JOC*Article*

Synthesis of Substituted Benzoxacycles via a Domino Ortho-Alkylation/Heck Coupling Sequence

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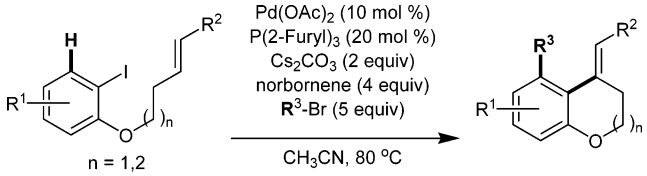
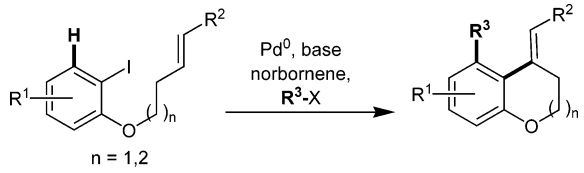


The synthesis of a variety of alkylidene benzoxacycles via a domino palladium-catalyzed ortho-alkylation/intramolecular Heck reaction is described. Under the optimized conditions [$Pd(OAc)_2$ (10 mol %), P(2-Furyl)$_3$ (20 mol %), norbornene (4 equiv), Cs_2CO_3 (2 equiv), CH_3CN, 80 °C], aryl iodides with oxygen-tethered Heck acceptors are coupled with alkyl bromides (5 equiv) to generate a variety of six- and seven-membered-ring benzoxacyclic products.

Introduction

Chromans (2,3-dihydrobenzopyrans) and benzoxepines represent families of oxygen-containing natural products that demonstrate activity toward a variety of biological targets.[1] Structure activity relationships of these compounds have been studied;[2] however, the effect of substituents on the aromatic ring remains to be fully explored. We sought to develop a method that could efficiently prepare substituted chromans and benzoxepines in a direct way. Domino[3] palladium catalysis[4] represents a class of reaction that can fulfill this objective. Herein we describe that the norbornene-mediated, palladium-catalyzed domino ortho-alkylation/Heck reaction initially reported by Catellani[5] and further developed in our laboratories[6] can be applied to the synthesis of chromen-4-ylidenes and 1-benzoxepin-5-ylidenes (Scheme 1). The modularity of this reaction can be demonstrated by employing a variety of alkyl halides (**R**^{3}-X) and aryl iodides containing ortho oxygen-tethered Heck acceptors (**1**). This approach is particularly interesting as it forms

SCHEME 1. Tandem Ortho-Alkylation/Heck Approach toward Benzoxacycles



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(1) Chromans are typically found as the core of the tocopherols, most importantly Vitamin E (α-tocopherol). For the subtype-specific translocation and activation of diacylglycerol kinase α by D-α-tocopherol, see: (a) Fukunaga-Takenaka, R.; Shirai, Y.; Yagi, K.; Adachi, N.; Sakai, N.; Merino, E.; Merida, I.; Saito, N. *Genes Cells* **2005**, *10*, 311−319. For the inhibition of LPS-induced nitric oxide production by chromans, see: (b) Kim, B.-H.; Reddy, A. M.; Lee, K.-H.; Chung, E. Y.; Cho, S. M.; Lee, H.; Min, K. R.; Kim, Y. *Biochem. Biophys. Res. Commun.* **2004**, *325*, 223−228. For the use of chromans in the treatment of cancer and inflammation, see: (c) Salvatore, B. A.; Solis, F. C. WO 2004103985, 2004. For the use of chromans as antiinflammatory agents, see: (d) Salman, M.; Arora, P. K.; Ray, S.; Srimal, R. C. *Indian J. Pharm. Sci.* **1987**, *49*, 43−47. For the use of 1-benzoxepines as inhibitors of farnesyl protein transferase, see: Wolin, R.; Connolly, M.; Kelly, J.; Weinstein, J.; Rosenblum, S.; Afonso, A.; James, L.; Kirschmeier, P.; Bishop, W. R. *Biorg. Med. Chem. Lett.* **1998**, *8*, 2521−2526.

(2) As kappa opioid receptor agonists, see: (a) Chu, G.-H.; Gu, M.; Cassel, J. A.; Belanger, S.; Graczyk, T. M.; DeHaven, R. N.; Conway-James, N.; Koblish, M.; Little, P. J.; DeHaven-Hudkins, D. L.; Dolle, R. E. *Bioorg. Med. Chem. Lett.* **2005**, *15*, 5114−5119. As estrogen receptor ligands, see: (b) Tan, Q.; Blizzard, T. A.; Morgan, J. D.; Birzin, E. T.; Chan, W.; Yang, Y. T.; Pai, L.-Y.; Hayes, E. C.; DaSilva, C. A.; Warrier, S.; Yudkovitz, J.; Wilkinson, H. A.; Sharma, N.; Fitzgerald, P. M. D.; Li, S.; Colwell, L.; Fisher, J. E.; Adamski, S.; Reszka, A. A.; Kimmel, D.; DiNinno, F.; Rohrer, S. P.; Freedman, L. P.; Schaeffer, J. M.; Hammond, M. L. *Bioorg. Med. Chem. Lett.* **2005**, *15*, 1675−1681. For redox inactivation of human 15-lipoxygenase, see: (c) Cichewicz, R. H.; Kenyon, V. A.; Whitman, S.; Morales, N. M.; Arguello, J. F.; Holman, T. R.; Crews, P. *J. Am. Chem. Soc.* **2004**, *126*, 14910−14920. As novel pesticides, see: (d) Yang, G.; Jiang, X.; Yang, H. *Pest Manage. Sci.* **2002**, *58*, 1063−1067. As nicotine agonists, see: (e) Efange, S. M. N.; Tu, Z.; von Hohenberg, K.; Francesconi, L.; Howell, R. C.; Rampersad, M. V.; Todaro, L. J.; Papke, R. L.; Kung, M.-P. *J. Med. Chem.* **2001**, *44*, 4704−4715. As IKs channel blockers, see: (f) Gerlach, U.; Brendel, J.; Lang, H.-J.; Paulus, E. F.; Weidmann, K.; Brueggemann, A.; Busch, A. E.; Suessbrich, H.; Bleich, M.; Greger, R. *J. Med. Chem.* **2001**, *44*, 3831−3837.

