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One-Pot Cyclizations of Dilithiated Oximes and Hydrazones with Epibromohydrin. Efficient Synthesis of 6-Hydroxymethyl-5,6-dihydro-4*H*-1,2-oxazines and Oxazolo[3,4-*b*]pyridazin-7-ones

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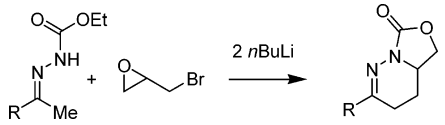

The one-pot cyclization of dilithiated oximes with epibromohydrin provided a convenient and regioselective approach to 6-hydroxymethyl-5,6-dihydro-4*H*-1,2-oxazines. The reaction of the latter with phosphorus tribromide resulted in a Beckmann rearrangement and formation of 5-bromomethyl-2-iminotetrahydrofurans. The reaction of dilithiated hydrazones with epibromohydrin afforded oxazolo[3,4-*b*]pyridazin-7-ones, which were formed by a novel domino cyclization.

Cyclization reactions of dianions[1] with dielectrophiles constitute a useful strategy[2] for the synthesis of carbo- and heterocyclic systems. Despite their simplicity and synthetic usefulness, cyclization reactions of dianions often suffer from side reactions, such as polymerization, decomposition, or formation of open-chained products. In addition, elimination reactions or reduction of the electrophile are frequently observed, due to the high basicity and electron-rich character of the dianions. It has been known for many years that treatment of oximes and hydrazones with 2 equiv of *n*-butyllithium results in formation of 1,4-dianions. The reaction of oxime dianions with esters has been reported to give isoxazoles.[3] Isoxazolin-5-ones have been prepared by cyclization of oxime dianions with carbon dioxide.[4] The cyclization of hydrazone dianions with esters,[5] acid chlorides,[6] and nitriles[7] has been reported to give pyrazoles. Pyrazolines are available by cyclization of hydrazone dianions with α-halo ketones.[5,8] Reactions of hydrazone dianions have been used for the synthesis of 1,2,3-thiazoles.[9] Recently, we have reported[10] the synthesis of functionalized 1,2-oxazines by cyclization of oxime dianions with epibromohydrin.[11] Herein, we report full details of these studies. With regard to our preliminary communication,[10] we also studied the reaction of the products with phosphorus(III) tribromide, which results in an interesting Beckmann rearrange-

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(1) For reviews of dianions, see: (a) Kaiser, E. M.; Petty, J. D.; Knutson, P. L. A. *Synthesis* **1977**, 509. (b) Thompson, C. M.; Green, D. *Tetrahedron* **1991**, *47*, 4223.
(2) For a review of cyclization reactions of dianions, see: Langer, P.; Freiberg, W. *Chem. Rev.* **2004**, *104*, 4125.
(3) Beam, C. F.; Dyer, M. C. D.; Schwarz, R. A.; Hauser, C. R. *J. Org. Chem.* **1970**, *35*, 1806.
(4) Griffiths, J. S.; Beam, C. F.; Hauser, C. R. *J. Chem. Soc. C* **1971**, 974.
(5) Matsumura, N.; Kunigihara, A.; Yoneda, S. *Tetrahedron. Lett.* **1983**, *24*, 3239.
(6) Matsumura, N.; Kunigihara, A.; Yoneda, S. *Tetrahedron. Lett.* **1984**, *25*, 4529.
(7) Duncan, D. C.; Trumbo, T. A.; Almquist, C. D.; Lentz, T. A.; Beam, C. F. *J. Heterocycl. Chem.* **1987**, *24*, 555.
(8) Beam, C. F.; Reames, D. C.; Harris, C. E.; Dasher, I. W.; Hollinger, W. M.; Shealy, N. L.; Sandifer, R. M.; Perkins, M.; Hauser, C. R. *J. Org. Chem.* **1975**, *40*, 514.
(9) Hurd, C. D.; Mori, R. J. *J. Am. Chem. Soc.* **1955**, *77*, 5359.
(10) Albrecht, U.; Gerwien, K.; Langer, P. *Tetrahedron Lett.* **2005**, *46*, 1017. For reactions with epichlorohydrin, see: Stevenson, T. M.; Patel, K. M.; Crouse, B. A.; Folgar, M. P.; Hutchison, C. D.; Pine, K. K. *ACS Symp. Ser.* **1995**, *584*, 197.
(11) For reactions of **2** from our laboratory, see: (a) Langer, P.; Freifeld, I. *Chem. Eur. J.* **2001**, *7*, 565. (b) Langer, P.; Freifeld, I. *Org. Lett.* **2001**, 3903. (c) Langer, P.; Armbrust, H.; Eckardt, T.; Magull, J. *Chem. Eur. J.* **2002**, *8*, 1443. (d) Albrecht, U.; Langer, P. *Synlett* **2004**, 2200.

