E*)-(2-allyloxy)cinnamyl alcohols from readily available salicylaldehydes (Scheme 2). *O*-Allylation of

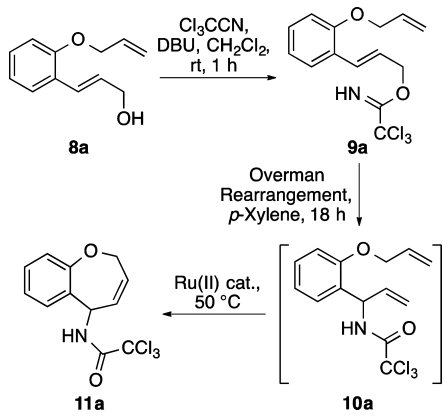
Scheme 2. Synthesis of Allylic Alcohols 8a−l



salicylaldehydes **5a−l** under standard conditions gave 2-allyloxybenzaldehydes **6a−l**, and these were subjected to a Horner−Wadsworth−Emmons (HWE) reaction with triethyl phosphonoacetate (TEPA) under mild Masamune−Roush conditions.[21] Reduction of the resulting (*E*)-α,β-unsaturated esters **7a−l** with DIBAL-H completed the three-step synthesis of (*E*)-(2-allyloxy)cinnamyl alcohols **8a−l** in high overall yields.

The one-pot multibond-forming process was then optimized for the synthesis of 5-amino-substituted 2,5-dihydro-1-benzoxepine **11a** (Table 1). (*E*)-(2-Allyloxy)cinnamyl alcohol **8a** was converted to the corresponding allylic trichloroacetimidate using trichloroacetonitrile and a catalytic amount of DBU and then subjected to an Overman rearrangement under thermal conditions (entry 1).[22] Grubbs first-generation catalyst was initially investigated for the RCM step and required a catalyst loading of 30 mol % and a reaction time of 120 h for complete conversion.[23] This gave 2,5-dihydro-1-benzoxepine **11a** in 15% yield over the three steps. On analysis of the process, it was

Table 1. Optimization of the One-Pot Process



entry	Overman rearrangement	RCM reaction	yield (%)
1[a]	K_2CO_3, 140 °C	Grubbs I (30 mol %), 120 h	15
2[b]	K_2CO_3, 140 °C	Grubbs I (30 mol %), 120 h	63
3[b]	$Pd(MeCN)_2Cl_2$ (10 mol %), rt	Grubbs I (30 mol %), 120 h	26
4[b]	K_2CO_3, 140 °C	Grubbs II (5 mol %), 20 h	68

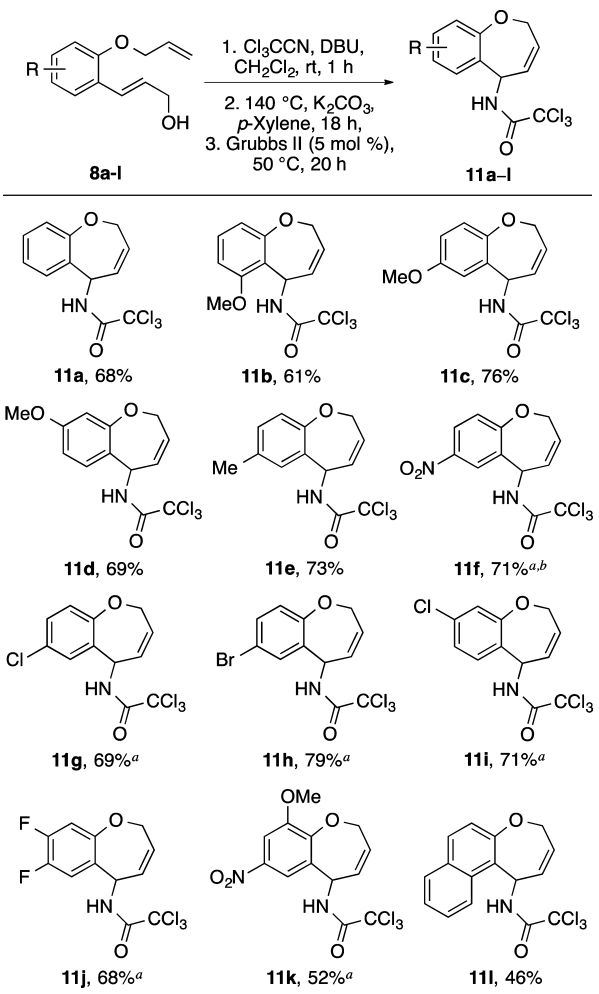
[a]Allylic trichloroacetimidate **9a** was isolated by filtration of the reaction mixture through a plug of silica gel. [b]Allylic trichloroacetimidate **9a** was isolated by filtration of the reaction mixture through a plug of neutral alumina.

found that the typical workup procedure of allylic trichloroacetimidate formation by filtration of the reaction mixture through a plug of silica gel, resulted in substantial decomposition of **9a**. This is likely promoted by the presence of the electron-rich *ortho*-ether unit and the acidic nature of the silica gel. In subsequent studies of the one-pot process, this issue was overcome by simply performing the filtration using neutral alumina. Using this modification, the one-pot process was repeated, and **11a** was isolated in a significantly improved 63% overall yield (entry 2). The use of a palladium(II)-catalyzed Overman rearrangement was next investigated, and while this transformation was conducted under mild conditions, 2,5-dihydro-1-benzoxepine **11a** was isolated in only 26% yield (entry 3). The low yield is likely due to a number of factors such as a competing 1,3-rearrangement as well as coordination of the palladium(II)-catalyst with the allylic ether moiety preventing effective activation and rearrangement of the allylic trichloroacetimidate.[15a] Finally, the use of a one-pot process involving a thermally mediated Overman rearrangement in combination with Grubbs second-generation catalyst was examined, and this resulted in a substantial improvement of reaction conditions for the RCM step (entry 4).[24] After 20 h, complete conversion could be achieved using a 5 mol % catalyst loading, resulting in the isolation of 2,5-dihydro-1-benzoxepine **11a** in 68% yield from allylic alcohol **8a**.

Using these optimized conditions, the scope of the one-pot process for the synthesis of a small library of 5-amino-substituted 2,5-dihydro-1-benzoxepines was explored (Scheme 3). Overall, this approach was found to be general for a range of substituents and substitution patterns. For example, comparison of the same substituent at *ortho*-, *meta*-, or *para*-positions showed no significant difference in reactivity, giving the final products in comparable yields (**11b**/**c**/**d** and **11g**/**i**). Substrates bearing strongly electron-deficient substituents did require

DOI: 10.1021/acs.joc.5b00583
J. Org. Chem. 2015, 80, 4683−4696

Scheme 3. Synthesis of 5-Amino-Substituted 2,5-Dihydro-1-benzoxepines 11a–l



[a]The Overman rearrangement required an extended reaction time (24 h, **11i** and **11j**; 48 h, **11h** and **11k**; 60 h, **11f** and **11g**). [b]7.5 mol % of Grubbs second-generation catalyst was used for the RCM step.

extended reaction times for the Overman rearrangement, however, these one-pot processes still produced the corresponding 2,5-dihydro-1-benzoxepines in high yields (**11f–j**). Only products **11k** and **11l** were isolated in modest yields, and this is likely due to the increased steric bulk associated with the aryl substituents.

Derivatives of 5-amino-substituted 2,3,4,5-tetrahydro-1-benzoxepines bearing aryl groups at the 8-postion (e.g., **20**, Scheme 4) have been shown to be potent inhibitors of acyl-CoA cholesterol *O*-acyl transferase (ACAT), the enzyme responsible for intracellular esterification of cholesterol.[19] Due to the significant biological activity of these compounds, the scope of our one-pot synthesis of 2,5-dihydro-1-benzoxepines was extended to investigate the rapid assembly of this type of oxepine skeleton (Scheme 4). Initially, Suzuki–Miyaura coupling of 4-fluorophenylboronic acid (**12**) and methyl 2-hydroxy-4-iodobenzoate (**13**) gave biaryl compound **14** in quantitative yield. Reduction of the ester with lithium aluminum hydride and selective allylation of the phenol gave benzyl alcohol **15**. This was then subjected to a one-pot Swern oxidation and HWE reaction, which gave (*E*)-α,β-unsaturated ester **16** as the sole product in 84% yield over the two steps. DIBAL-H reduction of the ester then completed the six-step synthesis of allylic alcohol **17**. Formation of the corresponding allylic trichloroacetimidate and application of the one-pot Overman rearrangement and RCM process using the optimized conditions proceeded smoothly, giving 2,5-dihydro-1-benzoxepine **18** in 98% yield. The synthesis of **18** in 61% overall yield from commercially available benzoate **13** demonstrates the robust nature of the one-pot strategy for the synthesis of pharmacologically important 5-amino-substituted 2,5-dihydro-1-benzoxepine building blocks.

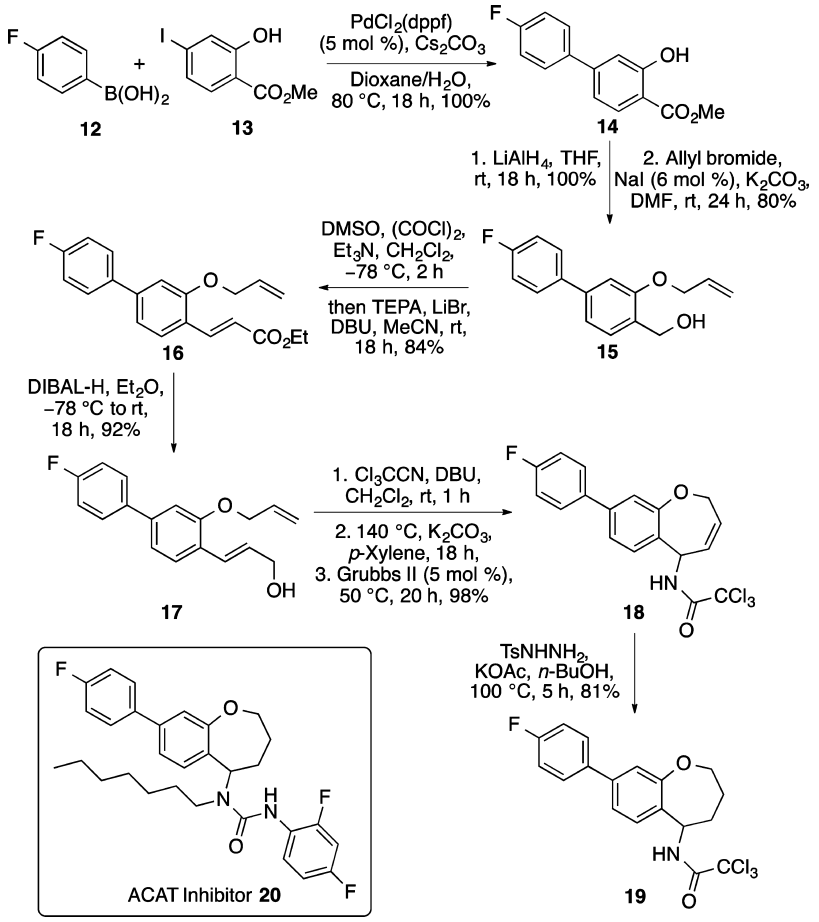
Having explored the scope of the one-pot process, the next stage of this research program investigated the synthetic utility of these compounds for the preparation of biologically active scaffolds. As 5-amino-substituted 2,3,4,5-tetrahydro-1-benzoxepines have wide ranging pharmacological activities,[17−20] chemoselective methods for their synthesis from 2,5-dihydro-1-benzoxepines were developed. A method that would allow preparation of the ACAT inhibitor core by reduction of the alkene moiety of **18** while retaining the trichloroacetamide as a protecting group was initially examined. Standard hydrogenation conditions (10% Pd/C in an atmosphere of H_2) gave **19** in 59% yield. However, several byproducts formed via reduction of the trichloromethyl group were also isolated. Instead, a more selective reaction for the preparation of **19** was achieved using diimide, which was generated in situ from *p*-toluenesulfonyl hydrazide and potassium acetate (Scheme 4).[25] This produced 2,3,4,5-tetrahydro-1-benzoxepine **19** more cleanly in 81% yield.

A synthesis of 8-chloro-5-guanidino-2,3,4,5-tetrahydro-1-benzoxepine (**4**), a known hypotensive agent was developed from 2,5-dihydro-1-benzoxepine **11i** (Scheme 5).[20] In this case, introduction of the guanidine moiety required removal of the trichloroacetamide, and so no effort was made to maintain this group during reduction of the alkene. Hydrogenation of **11i** under standard conditions resulted in reduction of both the alkene and the trichloromethyl group giving **21** as the sole product in 94% yield. Acid hydrolysis of the dichloromethylacetamide group required forcing conditions but did yield the corresponding amine cleanly. This was coupled with commercially available *N*,*N*′-bis(*tert*-butoxycarbonyl)-1*H*-pyrazole-1-carboxamidine (**22**) in the presence of Hünig's base, and this gave guanidine **23** in 75% yield over the two steps.[26,27] Finally, removal of the Boc-protecting groups using TFA completed the 10-step synthesis of hypotensive agent **4** in 40% overall yield from commercially available 4-chloro-2-hydroxybenzaldehyde (**5i**).

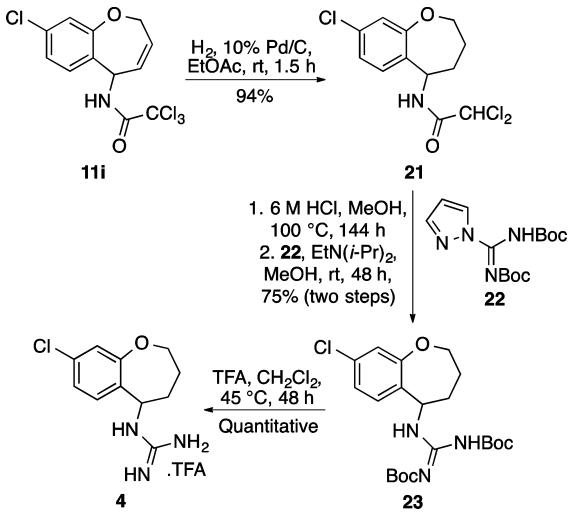
A number of 5-amino-substituted 2,3,4,5-tetrahydro-1-benzoxepines bearing hydroxyl groups have displayed pharmacological activity (e.g., **3**, Figure 1).[17a,c,18] For this reason and the considerable interest in the medicinal chemistry applications of the vicinal amino diol motif,[28] the final stage of this research program explored the directed oxidation of 5-amino-substituted 2,5-dihydro-1-benzoxepines for the preparation of *syn*- and *anti*-3,4-diol analogues. While directed dihydroxylation[29] and epoxidation[30] of a number of cyclic allylic trichloroacetamide systems has been described, we were interested in the outcome of these reactions using 5-amino-substituted 2,5-dihydro-1-benzoxepines as novel substrates. Reaction of 6-methoxy-2,5-dihydro-1-benzoxepine **11b** with osmium tetroxide and TMEDA under Donohoe conditions gave the corresponding (3*R**,4*S**,5*S**)-diol **24** in 74% yield (Scheme 6).[29] Inspection of the ^{1}H NMR spectra of the crude material from this reaction showed only one diastereomer, with

DOI: 10.1021/acs.joc.5b00583
J. Org. Chem. 2015, 80, 4683−4696

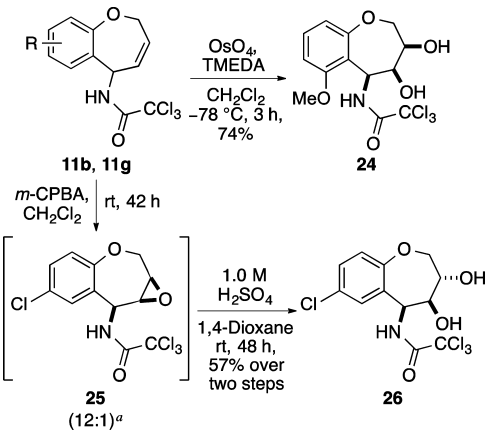
Scheme 4. Synthesis of 5-Amino-Substituted 2,3,4,5-Tetrahydro-1-benzoxepine 19



Scheme 5. Synthesis of 8-Chloro-5-guanidino-2,3,4,5-tetrahydro-1-benzoxepine (4)



Scheme 6. Dihydroxylation of 5-Amino-Substituted 2,5-Dihydro-1-benzoxepines



[a]Ratio of major (3*R**,4*S**,5*S**)-**25** and minor (3*S**,4*R**,5*S**) epoxide diastereomers.

NOE experiments clearly demonstrated the *syn*-relationship of the vicinal amino diol motif. This result suggests that the trichloroacetamide unit of the oxepine ring systems is able to facilitate a highly effective, directed dihydroxylation with the complex formed from osmium tetroxide and TMEDA.

Directed epoxidation of 7-chloro-2,5-dihydro-1-benzoxepine **11g** and subsequent acid mediated ring opening for the preparation of the *anti*-3,4-diol was next investigated and found to be less selective. Treatment of **11g** with *m*-CPBA gave the corresponding epoxide in a 12:1 diastereoselectivity (Scheme 6). Again NOE experiments confirmed the all *syn*-diastereomer **25** as the major product, formed via a substrate-directed process that is in agreement with Henbest's rule.[30,31] Without purification, regioselective hydrolysis of epoxide **25** under acidic conditions gave after purification, the (3*S**,4*S**,5*S**)-diol **26** in good yield over the two steps. The difference in selectivity

DOI: 10.1021/acs.joc.5b00583
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between the dihydroxylation and epoxidation processes is likely a direct reflection of the ability of the reagents of these reactions to undergo hydrogen-bonding substrate-directed reactions with the allylic trichloroacetamide oxepine unit. Seven-membered heterocyclic ring systems such as azepanes bearing an allylic trichloroacetamide moiety have demonstrated similar selectivity and overall yields for these oxidation processes.[15b]

CONCLUSIONS

In summary, a general approach has been developed for the preparation of 2,5-dihydro-1-benzoxepines. A three-step synthesis of 2-allyloxycinnamyl alcohol derivatives from readily available 2-hydroxybenzaldehydes was followed by imidate formation and a one-pot Overman rearrangement and RCM process, allowing access to a diverse library of 5-amino-2,5-dihydro-1-benzoxepines in high overall yields. Further functionalization of these privileged structures was explored. Chemoselective reduction or substrate-directed oxidation of the alkene moiety generated a series of 5-amino-2,3,4,5-tetrahydro-1-benzoxepines, compounds which display a wide range of pharmacological activities. Work is currently underway to extend the application of this one-pot multibond-forming reaction process for the preparation of biologically relevant polycyclic classes of compounds.