10.1021/jo060552l CCC: $33.50
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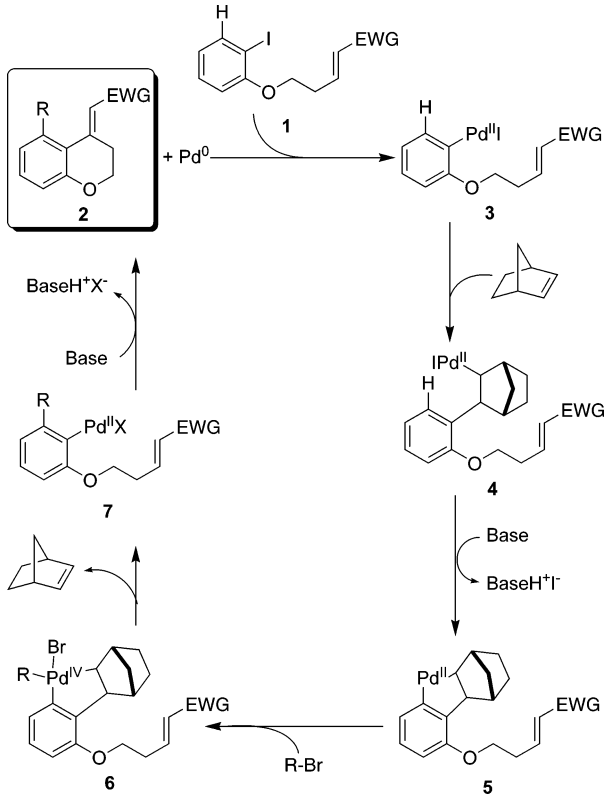
SCHEME 2. Proposed Reaction Mechanism



a 1,2,3-trisubstituted aromatic, which would be difficult to access via classical methods. Our previous studies suggest that the ortho-alkylation step benefits from the presence of electron-donating groups on the aryl iodide.[6b,d] This approach would thus benefit from electron-rich phenol-based systems.

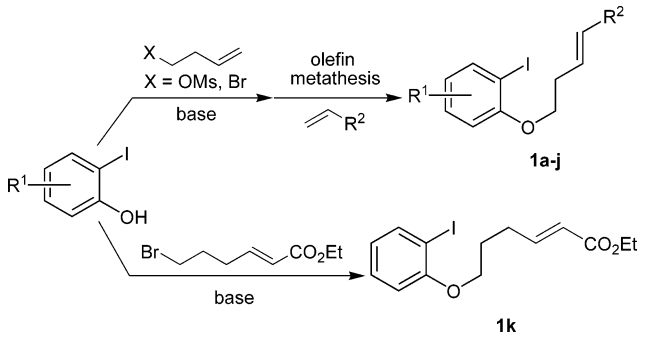
The proposed mechanism and catalytic cycle (Scheme 2), based upon the findings of Catellani and Pregosin,[5b] begins with the oxidative addition of Pd(0) to **1**, forming arylpalladium(II) species **3**. Carbopalladation of norbornene forms species **4**, followed by ortho C−H activation to generate palladacycle **5**. An alkyl bromide oxidatively adds to **5**, giving Pd(IV) species **6**. Reductive elimination of **6** forms a $C(sp^3)-C(sp^2)$ bond, and subsequent extrusion of norbornene generates **7**, which further undergoes an intramolecular Heck reaction to afford **2**.

Results and Discussion

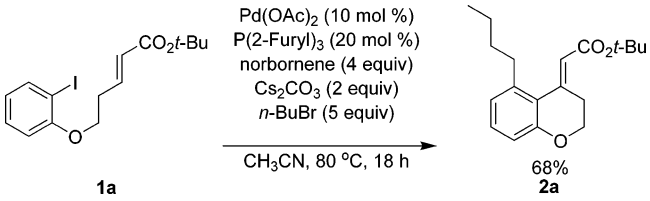
To create an efficient route toward the desired benzoxacycles, cyclization precursors should be accessible through common transformations with use of commercially available starting materials. For the most part, the substrates were attained through a two-step alkylation/olefin metathesis (n = 1), or direct alkylation with ethyl 6-bromohex-2-enoate (n = 2) (Scheme 3).

Synthesis of Chromen-4-ylidenes. (a) Optimization. With substrate **1a** in hand, the synthesis of chromen-4-ylidenes was explored. On the basis of the proposed reaction mechanism (Scheme 2), a suitable catalytic Pd^0 source,[7] norbornene, base, and alkyl halide are required. Through the examination of

SCHEME 3. Generalized Preparation of Cyclization Precursors



SCHEME 4. Optimized Reaction Conditions



palladium sources and phosphine ligands, we found that $Pd(OAc)_2$ and tri(2-furyl)phosphine[8] in acetonitrile was the ideal catalyst system. Screening of inorganic bases found Cs_2CO_3 to be optimal. Testing different alkyl halides, we found that alkyl bromides performed better than alkyl iodides, and that alkyl chlorides were inert to the reaction conditions. Substrate concentration had a small effect on the yield, and 0.35 M **1a** in CH_3CN was optimal. Varying the equivalents of each reagent led to the optimized conditions shown in Scheme 4. Finally, it was found that the order and the timing of addition of reagents were crucial to the efficiency of the reaction. We observed that the best yields were obtained if $Pd(OAc)_2$ and tri(2-furyl)-phosphine were added together and pre-stirred in CH_3CN for 10 to 15 minites under $N_{2(g)}$ until a homogeneous solution was obtained, followed by addition of Cs_2CO_3, norbornene, and a mixture of alkyl halide and aryl iodide in CH_3CN. The reaction vessel was then flushed with $N_{2(g)}$ and heated to 80 °C. Omitting the pre-stirring of the catalyst generally gave yields 5% to 10% lower, while under "open flask" conditions, yields were generally 30% lower. Under the optimized conditions, using *n*-BuBr as alkyl halide, **2a** was obtained in 68% yield, as solely the *E* isomer, as determined by 2D-ROESY experiments. Formation of the desired product and avoiding the "Heck-only" product indicates that the intermolecular ortho-alkylation reaction is

(3) Tietze, L. F. *Chem. Rev.* **1996**, *96*, 115−136.

(4) (a) Negishi, E. *Handbook of Organopalladium Chemistry for Organic Synthesis*; Negishi, E., Ed.; Wiley: New York, 2002. (b) Tsuji, J. *Palladium Reagents and Catalysts*: *New Perspectives for the 21st Century*; Tsuji, J., Ed.; Wiley: New York, 2004.

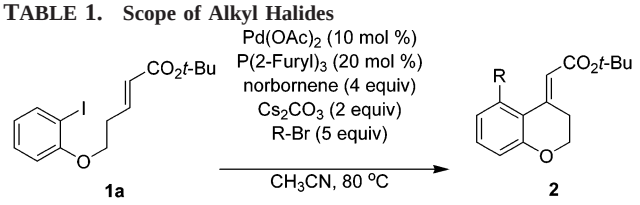
(5) (a) Catellani, M.; Frignani, F.; Rangoni, A. *Angew. Chem., Int. Ed. Engl.* **1997**, *36*, 119−122. (b) Catellani, M.; Mealli, C.; Motti, E.; Paoli, P.; Perez-Carreno, E.; Pregosin, P. S. *J. Am. Chem. Soc.* **2002**, *124*, 4336−4346. (c) Catellani, M. *Synlett* **2003**, 298−313. (d) Catellani, M. *Top. Organomet. Chem.* **2005**, *14*, 21−53.