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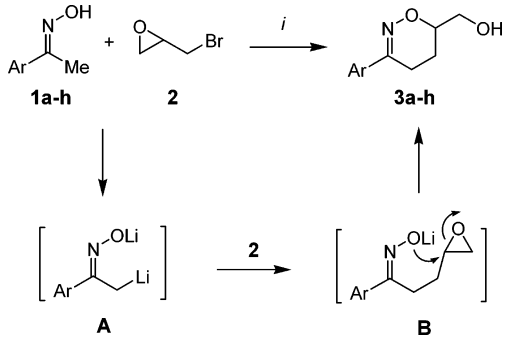
ment. In addition, we report what are, to the best of our knowledge, the first domino cyclizations of hydrazone dianions with epibromohydrin; these reactions provide a new and convenient approach to oxazolo[3,4-*b*]pyridazin-7-ones.

1,2-Oxazines are of pharmacological relevance and represent useful synthetic building blocks. They have been used, for instance, as intermediates during the synthesis of glycosidase inhibitor analogues[12,13] and of functionalized pyrroles.[14] Although a number of synthetic approaches to 1,2-oxazines are known,[15−25] the development of alternative strategies is of considerable interest. Oxazolo[3,4-*b*]pyridazin-7-ones have been previously prepared on the basis of cyclization reactions of 3-aminooxazolidin-2-ones.[26]

Results and Discussion

Cyclization of Dilithiated Oximes with Epibromohydrin. The reaction of the dianion of acetophenone oxime (**1a**), generated by *n*-butyllithium (2.5 equiv), with epibromohydrin (**2**) afforded the 1,2-oxazine **3a** (Scheme 1). The use of epichlorohydrin proved to be unsuccessful. The formation of **3a** can be explained by S_N2 reaction of the carbon atom of the dianion with the CBr functionality of **2** and subsequent cyclization via the oxygen atom or, alternatively, by attack of the dianion onto the sterically less hindered carbon atom of the epoxide, Payne rearrangement, and subsequent cyclization. The reaction proceeded with very good regioselectivity, due to the higher nucleophilicity of the carbanion compared to the alkoxide.

SCHEME 1. Synthesis of 1,2-oxazines 3a−h[a]



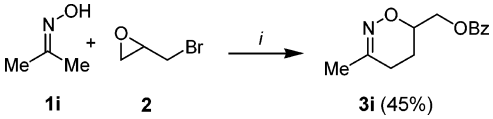
[a] Key: (i) (1) *n*-BuLi (2.5 equiv), 45 min, −78 °C, (2) 15 min, 20 °C, (3) **2**, −78 → +20 °C, 16 h.

TABLE 1. Products and Yields

3	Ar	% yield[a]
a	C_6H_5	30
b	4-MeC_6H_4	81
c	4-$(MeO)C_6H_4$	73
d	3-MeC_6H_4	36
e	3-$(MeO)C_6H_4$	72
f	2-MeC_6H_4	33
g	1-naphthyl	44
h	2-naphthyl	42

[a] Yields of isolated products.

SCHEME 2. Synthesis of 3i[a]



[a] Key: (i) (1) *n*-BuLi (2.5 equiv), 45 min, −78 °C, (2) 15 min, 20 °C, (3) **2**, −78 → +20 °C, 16 h, (4) BzCl (5.0 equiv), 20 °C, 16 h, 45%.

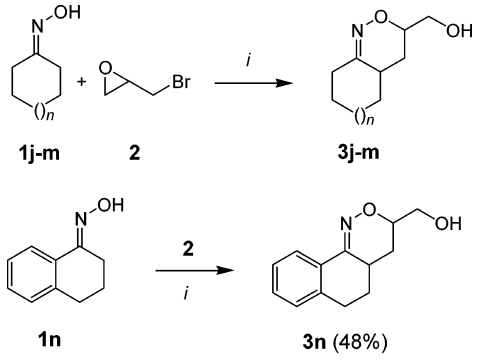
The preparative scope was studied next (Scheme 1, Table 1). The cyclization of **2** with dilithiated oximes **1b−h** afforded the 1,2-oxazines **3b−h**. The reaction of the acetone derived oxime **1i** with **2** proved to be unsuccessful, due to problems with the isolation of the product. The problem was solved when the product was isolated in the form of its benzoate ester **3i** (Scheme 2).