EXPERIMENTAL SECTION

All reagents and starting materials were obtained from commercial sources and used as received. All dry solvents were purified using a solvent purification system. All reactions were performed under an atmosphere of argon unless otherwise mentioned. Brine refers to a saturated solution of sodium chloride. Flash column chromatography was performed using silica gel 60 (35−70 μm). Aluminum-backed plates precoated with silica gel 60F_{254} were used for thin-layer chromatography and were visualized with a UV lamp or by staining with potassium permanganate. ^{1}H NMR spectra were recorded on a NMR spectrometer at either 400 or 500 MHz, and data are reported as follows: chemical shift in ppm relative to tetramethylsilane as the internal standard, multiplicity (s = singlet, d = doublet, t = triplet, q = quartet, m = multiplet or overlap of nonequivalent resonances, integration). ^{13}C NMR spectra were recorded on a NMR spectrometer at either 101 or 126 MHz, and data are reported as follows: chemical shift in ppm relative to tetramethylsilane or the solvent as internal standard ($CDCl_3$, δ 77.0 ppm or CD_3OD, δ 44.0 ppm), multiplicity with respect to hydrogen (deduced from DEPT experiments, C, CH, CH_2 or CH_3). Infrared spectra were recorded on a FTIR spectrometer; wavenumbers are indicated in cm^{-1}. Mass spectra were recorded using electron impact, chemical ionization, or electrospray techniques. HRMS spectra were recorded using a dual-focusing magnetic analyzer mass spectrometer. Melting points are uncorrected.

2-Allyloxybenzaldehyde (6a).[32] Allyl bromide (0.98 mL, 1.3 mmol) was added to a stirred solution of 2-hydroxybenzaldehyde (**5a**) (0.10 mL, 0.94 mmol) and potassium carbonate (0.26 g, 1.9 mmol) in *N*,*N*′-dimethylformamide (10 mL) and warmed to 70 °C for 2 h. The reaction was cooled to room temperature, diluted with 5% aqueous lithium chloride solution (20 mL), and extracted with diethyl ether (20 mL). The organic layer was washed with 5% aqueous lithium chloride solution (3 × 10 mL), brine (10 mL), dried ($MgSO_4$), filtered, and concentrated *in vacuo*. Purification by column chromatography (elution with 20% diethyl ether in petroleum ether) gave 2-allyloxybenzaldehyde (**6a**) (0.15 g, 99%) as a colorless oil. Spectroscopic data were in accordance with literature values.[32] ^{1}H NMR (400 MHz, $CDCl_3$) δ 4.66 (dt, J = 5.1, 1.5 Hz, 2H), 5.34 (dq, J = 10.5, 1.5 Hz, 1H), 5.45 (dq, J = 17.3, 1.5 Hz, 1H), 6.08 (ddt, J = 17.3, 10.5, 5.1 Hz, 1H), 6.98 (d, J = 8.4 Hz, 1H), 7.03 (br t, J = 7.5 Hz, 1H), 7.53 (ddd, J = 8.4, 7.5, 1.9 Hz, 1H), 7.84 (dd, J = 7.5, 1.9 Hz, 1H), 10.54 (d, J = 0.7 Hz, 1H); ^{13}C NMR (101 MHz, $CDCl_3$) δ 69.4 (CH_2), 113.0 (CH), 118.2 (CH_2), 121.0 (CH), 125.3 (C), 128.6 (CH), 132.6 (CH), 135.9 (CH), 161.1 (C), 189.9 (CH); MS (CI) m/z 163 (MH^+, 100), 135 (34), 121 (8), 85 (12), 79 (11).

2-Allyloxy-6-methoxybenzaldehyde (6b).[32] The reaction was carried out as described for the synthesis of 2-allyloxybenzaldehyde (**6a**) using 2-hydroxy-6-methoxybenzaldehyde (**5b**) (0.500 g, 3.29 mmol). This gave 2-allyloxy-6-methoxybenzaldehyde (**6b**) (0.559 g, 88%) as a yellow oil. Spectroscopic data were in accordance with literature values.[32] ^{1}H NMR (400 MHz, $CDCl_3$) δ 3.90 (s, 3H), 4.63 (dt, J = 5.0, 1.4 Hz, 2H), 5.31 (dq, J = 10.4, 1.4 Hz, 1H), 5.48 (dq, J = 17.3, 1.4 Hz, 1H), 6.05 (ddt, J = 17.3, 10.4, 5.0 Hz, 1H), 6.56 (d, J = 8.5 Hz, 1H), 6.58 (d, J = 8.5 Hz, 1H), 7.42 (t, J = 8.5 Hz, 1H), 10.56 (s, 1H); ^{13}C NMR (101 MHz, $CDCl_3$) δ 56.2 (CH_3), 69.7 (CH_2), 104.2 (CH), 105.3 (CH), 115.0 (C), 117.9 (CH_2), 132.6 (CH), 135.8 (CH), 161.6 (C), 162.0 (C), 189.4 (CH); MS (ESI) m/z 215 (MNa^+, 100), 187 (10), 174 (20), 137 (5).

2-Allyloxy-5-methoxybenzaldehyde (6c).[33] The reaction was carried out as described for the synthesis of 2-allyloxybenzaldehyde (**6a**) using 2-hydroxy-5-methoxybenzaldehyde (**5c**) (0.41 mL, 3.30 mmol). This gave 2-allyloxy-5-methoxybenzaldehyde (**6c**) (0.60 g, 96%) as a yellow oil. Spectroscopic data were in accordance with literature values.[33] ^{1}H NMR (400 MHz, $CDCl_3$) δ 3.80 (s, 3H), 4.61 (d, J = 5.2 Hz, 2H), 5.31 (dd, J = 10.6, 1.4 Hz, 1H), 5.43 (dd, J = 17.1, 1.4 Hz, 1H), 6.06 (ddt, J = 17.1, 10.6, 5.2 Hz, 1H), 6.93 (d, J = 9.1 Hz, 1H), 7.11 (dd, J = 9.1, 3.3 Hz, 1H), 7.33 (d, J = 3.3 Hz, 1H), 10.49 (s, 1H); ^{13}C NMR (101 MHz, $CDCl_3$) δ 56.0 (CH_3), 70.2 (CH_2), 110.4 (CH), 115.1 (CH), 118.1 (CH_2), 123.6 (CH), 125.6 (C), 132.8 (CH), 154.0 (C), 155.9 (C), 189.6 (CH); MS (ESI) m/z 215 (MNa^+, 40), 206 (30), 174 (100).

2-Allyloxy-4-methoxybenzaldehyde (6d).[33] The reaction was carried out as described for the synthesis of 2-allyloxybenzaldehyde (**6a**) using 2-hydroxy-4-methoxybenzaldehyde (**5d**) (0.500 g, 3.29 mmol). This gave 2-allyloxy-4-methoxybenzaldehyde (**6d**) (0.583 g, 92%) as a colorless oil. Spectroscopic data were in accordance with literature values.[33] ^{1}H NMR (500 MHz, $CDCl_3$) δ 3.85 (s, 3H), 4.62 (dt, J = 5.1, 1.5 Hz, 2H), 5.33 (dq, J = 10.5, 1.5 Hz, 1H), 5.45 (dq, J = 17.3, 1.5 Hz, 1H), 6.06 (ddt, J = 17.3, 10.5, 5.1 Hz, 1H), 6.43 (d, J = 2.2 Hz, 1H), 6.54 (ddd, J = 8.7, 2.2, 0.6 Hz, 1H), 7.81 (d, J = 8.7 Hz, 1H), 10.35 (d, J = 0.6 Hz, 1H); ^{13}C NMR (126 MHz, $CDCl_3$) δ 55.8 (CH_3), 69.3 (CH_2), 99.2 (CH), 106.2 (CH), 118.2 (CH_2), 119.4 (C), 130.6 (CH), 132.4 (CH), 162.8 (C), 166.2 (C), 188.4 (CH); MS (ESI) m/z 215 (MNa^+, 100), 187 (7), 174 (7), 159 (3).

2-Allyloxy-5-methylbenzaldehyde (6e).[33] The reaction was carried out as described for the synthesis of 2-allyloxybenzaldehyde (**6a**) using 2-hydroxy-5-methylbenzaldehyde (**5e**) (0.136 g, 1.00 mmol). This gave 2-allyloxy-5-methylbenzaldehyde (**6e**) (0.173 g, 98%) as a colorless oil. Spectroscopic data were in accordance with literature values.[33] ^{1}H NMR (500 MHz, $CDCl_3$) δ 2.31 (s, 3H), 4.63 (dt, J = 5.2, 1.6 Hz, 2H), 5.32 (dq, J = 10.6, 1.6 Hz, 1H), 5.44 (dq, J = 17.3, 1.6 Hz, 1H), 6.07 (ddt, J = 17.3, 10.6, 5.2 Hz, 1H), 6.88 (d, J = 8.5 Hz, 1H), 7.33 (ddd, J = 8.5, 2.3, 0.6 Hz, 1H), 7.64 (d, J = 2.3 Hz, 1H), 10.51 (s, 1H); ^{13}C NMR (126 MHz, $CDCl_3$) δ 20.3 (CH_3), 69.3 (CH_2), 113.0 (CH), 117.9 (CH_2), 124.9 (C), 128.5 (CH), 130.3 (C), 132.6 (CH), 136.5 (CH), 159.1 (C), 189.9 (CH); MS (ESI) m/z 199 (MNa^+, 100), 190 (3), 185 (4), 171 (5), 158 (16), 136 (2).

2-Allyloxy-5-nitrobenzaldehyde (6f).[34] The reaction was carried out as described for the synthesis of 2-allyloxybenzaldehyde (**6a**) using 2-hydroxy-5-nitrobenzaldehyde (**5f**) (0.050 g, 0.32 mmol). This gave 2-allyloxy-5-nitrobenzaldehyde (**6f**) (0.061 g, 98%) as a white solid. Mp 62−64 °C (lit.[34] 63−65 °C); ^{1}H NMR (400 MHz, $CDCl_3$) δ 4.80 (dt, J = 5.3, 1.4 Hz, 2H), 5.41 (ddt, J = 10.7, 2.5, 1.4 Hz, 1H), 5.48 (ddt, J = 17.3, 2.5, 1.4 Hz, 1H), 6.08 (ddt, J = 17.3, 10.7, 5.3 Hz, 1H), 7.11 (d, J = 9.2 Hz, 1H), 8.39 (dd, J = 9.2, 2.9 Hz, 1H), 8.67 (d, J = 2.9 Hz, 1H), 10.48 (s, 1H); ^{13}C NMR (101 MHz, $CDCl_3$) δ 70.3 (CH_2), 113.5 (CH), 119.6 (CH_2), 124.7 (CH), 124.8 (C) 130.6 (CH), 131.1 (CH), 141.7 (C), 164.7 (C), 187.6 (CH); MS (CI) m/z 208 (MH^+, 100), 178 (45), 168 (13), 138 (16), 113 (21), 97 (18), 81 (32), 69 (33).

DOI: 10.1021/acs.joc.5b00583
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2-Allyloxy-5-chlorobenzaldehyde (6g).[35] The reaction was carried out as described for the synthesis of 2-allyloxybenzaldehyde (**6a**) using 2-hydroxy-5-chlorobenzaldehyde (**5g**) (0.500 g, 3.18 mmol). This gave 2-allyloxy-5-chlorobenzaldehyde (**6g**) (0.61 g, 96%) as a white solid. Mp 99−101 °C (lit.[35] 101−102 °C); ^{1}H NMR (400 MHz, $CDCl_3$) δ 4.65 (dt, J = 5.2, 1.5 Hz, 2H), 5.35 (dq, J = 10.6, 1.5 Hz, 1H), 5.44 (dq, J = 17.3, 1.5 Hz, 1H), 6.06 (ddt, J = 17.3, 10.6, 5.2 Hz, 1H), 6.93 (d, J = 8.9 Hz, 1H), 7.47 (dd, J = 8.9, 2.8 Hz, 1H), 7.79 (d, J = 2.8 Hz, 1H), 10.46 (s, 1H); ^{13}C NMR (101 MHz, $CDCl_3$) δ 69.8 (CH_2), 114.7 (CH), 118.7 (CH_2), 126.1 (C), 126.7 (C), 128.1 (CH), 132.1 (CH), 135.4 (CH), 159.5 (C), 188.5 (CH); MS (CI) m/z 197 (MH^+, 100), 169 (13), 157 (4), 81 (11), 69 (18).

2-Allyloxy-5-bromobenzaldehyde (6h).[35] The reaction was carried out as described for the synthesis of 2-allyloxybenzaldehyde (**6a**) using 2-hydroxy-5-bromobenzaldehyde (**5h**) (0.500 g, 2.49 mmol). This gave 2-allyloxy-5-bromobenzaldehyde (**6h**) (0.591 g, 99%) as a white solid. Mp 35−37 °C; Spectroscopic data were in accordance with literature values.[35] ^{1}H NMR (400 MHz, $CDCl_3$) δ 4.65 (dt, J = 5.2, 1.5 Hz, 2H), 5.35 (dq, J = 10.6, 1.5 Hz, 1H), 5.44 (dq, J = 17.3, 1.5 Hz, 1H), 6.05 (ddt, J = 17.3, 10.6, 5.2 Hz, 1H), 6.88 (d, J = 8.9 Hz, 1H), 7.60 (dd, J = 8.9, 2.6 Hz, 1H), 7.93 (d, J = 2.6 Hz, 1H), 10.44 (s, 1H); ^{13}C NMR (101 MHz, $CDCl_3$) δ 69.7 (CH_2), 113.8 (C), 115.1 (CH), 118.7 (CH_2), 126.6 (C), 131.2 (CH), 132.1 (CH), 138.3 (CH), 160.0 (C), 188.4 (CH); MS (ESI) m/z 263 (MNa^+, 75), 236 (22), 219 (70), 201 (14), 184 (27).

2-Allyloxy-4-chlorobenzaldehyde (6i). The reaction was carried out as described for the synthesis of 2-allyloxybenzaldehyde (**6a**) using 4-chloro-2-hydroxybenzaldehyde (**5i**) (0.936 g, 6.00 mmol). This gave 2-allyloxy-4-chlorobenzaldehyde (**6i**) (1.17 g, 100%) as a white solid. Mp 48−49 °C; IR (neat) 2867, 1685, 1589, 1413, 1240, 1222, 996, 904 cm^{-1}; ^{1}H NMR (400 MHz, $CDCl_3$) δ 4.67 (dt, J = 5.2, 1.5 Hz, 2H), 5.39 (dq, J = 10.5, 1.5 Hz, 1H), 5.48 (dq, J = 17.2, 1.5 Hz, 1H), 6.08 (ddt, J = 17.2, 10.5, 5.2 Hz, 1H), 6.95 (d, J = 1.7 Hz, 1H), 7.03 (ddd, J = 8.3, 1.7, 0.7 Hz, 1H), 7.79 (d, J = 8.3 Hz, 1H), 10.46 (d, J = 0.7 Hz, 1H); ^{13}C NMR (101 MHz, $CDCl_3$) δ 69.5 (CH_2), 113.5 (CH), 118.6 (CH_2), 121.4 (CH), 123.6 (C), 129.5 (CH), 131.7 (CH), 141.8 (C), 161.2 (C), 188.4 (CH); MS (EI) m/z 196 (M^+, 44), 181 (9), 167 (38), 155 (100), 126 (25), 99 (27), 75 (14), 63 (26); HRMS (EI) calcd for $C_{10}H_9{}^{35}ClO_2$ (M^+), 196.0291, found 196.0288.

2-Allyloxy-4,5-difluorobenzaldehyde (6j). The reaction was carried out as described for the synthesis of 2-allyloxybenzaldehyde (**6a**) using 4,5-difluoro-2-hydroxybenzaldehyde (**5j**) (0.079 g, 0.500 mmol). This gave 2-allyloxy-4,5-difluorobenzaldehyde (**6j**) (0.099 g, 100%) as a white solid. Mp 35−36 °C; IR (neat) 2872, 1686, 1604, 1511, 1434, 1323, 1203, 990, 893, 758 cm^{-1}; ^{1}H NMR (500 MHz, $CDCl_3$) δ 4.63 (dt, J = 5.2, 1.6 Hz, 2H), 5.38 (dq, J = 10.6, 1.6 Hz, 1H), 5.46 (dq, J = 17.3, 1.6 Hz, 1H), 6.05 (ddt, J = 17.3, 10.6, 5.2 Hz, 1H), 6.81 (dd, $^3J_{HF}$ = 11.5, $^4J_{HF}$ = 5.2 Hz, 1H), 7.66 (dd, $^3J_{HF}$ = 11.5, $^4J_{HF}$ = 9.4 Hz, 1H), 10.39 (d, $^5J_{HF}$ = 3.1 Hz, 1H); ^{13}C NMR (126 MHz, $CDCl_3$) δ 70.2 (CH_2), 103.0 (d, $^2J_{CF}$ = 21.1 Hz, CH), 116.4 (dd, $^2J_{CF}$ = 18.5, $^3J_{CF}$ = 2.9 Hz, CH), 118.9 (CH_2), 121.5 (t, $^3J_{CF}$ = 3.2 Hz, C), 131.6 (CH), 145.2 (dd, $^1J_{CF}$ = 244.6, $^2J_{CF}$ = 13.0 Hz, C), 154.9 (dd, $^1J_{CF}$ = 258.5, $^2J_{CF}$ = 14.5 Hz, C), 157.8 (dd, $^3J_{CF}$ = 8.2, $^4J_{CF}$ = 1.8 Hz, C), 187.2 (CH); MS (EI) m/z 198 (M^+, 10), 156 (11), 119 (4), 101 (6), 84 (100); HRMS (EI) calcd for $C_{10}H_8F_2O_2$ (M^+), 198.0492, found 198.0489.

2-Allyloxy-3-methoxy-5-nitrobenzaldehyde (6k). The reaction was carried out as described for the synthesis of 2-allyloxybenzaldehyde (**6a**) using 2-hydroxy-3-methoxy-5-nitrobenzaldehyde (**5k**) (0.197 g, 1.00 mmol). This gave 2-allyloxy-3-methoxy-5-nitrobenzaldehyde (**6k**) (0.209 g, 88%) as a white solid. Mp 82−84 °C; IR (neat) 3101, 2898, 1695, 1684, 1583, 1527, 1480, 1336, 1278, 1230, 1091, 954, 938, 743 cm^{-1}; ^{1}H NMR (500 MHz, $CDCl_3$) δ 4.02 (s, 3H), 4.84 (dt, J = 6.2, 1.3 Hz, 2H), 5.32 (dq, J = 10.3, 1.3 Hz, 1H), 5.38 (dq, J = 17.1, 1.3 Hz, 1H), 6.05 (ddt, J = 17.1, 10.3, 6.2 Hz, 1H), 7.96 (d, J = 2.7 Hz, 1H), 8.33 (d, J = 2.7 Hz, 1H), 10.43 (s, 1H); ^{13}C NMR (126 MHz, $CDCl_3$) δ 56.6 (CH_3), 75.4 (CH_2), 111.5 (CH), 115.0 (CH), 120.0 (CH_2), 129.3 (C), 132.3 (CH), 143.6 (C), 153.3 (C), 155.8 (C), 188.2 (CH); MS (EI) m/z 237 (M^+, 24), 220 (4), 196 (27), 180 (27), 150 (15), 122 (11), 84 (100); HRMS (EI) calcd for $C_{11}H_{11}NO_5$ (M^+), 237.0637, found 237.0630.