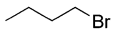
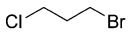
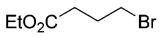
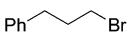
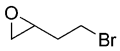
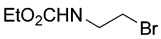
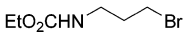
(6) (a) Lautens, M.; Piguel, S. *Angew. Chem., Int. Ed.* **2000**, *39*, 1045−1046. (b) Lautens, M.; Paquin, J.-F.; Piguel, S.; Dahlmann, M. *J. Org. Chem.* **2001**, *66*, 8127−8134. (c) Lautens, M.; Paquin, J.-F.; Piguel, S. *J. Org. Chem.* **2002**, *67*, 3972−3974. (d) Pache, S.; Lautens, M. *Org. Lett.* **2003**, *5*, 4827−4830. (e) Alberico, D.; Paquin, J.-F.; Lautens, M. *Tetrahedron* **2005**, *61*, 6283−6297. (f) Bressy, C.; Alberico, D.; Lautens, M. *J. Am. Chem. Soc.* **2005**, *127*, 13148−13149. (g) Wilhelm, T.; Lautens, M. *Org. Lett.* **2005**, *7*, 4053−4056.

(7) For investigations into "Pd^0" formation from Pd^{II} salts, see: (a) Amatore, C.; Jutand, A. *J. Organomet. Chem.* **1999**, *576*, 254−278. (b) Amatore, C.; Jutand, A. *Acc Chem. Res.* **2000**, *33*, 314−321.

(8) For a review of the use of tri(2-furyl)phosphine in transition metal mediated reactions, see: Andersen, N. G.; Keay, B. G. *Chem. Rev.* **2001**, *101*, 997−1030.

TABLE 1. Scope of Alkyl Halides



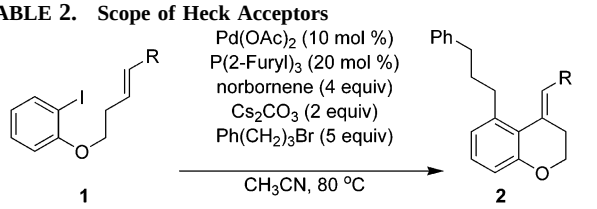
entry	R-Br	product	isolated yield (%)
1		**2a**	68
2		**2b**	80
3		**2c**	71
4		**2d**	96
5		**2e**	50
6		**2f**	75
7		**2g**	70

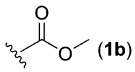
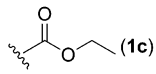
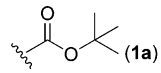
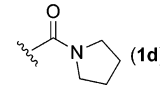
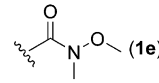
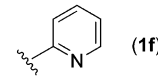
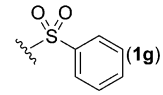
faster than an intramolecular 6-*exo-trig* Heck reaction under these reaction conditions. It should also be noted that when the analogous reaction was attempted with the intent of making 4-substituted benzofurans (n = 0), only intramolecular Heck product was obtained, with no ortho-alkylation observed.

(b) Scope of Alkyl Halides. The scope of the reaction was explored through variation of the alkyl halides used (Table 1). We elected to introduce *n*-alkyl chains containing remote reactive functional groups as potential handles for product elaboration. As mentioned above, alkyl chlorides were inert to the reaction conditions, thus introduction of a chloroalkyl chain by using 1-bromo-3-chloropropane was accomplished, affording product **2b** in 80% yield (entry 2). Furthermore, esters can be incorporated, as **2c** was obtained in 71% yield (entry 3). This reaction affords two easily differentiated ester moieties. When a phenyl ring was included at the 3-position of the alkyl bromide, **2d** was obtained in 96% yield (entry 4). Introduction of an epoxyalkyl chain, such as in **2e** (entry 5), is particularly interesting, as epoxides can undergo a variety of reactions.[9] Finally, the incorporation of nitrogen-containing side chains was demonstrated as **2f** and **2g** were synthesized in 75% and 70% yields, respectively (entries 6 and 7). These cases demonstrate that the ortho-alkylation and intramolecular Heck reactions are faster than aryl amination (either intramolecular or intermolecular), which is known to proceed under similar reaction conditions.[10]

(c) Scope of Heck Acceptors. In an effort to further demonstrate the flexibility of this approach, a variety of Heck acceptors were examined. As 1-bromo-3-phenylpropane afforded the best results during the screening of alkyl halides, it was used to examine the scope of Heck acceptors (Table 2). With alkyl esters as electron withdrawing groups (entries 1−3), it was observed that the lability of the ester factored into the product yield. Methyl ester **1b** afforded **2h** in 74% yield, whereas more stable ethyl and *tert*-butyl esters afforded **2i** and **2d** in 90% and 96% yields, respectively. Next, Heck acceptors

TABLE 2. Scope of Heck Acceptors



entry	R	product	isolated yield (%)
1	 (**1b**)	**2h**	74
2	 (**1c**)	**2i**	90
3	 (**1a**)	**2d**	96
4	 (**1d**)	**2j**	65
5	 (**1e**)	**2k**	75
6	 (**1f**)		trace
7	 (**1g**)		trace

containing a nitrogen atom were examined (entries 4 and 5). Amide **1d** afforded product **2j** in 65% yield, with significant amounts of "Heck-only" product observed. The synthetically useful Weinreb amide[11] **1e** afforded the desired product **2k** in 75% yield with no direct Heck reaction product observed. When Heck acceptors containing strongly Lewis basic functionalities were tried, such as in entries 6 and 7, only traces of product were observed. The low yield with **1f** may be attributed to catalyst poisoning by the pyridyl nitrogen, as this was one of the only cases where starting material was recovered. For vinyl sulfone **1g**, the Lewis basicity of sulfones may have led to catalyst poisoning, or other reactions[12] of phenyl vinyl sulfones under Pd-catalysis may have formed undesired products, although no such products could be isolated and identified.

(d) Aromatic Substitution. Aromatic substituents can have a profound effect on the rates of oxidative addition and carbopalladation, and thus can greatly affect the catalytic cycle. As previously mentioned, the ortho-alkylation reaction benefits from electron-rich aromatic rings, so methoxy-substituted **1h** was subjected to the reaction conditions (Scheme 5) and afforded **2l** in 55% yield. This lower than expected yield may be attributed to a slower rate of oxidative addition to **1h**,[13] or to the effect of steric crowding by the methoxy substituent. Conversely, electron-poor species **1i** gave **2m** in 74% yield, showing that electron-withdrawing groups are tolerated. In

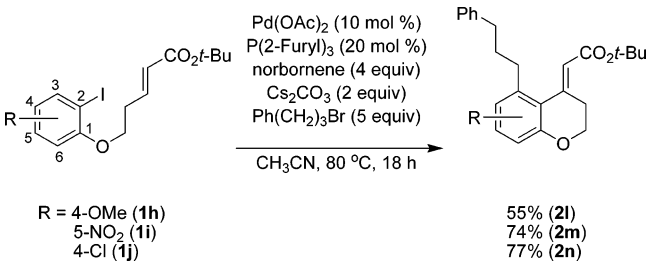
(9) Hassner, A. In *Heterocyclic Compounds*; Vol. 42, Part 3, Small Ring Heterocycles; Hassner, A., Ed.; John Wiley & Sons: Toronto, Canada, 1985; pp 3−152.

(10) We have preliminary results for a domino ortho-alkylation/aromatic amination reaction.