The cyclization of **2** with the dianions of cycloalkanone derived oximes **1j−m** afforded the corresponding 6,6-, 6,7-, 6,8-, and 6,12-bicyclic 1,2-oxazines **3j−m** (Scheme 3, Table 2). The cyclization of **2** with dilithiated oxime **1n**, prepared from tetralone, afforded the tricyclic 1,2-oxazine **3n** (Scheme 3). All products **3j−n** were formed as inseparable mixtures of diastereomers.

Beckmann Rearrangement of 1,2-Oxazines. The reaction of 1,2-oxazine **3a** with phosphorus tribromide (PBr_3) afforded the 5-bromomethyl-2-(phenylimino)tetrahydrofuran **4a** (Scheme 4, Table 3). The formation of the latter can be explained by transformation of the alcohol into a bromide functionality (intermediate **A**) and subsequent Beckmann rearrangement via intermediate **B**. A Dimroth rearrangement to give the corresponding lactam was not observed. The yield of **4a** strongly depended on the reaction conditions; during the optimization, the reaction time proved to be an important parameter. The reaction of 1,2-oxazines **3b−e** and **3h** with PBr_3 afforded the 5-bromomethyl-2-(phenylimino)tetrahydrofurans **4b−f**. The struc-

(12) (a) Streith, J.; Defoin, A. *Synlett* **1996**, 189. (b) Defoin, A.; Sarazin, H.; Streith, J. *Tetrahedron* **1997**, *53*, 13769.
(13) Bach, P.; Bols, M. *Tetrahedron Lett.* **1999**, *40*, 3460.
(14) Miyashita, M.; Awen, B. Z. E. Yoshikoshi, A. *Tetrahedron* **1990**, *46*, 7569.
(15) For hetero-Diels−Alder reactions of alkenes with ene-nitroso compounds, derived from α-haloximes, see: (a) Gilchrist, T. L. *J. Chem. Soc., Chem. Rev.* **1983**, *12*, 53. See also: (b) Gilchrist, T. L.; Roberts, T. G. *J. Chem. Soc., Chem. Commun.* **1978**, 847. (c) Zimmer, R.; Reissig, H. U. *Liebigs Ann. Chem.* **1991**, 553. (d) Yoon, S. C.; Kim, K.; Park, Y. J. *J. Org. Chem.* **2001**, *66*, 7334.
(16) For hetero-Diels−Alder reactions of dienes with nitroso compounds, see: Naruse, M., Aoyagi, S., Kibayashi, C. *Tetrahedron Lett.* **1994**, *35*, 595.
(17) For cyclizations of alkenyl-substituted oximes in the presence of NBS, see: (a) Bowman, W. R.; Davies, R. V.; Slawin, A. M. Z.; Sohal, G. S.; Titman, R. B.; Wilkins, D. J. *J. Chem. Soc., Perkin Trans. 1* **1997**, 155. (b) Dondas, H. A.; Grigg, R.; Hadjisoteriou, M.; Markandu, J.; Kennewell, P.; Thornson-Pett, M. *Tetrahedron* **2001**, *57*, 1119.
(18) For cyclizations of alkenyl-substituted oximes in the presence of diphenyldiselenide, see: (a) Tiecco, M.; Testaferri, L.; Tingoli, M.; Bagnoli, L.; Marini, F. *J. Chem. Soc., Perkin Trans. 1* **1993**, 1989. (b) Grigg, R.; Hadjisoteriou, M.; Kennewell, P.; Markandu, J. *J. Chem. Soc., Chem. Commun.* **1992**, 1537.
(19) For cyclizations of alkenyl-substituted oximes in the presence of acid, see: Bishop, R.; Hawkins, S. C.; Quibuyen, T. A. O.; Brooks, P. R. *Tetrahedron Lett.* **1988**, *29*, 6805
(20) For photochemical activation, see: Armesto, D.; Austin, M. A.; Griffiths, O. J.; Horspool, W. M.; Carpintero, M. *J. Chem. Soc., Chem. Commun.* **1996**, 2715.
(21) For base-mediated cyclizations of γ-chloroximes, see: (a) Kaiser, A.; Mayer, K. K.; Sellmer, A.; Wiegrebe, W. *Monatsh. Chem.* **2003**, *3*, 343. (b) Ellames, G. J.; Hewkin, C. T.; Jackson, R. F. W.; Smith, D. I.; Standen, S. P. *Tetrahedron Lett.* **1989**, *26*, 3471.
(22) For base-mediated cyclizations of γ-sulfonyloximes, see: Saiki, H.; Mukai, T. *Chem. Lett.* **1981**, 1561.
(23) For Lewis acid catalyzed reactions of allenoximes, see: Lathbury, D.; Gallagher, T. *J. Chem. Soc., Chem. Commun.* **1986**, 1017.
(24) For acid-catalyzed cyclization of cyclopropyloximes, see: Castin, V.; Rentzea, C. N. *Angew. Chem.* **1980**, *92*, 195.
(25) For cyclizations of γ-nitro ketones, see: Boberg, F.; Ruhr, M.; Garburg, K. H.; Garming, A. *J. Heterocycl. Chem.* **1986**, *23*, 759.
(26) Ciufolini, M. A.; Shimizu, T.; Swaminathan, S.; Xi, N. *Tetrahedron Lett.* **1997**, *38*, 4947.