2-Allyloxy-1-naphthaldehyde (6l).[32] The reaction was carried out as described for the synthesis of 2-allyloxybenzaldehyde (**6a**) using 2-hydroxy-1-naphthaldehyde (**5l**) (0.172 g, 1.00 mmol). This gave 2-allyloxy-1-naphthaldehyde (**6l**) (0.208 g, 98%) as a white solid. Mp 72−74 °C (lit.[32] 79−80 °C); ^{1}H NMR (400 MHz, $CDCl_3$) δ 4.83 (dt, J = 5.2, 1.6 Hz, 2H), 5.39 (dq, J = 10.6, 1.6 Hz, 1H), 5.50 (dq, J = 17.3, 1.6 Hz, 1H), 6.13 (ddt, J = 17.3, 10.6, 5.2 Hz, 1H), 7.30 (d, J = 9.3 Hz, 1H), 7.45 (ddd, J = 8.5, 8.4, 1.3 Hz, 1H), 7.65 (ddd, J = 8.5, 8.4, 1.3 Hz, 1H), 7.80 (br d, J = 8.4 Hz, 1H), 8.06 (d, J = 9.3 Hz, 1H), 9.31 (br d, J = 8.4 Hz, 1H), 10.98 (s, 1H); ^{13}C NMR (101 MHz, $CDCl_3$) δ 69.9 (CH_2), 113.7 (CH), 116.8 (C), 118.1 (CH_2), 124.7 (CH), 124.9 (CH), 128.3 (CH), 128.5 (C), 129.7 (CH), 131.5 (C), 132.4 (CH), 137.4 (CH), 163.0 (C), 191.8 (CH); MS (ESI) m/z 235 (MNa^+, 100), 218 (6), 194 (16).

Ethyl (2*E*)-3-(2′-Allyloxyphenyl)prop-2-enoate (7a).[36] Lithium bromide (0.47 g, 5.4 mmol) was added to a solution of triethyl phosphonoacetate (0.91 mL, 4.6 mmol) and 1,8-diazabicyclo[5.4.0]-undec-7-ene (0.68 mL, 4.6 mmol) in acetonitrile (20 mL) and stirred at room temperature for 0.5 h. 2-Allyloxybenzaldehyde (**6a**) (0.22 g, 1.4 mmol) was added, and the solution was stirred at room temperature for 18 h. The reaction was quenched by the addition of a saturated solution of ammonium chloride (30 mL), concentrated to half volume *in vacuo*, and extracted with diethyl ether (3 × 30 mL). The combined organic layers were washed with water (100 mL), brine (100 mL), dried ($MgSO_4$), filtered, and concentrated *in vacuo*. Purification by column chromatography (elution with 20% diethyl ether in petroleum ether) gave ethyl (2*E*)-3-(2′-allyloxyphenyl)prop-2-enoate (**7a**) (0.30 g, 95%) as a yellow oil. Spectroscopic data were in accordance with literature values.[36] ^{1}H NMR (400 MHz, $CDCl_3$) δ 1.34 (t, J = 7.1 Hz, 3H), 4.26 (q, J = 7.1 Hz, 2H), 4.62 (dt, J = 5.1, 1.5 Hz, 2H), 5.31 (dq, J = 10.6, 1.5 Hz, 1H), 5.43 (dq, J = 17.3, 1.5 Hz, 1H), 6.08 (ddt, J = 17.3, 10.6, 5.1 Hz, 1H), 6.53 (d, J = 16.2 Hz, 1H), 6.90 (d, J = 8.3 Hz, 1H), 6.96 (td, J = 7.7, 0.5 Hz, 1H), 7.29−7.35 (m, 1H), 7.52 (dd, J = 7.7, 1.7 Hz, 1H), 8.05 (d, J = 16.2 Hz, 1H); ^{13}C NMR (101 MHz, $CDCl_3$) δ 14.4 (CH_3), 60.3 (CH_2), 69.2 (CH_2), 112.5 (CH), 117.7 (CH_2), 118.8 (CH), 120.9 (CH), 123.8 (C), 128.8 (CH), 131.3 (CH), 132.9 (CH), 139.9 (CH), 157.3 (C), 167.5 (C); MS (EI) m/z 232 (M^+, 38), 187 (42), 158 (78), 144 (59), 129 (61), 118 (97), 84 (100), 77 (19), 49 (99).

Ethyl (2*E*)-3-(2′-Allyloxy-6′-methoxyphenyl)prop-2-enoate (7b). The reaction was carried out as described for the synthesis of ethyl (2*E*)-3-(2′-allyloxyphenyl)prop-2-enoate (**7a**) using 2-allyloxy-6-methoxybenzaldehyde (**6b**) (0.531 g, 2.76 mmol). This gave ethyl (2*E*)-3-(2′-allyloxy-6′-methoxyphenyl)prop-2-enoate (**7b**) (0.594 g, 85%) as a yellow oil. IR (neat) 2979, 1701, 1622, 1593, 1473, 1308, 1254, 1160, 1093 cm^{-1}; ^{1}H NMR (400 MHz, $CDCl_3$) δ 1.33 (t, J = 7.1 Hz, 3H), 3.88 (s, 3H), 4.26 (q, J = 7.1 Hz, 2H), 4.62 (dt, J = 5.1, 1.5 Hz, 2H), 5.30 (dq, J = 10.5, 1.5 Hz, 1H), 5.43 (dq, J = 17.3, 1.5 Hz, 1H), 6.08 (ddt, J = 17.3, 10.5, 5.1 Hz, 1H), 6.54 (d, J = 8.4 Hz, 1H), 6.56 (d, J = 8.4 Hz, 1H), 6.89 (d, J = 16.3 Hz, 1H), 7.23 (t, J = 8.4 Hz, 1H), 8.17 (d, J = 16.3 Hz, 1H); ^{13}C NMR (126 MHz, $CDCl_3$) δ 14.4 (CH_3), 55.7 (CH_3), 60.1 (CH_2), 69.4 (CH_2), 103.8 (CH), 105.0 (CH), 112.5 (C), 117.6 (CH_2), 120.8 (CH), 131.1 (CH), 132.9 (CH), 135.4 (CH), 158.9 (C), 160.1 (C), 168.6 (C); MS (ESI) m/z 285 (MNa^+, 100); HRMS (ESI) calcd for $C_{15}H_{18}NaO_4$ (MNa^+), 285.1097, found 285.1088.

Ethyl (2*E*)-3-(2′-Allyloxy-5′-methoxyphenyl)prop-2-enoate (7c). The reaction was carried out as described for the synthesis of ethyl (2*E*)-3-(2′-allyloxyphenyl)prop-2-enoate (**7a**) using 2-allyloxy-5-methoxybenzaldehyde (**6c**) (0.580 g, 3.02 mmol). This gave ethyl (2*E*)-3-(2′-allyloxy-5′-methoxyphenyl)prop-2-enoate (**7c**) (0.792 g, 100%) as a yellow oil. IR (neat) 2954, 1706, 1631, 1494, 1214, 1165, 1042, 862 cm^{-1}; ^{1}H NMR (400 MHz, $CDCl_3$) δ 1.34 (t, J = 7.1 Hz, 3H), 3.79 (s, 3H), 4.26 (q, J = 7.1 Hz, 2H), 4.56 (dt, J = 5.2, 1.5 Hz, 2H), 5.29 (dq, J = 10.6, 1.5 Hz, 1H), 5.41 (dq, J = 17.3, 1.5 Hz, 1H), 6.06 (ddt, J = 17.3, 10.6, 5.2 Hz, 1H), 6.49 (d, J = 16.2 Hz, 1H), 6.84 (d, J = 8.8 Hz, 1H), 6.88 (dd, J = 8.8, 2.9 Hz, 1H), 7.05 (d, J = 2.9 Hz, 1H), 8.02 (d, J = 16.2 Hz, 1H); ^{13}C NMR (126 MHz, $CDCl_3$) δ 14.5

DOI: 10.1021/acs.joc.5b00583
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(CH_3), 55.9 (CH_3), 60.5 (CH_2), 70.2 (CH_2), 113.0 (CH), 114.4 (CH), 117.2 (CH), 117.8 (CH_2), 119.1 (CH), 124.7 (C), 133.3 (CH), 139.8 (CH), 151.9 (C), 153.8 (C), 167.5 (C); MS (ESI) m/z 285 (MNa^+, 100); HRMS (ESI) calcd for $C_{15}H_{18}NaO_4$ (MNa^+), 285.1097, found 285.1090.

Ethyl (2*E*)-3-(2′-Allyloxy-4′-methoxyphenyl)prop-2-enoate (7d). The reaction was carried out as described for the synthesis of ethyl (2*E*)-3-(2′-allyloxyphenyl)prop-2-enoate (**7a**) using 2-allyloxy-4-methoxybenzaldehyde (**6d**) (0.580 g, 3.02 mmol). This gave ethyl (2*E*)-3-(2′-allyloxy-4′-methoxyphenyl)prop-2-enoate (**7d**) (0.79 g, 100%) as a yellow oil. IR (neat) 2980, 1701, 1601, 1505, 1300, 1252, 1155, 986 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$) δ 1.33 (t, J = 7.1 Hz, 3H), 3.82 (s, 3H), 4.24 (q, J = 7.1 Hz, 2H), 4.60 (dt, J = 5.2, 1.5 Hz, 2H), 5.32 (dq, J = 10.5, 1.5 Hz, 1H), 5.43 (dq, J = 17.3, 1.5 Hz, 1H), 6.08 (ddt, J = 17.3, 10.5, 5.2 Hz, 1H), 6.43 (d, J = 16.1 Hz, 1H), 6.44 (d, J = 2.4 Hz, 1H), 6.50 (dd, J = 8.6, 2.4 Hz, 1H), 7.46 (d, J = 8.6 Hz, 1H), 7.96 (d, J = 16.1 Hz, 1H); ^{13}C NMR (101 MHz, $CDCl_3$) δ 14.5 (CH_3), 55.6 (CH_3), 60.3 (CH_2), 69.3 (CH_2), 99.7 (CH), 105.6 (CH), 116.3 (C), 117.0 (CH_2), 118.1 (CH), 130.3 (CH), 132.9 (CH), 140.0 (CH), 158.8 (C), 162.6 (C), 168.0 (C); MS (ESI) m/z 285 (MNa^+, 100); HRMS (ESI) calcd for $C_{15}H_{18}NaO_4$ (MNa^+), 285.1097, found 285.1090.

Ethyl (2*E*)-3-(2′-Allyloxy-5′-methylphenyl)prop-2-enoate (7e). The reaction was carried out as described for the synthesis of ethyl (2*E*)-3-(2′-allyloxyphenyl)prop-2-enoate (**7a**) using 2-allyloxy-5-methylbenzaldehyde (**6e**) (0.167 g, 0.950 mmol). This gave ethyl (2*E*)-3-(2′-allyloxy-5′-methylphenyl)prop-2-enoate (**7e**) (0.206 g, 88%) as a yellow oil. IR (neat) 3021, 1701, 1631, 1494, 1217, 1178, 750 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$) δ 1.33 (t, J = 7.1 Hz, 3H), 2.29 (s, 3H), 4.25 (q, J = 7.1 Hz, 2H), 4.59 (dt, J = 5.2, 1.6 Hz, 2H), 5.29 (dq, J = 10.6, 1.6 Hz, 1H), 5.41 (dq, J = 17.3, 1.6 Hz, 1H), 6.07 (ddt, J = 17.3, 10.6, 5.2 Hz, 1H), 6.51 (d, J = 16.2 Hz, 1H), 6.80 (d, J = 8.4 Hz, 1H), 7.11 (dd, J = 8.4, 2.0 Hz, 1H), 7.32 (d, J = 2.0 Hz, 1H), 8.01 (d, J = 16.2 Hz, 1H); ^{13}C NMR (101 MHz, $CDCl_3$) δ 14.4 (CH_3), 20.4 (CH_3), 60.3 (CH_2), 69.4 (CH_2), 112.6 (CH), 117.6 (CH_2), 118.6 (CH), 123.5 (C), 129.2 (CH), 130.1 (C), 131.8 (CH), 133.1 (CH), 140.0 (CH), 155.3 (C), 167.5 (C); MS (ESI) m/z 269 (MNa^+, 100); HRMS (ESI) calcd for $C_{15}H_{18}NaO_3$ (MNa^+), 269.1148, found 269.1139.

Ethyl (2*E*)-3-(2′-Allyloxy-5′-nitrophenyl)prop-2-enoate (7f). The reaction was carried out as described for the synthesis of ethyl (2*E*)-3-(2′-allyloxyphenyl)prop-2-enoate (**7a**) using 2-allyloxy-5-nitrobenzaldehyde (**6f**) (0.049 g, 0.24 mmol). This gave ethyl (2*E*)-3-(2′-allyloxy-5′-nitrophenyl)prop-2-enoate (**7f**) (0.060 g, 91%) as a white solid. Mp 64−65 °C; IR (neat) 2986, 1690, 1631, 1580, 1512, 1341, 1273, 1150, 1032, 872 cm^{-1}; ^1H NMR (500 MHz, $CDCl_3$) δ 1.35 (t, J = 7.1 Hz, 3H), 4.29 (q, J = 7.1 Hz, 2H), 4.74 (dt, J = 5.2, 1.5 Hz, 2H), 5.39 (dq, J = 10.6, 1.5 Hz, 1H), 5.45 (dq, J = 17.3, 1.5 Hz, 1H), 6.07 (ddt, J = 17.3, 10.6, 5.2 Hz, 1H), 6.61 (d, J = 16.2 Hz, 1H), 6.98 (d, J = 9.2 Hz, 1H), 7.98 (d, J = 16.2 Hz, 1H), 8.22 (dd, J = 9.2, 2.8 Hz, 1H), 8.43 (d, J = 2.8 Hz, 1H); ^{13}C NMR (126 MHz, $CDCl_3$) δ 14.3 (CH_3), 60.7 (CH_2), 70.0 (CH_2), 112.2 (CH), 118.9 (CH_2), 121.5 (CH), 124.0 (CH), 124.3 (C), 126.6 (CH), 131.5 (CH), 137.3 (CH), 141.4 (C), 161.4 (C), 166.5 (C); MS (ESI) m/z 300 (MNa^+, 100); HRMS (ESI) calcd for $C_{14}H_{15}NNaO_5$ (MNa^+), 300.0842, found 300.0829.

Ethyl (2*E*)-3-(2′-Allyloxy-5′-chlorophenyl)prop-2-enoate (7g). The reaction was carried out as described for the synthesis of ethyl (2*E*)-3-(2′-allyloxyphenyl)prop-2-enoate (**7a**) using 2-allyloxy-5-chlorobenzaldehyde (**6g**) (0.595 g, 3.02 mmol). This gave ethyl (2*E*)-3-(2′-allyloxy-5′-chlorophenyl)prop-2-enoate (**7g**) (0.743 g, 92%) as a yellow oil. IR (neat) 2982, 1705, 1632, 1481, 1314, 1248, 1165, 1034, 984 cm^{-1}; ^1H NMR (500 MHz, $CDCl_3$) δ 1.33 (t, J = 7.1 Hz, 3H), 4.26 (q, J = 7.1 Hz, 2H), 4.60 (dt, J = 5.2, 1.4 Hz, 2H), 5.32 (dq, J = 10.5, 1.4 Hz, 1H), 5.41 (dq, J = 17.3, 1.4 Hz, 1H), 6.05 (ddt, J = 17.3, 10.5, 5.2 Hz, 1H), 6.49 (d, J = 16.2 Hz, 1H), 6.83 (d, J = 8.9 Hz, 1H), 7.25 (dd, J = 8.9, 2.5 Hz, 1H), 7.48 (d, J = 2.5 Hz, 1H), 7.95 (d, J = 16.2 Hz, 1H); ^{13}C NMR (126 MHz, $CDCl_3$) δ 14.5 (CH_3), 60.6 (CH_2), 69.7 (CH_2), 114.0 (CH), 118.2 (CH_2), 120.1 (CH), 125.4 (C), 126.1 (C), 128.3 (CH), 130.8 (CH), 132.6 (CH), 138.6 (CH), 155.8 (C), 167.2 (C); MS (ESI) m/z 289 (MNa^+, 100); HRMS (ESI) calcd for $C_{14}H_{15}{}^{35}ClNaO_3$ (MNa^+), 289.0602, found 289.0610.

Ethyl (2*E*)-3-(2′-Allyloxy-5′-bromophenyl)prop-2-enoate (7h). The reaction was carried out as described for the synthesis of ethyl (2*E*)-3-(2′-allyloxyphenyl)prop-2-enoate (**7a**) using 2-allyloxy-5-bromobenzaldehyde (**6h**) (0.545 g, 2.26 mmol). This gave ethyl (2*E*)-3-(2′-allyloxy-5′-bromophenyl)prop-2-enoate (**7h**) (0.685 g, 97%) as a white solid. Mp <30 °C; IR (neat) 2986, 1688, 1628, 1489, 1300, 1275, 1175, 986 cm^{-1}; ^1H NMR (500 MHz, $CDCl_3$) δ 1.33 (t, J = 7.1 Hz, 3H), 4.26 (q, J = 7.1 Hz, 2H), 4.60 (dt, J = 5.2, 1.4 Hz, 2H), 5.32 (dq, J = 10.6, 1.4 Hz, 1H), 5.41 (dq, J = 17.3, 1.4 Hz, 1H), 6.05 (ddt, J = 17.3, 10.6, 5.2 Hz, 1H), 6.49 (d, J = 16.2 Hz, 1H), 6.78 (d, J = 8.8 Hz, 1H), 7.39 (dd, J = 8.8, 2.5 Hz, 1H), 7.62 (d, J = 2.5 Hz, 1H), 7.94 (d, J = 16.2 Hz, 1H); ^{13}C NMR (126 MHz, $CDCl_3$) δ 14.5 (CH_3), 60.6 (CH_2), 69.6 (CH_2), 113.3 (C), 114.4 (CH), 118.3 (CH_2), 120.2 (CH), 125.9 (C), 131.2 (CH), 132.6 (CH), 133.8 (CH), 138.5 (CH), 156.3 (C), 167.2 (C); MS (ESI) m/z 333 (MNa^+, 100); HRMS (ESI) calcd for $C_{14}H_{15}{}^{79}BrNaO_3$ (MNa^+), 333.0097, found 333.0090.