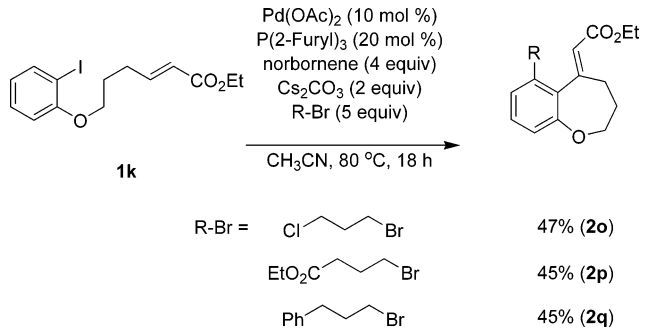
(11) For synthetic applications of Weinreb amides, see: (a) Sibi, M. P. *Org. Prep. Proc. Int.* **1993**, *25*, 15−42. (b) Keck, G. E.; McHardy, S. F.; Murry, J. A. *Tetrahedron Lett.* **1993**, *34*, 6215−6218.

(12) Mauleón, P.; Alonso, I.; Carretero, J. C. *Angew. Chem., Int. Ed.* **2001**, *40*, 1291−1293.

SCHEME 5. Aromatic Substitution



SCHEME 6. Synthesis of 1-Benzoxepin-5-ylidenes



addition, the nitro group can act as a precursor to a variety of transformations.[14] Finally, the presence of an aryl halide was examined. Our previous work demonstrated that extraneous I, Br, and OTf aromatic substitutents were not tolerated under the reaction conditions;[6b] thus an aromatic Cl was tried. Gratifyingly, aryl chlorides are inert to the reaction conditions, and **2n** was isolated in 77% yield. This is a useful result, as the aryl chloride can serve as a functional handle for a variety of recently developed cross-coupling reactions.[15]

Synthesis of 1-Benzoxepin-5-ylidenes. Our final effort was placed upon the synthesis of seven-membered rings through the intramolecular Heck reaction. Our previous efforts demonstrated success synthesizing benzoxepinylidenes;[6c] however, benzoxepines with phenolic oxygens could not be accessed by that method. This method provides access to a different family of benzoxepines with a different substitution pattern. With use of the optimized conditions listed in Scheme 3, **1k** was used to synthesize several 1-benzoxepin-5-ylidenes (Scheme 6). Yields were generally lower than those for the chromanylidene analogues; however, there was greater uniformity of isolated yield with a variety of alkyl halides.

Conclusion

We have developed a concise route toward the synthesis of alkylidene benzoxacyclic products. This method utilizes palladium-catalyzed ortho-alkylation with an intramolecular Heck reaction as the ring-forming step. In this sequence, two carbon−carbon bonds are formed in one pot, one from an unactivated aryl C−H bond. For six- and seven-membered rings, the intramolecular Heck reaction was slow enough for the reaction to proceed smoothly in the desired sequence. The modularity of this reaction was demonstrated by the variety of chroman-4-ylidenes and 1-benzoxepin-5-ylidenes which could be synthesized through variation of the alkyl halide and Heck acceptor moieties.

Experimental Section

The following represents experimental procedures toward the synthesis of products **2a**−**q**. This includes experimental details and characterization data for the aforementioned compounds. The information for all other compounds can be found in the Supporting Information.

General Procedure. In a round-bottom flask with a fused, water-cooled condenser were combined $Pd(OAc)_2$ (7.80 mg, 0.0350 mmol, 10 mol %) and P(2-Furyl)$_3$ (16.2 mg, 0.0700 mmol, 20 mol %), then the flask was capped and flushed with $N_{2(g)}$. Dry CH_3CN (0.5 mL) was added, and the mixture was stirred for 10−15 minutes at room temperature, until a homogeneous, orange-red solution was obtained. Next, Cs_2CO_3 (228 mg, 0.700 mmol, 2 equiv) was added, and the solution turned a dark brown color. Norbornene (132 mg, 1.40 mmol, 4 equiv) was added, followed by a mixture of **1** (0.350 mmol) and alkyl bromide (1.75 mmol, 5 equiv) in CH_3CN (0.5 mL). The system was capped, flushed with $N_{2(g)}$, and then stirred at 80 °C for 18 h. The mixture was quenched with 10 mL of saturated $NH_4Cl_{(aq)}$ and extracted with 3 × 10 mL of Et_2O. The combined organic phases were dried over $MgSO_4$, filtered, and concentrated in vacuo. The crude mixture was then purified by flash chromatography on silica gel to afford product **2**.

***tert*-Butyl (2*E*)-(5-Butyl-2,3-dihydro-4*H*-chromen-4-ylidene)-acetate (2a).** Following the general procedure, **1a** (80.0 mg, 0.210 mmol) and 1-bromobutane (113 μL, 1.05 mmol) were reacted. The crude mixture was purified by flash chromatography on silica gel (R_f 0.42 in 10% Et_2O/hexane), using 0−10% Et_2O/hexane, to afford product **2a** as a viscous, clear oil. Isolated yield: 43 mg (68%). ^{1}H NMR (300 MHz, $CDCl_3$) δ 0.96 (t, J = 7.3 Hz, 3H), 1.37−1.44 (m, 2H), 1.51 (s, 9H), 1.59−1.67 (m, 2H), 2.73−2.80 (m, 2H), 3.36 (td, J = 6.1, 1.2 Hz, 2H), 4.23−4.29 (m, 2H), 5.96 (s, 1H), 6.67 (dd, J = 8.2 1.2 Hz, 1H), 6.81 (dd, J = 7.6, 1.2 Hz, 1H), 7.09−7.15 (m, 1H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 13.8, 22.6, 27.5, 28.3, 32.9, 33.9, 66.7, 80.1, 114.6, 118.1, 122.9, 129.8, 141.3, 147.2, 156.6, 166.2; IR neat, ν (cm^{-1}) 734 (m), 753 (m), 861 (w), 885 (w), 1058 (m), 1144 (s), 1256 (m), 1367 (m), 1630 (m), 1707 (s), 2254 (w), 2872 (m), 2931 (m), 2959 (m); HRMS (EI) calcd for $C_{19}H_{26}O_3$ 302.1882 (M^+), found 302.1874.

***tert*-Butyl (2*E*)-[5-(3-Chloropropyl)-2,3-dihydro-4*H*-chromen-4-ylidene]acetate (2b).** Following the general procedure, **1a** (80.0 mg, 0.210 mmol) and 1-bromo-3-chloropropane (104 μL, 1.05 mmol) were reacted. The crude mixture was purified by flash chromatography on silica gel (R_f 0.40 in 10% Et_2O/hexane), using 0−10% Et_2O/hexane, to afford product **2b** as a viscous, clear oil. Isolated yield: 54 mg (80%). ^{1}H NMR (300 MHz, $CDCl_3$) δ 1.51 (s, 9H), 2.04−2.15 (m, 2H), 2.93−3.00 (m, 2H), 3.37 (t, J = 6.3 Hz, 2H), 3.57 (t, J = 6.5 Hz, 2H), 4.28 (t, J = 6.3 Hz, 2H), 5.96 (s, 1H), 6.70 (dd, J = 8.2, 1.1 Hz, 1H), 6.81 (dd, J = 7.7, 0.8 Hz, 1H), 7.14 (t, J = 8.0 Hz, 1H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 27.7, 28.5, 30.7, 34.3, 44.7, 67.1, 80.6, 115.4, 118.6, 123.1, 123.4, 130.2, 139.2, 147.2, 157.0, 166.2; IR neat, ν (cm^{-1}) 1076 (w), 1144 (s), 1249 (m), 1367 (m), 1448 (m), 1598 (w), 1632 (m), 1705 (s), 2976 (m); HRMS (EI) calcd for $C_{18}H_{23}ClO_3$ 322.1336 (M^+), found 322.1330.