SCHEME 3. Synthesis of Bicyclic 1,2-Oxazines 3j−n[a]



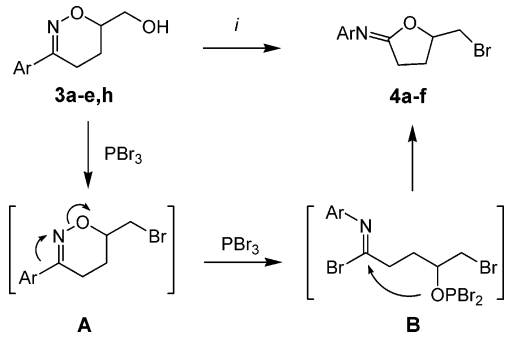
[a] Key: (i) (1) *n*-BuLi (2.5 equiv), 45 min, −78 °C, (2) 15 min, 20 °C, (3) **2**, −78 → +20 °C, 16 h, dr = 1:1 for all products.

TABLE 2. Products and Yields

3	*n*	% yield[a]
j	1	38
k	2	51
l	3	49
m	7	52

[a] Yields of isolated products; dr = 1:1 for all products.

SCHEME 4. Beckmann Rearrangement of 1,2-Oxazines 3[a]



[a] Key: (i) PBr_3, reflux, 12 h.

TABLE 3. Products and Yields

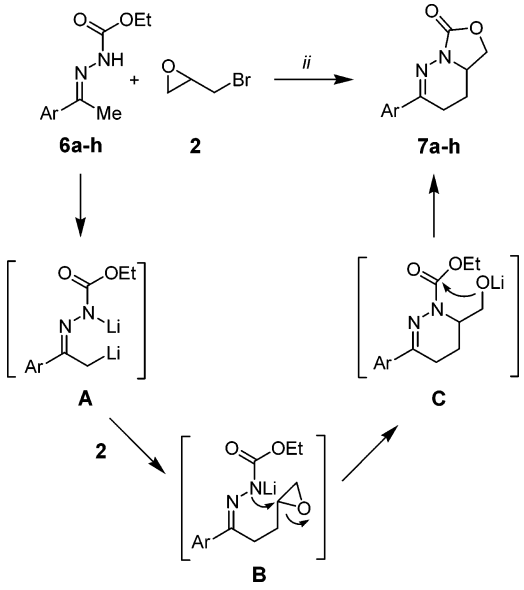
4	R	% yield[a]
a	4-C_6H_4	20
b	3-MeC_6H_4	21
c	4-(MeO)C_6H_4	35
d	3-(MeO)C_6H_4	32
e	2-$C_{10}H_7$	12

[a] Yields of isolated products.

ture of **4a**−**f** was established by NMR spectroscopy (analysis of chemical shifts and coupling constants, NOESY measurements). A few related reactions have been reported in the literature.[27]

Cyclization of Dilithiated Hydrazones with Epibromohydrin. The *N*-(ethoxycarbonyl)hydrazones **6a**−**h** were prepared from the corresponding acetophenones **5a**−**h** according to a literature procedure (Scheme 5, Table 4).[9,28,29] The reaction of epibromohydrin (**2**) with the dianion of hydrazone **6a**, generated

SCHEME 5. Cyclization of Dilithiated Hydrazones with Epibromohydrin[a]



[a] Key: (i) H_2NNHCO_2Et, HOAC, EtOH, H_2O, 20 °C, 2 h; (ii) (a) *n*-BuLi (2.5 equiv), THF, −78 °C, 1 h, (b) **2**, −78 → +20 °C, 16 h.