Ethyl (2*E*)-3-(2′-Allyloxy-4′-chlorophenyl)prop-2-eneoate (7i). The reaction was carried out as described for the synthesis of ethyl (2*E*)-3-(2′-allyloxyphenyl)prop-2-enoate (**7a**) using 2-allyloxy-4-chlorobenzaldehyde (**6i**) (0.150 g, 0.760 mmol). This gave ethyl (2*E*)-3-(2′-allyloxy-4′-chlorophenyl)prop-2-enoate (**7i**) (0.192 g, 94%) as an oil. IR (neat) 2989, 1707, 1632, 1592, 1486, 1312, 1178, 908, 732 cm^{-1}; ^1H NMR (500 MHz, $CDCl_3$) δ 1.35 (t, J = 7.1 Hz, 3H), 4.27 (q, J = 7.1 Hz, 2H), 4.63 (dt, J = 5.2, 1.3 Hz, 2H), 5.36 (dq, J = 17.2, 1.3 Hz, 1H), 5.46 (dq, J = 10.6, 1.3 Hz, 1H), 6.08 (ddt, J = 17.2, 10.6, 5.2 Hz, 1H), 6.51 (d, J = 16.2 Hz, 1H), 6.91 (d, J = 1.9 Hz, 1H), 6.97 (dd, J = 8.3, 1.9 Hz, 1H), 7.45 (d, J = 8.3 Hz, 1H), 7.96 (d, J = 16.2 Hz, 1H); ^{13}C NMR (126 MHz, $CDCl_3$) δ 14.3 (CH_3), 60.4 (CH_2), 69.5 (CH_2), 113.1 (CH), 118.2 (CH_2), 119.2 (CH), 121.1 (CH), 122.4 (C), 129.5 (CH), 132.2 (CH), 136.7 (C), 138.7 (CH), 157.6 (C), 167.2 (C); MS (ESI) m/z 289 (MNa^+, 100); HRMS (ESI) calcd for $C_{14}H_{15}{}^{35}ClNaO_3$ (MNa^+), 289.0602, found 289.0595.

Ethyl (2*E*)-3-(2′-Allyloxy-4′,5′-difluorophenyl)prop-2-enoate (7j). The reaction was carried out as described for the synthesis of ethyl (2*E*)-3-(2′-allyloxyphenyl)prop-2-enoate (**7a**) using 2-allyloxy-4,5-difluorobenzaldehyde (**6j**) (0.093 g, 0.470 mmol). This gave ethyl (2*E*)-3-(2′-allyloxy-4′,5′-difluorophenyl)prop-2-enoate (**7j**) (0.117 g, 93%) as a white solid. Mp 52−53 °C; IR (neat) 2985, 1690, 1599, 1511, 1273, 1224, 1174, 987, 857 cm^{-1}; ^1H NMR (500 MHz, $CDCl_3$) δ 1.33 (t, J = 7.1 Hz, 3H), 4.26 (q, J = 7.1 Hz, 2H), 4.57 (dt, J = 5.2, 1.6 Hz, 2H), 5.34 (dq, J = 10.6, 1.6 Hz, 1H), 5.43 (dq, J = 17.3, 1.6 Hz, 1H), 6.04 (ddt, J = 17.3, 10.6, 5.2 Hz, 1H), 6.41 (d, J = 16.2 Hz, 1H), 6.72 (dd, $^3J_{HF}$ = 11.5, $^4J_{HF}$ = 5.2 Hz, 1H), 7.32 (dd, $^3J_{HF}$ = 11.5, $^4J_{HF}$ = 9.0 Hz, 1H), 7.91 (dd, J = 16.2, $^5J_{HF}$ = 1.0 Hz, 1H); ^{13}C NMR (101 MHz, $CDCl_3$) δ 14.3 (CH_3), 60.5 (CH_2), 70.2 (CH_2), 102.6 (d, $^2J_{CF}$ = 20.9 Hz, CH), 116.2 (dd, $^2J_{CF}$ = 18.6, $^3J_{CF}$ = 1.8 Hz, CH), 118.5 (CH_2), 119.5 (CH), 120.1 (dd, $^3J_{CF}$ = 5.8, $^4J_{CF}$ = 4.3 Hz, C), 132.1 (CH), 137.7 (CH), 144.8 (dd, $^1J_{CF}$ = 241.6, $^2J_{CF}$ = 13.1 Hz, C), 151.5 (dd, $^1J_{CF}$ = 253.1, $^2J_{CF}$ = 14.0 Hz, C), 153.7 (dd, $^3J_{CF}$ = 7.3, $^4J_{CF}$ = 1.6 Hz, C), 167.0 (C); MS (ESI) m/z 291 (MNa^+, 100); HRMS (ESI) calcd for $C_{14}H_{14}F_2NaO_3$ (MNa^+), 291.0803, found 291.0797.

Ethyl (2*E*)-3-(2′-Allyloxy-3′-methoxy-5′-nitrophenyl)prop-2-enoate (7k). The reaction was carried out as described for the synthesis of ethyl (2*E*)-3-(2′-allyloxyphenyl)prop-2-enoate (**7a**) using 2-allyloxy-3-methoxy-5-nitrobenzaldehyde (**6k**) (0.617 g, 2.60 mmol). This gave ethyl (2*E*)-3-(2′-allyloxy-3′-methoxy-5′-nitrophenyl)prop-2-enoate (**7k**) (0.798 g, 100%) as a white solid. Mp 82−83 °C; IR (neat) 3022, 1711, 1641, 1582, 1527, 1466, 1340, 1278, 1179, 979 cm^{-1}; ^1H NMR (500 MHz, $CDCl_3$) δ 1.35 (t, J = 7.1 Hz, 3H), 3.97 (s, 3H), 4.28 (q, J = 7.1 Hz, 2H), 4.69 (dt, J = 6.1, 1.3 Hz, 2H), 5.28 (dq, J = 10.3, 1.3 Hz, 1H), 5.37 (dq, J = 17.2, 1.3 Hz, 1H), 6.05 (ddt, J = 17.2, 10.3, 6.1 Hz, 1H), 6.56 (d, J = 16.2 Hz, 1H), 7.77 (d, J = 2.6 Hz, 1H), 7.99 (d, J = 16.2 Hz, 1H), 8.10 (d, J = 2.6 Hz, 1H); ^{13}C NMR (126 MHz, $CDCl_3$) δ 14.2 (CH_3), 56.4 (CH_3), 60.7 (CH_2), 74.8 (CH_2), 108.0 (CH), 114.9 (CH), 119.2 (CH_2), 121.9 (CH), 129.1 (C), 132.9 (CH), 137.5 (CH), 143.7 (C), 151.8 (C), 153.1 (C), 166.3 (C); MS (ESI) m/z 330 (MNa^+, 100); HRMS (ESI) calcd for $C_{15}H_{17}NNaO_6$ (MNa^+), 330.0948, found 330.0934.

DOI: 10.1021/acs.joc.5b00583
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Ethyl (2*E*)-3-(2′-Allyloxynaphthalen-1′-yl)prop-2-enoate (7l). The reaction was carried out as described for the synthesis of ethyl (2*E*)-3-(2′-allyloxyphenyl)prop-2-enoate (**7a**) using 2-allyloxy-1-naphthaldehyde (**6l**) (0.620 g, 2.94 mmol). This gave ethyl (2*E*)-3-(2′-allyloxynaphthalen-1′-yl)prop-2-enoate (**7l**) (0.760 g, 92%) as a white solid. Mp 46−48 °C; IR (neat) 2981, 1701, 1617, 1264, 1159, 907, 727 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$) δ 1.37 (t, J = 7.1 Hz, 3H), 4.32 (q, J = 7.1 Hz, 2H), 4.75 (dt, J = 5.2, 1.6 Hz, 2H), 5.31 (dq, J = 10.6, 1.6 Hz, 1H), 5.44 (dq, J = 17.3, 1.6 Hz, 1H), 6.10 (ddt, J = 17.3, 10.6, 5.2 Hz, 1H), 6.77 (d, J = 16.2 Hz, 1H), 7.25 (d, J = 9.3 Hz, 1H), 7.38 (ddd, J = 8.5, 8.4, 1.0 Hz, 1H), 7.52 (ddd, J = 8.5, 8.4, 1.0 Hz, 1H), 7.78 (dd, J = 8.4, 1.0 Hz, 1H), 7.81 (d, J = 9.3 Hz, 1H), 8.19 (dd, J = 8.4, 1.0 Hz, 1H), 8.36 (d, J = 16.2 Hz, 1H); ^{13}C NMR (101 MHz, $CDCl_3$) δ 14.4 (CH_3), 60.4 (CH_2), 70.0 (CH_2), 114.3 (CH), 117.4 (C), 117.8 (CH_2), 123.5 (CH), 123.7 (CH), 124.0 (CH), 127.3 (CH), 128.5 (CH), 129.1 (C), 131.3 (CH), 132.8 (C), 133.0 (CH), 137.7 (CH), 155.6 (C), 167.8 (C); MS (ESI) m/z 305 (MNa^+, 100); HRMS (ESI) calcd for $C_{18}H_{18}NaO_3$ (MNa^+), 305.1148, found 305.1139.

(2*E*)-3-(2′-Allyloxyphenyl)prop-2-en-1-ol (8a).[36] Diisobutylaluminum hydride (3.21 mL, 1 M solution in hexanes) was added dropwise with stirring to a solution of ethyl (2*E*)-3-(2′-vinylphenyl)-prop-2-enoate (**7a**) (0.298 g, 1.28 mmol) in diethyl ether (30 mL) at −78 °C. The solution was stirred at −78 °C for 3 h, then allowed to return to room temperature over 15 h. The reaction was quenched with 10% aqueous potassium sodium tartrate solution (30 mL), extracted with diethyl ether (2 × 20 mL), washed with water (100 mL), brine (100 mL), dried ($MgSO_4$), filtered, and concentrated *in vacuo*. Purification by column chromatography (elution with 30% diethyl ether in petroleum ether) gave (2*E*)-3-(2′-allyloxyphenyl)prop-2-en-1-ol (**8a**) (0.211 g, 87%) as a white solid. Mp 44−46 °C; spectroscopic data were in accordance with literature values.[36] ^1H NMR (400 MHz, $CDCl_3$) δ 1.41 (t, J = 5.9 Hz, 1H), 4.33 (td, J = 5.9, 0.8 Hz, 2H), 4.58 (dt, J = 5.2, 1.5 Hz, 2H), 5.29 (dq, J = 10.5, 1.5 Hz, 1H), 5.42 (dq, J = 17.3, 1.5 Hz, 1H), 6.08 (ddt, J = 17.3, 10.5, 5.2 Hz, 1H), 6.40 (dt, J = 16.0, 5.9 Hz, 1H), 6.87 (dd, J = 8.2, 0.8 Hz, 1H), 6.91−7.02 (m, 2H), 7.21 (ddd, J = 8.2, 7.5, 1.7 Hz, 1H), 7.46 (dd, J = 7.5, 1.7 Hz, 1H); ^{13}C NMR (101 MHz, $CDCl_3$) δ 64.5 (CH_2), 69.4 (CH_2), 112.5 (CH), 117.6 (CH_2), 121.1 (CH), 126.2 (C), 126.4 (CH), 127.2 (CH), 128.8 (CH), 129.3 (CH), 133.5 (CH), 156.0 (C); MS (EI) m/z 190 (M^+, 57), 149 (59), 131 (92), 121 (60), 119 (46), 91 (100), 77 (40).

(2*E*)-3-(2′-Allyloxy-6′-methoxyphenyl)prop-2-en-1-ol (8b). The reaction was carried out as described for the synthesis of (2*E*)-3-(2′-allyloxyphenyl)prop-2-en-1-ol (**8a**) using ethyl (2*E*)-3-(2′-allyloxy-6′-methoxyphenyl)prop-2-enoate (**7b**) (0.569 g, 2.17 mmol). This gave (2*E*)-3-(2′-allyloxy-6′-methoxyphenyl)prop-2-en-1-ol (**8b**) (0.427 g, 90%) as a colorless oil. IR (neat) 3372, 2953, 1584, 1470, 1251, 1200, 1112, 1079 cm^{-1}; ^1H NMR (500 MHz, $CDCl_3$) δ 1.41 (t, J = 5.9 Hz, 1H), 3.85 (s, 3H), 4.33 (td, J = 5.9, 1.0 Hz, 2H), 4.58 (dt, J = 5.2, 1.5 Hz, 2H), 5.28 (dq, J = 10.5, 1.5 Hz, 1H), 5.42 (dq, J = 17.3, 1.5 Hz, 1H), 6.08 (ddt, J = 17.3, 10.5, 5.2 Hz, 1H), 6.55 (d, J = 8.3 Hz, 1H), 6.56 (d, J = 8.3 Hz, 1H), 6.82 (dt, J = 16.2, 5.9 Hz, 1H), 6.92 (br d, J = 16.2 Hz, 1H), 7.13 (t, J = 8.3 Hz, 1H); ^{13}C NMR (126 MHz, $CDCl_3$) δ 55.8 (CH_3), 65.7 (CH_2), 69.6 (CH_2), 104.1 (CH), 105.4 (CH), 114.4 (C), 117.6 (CH_2), 122.0 (CH), 128.3 (CH), 132.8 (CH), 133.5 (CH), 157.6 (C), 158.7 (C); MS (ESI) m/z 243 (MNa^+, 100); HRMS (ESI) calcd for $C_{13}H_{16}NaO_3$ (MNa^+), 243.0992, found 243.0987.

(2*E*)-3-(2′-Allyloxy-5′-methoxyphenyl)prop-2-en-1-ol (8c). The reaction was carried out as described for the synthesis of (2*E*)-3-(2′-allyloxyphenyl)prop-2-en-1-ol (**8a**) using ethyl (2*E*)-3-(2′-allyloxy-5′-methoxyphenyl)prop-2-enoate (**7c**) (0.126 g, 2.94 mmol). This gave (2*E*)-3-(2′-allyloxy-5′-methoxyphenyl)prop-2-en-1-ol (**8c**) (0.534 g, 83%) as a white solid. Mp 41−43 °C; IR (neat) 3387, 2915, 1585, 1493, 1424, 1213, 1123, 1011 cm^{-1}; ^1H NMR (500 MHz, $CDCl_3$) δ 1.48 (br s, 1H), 3.78 (s, 3H), 4.33 (br d, J = 5.7 Hz, 2H), 4.51 (dt, J = 5.2, 1.5 Hz, 2H), 5.27 (dq, J = 10.5, 1.5 Hz, 1H), 5.40 (dq, J = 17.3, 1.5 Hz, 1H), 6.06 (ddt, J = 17.3, 10.5, 5.2 Hz, 1H), 6.38 (dt, J = 16.0, 5.7 Hz, 1H), 6.75 (dd, J = 8.9, 3.0 Hz, 1H), 6.81 (d, J = 8.9 Hz, 1H), 6.94 (dt, J = 16.0, 1.3 Hz, 1H), 7.01 (d, J = 3.0 Hz, 1H); ^{13}C NMR (126 MHz, $CDCl_3$) δ 55.9 (CH_3), 64.3 (CH_2), 70.3 (CH_2), 112.2 (CH), 114.0 (CH), 114.3 (CH), 117.5 (CH_2), 126.2 (CH), 127.2 (C), 129.6 (CH), 133.7 (CH), 150.4 (C), 154.0 (C); MS (ESI) m/z 243 (MNa^+, 100); HRMS (ESI) calcd for $C_{13}H_{16}NaO_3$ (MNa^+), 243.0992, found 243.0990.

(2*E*)-3-(2′-Allyloxy-4′-methoxyphenyl)prop-2-en-1-ol (8d). The reaction was carried out as described for the synthesis of (2*E*)-3-(2′-allyloxyphenyl)prop-2-en-1-ol (**8a**) using ethyl (2*E*)-3-(2′-allyloxy-4′-methoxyphenyl)prop-2-enoate (**7d**) (0.676 g, 2.58 mmol). This gave (2*E*)-3-(2′-allyloxy-4′-methoxyphenyl)prop-2-en-1-ol (**8d**) (0.566 g, 100%) as a white solid. Mp <30 °C; IR (neat) 3379, 2914, 1609, 1576, 1500, 1420, 1261, 1197, 1003 cm^{-1}; ^1H NMR (500 MHz, $CDCl_3$) δ 1.89 (s, 1H), 3.78 (s, 3H), 4.28 (dd, J = 6.1, 1.2 Hz, 2H), 4.53 (d, J = 5.2 Hz, 2H), 5.28 (dd, J = 10.5, 1.5 Hz, 1H), 5.41 (dd, J = 17.3, 1.5 Hz, 1H), 6.06 (ddt, J = 17.3, 10.5, 5.2 Hz, 1H), 6.27 (dt, J = 16.0, 6.1 Hz, 1H), 6.42 (d, J = 2.4 Hz, 1H), 6.47 (dd, J = 8.5, 2.4 Hz, 1H), 6.86 (br d, J = 16.0 Hz, 1H), 7.35 (d, J = 8.5 Hz, 1H); ^{13}C (126 MHz, $CDCl_3$) δ 55.4 (CH_3), 64.5 (CH_2), 69.2 (CH_2), 99.7 (CH), 105.3 (CH), 117.7 (CH_2), 119.1 (C), 126.2 (CH), 127.1 (CH), 127.8 (CH), 133.2 (CH), 156.9 (C), 160.4 (C); MS (CI) m/z 221 (MH^+, 18), 203 (100), 177 (3), 163 (2), 81 (5), 69 (7); HRMS (CI) calcd for $C_{13}H_{17}O_3$ (MH^+), 221.1178, found 221.1177.

(2*E*)-3-(2′-Allyloxy-5′-methylphenyl)prop-2-en-1-ol (8e). The reaction was carried out as described for the synthesis of (2*E*)-3-(2′-allyloxyphenyl)prop-2-en-1-ol (**8a**) using ethyl (2*E*)-3-(2′-allyloxy-5′-methylphenyl)prop-2-enoate (**7e**) (0.198 g, 0.750 mmol). This gave (2*E*)-3-(2′-allyloxy-5′-methylphenyl)prop-2-en-1-ol (**8e**) (0.164 g, 100%) as a colorless oil. IR (neat) 3370, 2922, 1494, 1243, 1220, 997, 909 cm^{-1}; ^1H NMR (500 MHz, $CDCl_3$) δ 1.39 (br s, 1H), 2.29 (s, 3H), 4.32 (d, J = 5.2 Hz, 2H), 4.54 (dt, J = 5.2, 1.6 Hz, 2H), 5.27 (dq, J = 10.6, 1.6 Hz, 1H), 5.40 (dq, J = 17.3, 1.6 Hz, 1H), 6.07 (ddt, J = 17.3, 10.6, 5.2 Hz, 1H), 6.38 (dt, J = 16.2, 5.2 Hz, 1H), 6.76 (d, J = 8.3 Hz, 1H), 6.94 (d, J = 16.2 Hz, 1H), 7.00 (dd, J = 8.3, 2.1 Hz, 1H), 7.27 (d, J = 2.1 Hz, 1H); ^{13}C NMR (126 MHz, $CDCl_3$) δ 20.6 (CH_3), 64.2 (CH_2), 69.4 (CH_2), 112.5 (CH), 117.4 (CH_2), 125.8 (C), 126.1 (CH), 127.6 (CH), 129.1 (2 × CH), 130.1 (C), 133.6 (CH), 153.8 (C); MS (EI) m/z 204 (M^+, 49), 163 (31), 145 (61), 133 (64), 105 (97), 84 (100), 77 (24), 69 (13); HRMS (EI) calcd for $C_{13}H_{16}O_2$ (M^+), 204.1150, found 204.1153.