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Ethyl 4-[(4*E*)-4-(2-*tert*-Butoxy-2-oxoethylidene)-3,4-dihydro-2*H*-chromen-5-yl]butanoate (2c). Following the general procedure, **1a** (131 mg, 0.350 mmol) and ethyl 4-bromobutyrate (252 μL, 1.75 mmol) were reacted. The crude mixture was purified by flash chromatography on silica gel (R_f 0.36 in 20% Et_2O/hexane), using 0−20% Et_2O/hexane, affording product **2c** as a clear, pale yellow oil. Isolated yield: 90 mg (71%). ^{1}H NMR (300 MHz, $CDCl_3$) δ 1.26 (t, J = 7.1 Hz, 3H), 1.52 (s, 9H), 1.90−2.01 (m, 2H), 2.34 (t, J = 7.4 Hz, 2H), 2.80−2.87 (m, 2H), 3.36 (t, J = 6.2 Hz, 2H), 4.13 (q, J = 7.1 Hz, 2H), 4.27 (t, J = 6.2 Hz, 2H), 5.92 (s, 1H), 6.69 (dd, J = 8.0, 1.1 Hz, 1H), 6.83 (d, J = 7.5 Hz, 1H), 7.13 (t, J = 8.0 Hz, 1H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 14.5, 26.8, 27.9, 28.5, 32.5, 34.1, 60.5, 67.0, 80.5, 115.2, 118.6, 122.9, 123.4, 130.1, 139.9, 147.3, 156.9, 166.3, 173.5; IR neat, ν (cm^{-1}) 734 (m), 861 (w), 885 (w), 1045 (m), 1078 (m), 1143 (s), 1250 (s), 1368 (s), 1447 (m), 1574 (m), 1598 (m), 1631 (m), 1705 (s), 1732 (s), 2876 (m), 2934 (m), 2977 (s), 3447 (w); HRMS (ESI) calcd for $C_{21}H_{29}O_5$ 361.2009 (M + H^+), found 361.2018.

***tert*-Butyl (2*E*)-[5-(3-Phenylpropyl)-2,3-dihydro-4*H*-chromen-4-ylidene]acetate (2d).** Following the general procedure, **1a** (187 mg, 0.500 mmol) and $Ph(CH_2)_3Br$ (380 μL, 2.50 mmol) were reacted. The crude mixture was purified by flash chromatography on silica gel (R_f 0.33 in 10% Et_2O/hexane), using 0−10% Et_2O/hexane, to afford product **2d** as a viscous, clear oil, slowly solidifying to a waxy, white solid with needlelike crystals (mp 42−45 °C). Isolated yield: 175 mg (96%). ^{1}H NMR (300 MHz, $CDCl_3$) δ 1.53 (s, 9H), 1.90−2.02 (m, 2H), 2.65−2.72 (m, 2H), 2.78−2.85 (m, 2 H), 3.34−3.39 (m, 2H), 4.26 (t, J = 6.1 Hz, 2H), 5.94 (s, 1H), 6.67 (dd, J = 8.1, 1.2 Hz, 1H), 6.81 (dd, J = 7.7, 1.1 Hz, 1H), 7.11 (t, J = 8.0 Hz, 1H), 7.15−7.22 (m, 3H), 7.24−7.32 (m, 2H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 27.8, 28.6, 33.3, 33.7, 36.1, 67.0, 80.5, 115.0, 118.3, 122.9, 123.2, 126.0, 128.6 (2 C), 130.1, 140.9, 142.3, 147.5, 156.9, 166.4; IR neat, ν (cm^{-1}) 695 (s), 760 (m), 794 (m), 861 (m), 883 (m), 944 (m), 1080 (s), 1140 (s), 1248 (s), 1311 (m), 1699 (s), 2971 (s); HRMS (ESI) calcd for $C_{24}H_{29}O_3$ 365.2111 (M + H^+), found 365.2124.

***tert*-Butyl (2*E*)-[5-(2-Oxiran-2-ylethyl)-2,3-dihydro-4*H*-chromen-4-ylidene]acetate (2e).** Following the general procedure, **1a** (131 mg, 0.350 mmol) and 2-(2-bromoethyl)oxirane (264 mg, 1.75 mmol) were reacted. The crude mixture was purified by flash chromatography on silica gel (R_f 0.55 in 10% Et_2O/hexane), using 0−5% Et_2O/hexane, affording product **2e** as a clear, pale yellow oil. Isolated yield: 55 mg (50%). ^{1}H NMR (400 MHz, $CDCl_3$) δ 1.52 (s, 9H), 1.79−1.96 (m, 2H), 2.53 (dd, J = 4.9, 2.7 Hz, 1H), 2.76−2.79 (m, 1H), 2.94−3.00 (m, 3H), 3.30−3.44 (m, 2H), 4.27 (t, J = 6.2 Hz, 2H), 5.94 (s, 1H), 6.70 (dd, J = 8.1, 1.1 Hz, 1H), 6.83 (dd, J = 7.7, 1.1 Hz, 1H), 7.13 (t, J = 7.9 Hz, 1H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 27.8, 28.5, 29.7, 34.5, 47.4, 52.0, 67.0, 80.6, 115.4, 118.5, 122.9, 123.2, 130.2, 139.6, 147.4, 157.0, 166.2; IR neat, ν (cm^{-1}) 750 (m), 858 (m), 1079 (m), 1144 (s), 1251 (m), 1367 (m), 1475 (m), 1574 (m), 1597 (m), 1633 (m), 1704 (s), 2975 (m); HRMS (EI) calcd for $C_{19}H_{24}O_4$ 316.1675 (M^+), found 316.1674.