TABLE 4. Products and Yields

6, 7	Ar	% yield (**6**)[a]	% yield (**7**)[a]
a	C_6H_5	60	38
b	4-MeC_6H_4	37	56
c	4-(MeO)C_6H_4	32	41
d	3-MeC_6H_4	34	53
e	3-(MeO)C_6H_4	38	62
f	2-MeC_6H_4	43	24
g	1-naphthyl	30	31
h	2-naphthyl	21	52

[a] Yields of isolated products.

by means of *n*-BuLi (2.5 equiv), afforded the 3,4,4a,5-tetrahydro-2-phenyloxazolo[3,4-*b*]pyridazin-7-one **7a** (Scheme 5, Table 4). The use of epichlorohydrin proved to be unsuccessful. Product **7a** was regioselectively formed by attack of the carbon atom of the dianion (intermediate **A**) onto **2** to give intermediate **B**, attack of the nitrogen atom onto the epoxide (intermediate **C**), and subsequent cyclization by attack of the alkoxide onto the carbamate functionality. Alternatively, an attack of the dianion onto the epoxide, Payne rearrangement, and subsequent cyclization is possible. The cyclization of dilithiated hydrazones **6b**−**h** with **2** afforded the oxazolopyridazinones **7b**−**h** (Scheme 5, Table 4).

The cyclization of **2** with the dianions of hydrazones **6i**−**m**, prepared from the corresponding cycloalkanones,[30] afforded the 5,6,5-, 5,6,6-, 5,6,7-, 5,6,8-, and 5,6,12-tricyclic oxazolo[3,4-*b*]pyridazin-7-ones **7i**−**m** (Scheme 6, Table 5). The cyclization of **2** with the dianion of hydrazone **6n**, prepared from tetralone, afforded the tetracyclic product **7n** (Scheme 6). The oxazolo-[3,4-*b*]pyridazin-7-ones **7j**−**n** were formed as unseparable mixtures of diastereomers. Product **7i** was isolated as a single diastereomer; however, the relative configuration remains unknown at present.

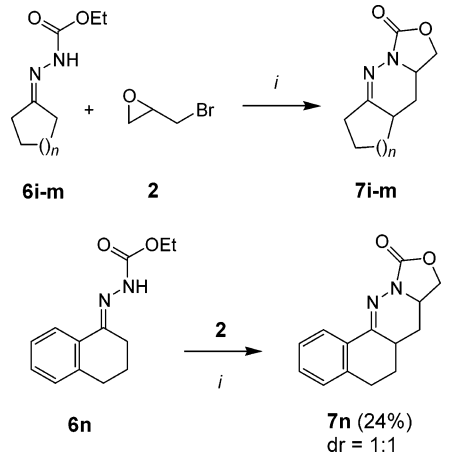
(27) (a) Adams, R.; Burney, D. E. *J. Am. Chem. Soc.* **1941**, *63*, 1103. (b) Denmark, S. E.; Dappen, M. S.; Cramer, C. J. *J. Am. Chem. Soc.* **1986**, *108*, 1306. (c) Denmark, S. E.; Moon, Y.-C.; Cramer, C. J.; Dappen, M. S.; Senanayake, C. B. W. *Tetrahedron* **1990**, *46*, 7373.

(28) Seltzer, S.; Dunne, F. T. *J. Am. Chem. Soc.* **1965**, *87*, 2628.

(29) Amer, A. M. *Monatsh. Chem.* **1995**, *126*, 431.

(30) Wang, Q.; Amer, A.; Mohr, S.; Ertel, E.; Jochims, J. C. *Tetrahedron* **1993**, *49*, 9973.

SCHEME 6. Synthesis of 7i−n[a]



[a] Key: (i) 1) *n*-BuLi (2.5 equiv), 1 h, −78 °C, (2) 10 min, 20 °C, (3) **2**, −78 → +20 °C, 16 h.

TABLE 5. Products and Yields

6, **7**	*n*	% yield (**6**)[a]	% yield (**7**)[a]	dr (**7**)[b]
i	1	65	38	>98:2
j	2	18	30	1:1
k	3	36	44	3:1
l	4	22	60	3:2
m	8	20	37	1:1

[a] Yields of isolated products. [b] By NMR, assignment arbitrary.