(2*E*)-3-(2′-Allyloxy-5′-nitrophenyl)prop-2-en-1-ol (8f). The reaction was carried out as described for the synthesis of (2*E*)-3-(2′-allyloxyphenyl)prop-2-en-1-ol (**8a**) using ethyl (2*E*)-3-(2′-allyloxy-5′-nitrophenyl)prop-2-enoate (**7f**) (0.629 g, 2.27 mmol). This gave (2*E*)-3-(2′-allyloxy-5′-nitrophenyl)prop-2-en-1-ol (**8f**) (0.469 g, 88%) as a yellow solid. Mp 62−66 °C; IR (neat) 2864, 1611, 1508, 1335, 1246, 1078, 990 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$) δ 1.89 (br s, 1H), 4.37 (dd, J = 5.4, 1.7 Hz, 2H), 4.67 (dt, J = 5.2, 1.5 Hz, 2H), 5.35 (dq, J = 10.6, 1.5 Hz, 1H), 5.43 (dq, J = 17.3, 1.5 Hz, 1H), 6.05 (ddt, J = 17.3, 10.6, 5.2 Hz, 1H), 6.49 (dt, J = 16.2, 5.4 Hz, 1H), 6.88 (d, J = 9.2 Hz, 1H), 6.92 (dt, J = 16.2, 1.7 Hz, 1H), 8.08 (dd, J = 9.2, 2.8 Hz, 1H), 8.30 (d, J = 2.8 Hz, 1H); ^{13}C NMR (101 MHz, $CDCl_3$) δ 63.7 (CH_2), 69.8 (CH_2), 111.6 (CH), 118.8 (CH_2), 122.6 (CH), 123.6 (CH), 124.5 (CH), 127.0 (C), 132.0 (CH), 132.3 (CH), 141.5 (C), 160.3 (C); MS (ESI) m/z 258 (MNa^+, 100); HRMS (ESI) calcd for $C_{12}H_{13}NNaO_4$ (MNa^+), 258.0737, found 258.0737.

(2*E*)-3-(2′-Allyloxy-5′-chlorophenyl)prop-2-en-1-ol (8g). The reaction was carried out as described for the synthesis of (2*E*)-3-(2′-allyloxyphenyl)prop-2-en-1-ol (**8a**) using ethyl (2*E*)-3-(2′-allyloxy-5′-chlorophenyl)prop-2-enoate (**7g**) (0.126 g, 0.472 mmol). This gave (2*E*)-3-(2′-allyloxy-5′-chlorophenyl)prop-2-en-1-ol (**8g**) (0.101 g, 95%) as a yellow oil. IR (neat) 3336, 2918, 1592, 1481, 1242, 1129, 1015, 970 cm^{-1}; ^1H NMR (500 MHz, $CDCl_3$) δ 2.24 (br s, 1H), 4.30 (dd, J = 5.7, 1.5 Hz, 2H), 4.51 (dt, J = 5.2, 1.4 Hz, 2H), 5.28 (dq, J = 10.6, 1.4 Hz, 1H), 5.39 (dq, J = 17.3, 1.4 Hz, 1H), 6.03 (ddt, J = 17.3, 10.6, 5.2 Hz, 1H), 6.34 (dt, J = 16.1, 5.7 Hz, 1H), 6.74 (d, J = 8.8 Hz, 1H), 6.87 (dt, J = 16.1, 1.5 Hz, 1H), 7.11 (dd, J = 8.8, 2.6 Hz, 1H), 7.37 (d, J = 2.6 Hz, 1H); ^{13}C NMR (126 MHz, $CDCl_3$) δ 63.8 (CH_2), 69.6 (CH_2), 113.7 (CH), 117.8 (CH_2), 124.7 (CH), 126.0 (C), 126.7 (CH), 127.8 (C), 128.1 (CH), 130.7 (CH), 133.0 (CH), 154.3 (C); MS (EI) m/z 224 (M^+, 100), 183 (58), 165 (89), 155 (78), 125 (86),

DOI: 10.1021/acs.joc.5b00583
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91 (36), 63 (12); HRMS (EI) calcd for $C_{12}H_{13}{}^{35}ClO_2$ (M^+), 224.0604, found 224.0606.

(2*E*)-3-(2′-Allyloxy-5′-bromophenyl)prop-2-en-1-ol (8h). The reaction was carried out as described for the synthesis of (2*E*)-3-(2′-allyloxyphenyl)prop-2-en-1-ol (**8a**) using ethyl (2*E*)-3-(2′-allyloxy-5′-bromophenyl)prop-2-enoate (**7h**) (0.075 g, 0.24 mmol). This gave (2*E*)-3-(2′-allyloxy-5′-bromophenyl)prop-2-en-1-ol (**8h**) (0.058 g, 90%) as a white solid. Mp <30 °C; IR (neat) 3297, 2857, 1588, 1482, 1249, 1127, 1016, 974 cm^{-1}; ^1H NMR (500 MHz, $CDCl_3$) δ 2.07 (s, 1H), 4.30 (dd, J = 5.7, 1.4 Hz, 2H), 4.51 (dt, J = 5.2, 1.3 Hz, 2H), 5.28 (dq, J = 10.5, 1.3 Hz, 1H), 5.38 (dq, J = 17.2, 1.3 Hz, 1H), 6.03 (ddt, J = 17.2, 10.5, 5.2 Hz, 1H), 6.34 (dt, J = 16.1, 5.7 Hz, 1H), 6.70 (d, J = 8.8 Hz, 1H), 6.86 (dt, J = 16.1, 1.4 Hz, 1H), 7.25 (dd, J = 8.8, 2.5 Hz, 1H), 7.52 (d, J = 2.5 Hz, 1H); ^{13}C NMR (126 MHz, $CDCl_3$) δ 63.9 (CH_2), 69.5 (CH_2), 113.4 (C), 114.1 (CH), 117.9 (CH_2), 124.6 (CH), 128.3 (C), 129.6 (CH), 130.7 (CH), 131.1 (CH), 133.0 (CH), 154.8 (C); MS (EI) m/z 268 (M^+, 65), 229 (40), 199 (50), 131 (20), 118 (100), 91 (27), 63 (11); HRMS (EI) calcd for $C_{12}H_{13}{}^{79}BrO_2$ (M^+), 268.0099, found 268.0101.

(2*E*)-3-(2′-Allyloxy-4′-chlorophenyl)prop-2-en-1-ol (8i). The reaction was carried out as described for the synthesis of (2*E*)-3-(2′-allyloxyphenyl)prop-2-en-1-ol (**8a**) using ethyl (2*E*)-3-(2′-allyloxy-4′-chlorophenyl)prop-2-enoate (**7i**) (0.193 g, 0.720 mmol). This gave (2*E*)-3-(2′-allyloxy-4′-chlorophenyl)prop-2-en-1-ol (**8i**) (0.138 g, 85%) as a white solid. Mp 45−47 °C; IR (neat) 3350, 2869, 1590, 1485, 1408, 1245, 1226, 1015, 998, 972, 905, 730 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$) δ 1.59 (t, J = 5.1 Hz, 1H), 4.34 (br t, J = 5.1 Hz, 2H), 4.57 (dt, J = 5.2, 1.4 Hz, 2H), 5.33 (dq, J = 10.6, 1.4 Hz, 1H), 5.44 (dq, J = 17.2, 1.4 Hz, 1H), 6.07 (ddt, J = 17.2, 10.6, 5.2 Hz, 1H), 6.38 (dt, J = 16.0, 5.1 Hz, 1H), 6.86 (d, J = 1.8 Hz, 1H), 6.88−6.94 (m, 2H), 7.37 (d, J = 8.3 Hz, 1H); ^{13}C NMR (126 MHz, $CDCl_3$) δ 64.1 (CH_2), 69.4 (CH_2), 112.9 (CH), 118.0 (CH_2), 121.0 (CH), 124.6 (C), 125.2 (CH), 127.7 (CH), 129.6 (CH), 132.6 (CH), 133.8 (C), 156.2 (C); MS (EI) m/z 224 (M^+, 93), 183 (99), 165 (73), 155 (100), 125 (55), 120 (10), 91 (48), 77 (14); HRMS (EI) calcd for $C_{12}H_{13}{}^{35}ClO_2$ (M^+), 224.0604, found 224.0600.

(2*E*)-3-(2′-Allyloxy-4′,5′-difluorophenyl)prop-2-en-1-ol (8j). The reaction was carried out as described for the synthesis of (2*E*)-3-(2′-allyloxyphenyl)prop-2-en-1-ol (**8a**) using ethyl (2*E*)-3-(2′-allyloxy-4′,5′-difluoro-phenyl)prop-2-enoate (**7j**) (0.090 g, 0.340 mmol). This gave (2*E*)-3-(2′-allyloxy-4′,5′-difluorophenyl)prop-2-en-1-ol (**8j**) (0.071 g, 94%) as a yellow oil. IR (neat) 3341, 2867, 1610, 1507, 1422, 1192, 991, 969 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$) δ 1.57 (br s, 1H), 4.32 (br d, J = 5.2 Hz, 2H), 4.51 (dt, J = 5.2, 1.6 Hz, 2H), 5.31 (dq, J = 10.6, 1.6 Hz, 1H), 5.41 (dq, J = 17.3, 1.6 Hz, 1H), 6.03 (ddt, J = 17.3, 10.6, 5.2 Hz, 1H), 6.28 (dt, J = 16.0, 5.2 Hz, 1H), 6.67 (dd, $^3J_{HF}$ = 11.5, $^4J_{HF}$ = 5.2 Hz, 1H), 6.85 (dd, J = 16.0, 1.6 Hz, 1H), 7.23 (dd, $^3J_{HF}$ = 11.5, $^4J_{HF}$ = 9.0 Hz, 1H); ^{13}C NMR (101 MHz, $CDCl_3$) δ 63.9 (CH_2), 70.1 (CH_2), 102.5 (d, $^2J_{CF}$ = 20.8 Hz, CH), 114.7 (dd, $^2J_{CF}$ = 18.3, $^3J_{CF}$ = 1.4 Hz, CH), 118.1 (CH_2), 122.5 (dd, $^3J_{CF}$ = 5.1, $^4J_{CF}$ = 3.8 Hz, C), 124.2 (CH), 129.9 (d, $^4J_{CF}$ = 2.2 Hz, CH), 132.6 (CH), 144.8 (dd, $^1J_{CF}$ = 240.5, $^2J_{CF}$ = 13.0 Hz, C), 149.7 (dd, $^1J_{CF}$ = 248.7, $^2J_{CF}$ = 13.9 Hz, C), 151.8 (dd, $^3J_{CF}$ = 7.1, $^4J_{CF}$ = 1.8 Hz, C); MS (EI) m/z 226 (M^+, 79), 185 (74), 167 (100), 157 (60), 127 (94), 119 (22), 84 (97); HRMS (EI) calcd for $C_{12}H_{12}F_2O_2$ (M^+), 226.0805, found 226.0806.

(2*E*)-3-(2′-Allyloxy-3′-methoxy-5′-nitrophenyl)prop-2-en-1-ol (8k). The reaction was carried out as described for the synthesis of (2*E*)-3-(2′-allyloxyphenyl)prop-2-en-1-ol (**8a**) using ethyl (2*E*)-3-(2′-allyloxy-3′-methoxy-5′-nitrophenyl)prop-2-enoate (**7k**) (0.798 g, 2.59 mmol). This gave (2*E*)-3-(2′-allyloxy-3′-methoxy-5′-nitrophenyl)-prop-2-en-1-ol (**8k**) (0.604 g, 88%) as a white solid. Mp 58−60 °C; IR (neat) 3267, 2933, 1657, 1579, 1511, 1471, 1336, 1265, 1210, 1104, 1071, 977 cm^{-1}; ^1H NMR (500 MHz, $CDCl_3$) δ 1.59 (t, J = 5.6 Hz, 1H), 3.95 (s, 3H), 4.38 (td, J = 5.6, 1.6 Hz, 2H), 4.60 (dt, J = 6.0, 1.3 Hz, 2H), 5.26 (dq, J = 10.5, 1.3 Hz, 1H), 5.37 (dq, J = 17.1, 1.3 Hz, 1H), 6.06 (ddt, J = 17.1, 10.5, 6.0 Hz, 1H), 6.50 (dt, J = 16.2, 5.6 Hz, 1H), 6.95 (dt, J = 16.2, 1.6 Hz, 1H), 7.66 (d, J = 2.6 Hz, 1H), 8.04 (d, J = 2.6 Hz, 1H); ^{13}C NMR (126 MHz, $CDCl_3$) δ 56.2 (CH_3), 63.4 (CH_2), 74.4 (CH_2), 105.9 (CH), 114.1 (CH), 118.6 (CH_2), 123.4 (CH), 131.5 (C), 132.7 (CH), 133.3 (CH), 143.8 (C), 150.3 (C), 153.0 (C); MS (ESI) m/z 288 (MNa^+, 100); HRMS (ESI) calcd for $C_{13}H_{15}NNaO_5$ (MNa^+), 288.0842, found 288.0837.

(2*E*)-3-(2′-Allyloxynaphthalen-1′-yl)prop-2-en-1-ol (8l). The reaction was carried out according to the procedure described for the synthesis of (2*E*)-3-(2′-allyloxyphenyl)prop-2-en-1-ol (**8a**) using ethyl (2*E*)-3-(2′-allyloxynaphthalen-1′-yl)prop-2-enoate (**7l**) (0.760 g, 2.69 mmol). This gave (2*E*)-3-(2′-allyloxynaphthalen-1′-yl)prop-2-en-1-ol (**8l**) (0.592 g, 92%) as a yellow solid. Mp 56−58 °C; IR (neat) 3391, 2865, 1591, 1510, 1217, 1011, 805 cm^{-1}; ^1H NMR (500 MHz, $CDCl_3$) δ 1.52 (t, J = 6.0 Hz, 1H), 4.47 (td, J = 6.0, 1.6 Hz, 2H), 4.70 (dt, J = 5.2, 1.6 Hz, 2H), 5.29 (dq, J = 10.5, 1.6 Hz, 1H), 5.44 (dq, J = 17.3, 1.6 Hz, 1H), 6.10 (ddt, J = 17.3, 10.5, 5.2 Hz, 1H), 6.46 (dt, J = 16.2, 6.0 Hz, 1H), 7.04 (dt, J = 16.2, 1.6 Hz, 1H), 7.25 (d, J = 9.0 Hz, 1H), 7.35 (ddd, J = 8.5, 8.4, 1.0 Hz, 1H), 7.46 (ddd, J = 8.5, 8.4, 1.0 Hz, 1H), 7.74 (d, J = 9.0 Hz, 1H), 7.78 (dd, J = 8.4, 1.0 Hz, 1H), 8.16 (dd, J = 8.4, 1.0 Hz, 1H); ^{13}C NMR (126 MHz, $CDCl_3$) δ 64.4 (CH_2), 70.2 (CH_2), 114.9 (CH), 117.5 (CH_2), 120.7 (C), 123.7 (CH), 123.9 (CH), 124.3 (CH), 126.5 (CH), 128.3 (CH), 128.8 (CH), 129.4 (C), 132.6 (C), 133.6 (CH), 135.3 (CH), 153.5 (C); MS (EI) m/z 240 (M^+, 40), 199 (25), 181 (56), 169 (93), 141 (100), 115 (38), 83 (95), 69 (10); HRMS (EI) calcd for $C_{16}H_{16}O_2$ (M^+), 240.1150, found 240.1153.

5-(2′,2′,2′-Trichloromethylcarbonylamino)-2,5-dihydro-1-benzoxepine (11a). (2*E*)-3-(2′-Allyloxyphenyl)prop-2-en-1-ol (**8a**) (0.050 g, 0.260 mmol) was dissolved in dichloromethane (15 mL) and cooled to 0 °C under argon with stirring. Trichloroacetonitrile (0.040 mL, 0.400 mmol) was added to the solution, followed by 1,8-diazabicyclo[5.4.0]undec-7-ene (0.020 mL, 0.130 mmol), and the reaction was allowed to return to room temperature over 1 h. The reaction mixture was filtered through a short pad of alumina (neutral, Brockman V) with diethyl ether (150 mL) and concentrated *in vacuo* to yield the crude allylic trichloroacetimidate **9a** as a yellow oil which was used without further purification. Allylic trichloroacetimidate **9a** was transferred to a dry Schlenk tube containing a stirrer bar and potassium carbonate (15 mg, 3 mg/mL) to which *p*-xylene (5 mL) was then added. The tube was purged with argon, sealed, and heated to 140 °C for 18 h. The reaction was allowed to cool to room temperature, and Grubbs second-generation catalyst (0.110 g, 0.013 mmol) was added. The reaction mixture was heated to 50 °C for 20 h. The reaction mixture was concentrated *in vacuo* and purified by column chromatography (elution with 10% diethyl ether in petroleum ether) that gave 5-(2′,2′,2′-trichloromethylcarbonylamino)-2,5-dihydro-1-benzoxepine (**11a**) (0.055 g, 68%) as a white solid. Mp 96−98 °C; IR (neat) 3260, 3055, 1686, 1539, 1269, 1227, 1072, 822, 725 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$) δ 4.44 (dddd, J = 17.6, 2.6, 2.0, 1.0 Hz, 1H), 4.82 (dddd, J = 17.6, 3.5, 2.0, 1.0 Hz, 1H), 5.41 (br t, J = 7.7 Hz, 1H), 5.70 (ddd, J = 11.5, 3.5, 2.6 Hz, 1H), 6.11 (ddt, J = 11.5, 7.7, 2.0 Hz, 1H), 7.10−7.16 (m, 2H), 7.27−7.34 (m, 2H), 7.63 (br d, J = 7.7 Hz, 1H); ^{13}C NMR (101 MHz, $CDCl_3$) δ 51.5 (CH), 71.1 (CH_2), 92.7 (C), 122.1 (CH), 125.1 (CH), 126.0 (CH), 128.3 (CH), 130.1 (CH), 131.6 (CH), 134.9 (C), 157.3 (C), 160.6 (C); MS (CI) m/z 307 (MH^+, 100), 272 (37), 257 (62), 197 (13), 157 (28), 145 (64), 113 (35), 71 (53); HRMS (CI) calcd for $C_{12}H_{11}{}^{35}Cl_2{}^{37}ClNO_2$ (MH^+), 307.9827, found 307.9830.