***tert*-Butyl (2*E*)-(5-{2-[(Ethoxycarbonyl)amino]ethyl}-2,3-dihydro-4*H*-chromen-4-ylidene)acetate (2f).** Following the general procedure, **1a** (131 mg, 0.350 mmol) and ethyl 2-bromoethylcarbamate (343 mg, 1.75 mmol) were reacted. The crude mixture was purified by flash chromatography on silica gel (R_f 0.49 in 30% EtOAc/hexane), using 15−35% Et_2O/hexane, to afford product **2f** as a clear, pale yellow oil. Isolated yield: 95 mg (75%). ^{1}H NMR (300 MHz, $CDCl_3$) δ 1.19−1.27 (m, 3H), 1.52 (s, 9H), 3.04 (t, J = 7.1 Hz, 2H), 3.37 (t, J = 5.8 Hz, 2H), 3.41−3.51 (m, 2H), 4.11 (q, J = 7.0 Hz, 2H), 4.28 (t, J = 6.2 Hz, 2H), 4.64 (br s, 1H), 5.92 (s, 1H), 6.72 (d, J = 8.2 Hz, 1H), 6.83 (d, J = 7.4 Hz, 1H), 7.15 (t, J = 8.0 Hz, 1H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 14.7, 27.6, 28.3, 29.8, 33.2, 41.7, 60.8, 67.0, 80.5, 92.0, 107.2, 115.6, 118.7, 122.6, 130.1, 156.5, 156.8, 165.9; IR neat, ν (cm^{-1}) 778 (m), 942 (w), 1051 (m), 1145 (s), 1253 (s), 1367 (m), 1448 (m), 1534 (s), 1701 (s, br), 2933 (m), 2978 (m), 3337 (m, br); HRMS (EI) calcd for $C_{20}H_{27}NO_5$ 362.1967 (M^+), found 362.1964.

***tert*-Butyl (2*E*)-(5-{3-[(Ethoxycarbonyl)amino]propyl}-2,3-dihydro-4*H*-chromen-4-ylidene)acetate (2g).** Following the general procedure, **1a** (131 mg, 0.350 mmol) and ethyl 3-bromopropylcarbamate (368 mg, 1.75 mmol) were reacted. The crude mixture was purified by flash chromatography on silica gel (R_f 0.47 in 30% EtOAc/hexane), using 15−35% Et_2O/hexane, to afford product **2g** as a clear, pale yellow oil. Isolated yield: 92 mg (70%). ^{1}H NMR (400 MHz, $CDCl_3$) δ 1.24 (t, J = 6.9 Hz, 3H), 1.52 (s, 9H), 1.79−1.89 (m, 2H), 2.80−2.86 (m, 2H), 3.20−3.29 (m, 2H), 3.36 (t, J = 6.3 Hz, 2H), 4.11 (q, J = 6.9 Hz, 2H), 4.27 (t, J = 6.1 Hz, 2H), 4.65 (br s, 1H), 5.91 (s, 1H), 6.70 (d, J = 8.1 Hz, 1H), 6.81 (d, J = 7.2 Hz, 1H), 7.13 (t, J = 7.8 Hz, 1H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 14.7, 27.6, 28.3, 30.4, 31.7, 40.6, 60.7, 66.8, 80.4, 115.1, 118.1, 122.8, 123.0, 130.0, 139.7, 147.3, 156.7, 156.8, 166.0; IR neat, ν (cm^{-1}) 778 (m), 883 (m), 947 (w), 1039 (s), 1143 (s), 1250 (s), 1367 (s), 1537 (s), 1699 (s), 2977 (s), 3065 (w), 3334 (br, s); HRMS (ESI) calcd for $C_{20}H_{27}NO_5Na$ 398.1937 (M + Na^+), found 398.1952.

Methyl (2*E*)-[5-(3-Phenylpropyl)-2,3-dihydro-4*H*-chromen-4-ylidene]acetate (2h). Following the general procedure, **1b** (70.0 mg, 0.210 mmol) and $Ph(CH_2)_3Br$ (159 μL, 1.05 mmol) were reacted. The crude mixture was purified by flash chromatography on silica gel (R_f 0.36 in 10% Et_2O/hexane), using 0−10% Et_2O/hexane, to afford product **2h** as a viscous, clear oil. Isolated yield: 50 mg (74%). ^{1}H NMR (300 MHz, $CDCl_3$) δ 1.90−2.02 (m, 2H), 2.66−2.72 (m, 2H), 2.78−2.85 (m, 2H), 3.37−3.42 (m, 2H), 3.76 (s, 3H), 4.24−4.29 (m, 2H), 5.99 (s, 1H), 6.69 (dd, J = 8.2, 1.1 Hz, 1H), 6.82 (dd, J = 7.8, 1.1 Hz, 1H), 7.11−7.21 (m, 4H), 7.26−7.32 (m, 2H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 28.0, 33.2, 33.4, 36.0, 51.4, 66.9, 115.2, 115.9, 123.1, 126.0, 128.6, 128.7, 130.4, 142.1, 149.3, 157.0, 167.2; IR neat, ν (cm^{-1}) 700 (m), 753 (m), 787 (w), 878 (w), 1047 (w), 1081 (m), 1158 (s), 1250 (m), 1309 (m), 1353 (m), 1447 (m), 1474 (m), 1573 (m), 1597 (m), 1631 (m), 1714 (s), 2946 (m), 3024 (m); HRMS (ESI) calcd for $C_{21}H_{23}O_3$ 323.1641 (M + H^+), found 323.1642.

Ethyl (2*E*)-[5-(3-Phenylpropyl)-2,3-dihydro-4*H*-chromen-4-ylidene]acetate (2i). Following the general procedure, **1c** (118 mg, 0.340 mmol) and $Ph(CH_2)_3Br$ (258 μL, 1.70 mmol) were reacted. The crude mixture was purified by flash chromatography on silica gel (R_f 0.30 in 10% Et_2O/hexane), using 5−10% Et_2O/hexane, to afford product **2i** as a viscous, clear oil. Isolated yield: 103 mg (90%). ^{1}H NMR (400 MHz, $CDCl_3$) δ 1.33 (t, J = 7.1 Hz, 3H), 1.91−2.01 (m, 2H), 2.66−2.71 (m, 2H), 2.79−2.84 (m, 2H), 3.39 (t, J = 6.3 Hz, 2H), 4.21 (q, J = 7.0 Hz, 2H), 4.26 (t, J = 6.3 Hz, 2H), 6.00 (s, 1H), 6.68 (d, J = 8.3 Hz, 1H), 6.81 (d, J = 7.7 Hz, 1H), 7.13 (t, J = 7.9 Hz, 1H), 7.15−7.21 (m, 3H), 7.24−7.30 (m, 2H); ^{13} C NMR (100 MHz, $CDCl_3$) δ 14.5, 28.0, 33.2, 33.5, 36.0, 60.2, 66.9, 115.1, 116.4, 123.0, 126.0, 128.5, 128.6, 130.3, 140.9, 142.2, 148.9, 157.0, 166.8; IR, neat, ν (cm^{-1}) 700 (s), 751 (s), 787 (w), 883 (w), 909 (w), 1050 (m), 1081 (m), 1157 (s), 1249 (s), 1366 (m), 1447 (s), 1475 (s), 1496 (m), 1574 (m), 1597 (s), 1632 (s), 1709 (s), 1738 (s), 2935 (m); HRMS (EI) calcd for $C_{22}H_{24}O_3$ 336.1725 (M^+), found 336.1726.