In conclusion, we have reported one-pot cyclizations of dilithiated oximes with epibromohydrin which provide a convenient and regioselective access to 6-hydroxymethyl-5,6-dihydro-4*H*-1,2-oxazines. The reaction of the latter with phosphorus tribromide resulted in a Beckmann rearrangement and formation of 5-bromomethyl-2-iminotetrahydrofurans. The reaction of dilithiated hydrazones with epibromohydrin afforded oxazolo[3,4-*b*]pyridazin-7-ones, which were formed by a novel domino cyclization.

Experimental Section

General Comments. All solvents were dried by standard methods, and all reactions were carried out under an inert atmosphere. For ^{1}H and ^{13}C NMR spectra, the deuterated solvents indicated were used. Mass spectrometric data (MS) were obtained by electron ionization (EI, 70 eV), chemical ionization (CI, H_2O), or electrospray ionization (ESI). For preparative-scale chromatography, silica gel (60−200 mesh) was used. Melting points are uncorrected.

General Procedure for the Synthesis of 6-Hydroxymethyl-1,2-oxazines (3a−h). To a THF solution of oxime **1** was added *n*-butyllithium −78 °C. After being stirred for 45 min at −78 °C, the mixture was stirred for 15 min at 20 °C. Subsequently, epibromohydrin was added at −78 °C. After warming of the mixture to 20 °C during 16 h, a saturated aqueous solution of NH_4Cl (30 mL) was added. The organic and the aqueous layers were separated, and the latter was extracted with ethyl acetate (3 × 30 mL). The combined organic layers were dried (Na_2SO_4) and filtered, and the solvent of the filtrate was removed in vacuo. The residue was purified by chromatography (silica gel, *n*-hexane/EtOAc = 1:1).

6-Hydroxymethyl-3-phenyl-5,6-dihydro-4*H*-1,2-oxazine (3a). Starting with **1a** (0.270 g, 2.0 mmol), *n*-BuLi (2.0 mL, 5.0 mmol, 1.6 M), and **2** (0.301 g, 2.2 mmol) in THF (10 mL), **3a** was isolated as a colorless solid (0.116 g, 30%). Mp = 87 °C. IR (KBr): $\tilde{\nu}$ = 3370 (s), 3057 (w), 2925 (m), 2872 (w), 1492 (w), 1445 (s), 1423 (w) cm^{-1}. ^{1}H NMR ($CDCl_3$, 300 MHz): δ = 1.88−2.09 (m, 2 H, CH_2), 2.14 (br, 1 H, OH), 2.58−2.79 (m, 2 H, CH_2), 3.78−3.96 (m, 3 H, CH, CH_2), 7.39 (t, ^3J = 6 Hz, 2 H, CH), 7.67−7.70 (m, 3 H, CH). ^{13}C NMR (75 MHz, $CDCl_3$): δ = 20.4, 21.4, 64.1, 75.4, 125.3, 128.4, 129.5, 135.5, 155.1. MS (EI, 70 eV): *m*/*z* = 191 (M^+, 100), 160 (89), 132 (39), 117 (46), 104 (67). The exact molecular mass for $C_{11}H_{13}NO_2$ *m*/*z* = 191.0946 ± 2 ppm [M^+] was confirmed by HRMS (EI, 70 eV).

6-Hydroxymethyl-3-(4-tolyl)-5,6-dihydro-4*H*-1,2-oxazine (3b). Starting with **1b** (0.298 g, 2.0 mmol), *n*-BuLi (2.0 mL, 5.0 mmol, 2.5 M), and **2** (0.301 g, 2.2 mmol) in THF (10 mL), **3b** was isolated as a colorless solid (0.333 g, 81%). Mp = 80 °C. IR (KBr): $\tilde{\nu}$ = 3392 (s), 2964 (w), 2924 (m), 2869 (w), 1612 (w), 1511 (w), 1456 (w), 1444 (w), 1423 (w) cm^{-1}. UV−vis (MeCN): λ_{max} (lg ϵ) = 202 (4.25), 252 (4.05) nm. ^{1}H NMR ($CDCl_3$, 300 MHz): δ = 1.89−2.07 (m, 2 H, CH_2), 2.12 (br. s, 1 H, OH), 2.38 (s, 3 H, CH_3), 2.55−2.76 (m, 2 H, CH_2), 3.73−3.92 (m, 3 H, CH_2, CH), 7.19 (dd, ^3J = 6 Hz, ^4J = 2 Hz, 2 H, CH), 7.58 (dd, ^3J = 6 Hz, ^4J = 2 Hz, 2 H, CH). ^{13}C NMR (75 MHz, $CDCl_3$): δ = 20.4, 21.1, 21.3, 63.9, 75.3, 125.1, 128.1, 132.6, 139.4, 155.0. MS (EI, 70 eV): *m*/*z* = 205 (M^+, 86), 174 (100), 146 (18), 131 (27), 118 (46). Anal. Calcd for $C_{12}H_{15}NO_2$: C, 70.22; H, 7.37; N, 6.82. Found: C, 70.35; H, 7.66; N, 7.10.