6-Methoxy-5-(2′,2′,2′-trichloromethylcarbonylamino)-2,5-dihydro-1-benzoxepine (11b). The reaction was carried out as described for the synthesis of 5-(2′,2′,2′-trichloromethylcarbonylamino)-2,5-dihydro-1-benzoxepine (**11a**) using (2*E*)-3-(2′-allyloxy-6′-methoxyphenyl)prop-2-en-1-ol (**8b**) (0.049 g, 0.22 mmol). This gave 6-methoxy-5-(2′,2′,2′-trichloromethylcarbonylamino)-2,5-dihydro-1-benzoxepine (**11b**) (0.046 g, 61%) as colorless oil. IR (neat) 3412, 2938, 1710, 1602, 1471, 1278, 1088, 818 cm^{-1}; ^1H NMR (500 MHz, $CDCl_3$) δ 3.85 (s, 3H), 4.36−4.43 (m, 1H), 4.83 (ddd, J = 17.6, 3.6, 2.1 Hz, 1H), 5.65 (ddd, J = 10.7, 3.6, 1.9 Hz, 1H), 6.00 (t, J = 8.1 Hz, 1H), 6.17 (dddd, J = 10.7, 8.1, 2.6, 2.1 Hz, 1H), 6.73 (dd, J = 8.2, 0.7 Hz, 1H), 6.75 (dd, J = 8.2, 0.7 Hz, 1H), 7.24 (t, J = 8.2 Hz, 1H), 7.78 (d, J = 8.1 Hz, 1H); ^{13}C NMR (126 MHz, $CDCl_3$) δ 43.0 (CH), 56.3 (CH_3), 71.3 (CH_2), 93.0 (C), 108.2 (CH), 114.3 (CH), 123.9 (C), 126.7 (CH), 130.1 (CH), 131.3 (CH), 156.3 (C), 158.8 (C),

DOI: 10.1021/acs.joc.5b00583
J. Org. Chem. 2015, 80, 4683−4696

160.6 (C); MS (ESI) m/z 358 (MNa^+, 100); HRMS (ESI) calcd for $C_{13}H_{12}{}^{35}Cl_3NNaO_3$ (MNa^+), 357.9775, found 357.9766.

7-Methoxy-5-(2′,2′,2′-trichloromethylcarbonylamino)-2,5-dihydro-1-benzoxepine (11c). The reaction was carried out as described for the synthesis of 5-(2′,2′,2′-trichloromethylcarbonylamino)-2,5-dihydro-1-benzoxepine (**11a**) using (2*E*)-3-(2′-allyloxy-5′-methoxyphenyl)prop-2-en-1-ol (**8c**) (0.064 g, 0.29 mmol). This gave 7-methoxy-5-(2′,2′,2′-trichloromethylcarbonylamino)-2,5-dihydro-1-benzoxepine (**11c**) (0.075 g, 76%) as yellow oil. IR (neat) 3329, 2938, 1702, 1490, 1265, 1205, 1034, 818 cm^{-1}; ^1H NMR (500 MHz, $CDCl_3$) δ 3.78 (s, 3H), 4.34−4.44 (m, 1H), 4.76 (ddd, J = 17.7, 3.3, 2.3 Hz, 1H), 5.34 (t, J = 8.0 Hz, 1H), 5.68 (ddd, J = 11.6, 3.3, 2.0 Hz, 1H), 6.09 (ddt, J = 11.6, 8.0, 2.3 Hz, 1H), 6.79 (dd, J = 8.3, 3.0 Hz, 1H), 6.81 (d, J = 3.0 Hz, 1H), 7.05 (d, J = 8.3 Hz, 1H), 7.66 (d, J = 8.0 Hz, 1H); ^{13}C NMR (126 MHz, $CDCl_3$) δ 51.6 (CH), 55.8 (CH_3), 71.5 (CH_2), 92.8 (C), 113.6 (CH), 114.7 (CH), 122.8 (CH), 126.0 (CH), 131.9 (CH), 135.8 (C), 150.9 (C), 156.5 (C), 160.8 (C); MS (ESI) m/z 358 (MNa^+, 100); HRMS (ESI) calcd for $C_{13}H_{12}{}^{35}Cl_3NNaO_3$ (MNa^+), 357.9775, found 357.9769.

8-Methoxy-5-(2′,2′,2′-trichloromethylcarbonylamino)-2,5-dihydro-1-benzoxepine (11d). The reaction was carried out as described for the synthesis of 5-(2′,2′,2′-trichloromethylcarbonylamino)-2,5-dihydro-1-benzoxepine (**11a**) using (2*E*)-3-(2′-allyloxy-4′-methoxyphenyl)prop-2-en-1-ol (**8d**) (0.048 g, 0.22 mmol). This gave 8-methoxy-5-(2′,2′,2′-trichloromethylcarbonylamino)-2,5-dihydro-1-benzoxepine (**11d**) (0.051 g, 69%) as colorless oil. IR (neat) 3419, 2935, 1706, 1613, 1496, 1156, 1122, 1032, 819 cm^{-1}; ^1H NMR (500 MHz, $CDCl_3$) δ 3.79 (s, 3H), 4.43 (br d, J = 17.6 Hz, 1H), 4.79 (ddd, J = 17.6, 3.6, 1.9 Hz, 1H), 5.33 (t, J = 8.3 Hz, 1H), 5.69 (ddd, J = 11.5, 3.6, 1.9 Hz, 1H), 6.09 (ddt, J = 11.5, 8.3, 1.9 Hz, 1H), 6.64 (dd, J = 8.3, 2.6 Hz, 1H), 6.68 (d, J = 2.6 Hz, 1H), 7.20 (d, J = 8.3 Hz, 1H), 7.53 (d, J = 8.3 Hz, 1H); ^{13}C NMR (126 MHz, $CDCl_3$) δ 51.3 (CH), 55.6 (CH_3), 71.2 (CH_2), 92.8 (C), 108.3 (CH), 110.0 (CH), 126.3 (CH), 127.1 (C), 129.3 (CH), 131.5 (CH), 158.4 (C), 160.7 (C), 161.1 (C); MS (ESI) m/z 358 (MNa^+, 100); HRMS (ESI) calcd for $C_{13}H_{12}{}^{35}Cl_3NNaO_3$ (MNa^+), 357.9775, found 357.9781.

7-Methyl-5-(2′,2′,2′-trichloromethylcarbonylamino)-2,5-dihydro-1-benzoxepine (11e). The reaction was carried out as described for the synthesis of 5-(2′,2′,2′-trichloromethylcarbonylamino)-2,5-dihydro-1-benzoxepine (**11a**) using (2*E*)-3-(2′-allyloxyphenyl-5′-methyl)prop-2-en-1-ol (**8e**) (0.150 g, 0.730 mmol). This gave 7-methyl-5-(2′,2′,2′-trichloromethylcarbonylamino)-2,5-dihydro-1-benzoxepine (**11e**) (0.173 g, 73%) as a white solid. Mp 146−148 °C; IR (neat) 3306, 1713, 1530, 1494, 1234, 1064, 825 cm^{-1}; ^1H NMR (500 MHz, $CDCl_3$) δ 2.31 (s, 3H), 4.40 (br dt, J = 17.6, 2.1 Hz, 1H), 4.79 (ddd, J = 17.6, 3.5, 2.1 Hz, 1H), 5.33 (t, J = 8.1 Hz, 1H), 5.69 (ddd, J = 11.5, 3.5, 2.1 Hz, 1H), 6.11 (ddt, J = 11.5, 8.1, 2.1 Hz, 1H), 7.01 (d, J = 8.3 Hz, 1H), 7.08−7.12 (m, 2H), 7.65 (d, J = 8.1 Hz, 1H); ^{13}C NMR (126 MHz, $CDCl_3$) δ 20.8 (CH_3), 51.5 (CH), 71.2 (CH_2), 92.7 (C), 121.7 (CH), 126.0 (CH), 128.9 (CH), 130.4 (CH), 131.7 (CH), 134.5 (C), 134.7 (C), 155.0 (C), 160.6 (C); MS (ESI) m/z 342 (MNa^+, 100); HRMS (ESI) calcd for $C_{13}H_{12}{}^{35}Cl_3NNaO_2$ (MNa^+), 341.9826, found 341.9811.

7-Nitro-5-(2′,2′,2′-trichloromethylcarbonylamino)-2,5-dihydro-1-benzoxepine (11f). The reaction was carried out as described for the synthesis of 5-(2′,2′,2′-trichloromethylcarbonylamino)-2,5-dihydro-1-benzoxepine (**11a**) using (2*E*)-3-(2′-allyloxy-5′-nitrophenyl)prop-2-en-1-ol (**8f**) (0.060 g, 0.26 mmol), except that the Overman rearrangement was heated at 140 °C for 60 h and 7.5 mol % of Grubbs second-generation catalyst was used for the RCM step. This gave 7-nitro-5-(2′,2′,2′-trichloromethylcarbonylamino)-2,5-dihydro-1-benzoxepine (**11f**) (0.063 g, 71%) as a white solid. Mp 170 °C (decomposition); IR (neat) 3337, 2841, 1694, 1522, 1491, 1344, 1236, 1047, 820 cm^{-1}; ^1H NMR (500 MHz, $CDCl_3$) δ 4.50−4.59 (m, 1H), 4.85−4.92 (m, 1H), 5.57 (t, J = 7.5 Hz, 1H), 5.78 (ddd, J = 11.6, 3.0, 2.4 Hz, 1H), 6.09 (ddt, J = 11.6, 7.5, 2.4 Hz, 1H), 7.24−7.30 (m, 1H), 7.45 (br d, J = 7.5 Hz, 1H), 8.21 (dd, J = 9.5, 4.5 Hz, 1H), 8.22 (d, J = 4.5 Hz, 1H); ^{13}C NMR (126 MHz, $CDCl_3$) δ 51.0 (CH), 71.4 (CH_2), 92.4 (C), 123.4 (CH), 123.8 (CH), 125.4 (CH), 125.9 (CH), 131.5 (CH), 136.4 (C), 144.6 (C), 161.1 (C), 162.4 (C); MS (ESI) m/z 373 (MNa^+, 100); HRMS (ESI) calcd for $C_{12}H_9{}^{35}Cl_3N_2NaO_4$ (MNa^+), 372.9520, found 372.9514.

7-Chloro-5-(2′,2′,2′-trichloromethylcarbonylamino)-2,5-dihydro-1-benzoxepine (11g). The reaction was carried out as described for the synthesis of 5-(2′,2′,2′-trichloromethylcarbonylamino)-2,5-dihydro-1-benzoxepine (**11a**) using (2*E*)-3-(2′-allyloxy-5′-chlorophenyl)prop-2-en-1-ol (**8g**) (0.055 g, 0.25 mmol), except that the Overman rearrangement was heated at 140 °C for 60 h. This gave 7-chloro-5-(2′,2′,2′-trichloromethylcarbonylamino)-2,5-dihydro-1-benzoxepine (**11g**) (0.058 g, 69%) as white solid. Mp 136−138 °C; IR (neat) 3260, 2943, 1708, 1687, 1539, 1480, 1267, 1066, 825 cm^{-1}; ^1H NMR (500 MHz, $CDCl_3$) δ 4.42 (br d, J = 17.7 Hz, 1H), 4.75−4.85 (m, 1H), 5.36 (t, J = 7.9 Hz, 1H), 5.72 (ddd, J = 11.7, 3.4, 2.0 Hz, 1H), 6.07 (ddt, J = 11.7, 7.9, 2.3 Hz, 1H), 7.07 (d, J = 8.3 Hz, 1H), 7.23−7.30 (m, 2H), 7.55 (d, J = 7.9 Hz, 1H); ^{13}C NMR (126 MHz, $CDCl_3$) δ 51.0 (CH), 71.3 (CH_2), 92.6 (C), 123.6 (CH), 125.6 (CH), 128.3 (CH), 130.0 (CH), 130.2 (C), 131.8 (CH), 136.6 (C), 155.9 (C), 160.8 (C); MS (ESI) m/z 362 (MNa^+, 100); HRMS (ESI) calcd for $C_{12}H_9{}^{35}Cl_4NNaO_2$ (MNa^+), 361.9280, found 361.9268.

7-Bromo-5-(2′,2′,2′-trichloromethylcarbonylamino)-2,5-dihydro-1-benzoxepine (11h). The reaction was carried out as described for the synthesis of 5-(2′,2′,2′-trichloromethylcarbonylamino)-2,5-dihydro-1-benzoxepine (**11a**) using (2*E*)-3-(2′-allyloxy-5′-bromophenyl)prop-2-en-1-ol (**8h**) (0.10 g, 0.29 mmol), except that the Overman rearrangement was heated at 140 °C for 48 h. This gave 7-bromo-5-(2′,2′,2′-trichloromethylcarbonylamino)-2,5-dihydro-1-benzoxepine (**11h**) (0.11 g, 79%) as white solid. Mp 147−149 °C; IR (neat) 3267, 2890, 1707, 1687, 1535, 1478, 1267, 1067, 822 cm^{-1}; ^1H NMR (500 MHz, $CDCl_3$) δ 4.37−4.46 (m, 1H), 4.81 (ddd, J = 17.7, 3.3, 2.3 Hz, 1H), 5.36 (t, J = 8.2 Hz, 1H), 5.71 (ddd, J = 11.7, 3.3, 2.0 Hz, 1H), 6.07 (ddt, J = 11.7, 8.2, 2.3 Hz, 1H), 7.01 (d, J = 8.2 Hz, 1H), 7.42 (dd, J = 8.2, 2.5 Hz, 1H), 7.43 (d, J = 2.5 Hz, 1H), 7.54 (d, J = 8.2 Hz, 1H); δ_C (126 MHz, $CDCl_3$) δ 51.0 (CH), 71.3 (CH_2), 92.6 (C), 117.8 (C), 124.0 (CH), 125.6 (CH), 131.2 (CH), 131.8 (CH), 133.0 (CH), 137.0 (C), 156.4 (C), 160.8 (C); MS (ESI) m/z 406 (MNa^+, 100); HRMS (ESI) calcd for $C_{12}H_9{}^{79}Br{}^{35}Cl_3NNaO_2$ (MNa^+), 405.8774, found 405.8764.

8-Chloro-5-(2′,2′,2′-trichloromethylcarbonylamino)-2,5-dihydro-1-benzoxepine (11i). The reaction was carried out as described for the synthesis of 5-(2′,2′,2′-trichloromethylcarbonylamino)-2,5-dihydro-1-benzoxepine (**11a**) using (2*E*)-3-(2′-allyloxy-4′-chlorophenyl)prop-2-en-1-ol (**8i**) (0.130 g, 0.580 mmol), except that the Overman rearrangement was heated at 140 °C for 24 h. This gave 8-chloro-5-(2′,2′,2′-trichloromethylcarbonylamino)-2,5-dihydro-1-benzoxepine (**11i**) (0.141 g, 71%) as a yellow oil. IR (neat) 3416, 2960, 1700, 1598, 1490, 1480, 1271, 1225, 1077, 906, 836, 821, 731 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$) δ 4.45 (br dt, J = 17.6, 2.1 Hz, 1H), 4.82 (ddd, J = 17.6, 3.4, 2.1 Hz, 1H), 5.38 (t, J = 7.8 Hz, 1H), 5.72 (ddd, J = 11.5, 3.4, 2.1 Hz, 1H), 6.07 (ddt, J = 11.5, 7.8, 2.1 Hz, 1H), 7.11 (dd, J = 8.1, 2.0 Hz, 1H), 7.14 (d, J = 2.0 Hz, 1H), 7.23 (d, J = 8.1 Hz, 1H), 7.50 (d, J = 7.8 Hz, 1H); ^{13}C NMR (101 MHz, $CDCl_3$) δ 51.0 (CH), 71.2 (CH_2), 92.5 (C), 122.8 (CH), 125.2 (CH), 125.6 (CH), 129.3 (CH), 131.6 (CH), 133.4 (C), 134.9 (C), 157.8 (C), 160.7 (C); MS (ESI) m/z 362 (MNa^+, 100); HRMS (ESI) calcd for $C_{12}H_9{}^{35}Cl_4NNaO_2$ (MNa^+), 361.9280, found 361.9264.

7,8-Difluoro-5-(2′,2′,2′-trichloromethylcarbonylamino)-2,5-dihydro-1-benzoxepine (11j). The reaction was carried out as described for the synthesis of 5-(2′,2′,2′-trichloromethylcarbonylamino)-2,5-dihydro-1-benzoxepine (**11a**) using (2*E*)-3-(2′-allyloxy-4′,5′-difluorophenyl)prop-2-en-1-ol (**8j**) (0.040 g, 0.180 mmol), except that the Overman rearrangement was heated at 140 °C for 24 h. This gave 7,8-difluoro-5-(2′,2′,2′-trichloromethylcarbonylamino)-2,5-dihydro-1-benzoxepine (**11j**) (0.042 g, 68%) as a white solid. Mp 106−108 °C; IR (neat) 3264, 2925, 1711, 1691, 1620, 1542, 1500, 1267, 1161, 888 cm^{-1}; ^1H NMR (500 MHz, $CDCl_3$) δ 4.44 (ddd, J = 17.6, 3.5, 2.1 Hz, 1H), 4.79 (ddd, J = 17.6, 2.8, 2.1 Hz, 1H), 5.34 (t, J = 7.8 Hz, 1H), 5.73 (ddd, J = 11.5, 3.5, 2.8 Hz, 1H), 6.05 (ddt, J = 11.5, 7.8, 2.1 Hz, 1H), 6.97 (dd, $^3J_{HF}$ = 10.2, $^4J_{HF}$ = 6.8 Hz, 1H), 7.14 (dd, $^3J_{HF}$ = 10.2, $^4J_{HF}$ = 8.7 Hz, 1H), 7.47 (d, J = 7.8 Hz, 1H); ^{13}C NMR (101 MHz, $CDCl_3$) δ 50.7 (CH), 71.2 (CH_2), 92.4 (C), 111.8 (d, $^2J_{CF}$ = 18.3 Hz,

DOI: 10.1021/acs.joc.5b00583
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CH), 116.8 (dd, $^2J_{CF}$ = 19.0, $^3J_{CF}$ = 1.4 Hz, CH), 125.4 (CH), 131.3 (dd, $^3J_{CF}$ = 5.1, $^4J_{CF}$ = 3.6 Hz, C), 131.6 (CH), 147.0 (dd, $^1J_{CF}$ = 247.0, $^2J_{CF}$ = 12.5 Hz, C), 150.1 (dd, $^1J_{CF}$ = 251.6, $^2J_{CF}$ = 13.7 Hz, C), 153.1 (dd, $^3J_{CF}$ = 8.3, $^4J_{CF}$ = 3.1 Hz, C), 160.8 (C); MS (CI) *m*/*z* 342 (MH^+, 100), 308 (49), 274 (8), 238 (18), 181 (96), 81 (20), 69 (28); HRMS (CI) calcd for $C_{12}H_9{}^{35}Cl_3F_2NO_2$ (MH^+), 341.9667, found 341.9665.