1-{(2*E*)-2-[5-(3-Phenylpropyl)-2,3-dihydro-4*H*-chromen-4-ylidene]ethanoyl}pyrrolidine (2j). Following the general procedure, **1d** (31.0 mg, 0.0850 mmol) and $Ph(CH_2)_3Br$ (65.0 μL, 0.425 mmol) were reacted. The crude mixture was purified by flash chromatography on silica gel (R_f 0.21 in 50% EtOAc/hexane), using 50−60% EtOAc/hexane, to afford product **2j** as a viscous, clear, colorless oil. Isolated yield: 20 mg (65%). ^{1}H NMR (400 MHz, $CDCl_3$) δ 1.85−2.03 (m, 6H), 2.69 (t, J = 7.5 Hz, 2H), 2.80−2.86 (m, 2H), 3.28 (t, J = 6.1 Hz, 2H), 3.32 (t, J = 6.5 Hz, 2H), 3.54 (t, J = 6.6 Hz, 2H), 4.28 (t, J = 6.1 Hz, 2H), 6.08 (s, 1H), 6.68 (dd, J = 8.1, 1.1 Hz, 1H), 6.82 (dd, J = 7.5, 1.1 Hz, 1H), 7.11 (t, J = 7.9 Hz, 1H), 7.15−7.21 (m, 3H), 7.25−7.30 (m, 2H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 24.4, 26.2, 27.8, 32.8, 33.1, 35.8, 45.6, 46.9, 67.3, 114.8, 118.8, 122.5, 125.8, 128.3, 128.4, 129.4, 140.1, 141.9,

142.8, 156.3, 165.5; IR neat, ν (cm^{-1}) 699 (m), 747 (m), 1080 (m), 1248 (m), 1343 (m), 1418 (s), 1450 (s), 1615 (s), 1640 (s), 2926 (s); HRMS (ESI) calcd for $C_{24}H_{27}NO_2$ 361.2042 (M^+), found 361.2047.

(2*E*)-*N*-Methoxy-*N*-methyl-2-[5-(3-phenylpropyl)-2,3-dihydro-4*H*-chromen-4-ylidene]acetamide (2k). Following the general procedure, **1e** (180 mg, 0.500 mmol) and $Ph(CH_2)_3Br$ (380 μL, 2.50 mmol) were reacted. The crude mixture was purified by flash chromatography on silica gel (R_f 0.35 in 25% EtOAc/hexane), using 10−45% EtOAc/hexane, to afford product **2k** as a viscous, red-orange oil. Isolated yield: 132 mg (75%). ^{1}H NMR (300 MHz, $CDCl_3$) δ 1.94−2.05 (m, 2H), 2.69 (t, J = 7.7 Hz, 2H), 2.83−2.88 (m, J = 6.3 Hz, 2H), 3.26 (s, 3H), 3.36 (t, J = 6.2 Hz, 2H), 3.63 (s, 3H), 4.28 (t, J = 6.3 Hz, 2H), 6.49 (s, 1H), 6.69 (dd, J = 8.2, 1.2 Hz, 1H), 6.83 (dd, J = 7.6, 1.2 Hz, 1H), 7.10−7.20 (m, 4H), 7.25−7.30 (m, 2H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 27.8, 33.0, 33.2, 35.7, 61.7, 67.1, 100.0, 114.8, 115.1, 122.6, 123.4, 125.8, 128.3 (4 C), 129.7, 140.4, 141.9, 156.6; IR neat, ν (cm^{-1}) 700 (s), 1080 (m), 1456 (s), 2935 (s); HRMS (EI) calcd for $C_{22}H_{26}NO_3$ 352.1913 ($M + H^+$), found 352.1909.

tert*-Butyl (2*E*)-[6-Methoxy-5-(3-phenylpropyl)-2,3-dihydro-4*H*-chromen-4-ylidene]acetate (2*l*).** Following the general procedure, **1h** (134 mg, 0.330 mmol) and $Ph(CH_2)_3Br$ (251 μL, 1.65 mmol) were reacted. The crude mixture was purified by flash chromatography on silica gel (R_f 0.41 in 50% CH_2Cl_2/hexane), using 40−60% CH_2Cl_2/hexane, affording product **2*l as a clear, colorless viscous oil. Isolated yield: 71 mg (55%). ^{1}H NMR (300 MHz, $CDCl_3$) δ 1.54 (s, 9H), 1.88−2.01 (m, 2H), 2.69−2.82 (m, 4H), 3.36 (t, J = 5.9 Hz, 2H), 3.76 (s, 3H), 4.21 (t, J = 6.2 Hz, 2H), 5.97 (s, 1 H), 6.67 (d, J = 8.8 Hz, 1H), 6.78 (d, J = 9.1 Hz, 1H), 7.14−7.31 (m, 7H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 16.9, 27.7, 28.2, 28.4, 32.1, 36.3, 56.2, 66.7, 80.2, 110.0, 113.1, 114.4, 118.6, 125.7, 128.2, 128.4, 142.4, 147.5, 150.7, 152.5, 166.1; IR thin film, ν (cm^{-1}) 699 (m), 807 (w), 884 (w), 946 (w), 1064 (m), 1081 (m), 1142 (s), 1231 (m), 1366 (m), 1461 (s), 1634 (m), 1705 (s), 2935 (s); HRMS (EI) calcd for $C_{25}H_{30}O_4$ 394.2144 (M^+), found 394.2141.

***tert*-Butyl (2*E*)-[7-Nitro-5-(3-phenylpropyl)-2,3-dihydro-4*H*-chromen-4-ylidene]acetate (2m).** Following the general procedure, **1i** (145 mg, 0.350 mmol) and $Ph(CH_2)_3Br$ (266 μL, 1.75 mmol) were reacted. The crude mixture was purified by flash chromatography on silica gel (R_f 0.37 in 10% Et_2O/hexane), using 0−12% Et_2O/hexane, affording product **2m** as a yellow oil. Isolated yield: 106 mg (74%). ^{1}H NMR (300 MHz, $CDCl_3$) δ 1.54 (s, 9H), 1.93−2.05 (m, 2H), 2.71 (t, J = 7.6 Hz, 2H), 2.87 (m, 2H), 3.37 (t, J = 6.3 Hz, 2H), 4.34 (t, J = 6.1 Hz, 2H), 6.00 (s, 1H), 7.16−7.23 (m, 3H), 7.25−7.33 (m, 2H), 7.49 (d, J = 2.3 Hz, 1H), 7.66 (d, J = 2.3 Hz, 1H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 26.9, 28.5, 33.2 (2C), 35.9, 67.7, 81.3, 110.2, 116.8, 121.1, 126.3, 128.6, 128.7, 129.2, 141.6, 142.3, 145.1, 148.3, 157.0, 165.6; IR neat, ν (cm^{-1}) 700 (s), 1145 (s), 1347 (s), 1523 (s), 1603 (m), 1636 (m), 1708 (s), 1739 (m), 2935 (s), 2976 (s); HRMS (EI) calcd for $C_{24}H_{27}NO_5$ 409.1889 (M^+), found 409.1885.