6-Hydroxymethyl-3-(4-methoxyphenyl)-5,6-dihydro-4*H*-1,2-oxazine (3c). Starting with **1c** (0.330 g, 2.0 mmol), *n*-BuLi (2.0 mL, 5.0 mmol, 2.5 M), and **2** (0.301 g, 2.2 mmol) in THF (10 mL), **3c** was isolated as a colorless solid (0.322 g, 73%). Mp = 116 °C. IR (KBr): $\tilde{\nu}$ = 3360 (s), 2950 (s), 2934 (m), 2878 (w), 2836 (w), 1611 (s), 1514 (s), 1461 (m), 1445 (w), 1418 (w) cm^{-1}. UV−vis (MeCN): λ_{max} (lg ϵ) = 203 (4.21), 265 (4.15) nm. ^{1}H NMR ($CDCl_3$, 300 MHz): δ = 1.95−2.06 (m, 3 H, CH_2, OH), 2.55−2.76 (m, 2 H, CH_2), 3.72−3.94 (m, 6 H, CH_3, CH_2, CH), 6.90 (dd, ^3J = 7 Hz, ^4J = 2 Hz, 2 H, CH), 7.64 (dd, ^3J = 7 Hz, ^4J = 2 Hz, 2 H, CH). ^{13}C NMR (75 MHz, $CDCl_3$): δ = 20.7, 21.5, 55.3, 64.3, 75.4, 113.8, 126.8, 128.1, 154.9, 160.8. MS (EI, 70 eV): *m*/*z* = 221 (M^+, 100), 190 (63), 162 (11), 148 (14), 134 (35). HRMS (FT-ICR): calcd for $C_{12}H_{16}NO_3$ *m*/*z* = 222.11247, found 222.11250 ± 2 ppm.

6-Hydroxymethyl-3-(3-tolyl)-5,6-dihydro-4*H*-1,2-oxazine (3d). Starting with **1d** (0.298 g, 2.0 mmol), *n*-BuLi (2.0 mL, 5.0 mmol, 2.5 M), and **2** (0.301 g, 2.2 mmol) in THF (10 mL), **3d** was isolated as a colorless solid (0.149 g, 36%). Mp = 87 °C. IR (KBr): $\tilde{\nu}$ = 3336 (s), 2949 (s), 2906 (m), 2858 (w), 1604 (w), 1487 (w), 1448 (s), 1407 (s) cm^{-1}. UV−vis (MeCN): λ_{max} (lg ϵ) = 208 (4.30) nm. ^{1}H NMR ($CDCl_3$, 300 MHz): δ = 1.90−2.07 (m, 2 H, CH_2), 2.37 (s, 3 H, CH_3), 2.56−2.75 (m, 3 H, CH_2, CH), 7.19−7.22 (m, 1 H, CH), 7.28 (t, ^3J = 7 Hz, 1 H, CH), 7.44−7.45 (m, 1 H, CH), 7.51 (br. s, 1 H, CH). ^{13}C NMR (75 MHz, $CDCl_3$): δ = 20.4, 21.5, 21.4, 63.9 (CH_2), 75.4, 122.4, 125.9, 128.2, 130.2, 135.4, 137.9, 155.3. MS (EI, 70 eV): *m*/*z* = 205 (M^+, 60), 174 (68), 136 (27), 119 (39), 91 (100). HRMS (FT-ICR): calcd for $C_{12}H_{16}NO_2$ *m*/*z* = 206.11756, found 206.11753 ± 2 ppm.