9-Methoxy-7-nitro-5-(2′,2′,2′-trichloromethylcarbonylamino)-2,5-dihydro-1-benzoxepine (11k). The reaction was carried out as described for the synthesis of 5-(2′,2′,2′-trichloromethylcarbonylamino)-2,5-dihydro-1-benzoxepine (**11a**) using (2*E*)-3-(2′-allyloxy-3′-methoxy-5′-nitrophenyl)prop-2-en-1-ol (**8k**) (0.215 g, 0.810 mmol), except that the Overman rearrangement was heated at 140 °C for 48 h. This gave 9-methoxy-7-nitro-5-(2′,2′,2′-trichloromethylcarbonylamino)-2,5-dihydro-1-benzoxepine (**11k**) (0.162 g, 52%) as a white solid. Mp 180−182 °C; IR (neat) 3327, 2943, 1702, 1526, 1342, 1056, 909, 822 cm^{-1}; ^1H NMR (500 MHz, $CDCl_3$) δ 3.99 (s, 3H), 4.52 (ddd, *J* = 17.8, 3.5, 2.1 Hz, 1H), 4.89 (ddd, *J* = 17.8, 2.8, 2.1 Hz, 1H), 5.54 (t, *J* = 8.1 Hz, 1H), 5.76 (ddd, *J* = 11.6, 3.5, 2.8 Hz, 1H), 6.09 (ddt, *J* = 11.6, 8.1, 2.1 Hz, 1H), 7.54 (br d, *J* = 8.1 Hz, 1H), 7.83 (d, *J* = 2.5 Hz, 1H), 7.86 (d, *J* = 2.5 Hz, 1H); ^{13}C NMR (126 MHz, $CDCl_3$) δ 50.8 (CH), 56.6 (CH_3), 70.4 (CH_2), 92.3 (C), 108.1 (CH), 115.3 (CH), 125.4 (CH), 131.4 (CH), 137.3 (C), 144.6 (C), 150.7 (C), 152.9 (C), 160.9 (C); MS (ESI) *m*/*z* 403 (MNa^+, 100); HRMS (ESI) calcd for $C_{13}H_{11}{}^{35}Cl_3N_2NaO_5$ (MNa^+), 402.9626, found 402.9609.

5-(2′,2′,2′-Trichloromethylcarbonylamino)-2,5-dihydro-1-naphtho[2,1-*b*]oxepine (11l). The reaction was carried out as described for the synthesis of 5-(2′,2′,2′-trichloromethylcarbonylamino)-2,5-dihydro-1-benzoxepine (**11a**) using (2*E*)-3-(2′-allyloxynaphthyl)prop-2-en-1-ol (**8l**) (0.205 g, 0.850 mmol). This gave 5-(2′,2′,2′-trichloromethylcarbonylamino)-2,5-dihydro-1-naphtho[2,1-*b*]oxepine (**11l**) (0.140 g. 46%) as a white solid. Mp 136−138 °C; IR (neat) 3406, 2940, 1701, 1492, 1220, 1045, 818 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$) δ 4.48 (br dt, *J* = 17.6, 2.1 Hz, 1H), 4.93 (ddd, *J* = 17.6, 3.5, 2.1 Hz, 1H), 5.76 (ddd, *J* = 11.0, 3.5, 2.1 Hz, 1H), 6.25−6.30 (m, 1H), 6.32 (br t, *J* = 8.4 Hz, 1H), 7.32 (d, *J* = 8.4 Hz, 1H), 7.47 (ddd, *J* = 8.5, 8.4, 1.3 Hz, 1H), 7.60 (ddd, *J* = 8.5, 8.4, 1.3 Hz, 1H), 7.83−7.87 (m, 2H), 7.99 (d, *J* = 8.4 Hz, 1H), 8.29 (br d, *J* = 8.4 Hz, 1H); ^{13}C NMR (126 MHz, $CDCl_3$) δ 44.9 (CH), 70.5 (CH_2), 92.7 (C), 121.5 (CH), 122.9 (CH), 125.3 (CH), 126.0 (CH), 127.4 (CH), 128.6 (CH), 129.7 (C), 130.6 (C), 130.8 (CH), 131.4 (C), 131.8 (CH), 155.4 (C), 160.8 (C); MS (ESI) *m*/*z* 378 (MNa^+, 100); HRMS (ESI) calcd for $C_{16}H_{12}{}^{35}Cl_3NNaO_2$ (MNa^+), 377.9826, found 377.9808.

Methyl 4-(4′-fluorophenyl)-2-hydroxybenzoate (14).[37] 4-Fluorophenylboronic acid (**12**) (0.378 g, 2.70 mmol), cesium carbonate (1.47 g, 4.50 mmol), and [1,1′-bis(diphenylphosphino)-ferrocene]palladium(II) dichloride (0.0735 g, 0.0899 mmol) were added to a degassed solution of methyl 2-hydroxy-4-iodobenzoate (**13**) (0.500 g, 1.80 mmol) in 1,4-dioxane (17 mL) and water (1 mL). The solution was heated to 80 °C for 18 h, cooled to room temperature, and concentrated *in vacuo*. The reaction mixture was purified by column chromatography (elution with 20% diethyl ether in petroleum ether) to yield methyl 4-(4′-fluorophenyl)-2-hydroxybenzoate (**14**) (0.442 g, 100%) as a white solid. Mp 110−112 °C; Spectroscopic data were in accordance with literature values.[37] ^1H NMR (500 MHz, $CDCl_3$) δ 3.97 (s, 3H), 7.06 (dd, *J* = 8.4, 1.0 Hz, 1H), 7.10−7.17 (m, 3H), 7.57 (dd, *J* = 8.4, $^3J_{HF}$ = 5.4 Hz, 2H), 7.87 (d, *J* = 8.4 Hz, 1H), 10.82 (br s, 1H); ^{13}C NMR (126 MHz, $CDCl_3$) δ 52.4 (CH_3), 111.3 (C), 115.7 (CH), 116.0 (2 × CH, d, $^2J_{CF}$ = 21.6 Hz), 118.1 (CH), 129.0 (2 × CH, d, $^3J_{CF}$ = 8.2 Hz), 130.5 (CH), 135.9 (C, d, $^4J_{CF}$ = 3.2 Hz), 147.6 (C), 162.0 (C), 163.2 (C, d, $^1J_{CF}$ = 248.3 Hz), 170.6 (C); MS (EI) *m*/*z* 246 (M^+, 82), 214 (100), 186 (45), 157 (30), 133 (10), 93 (9), 84 (30), 49 (34).

4-(4′-Fluorophenyl)-2-hydroxybenzyl alcohol. Lithium aluminum hydride (0.663 g, 17.5 mmol) was added to a solution of methyl 4-(4′-fluorophenyl)-2-hydroxybenzoate (**14**) (1.72 g, 6.98 mmol) in tetrahydrofuran (70 mL) and stirred at room temperature for 18 h. The reaction mixture was cooled to 0 °C and quenched by addition of 2 M hydrochloric acid (70 mL). The solution was extracted with dichloromethane (2 × 70 mL), washed with water (2 × 50 mL), and brine (70 mL), dried ($MgSO_4$), filtered, and concentrated *in vacuo* to yield 4-(4′-fluorophenyl)-2-hydroxybenzyl alcohol (1.52 g, 100%) as a white solid. Mp 105−107 °C; IR (neat) 3441, 3395, 2918, 1491, 1241, 1184, 988, 822 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$) δ 2.23 (br s, 1H), 4.92 (s, 2H), 7.03 (dd, *J* 7.9, 1.6 Hz, 1H), 7.06−7.16 (m, 4H), 7.40 (br s, 1H), 7.48−7.56 (m, 2H); ^{13}C NMR (126 MHz, $CDCl_3$) δ 64.6 (CH_2), 115.3 (CH), 115.8 (2 × CH, d, $^2J_{CF}$ = 21.5 Hz), 118.8 (CH), 123.6 (C), 128.4 (CH), 128.7 (2 × CH, d, $^3J_{CF}$ = 8.1 Hz), 136.7 (C), 141.9 (C), 156.6 (C), 162.7 (C, d, $^1J_{CF}$ = 246.4 Hz); MS (EI) *m*/*z* 218 (M^+, 63), 200 (68), 172 (100), 133 (17), 120 (80), 85 (7); HRMS (EI) calcd for $C_{13}H_{11}FO_2$ (M^+), 218.0743, found 218.0742.

2-Allyloxy-4-(4′-fluorophenyl)benzyl alcohol (15). Allyl bromide (0.79 mL, 9.2 mmol) was added to a solution of 4-(4′-fluorophenyl)-2-hydroxybenzyl alcohol (1.0 g, 4.6 mmol), potassium carbonate (0.95 g, 6.9 mmol), and sodium iodide (0.041 g, 0.28 mmol) in *N*,*N*′-dimethylformamide (31 mL) and stirred at room temperature for 24 h. The solution was diluted with diethyl ether (60 mL), washed with 5% lithium chloride solution (3 × 50 mL), and brine (50 mL), dried ($MgSO_4$), filtered, and concentrated *in vacuo*. Purification by column chromatography (elution with 20% diethyl ether in petroleum ether) gave 2-allyloxy-4-(4′-fluorophenyl)benzyl alcohol (**15**) (0.95 g, 80%) as a white solid. Mp 54−56 °C; IR (neat) 3354, 2853, 1610, 1496, 1221, 1001, 819 cm^{-1}; ^1H NMR (500 MHz, $CDCl_3$) δ 2.38 (t, *J* 5.6 Hz, 1H), 4.66 (dt, *J* = 5.2, 1.5 Hz, 2H), 4.75 (d, *J* = 5.6 Hz, 2H), 5.32 (ddt, *J* = 10.5, 2.9, 1.5 Hz, 1H), 5.44 (ddt, *J* = 17.3, 2.9, 1.5 Hz, 1H), 6.09 (ddt, *J* = 17.3, 10.5, 5.2 Hz, 1H), 7.02 (d, *J* = 1.5 Hz, 1H), 7.06−7.15 (m, 3H), 7.34 (d, *J* = 7.7 Hz, 1H), 7.44−7.65 (m, 2H); ^{13}C NMR (126 MHz, $CDCl_3$) δ 61.9 (CH_2), 69.0 (CH_2), 110.6 (CH), 115.8 (2 × CH, d, $^2J_{CF}$ = 21.4 Hz), 118.0 (CH_2), 119.7 (CH), 128.6 (C), 128.8 (2 × CH, d, $^3J_{CF}$ = 8.0 Hz), 129.3 (CH), 133.1 (CH), 137.3 (C, d, $^4J_{CF}$ = 3.2 Hz), 141.4 (C), 156.9 (C), 162.7 (C, d, $^1J_{CF}$ = 246.6 Hz); MS (EI) *m*/*z* 258 (M^+, 100), 228 (17), 215 (27), 200 (57), 172 (70), 133 (17), 120 (6); HRMS (EI) calcd for $C_{16}H_{15}FO_2$ (M^+), 258.1056, found 258.1054.

Ethyl (2*E*)-3-(2′-Allyloxy-4′-[4‴-fluorophenyl]phenyl)prop-2-enoate (16). Dimethyl sulfoxide (0.64 mL, 9.0 mmol) was added to a stirred solution of oxalyl chloride (0.40 mL, 4.5 mmol) in dichloromethane (15 mL) at −78 °C. The reaction mixture was stirred for 0.3 h, then 2-allyloxy-4-(4′-fluorophenyl)benzyl alcohol (**15**) (0.78 g, 3.0 mmol) in dichloromethane (15 mL) was slowly added. The mixture was stirred for a further 0.3 h, then triethylamine (2.1 mL, 15 mmol) was added. This reaction mixture was stirred for 0.5 h at −78 °C and then allowed to warm to room temperature and stirred for a further 2 h. Meanwhile, a solution of lithium bromide (1.0 g, 12 mmol), triethyl phosphonoacetate (2.0 mL, 10 mmol), and 1,8-diazabicyclo[5.4.0]undec-7-ene (1.5 mL, 10 mmol) in acetonitrile (30 mL) was prepared and stirred for 1.0 h. The Swern solution was concentrated *in vacuo*, and the Horner−Wadsworth−Emmons solution was added. The reaction mixture was stirred at room temperature for 18 h. The reaction mixture was quenched by the addition of a saturated solution of ammonium chloride (20 mL) and concentrated to give an orange residue, which was then extracted with diethyl ether (2 × 30 mL). The organic layers were combined, washed with water (50 mL), and brine (50 mL), then dried ($MgSO_4$) and concentrated to give a yellow oil. Purification by column chromatography (elution with 5% diethyl ether in petroleum ether) gave ethyl (2*E*)-3-(2′-allyloxy-4′-[4‴-fluorophenyl]phenyl)prop-2-enoate (**16**) (0.83 g, 84%) as a white solid. Mp 75−76 °C; IR (neat) 2981, 1702, 1628, 1604, 1492, 1307, 1217, 1158, 986, 811 cm^{-1}; ^1H NMR (500 MHz, $CDCl_3$) δ 1.35 (t, *J* = 7.1 Hz, 3H), 4.27 (q, *J* = 7.1 Hz, 2H), 4.69 (d, *J* = 5.2 Hz, 2H), 5.34 (dd, *J* = 10.5, 1.4 Hz, 1H), 5.46 (dd, *J* = 17.2, 1.4 Hz, 1H), 6.11 (ddt, *J* = 17.2, 10.5, 5.2 Hz, 1H), 6.56 (d, *J* = 16.2 Hz, 1H), 7.04 (d, *J* = 1.3 Hz, 1H), 7.09−7.18 (m, 3H), 7.48−7.55 (m, 2H), 7.56 (d, *J* = 8.0 Hz, 1H), 8.06 (d, *J* = 16.2 Hz, 1H); ^{13}C NMR (126 MHz, $CDCl_3$) δ 14.5 (CH_3), 60.4 (CH_2), 69.4 (CH_2), 111.2 (CH), 115.9 (2 × CH, d, $^2J_{CF}$ = 21.5 Hz), 118.0 (CH_2), 118.8 (CH), 119.7 (CH), 122.9 (C), 128.8 (2 × CH, d, $^3J_{CF}$ = 8.1 Hz), 129.3 (CH), 132.9 (CH), 136.6 (C, d, $^4J_{CF}$ = 3.2 Hz), 139.5 (CH), 143.4 (C), 157.7 (C), 162.9 (C, d, $^1J_{CF}$ = 247.6 Hz),

DOI: 10.1021/acs.joc.5b00583
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167.6 (C); MS (EI) *m*/*z* 326 (M^+, 100), 281 (23), 252 (20), 238 (37), 225 (17), 212 (83), 183 (64), 165 (9), 157 (7), 133 (6), 113 (5); HRMS (EI) calcd for $C_{20}H_{19}FO_3$ (M^+), 326.1318, found 326.1316.

(2*E*)-3-(2′-Allyloxy-4′-[4‴-fluorophenyl]phenyl)prop-2-en-1-ol (17). The reaction was carried out as described for the synthesis of (2*E*)-3-(2′-allyloxyphenyl)prop-2-en-1-ol (**8a**) using ethyl (2*E*)-3-(2′-allyloxy-4′-[4‴-fluorophenyl]phenyl)prop-2-enoate (**16**) (0.79 g, 2.4 mmol). This gave (2*E*)-3-(2′-allyloxy-4′-[4‴-fluorophenyl]phenyl)-prop-2-en-1-ol (**17**) (0.63 g, 92%) as a white solid. Mp 84−86 °C; IR (neat) 3335, 2867, 1602, 1519, 1493, 1392, 1220, 1014, 972, 827 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$) δ 1.50 (br s, 1H), 4.36 (dd, *J* = 5.9, 1.1 Hz, 2H), 4.65 (dt, *J* = 5.2, 1.5 Hz, 2H), 5.32 (dq, *J* = 10.5, 1.5 Hz, 1H), 5.45 (dq, *J* = 17.3, 1.5 Hz, 1H), 6.11 (ddt, *J* = 17.3, 10.5, 5.2 Hz, 1H), 6.45 (dt, *J* = 16.1, 5.9 Hz, 1H), 6.99 (dt, *J* = 16.1, 1.1 Hz, 1H), 7.02 (d, *J* = 1.7 Hz, 1H), 7.08−7.16 (m, 3H), 7.47−7.57 (m, 3H); ^{13}C NMR (101 MHz, $CDCl_3$) δ 64.4 (CH_2), 69.5 (CH_2), 111.2 (CH), 115.8 (2 × CH, d, $^2J_{CF}$ = 21.4 Hz), 117.8 (CH_2), 119.8 (CH), 125.2 (C), 125.9 (CH), 127.5 (CH), 128.6 (2 × CH, d, $^3J_{CF}$ = 8.0 Hz), 129.5 (CH), 133.4 (CH), 137.1 (C, d, $^4J_{CF}$ = 3.2 Hz), 140.9 (C), 156.2 (C), 162.7 (C, d, $^1J_{CF}$ = 246.8 Hz); MS (EI) *m*/*z* 284 (M^+, 100), 243 (49), 225 (47), 215 (42), 196 (26), 183 (38), 165 (19), 133 (11), 107 (6), 55 (6); HRMS (EI) calcd for $C_{18}H_{17}FO_2$ (M^+), 284.1213, found 284.1214.

8-(4″-Fluorophenyl)-5-(2′,2′,2′-trichloromethylcarbonylamino)-2,5-dihydro-1-benzoxepine (18). The reaction was carried out as described for the synthesis of 5-(2′,2′,2′-trichloromethylcarbonylamino)-2,5-dihydro-1-benzoxepine (**11a**) using (2*E*)-3-(2′-allyloxy-4′-[4‴-fluorophenyl]phenyl)prop-2-en-1-ol (**17**) (0.200 g, 0.700 mmol). This gave 8-(4″-fluorophenyl)-5-(2′,2′,2′-trichloromethylcarbonylamino)-2,5-dihydro-1-benzoxepine (**18**) (0.277 g, 98%) as a white solid. Mp 115−117 °C; IR (neat) 3416, 2932, 1703, 1489, 1223, 907, 816, 729 cm^{-1}; ^1H NMR (500 MHz, $CDCl_3$) δ 4.50 (br d, *J* = 17.7 Hz, 1H), 4.86 (ddd, *J* = 17.7, 3.3, 2.2 Hz, 1H), 5.45 (t, *J* = 8.2 Hz, 1H), 5.74 (ddd, *J* = 11.6, 3.3, 1.9 Hz, 1H), 6.13 (ddt, *J* = 11.6, 8.2, 2.2 Hz, 1H), 7.09−7.15 (m, 2H), 7.30 (dd, *J* = 7.8, 1.5 Hz, 1H), 7.32 (d, *J* = 1.5 Hz, 1H), 7.35 (d, *J* = 7.8 Hz, 1H), 7.50−7.56 (m, 2H), 7.63 (d, *J* = 8.2 Hz, 1H); ^{13}C NMR (126 MHz, $CDCl_3$) δ 51.4 (CH), 71.3 (CH_2), 92.8 (C), 115.9 (2 × CH, d, $^2J_{CF}$ = 21.5 Hz), 120.8 (CH), 123.6 (CH), 126.1 (CH), 128.7 (2 × CH, d, $^3J_{CF}$ = 8.1 Hz), 128.9 (CH), 131.8 (CH), 133.7 (C), 136.1 (C, d, $^4J_{CF}$ = 3.2 Hz), 142.5 (C), 157.7 (C), 160.8 (C), 162.8 (C, d, $^1J_{CF}$ = 247.2 Hz); MS (EI) *m*/*z* 399 (M^+, 12), 364 (100), 328 (59), 294 (12), 252 (20), 238 (67), 225 (18), 209 (20), 196 (23), 183 (21), 157 (8), 133 (7), 120 (6); HRMS (EI) calcd for $C_{18}H_{13}{}^{35}Cl_3FNO_2$ (M^+), 398.9996, found 398.9980.