***tert*-Butyl (2*E*)-[6-Chloro-5-(3-phenylpropyl)-2,3-dihydro-4*H*-chromen-4-ylidene]acetate (2n).** Following the general procedure, **1j** (143 mg, 0.350 mmol) and $Ph(CH_2)_3Br$ (266 μL, 1.75 mmol) were reacted. The crude mixture was purified by flash chromatography on silica gel (R_f 0.54 in 10% Et_2O/hexane), using 0−4% Et_2O/hexane, to afford product **2n** as a clear, pale pink oil. Isolated yield: 107 mg (77%). ^{1}H NMR (400 MHz, $CDCl_3$) δ 1.54 (s, 9H), 1.95−2.04 (m, 2H), 2.74 (dd, J = 8.1, 8.0 Hz, 2H), 2.86−2.90 (m, 2H), 3.36 (t, J = 6.0 Hz, 2H), 4.27 (t, J = 6.2 Hz, 2H), 5.98 (s, 1H), 6.64 (d, J = 8.8 Hz, 1H), 7.16−7.21 (m, 2H), 7.23−7.31 (m, 4H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 27.1, 28.3, 31.1, 31.6, 35.9, 67.0, 80.6, 116.1, 118.9, 124.8, 125.9, 127.2, 128.3, 128.4, 131.1, 137.7, 141.9, 147.0, 155.2, 165.8; IR neat, ν (cm^{-1}) 815 (m), 885 (m), 1081 (m), 1144 (s), 1446 (s), 1634 (s), 1709 (s), 1870 (w), 2976 (s); HRMS (EI) calcd for $C_{24}H_{27}ClO_3$ 398.1649 (M^+), found 398.1645.

Ethyl (2*E*)-[6-(3-Chloropropyl)-3,4-dihydro-1-benzoxepin-5(2*H*)-ylidene]acetate (2o). Following the general procedure, **1k** (178 mg, 0.500 mmol) and 1-bromo-3-chloropropane (247 μL, 2.50 mmol) were reacted. The crude mixture was purified by flash chromatography on silica gel (R_f 0.13 in 70% CH_2Cl_2/hexane), using 70−80% CH_2Cl_2/hexane, to afford product **2o** as a clear, colorless oil. Isolated yield: 73 mg (47%). ^{1}H NMR (400 MHz, $CDCl_3$) δ 1.31 (t, J = 7.1 Hz, 3H), 1.94−2.09 (m, 4H), 2.83 (br s, 2H), 3.50 (t, J = 6.5 Hz, 2H), 4.09 (br s, 2H), 4.21 (q, J = 7.0 Hz, 2H), 5.78 (s, 1H), 6.88 (dd, J = 7.9, 1.1 Hz, 1H), 7.00 (dd, J = 7.6, 0.8 Hz, 1H), 7.16 (t, J = 7.9 Hz, 1H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 14.3, 29.2, 30.1, 30.4, 34.0, 44.2, 59.9, 72.9, 119.4, 119.9, 125.3, 128.8, 135.9, 138.2, 156.5, 157.8, 166.0; IR neat, ν (cm^{-1}) 755 (w), 881 (w), 998 (w), 1044 (m), 1068 (m), 1174 (s), 1236 (m), 1275 (m), 1368 (m), 1444 (m), 1571 (w), 1639 (m), 1713 (s), 2956 (m); HRMS (EI) calcd for $C_{17}H_{21}ClO_3$ 308.1179 (M^+), found 308.1183.

Ethyl 4-[(5*E*)-5-(2-Ethoxy-2-oxoethylidene)-2,3,4,5-tetrahydro-1-benzoxepin-6-yl]butanoate (2p). Following the general procedure, **1k** (178 mg, 0.500 mmol) and ethyl 4-bromobutyrate (358 μL, 2.50 mmol) were reacted. The crude mixture was purified by flash chromatography on silica gel (R_f 0.32 in 20% Et_2O/hexane), using 10−25% Et_2O/hexane, to afford product **2p** as a clear, colorless oil. Isolated yield: 77 mg (45%). ^{1}H NMR (400 MHz, $CDCl_3$) δ 1.18−1.29 (m, 2H), 1.24 (t, J = 7.1 Hz, 3H), 1.31 (t, J = 7.1 Hz, 3H), 1.80−1.89 (m, 2H), 1.96, 2.04 (m, 2H), 2.28 (t, J = 7.5 Hz, 2H), 2.70 (br s, 2H), 4.09 (br s, 2H), 4.11 (q, J = 7.2 Hz, 2H), 4.21 (q, J = 7.0 Hz, 2H), 5.77 (s, 1H), 6.86 (dd, J = 7.9, 1.1 Hz, 1H), 6.99 (dd, J = 7.7, 0.9 Hz, 1H), 7.15 (t, J = 7.8 Hz, 1H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 14.2, 14.3, 26.5, 29.1, 30.4, 32.2, 33.9, 59.9, 60.3, 72.9, 119.2, 119.7, 125.3, 128.7, 135.8, 138.9, 156.3, 158.1, 166.0, 173.2; IR neat, ν (cm^{-1}) 755 (w), 880 (w), 997 (w), 1044 (m), 1068 (m), 1096 (w), 1174 (s), 1242 (s), 1275 (m), 1369 (m), 1445 (m), 1638 (m), 1713 (s), 1732 (s), 2941 (m); HRMS (EI) calcd for $C_{20}H_{26}O_5$ 346.1780 (M^+), found 346.1797.

Ethyl (2*E*)-[6-(3-Phenylpropyl)-3,4-dihydro-1-benzoxepin-5(2*H*)-ylidene]acetate (2q). Following the general procedure, **1k** (178 mg, 0.500 mmol) and 1-bromo-3-phenylpropane (380 μL, 2.50 mmol) were reacted. The crude mixture was purified by flash chromatography on silica gel (R_f 0.21 in 10% Et_2O/hexane), using 5−12% Et_2O/hexane, to afford product **2q** as a clear, colorless oil. Isolated yield: 79 mg (45%). ^{1}H NMR (300 MHz, $CDCl_3$) δ 1.17−1.31 (m, 2H), 1.31 (t, J = 7.1 Hz, 3H), 1.80−1.88 (m, 2H), 1.96−2.03 (m, 2H), 2.59−2.64 (m, 2H), 2.68 (br s, 2H), 3.96−4.17 (m, 2H), 4.21 (t, J = 7.0 Hz, 2H), 5.76 (s, 1H), 6.85 (dd, J = 7.9, 1.3 Hz, 1H), 6.97 (dd, J = 7.7, 1.1 Hz, 1H), 7.14 (t, J = 7.8 Hz, 1H), 7.14−7.20 (m, 3H), 7.23−7.29 (m, 2H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 14.3, 29.1, 30.4, 32.8, 33.2, 35.7, 59.9, 72.9, 119.0, 119.6, 125.3, 125.8, 128.3, 128.6, 135.7, 139.9, 142.0, 156.3, 158.2, 166.1; IR neat, ν (cm^{-1}) 700 (m), 751 (m), 880 (w), 998 (m), 1044 (m), 1173 (s), 1243 (m), 1275 (m), 1368 (m), 1445 (m), 1639 (m), 1713 (s), 2940 (m); HRMS (EI) calcd for $C_{23}H_{26}O_3$ 350.1882 (M^+), found 350.1873.

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Supporting Information Available: Experimental details and characterization data for compounds **1a** to **1k** and their precursors. This material is available free of charge via the Internet at http://pubs.acs.org.

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