8-(4″-Fluorophenyl)-5-(2′,2′,2′-trichloromethylcarbonylamino)-2,3,4,5-tetrahydro-1-benzoxepine (19). *p*-Toluenesulfonyl hydrazide (0.030 g, 0.16 mmol) and potassium acetate (0.016 g, 0.16 mmol) were added to a stirred solution of 8-(4″-fluorophenyl)-5-(2′,2′,2′-trichloromethylcarbonylamino)-2,5-dihydro-1-benzoxepine (**18**) (0.033 g, 0.082 mmol) in butan-1-ol (0.8 mL) at 50 °C. The reaction mixture was heated to 100 °C, and four additional portions of *p*-toluenesulfonyl hydrazide (0.030 g, 0.16 mmol) and potassium acetate (0.016 g, 0.16 mmol) were added at 1 h intervals. After 5 h, the reaction mixture was cooled to room temperature and diluted with diethyl ether (10 mL), washed with 1 M sodium hydroxide (10 mL), water (10 mL), and brine (10 mL), then dried ($MgSO_4$), filtered, and concentrated *in vacuo*. Purification by column chromatography (elution with 10% diethyl ether in petroleum ether) gave 8-(4″-fluorophenyl)-5-(2′,2′,2′-trichloromethylcarbonylamino)-2,3,4,5-tetrahydro-1-benzoxepine (**19**) (0.027 g, 81%) as a white solid. Mp 128−130 °C; IR (neat) 3415, 2941, 1712, 1491, 1226, 817 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$) δ 1.77−1.95 (m, 2H), 2.22−2.42 (m, 2H), 3.79 (td, *J* = 11.9, 1.7 Hz, 1H), 4.43−4.50 (m, 1H), 5.18 (ddd, *J* = 8.1, 6.1, 1.7 Hz, 1H), 7.09−7.17 (m, 2H), 7.23−7.29 (m, 2H), 7.33 (d, *J* = 8.5 Hz, 1H), 7.45−7.56 (m, 3H); ^{13}C NMR (126 MHz, $CDCl_3$) δ 26.6 (CH_2), 29.8 (CH_2), 54.9 (CH), 74.2 (CH_2), 92.9 (C), 115.9 (2 × CH, d, $^2J_{CF}$ = 21.5 Hz), 121.1 (CH), 123.1 (CH), 128.7 (2 × CH, d, $^3J_{CF}$ = 8.1 Hz), 130.2 (CH), 132.3 (C), 136.1 (C, d, $^4J_{CF}$ = 3.3 Hz), 142.3 (C), 160.0 (C), 161.0 (C), 162.9 (C, d, $^1J_{CF}$ = 247.2 Hz); MS (EI) *m*/*z* 401 (M^+, 11), 366 (100), 330 (27), 296 (15), 283 (12), 241 (38), 212 (24), 183 (22), 170 (16), 84 (61); HRMS (EI) calcd for $C_{18}H_{15}{}^{35}Cl_3FNO_2$ (M^+), 401.0152, found 401.0150.

8-Chloro-5-(2′,2′-dichloromethylcarbonylamino)-2,3,4,5-tetrahydro-1-benzoxepine (21). 10% Palladium on charcoal (0.03 g) was added to a solution of 8-chloro-5-(2′,2′,2′-trichloromethylcarbonylamino)-2,5-dihydro-1-benzoxepine (**11i**) (0.120 g, 0.350 mmol) in ethyl acetate (7 mL). The mixture was stirred under an atmosphere of hydrogen at room temperature for 1.5 h. The reaction mixture was filtered through a short pad of Celite with diethyl ether (100 mL), concentrated *in vacuo*, and purified by column chromatography (elution with 10% diethyl ether in petroleum ether). This gave 8-chloro-5-(2′,2′-dichloromethylcarbonylamino)-2,3,4,5-tetrahydrobenzoxepine (**21**) (0.102 g, 94%) as a white solid. Mp 106−108 °C; IR (neat) 3263, 2936, 1670, 1561, 1479, 1284, 1223, 1213, 1080, 1042, 983, 952, 808 cm^{-1}; ^1H NMR (500 MHz, $CDCl_3$) δ 1.73−1.93 (m, 2H), 2.18−2.30 (m, 2H), 3.76 (td, *J* = 12.0, 2.0 Hz, 1H), 4.38 (dt, *J* = 12.0, 1.1 Hz, 1H), 5.16 (ddd, *J* = 7.8, 6.2, 1.6 Hz, 1H), 5.94 (s, 1H), 7.05 (dd, *J* = 8.0, 2.1 Hz, 1H), 7.07 (d, *J* = 2.1 Hz, 1H), 7.17 (d, *J* = 8.0 Hz, 1H), 7.20 (d, *J* = 7.8 Hz, 1H); ^{13}C NMR (126 MHz, $CDCl_3$) δ 26.4 (CH_2), 29.8 (CH_2), 53.2 (CH), 66.5 (CH), 74.1 (CH_2), 122.9 (CH), 124.6 (CH), 130.3 (CH), 132.3 (C), 134.5 (C), 160.1 (C), 163.0 (C); MS (ESI) *m*/*z* 330 (MNa^+, 100); HRMS (ESI) calcd for $C_{12}H_{12}{}^{35}Cl_3NNaO_2$ (MNa^+), 329.9826, found 329.9812.

5-*N*,*N*′-Bis(*tert*-butoxycarbonyl)guanidino-8-chloro-2,3,4,5-tetrahydro-1-benzoxepine (23). A solution of 8-chloro-5-(2′,2′-dichloromethylcarbonylamino)-2,3,4,5-tetrahydro-1-benzoxepine (**21**) (0.067 g, 0.219 mmol) was dissolved in methanol (1 mL) and added to 6 M hydrochloric acid (10 mL). The reaction mixture was heated at 100 °C for 144 h. The methanol was removed *in vacuo*, and the aqueous layer was extracted with diethyl ether (3 × 10 mL). The remaining aqueous layer was basified by adding sodium carbonate solution and extracted with diethyl ether (3 × 10 mL). The combined organic extracts were concentrated to afford 5-amino-8-chloro-2,3,4,5-tetrahydro-1-benzoxepine (0.033 g) as a white solid. This was used in the next step without further purification. Diisopropylethylamine (0.237 mL, 1.40 mmol) and *N*,*N*′-bis(*tert*-butoxycarbonyl-1*H*-pyrazole-1-carboxamidine (**22**) (0.079 g, 0.260 mmol) were added to a solution of 5-amino-8-chloro-2,3,4,5-tetrahydro-1-benzoxepine (0.033 g, 0.170 mmol) in methanol (10 mL) and stirred for 48 h at room temperature. The methanol was removed *in vacuo*. The resulting residue was dissolved in diethyl ether (10 mL) and acidified by 0.2 M hydrochloric acid (1 mL). The solution was washed with water (10 mL), brine (10 mL), dried ($MgSO_4$), and concentrated *in vacuo*. Purification by column chromatography (elution with 7% diethyl ether in petroleum ether) gave 5-*N*,*N*′-bis(*tert*-butoxycarbonyl)guanidino-8-chloro-2,3,4,5-tetrahydro-1-benzoxpine (**23**) (0.071 g, 75%) as a white solid. Mp 169−171 °C (decomposition); IR (neat) 3321, 2981, 1722, 1637, 1612, 1560, 1479, 1412, 1324, 1227, 1154, 1124, 1057, 909, 732 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$) δ 1.48 (s, 9H), 1.50 (s, 9H), 1.72−1.80 (m, 1H), 1.85−1.93 (m, 1H), 2.15−2.27 (m, 2H), 3.80 (ddd, *J* = 12.0, 10.1, 2.1 Hz, 1H), 4.31 (dt, *J* = 12.0, 4.2 Hz, 1H), 5.50 (ddd, *J* = 9.0, 6.6, 2.0 Hz, 1H), 7.02 (dd, *J* = 8.1, 2.1 Hz, 1H), 7.05 (d, *J* = 2.1 Hz, 1H), 7.24 (d, *J* = 8.1 Hz, 1H), 9.01 (d, *J* = 9.0 Hz, 1H), 11.46 (s, 1H); ^{13}C NMR (101 MHz, $CDCl_3$) δ 26.9 (CH_2), 28.1 (3 × CH_3), 28.3 (3 × CH_3), 30.4 (CH_2), 52.5 (CH), 73.9 (CH_2), 79.2 (C), 83.1 (C), 122.7 (CH), 124.1 (CH), 130.5 (CH), 133.1 (C), 133.8 (C), 153.0 (C), 155.1 (C), 160.3 (C), 163.7 (C); MS (EI) *m*/*z* 439 (M^+, 10), 383 (8), 327 (63), 266 (35), 196 (11), 181 (24), 82 (44), 59 (100); HRMS (EI) calcd for $C_{21}H_{30}{}^{35}ClN_3O_5$ (M^+), 439.1874, found 439.1873.

8-Chloro-5-guanidino-2,3,4,5-tetrahydro-1-benzoxepine trifluoroacetic acid (4). A solution of 5-*N*,*N*′-bis(*tert*-butoxycarbonyl)-guanidino-8-chloro-2,3,4,5-tetrahydro-1-benzoxpine (**23**) (0.012 g, 0.027 mmol) in dichloromethane (0.450 mL) and trifluoroacetic acid (0.011 mL, 0.140 mmol) was stirred at 45 °C for 48 h. The reaction mixture was concentrated *in vacuo* to afford 8-chloro-5-guanidino-2,3,4,5-tetrahydro-1-benzoxepine trifluoroacetic acid (**4**) (0.007 g, 100%) as a white solid. Mp 229−231 °C (decomposition); IR (neat) 3364, 3160, 2925, 1679, 1613, 1481, 1201, 1187, 1144, 972, 843, 801, 724 cm^{-1}; ^1H NMR (400 MHz, CD_3OD) δ 1.96−2.16 (m,

DOI: 10.1021/acs.joc.5b00583
J. Org. Chem. 2015, 80, 4683−4696

4H), 4.00 (ddd, J = 9.6, 5.2, 2.4 Hz, 1H), 4.07 (ddd, J = 9.6, 5.6, 2.8 Hz, 1H), 4.84 (t, J = 4.0 Hz, 1H), 7.08 (d, J = 2.1 Hz, 1H), 7.12 (dd, J = 8.2, 2.1 Hz, 1H), 7.21 (d, J = 8.2 Hz, 1H); ^{13}C NMR (101 MHz, CD_3OD) δ 27.2 (CH_2), 31.2 (CH_2), 53.7 (CH), 73.1 (CH_2), 122.4 (CH), 123.8 (CH), 128.1 (CH), 132.5 (C), 133.9 (C), 156.5 (C), 159.7 (C); MS (ESI) m/z 240 (MH^+, 25); HRMS (ESI) calcd for $C_{11}H_{15}{}^{35}ClN_3O$ (MH^+), 240.0898, found 240.0902.

(3*R,4*S**,5*S**)-3,4-Dihydroxy-6-methoxy-5-(2′,2′,2′-trichloromethylcarbonylamino)-2,3,4,5-tetrahydro-1-benzoxepine (24).** Tetramethylethylenediamine (0.019 mL, 0.13 mmol) was added to a solution of 6-methoxy-5-(2′,2′,2′-trichloromethylcarbonylamino)-2,5-dihydro-1-benzoxepine (**11b**) (0.039 g, 0.12 mmol) in dichloromethane (2 mL) and cooled to −78 °C. After 0.2 h, a solution of osmium tetroxide (0.032 g, 0.13 mmol) in dichloromethane (1 mL) was added dropwise. The solution was stirred at −78 °C for 1 h, allowed to return to room temperature over 2 h, then concentrated *in vacuo*. The residue was taken up in a solution of methanol (4 mL) and 12 M hydrochloric acid (0.5 mL) and stirred at room temperature for 2 h. The reaction mixture was concentrated *in vacuo*. The resulting residue was purified by column chromatography (elution with 50% ethyl acetate in petroleum ether) to yield (3*R**,4*S**,5*S**)-3,4-dihydroxy-6-methoxy-5-(2′,2′,2′-trichloromethylcarbonylamino)-2,3,4,5-tetrahydro-1-benzoxepine (**24**) (0.032 g, 74%) as a colorless oil. IR (neat) 3464, 3417, 2928, 1711, 1505, 1473, 1249, 1086, 820 cm^{-1}; ^{1}H NMR (500 MHz, $CDCl_3$) δ 2.72 (s, 1H), 2.95 (s, 1H), 3.68 (t, J = 12.4 Hz, 1H), 3.85 (s, 3H), 4.16−4.26 (m, 2H), 4.50 (dd, J = 6.6, 4.0 Hz, 1H), 6.01 (dd, J = 8.4, 6.6 Hz, 1H), 6.72 (d, J = 8.2 Hz, 1H), 6.75 (d, J = 8.2 Hz, 1H), 7.27 (t, J = 8.2 Hz, 1H), 7.31 (d, J = 8.4 Hz, 1H); ^{13}C NMR (126 MHz, $CDCl_3$) δ 47.5 (CH), 56.4 (CH_3), 68.4 (CH), 69.0 (CH), 71.2 (CH_2), 92.5 (C), 107.9 (CH), 114.4 (CH), 117.3 (C), 130.8 (CH), 158.9 (C), 160.2 (C), 161.7 (C); MS (ESI) m/z 392 (MNa^+, 100); HRMS (ESI) calcd for $C_{13}H_{14}{}^{35}Cl_3NNaO_5$ (MNa^+), 391.9830, found 391.9818.

(3*S,4*S**,5*S**)-7-Chloro-3,4-dihydroxy-5-(2′,2′,2′-trichloromethylcarbonylamino)-2,3,4,5-tetrahydro-1-benzoxepine (26).** 3-Chloroperbenzoic acid (0.10 g, 0.59 mmol) was added to a stirred solution of 7-chloro-5-(2′,2′,2′-trichloromethylcarbonylamino)-2,5-dihydro-1-benzoxepine (**11g**) (0.050 g, 0.15 mmol) in dichloromethane (3 mL) at 0 °C. The reaction mixture was stirred and allowed to warm from 0 °C to room temperature over 18 h, then cooled to 0 °C before 3-chloroperbenzoic acid (0.10 g, 0.59 mmol) was added. The reaction mixture was stirred for a further 24 h, quenched by the addition of a saturated solution of sodium sulfite (5 mL), and extracted with dichloromethane (2 × 5 mL). The combined organic layers were washed with a saturated solution of sodium hydrogen carbonate (3 × 10 mL), water (10 mL), and brine (10 mL), then dried ($MgSO_4$), filtered, and concentrated *in vacuo*. This gave a crude mixture containing (3*R**,4*S**,5*S**)-7-chloro-3,4-epoxy-5-(2′,2′,2′-trichloromethylcarbonylamino)-2,3,4,5-tetrahydro-1-benzoxepine (**25**) which was used in the next step without further purification. 1.0 M Sulfuric acid (2 mL) was added to a solution of the crude mixture containing (3*R**,4*S**,5*S**)-7-chloro-3,4-epoxy-5-(2′,2′,2′-trichloromethylcarbonylamino)-2,3,4,5-tetrahydro-1-benzoxepine (**25**) in 1,4-dioxane (2 mL) and stirred at room temperature for 48 h. The reaction was quenched by addition of a saturated solution of sodium hydrogen carbonate (3 mL) and extracted with diethyl ether (2 × 10 mL). The organic layer was washed with water (10 mL), brine (10 mL), then dried ($MgSO_4$), filtered, and concentrated *in vacuo*. Purification by column chromatography (elution with 50% ethyl acetate in petroleum ether) gave (3*S**,4*S**,5*S**)-7-chloro-3,4-dihydroxy-5-(2′,2′,2′-trichloromethylcarbonylamino)-2,3,4,5-tetrahydro-1-benzoxepine (**26**) (0.031 g, 57%) as a white foam. IR (neat) 3404, 2927, 1696, 1507, 1482, 1228, 1081, 823 cm^{-1}; ^{1}H NMR (400 MHz, $CDCl_3$) δ 2.70 (d, J = 3.7 Hz, 1H), 3.33 (d, J = 5.3 Hz, 1H), 3.76 (dd, J = 12.3, 8.4 Hz, 1H), 3.85−3.92 (m, 1H), 4.07 (ddd, J = 11.7, 8.4, 3.6 Hz, 1H), 4.35 (dd, J = 12.3, 3.6 Hz, 1H), 5.33 (dd, J = 8.0, 1.5 Hz, 1H), 7.02−7.10 (m, 1H), 7.27−7.31 (m, 2H), 7.35 (d, J = 8.0 Hz, 1H); ^{13}C NMR (126 MHz, $CDCl_3$) δ 57.1 (CH), 71.1 (CH), 73.9 (CH_2), 75.8 (CH), 92.3 (C), 123.9 (CH), 129.7 (CH), 130.5 (C), 130.6 (C), 130.7 (CH), 157.3 (C), 163.2 (C); MS (ESI) m/z 396 (MNa^+, 100); HRMS (ESI) calcd for $C_{12}H_{11}{}^{35}Cl_4NNaO_4$ (MNa^+), 395.9334, found 395.9321.

■ ASSOCIATED CONTENT

Supporting Information

NOE data for compounds **24**−**26** and ^{1}H and ^{13}C NMR spectra for all compounds. This material is available free of charge via the Internet at http://pubs.acs.org.

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Notes

The authors declare no competing financial interest.

■ ACKNOWLEDGMENTS

Financial support from the EPSRC (studentship to E.D.D.C., EP/P505534/1), the Scottish Funding Council (studentship to F.I.M.), MSD, the Ministry of Higher Education and Scientific Research and the University of Benghazi, Libya (studentship to S.A.I.S.) is gratefully acknowledged.

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DOI: 10.1021/acs.joc.5b00583
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