6-Hydroxymethyl-3-(3-methoxyphenyl)-5,6-dihydro-4*H*-1,2-oxazine (3e). Starting with **1e** (0.330 g, 2.0 mmol), *n*-BuLi (2.0 mL, 5.0 mmol, 2.5 M), and **2** (0.301 g, 2.2 mmol) in THF (10 mL), **3e** was isolated as a yellow oil (0.320 g, 72%). IR (KBr): $\tilde{\nu}$ = 3380 (s), 3076 (w), 3001 (w), 2935 (s), 2875 (w), 2840 (w), 1639 (w), 1603 (s), 1572 (s), 1487 (m), 1456 (s), 1428 (s) cm^{-1}. UV−vis (MeCN): λ_{max} (lg ϵ) = 213 (4.33) nm. ^{1}H NMR ($CDCl_3$, 300 MHz): δ = 1.82−1.92 (m, 1 H, CH_2), 1.96−2.05 (m, 1 H, CH_2), 2.55−2.64 (m, 2 H, CH_2), 3.37 (br. s, 1 H, OH), 3.72−3.89 (m, 6 H, CH, CH_2, CH_3), 6.91 (dd, ^3J = 8 Hz, ^4J = 1 Hz, 1 H, CH), 7.16−7.29 (m, 3 H, CH). ^{13}C NMR (75 MHz, $CDCl_3$): δ = 20.2, 21.3, 55.0, 63.7, 75.4, 110.2, 115.3, 117.6, 129.1, 136.7, 154.8, 159.3. MS (EI, 70 eV): *m*/*z* = 221 (M^+, 15), 190 (18), 134 (5), 84 (78), 49 (100). HRMS (FT-ICR): calcd for $C_{12}H_{16}NO_3$ *m*/*z* = 222.11247, found 222.11254 ± 2 ppm.

6-Hydroxymethyl-3-(2-tolyl)-5,6-dihydro-4*H*-1,2-oxazine (3f). Starting with **1f** (0.298 g, 2.0 mmol), *n*-BuLi (2.0 mL, 5.0 mmol,

2.5 M), and **2** (0.301 g, 2.2 mmol) in THF (10 mL), **3f** was isolated as a colorless solid (0.136 g, 0.60 mmol, 33%). Mp = 69 °C. IR (KBr): $\tilde{\nu}$ = 3361 (s), 2925 (s), 2361 (w), 1445 (m) cm^{-1}. ^{1}H NMR ($CDCl_3$, 300 MHz): δ = 1.88−1.99 (m, 2 H, CH_2), 2.36 (s, 3 H, CH_3), 2.44−2.52 (m, 2 H, CH_2), 3.71−3.95 (m, 3 H, CH_2, CH), 7.16−7.29 (m, 4 H, CH). ^{13}C NMR (75 MHz, $CDCl_3$): δ = 19.9, 20.8, 25.2, 64.2, 75.3, 125.9, 127.8, 128.7, 130.7, 135.6, 136.4, 158.9. MS (EI, 70 eV): *m*/*z* = 205 (M^+, 100), 174 (48), 144 (47), 130 (52), 91 (98). HRMS (FT-ICR): calcd for $C_{12}H_{16}NO_2$ *m*/*z* = 206.11756, found 206.11756 ± 2 ppm.

6-Hydroxymethyl-3-(1-naphthyl)-5,6-dihydro-4*H*-1,2-oxazine (3g). Starting with **1g** (0.370 g, 2.0 mmol), *n*-BuLi (2.0 mL, 5.0 mmol, 2.5 M), and **2** (0.301 g, 2.2 mmol) in THF (10 mL), **3g** was isolated as a colorless solid (0.215 g, 44%). Mp = 110 °C. IR (KBr): $\tilde{\nu}$ = 3370 (s), 2927 (w), 2874 (w) cm^{-1}. UV−vis (MeCN): λ_{max} (lg ϵ) = 223 (4.76) nm. ^{1}H NMR ($CDCl_3$, 300 MHz): δ = 1.90−1.97 (m, 2 H, CH_2), 2.53−2.58 (m, 2 H, CH_2), 3.24 (br. s, 1 H, OH), 3.72−3.80 (m, 2 H, CH_2), 3.94−4.00 (m, 1 H, CH), 7.35−7.51 (m, 4 H, CH), 7.80−7.84 (m, 2 H, CH), 8.03−8.06 (m, 1 H, CH). ^{13}C NMR (75 MHz, $CDCl_3$): δ = 20.6, 25.8, 63.9, 75.4, 124.8, 124.9, 125.4, 125.9, 126.5, 128.2, 129.1, 130.5, 133.6, 134.3, 158.1. MS (EI, 70 eV): *m*/*z* = 241 (M^+, 100), 210 (46), 182 (14), 170 (11), 153 (36). HRMS (FT-ICR): calcd for $C_{15}H_{16}NO_2$ *m*/*z* = 242.11756, found 242.11752 ± 2 ppm.

6-Hydroxymethyl-3-(2-naphthyl)-5,6-dihydro-4*H*-1,2-oxazine (3h). Starting with **1h** (0.370 g, 2.0 mmol), *n*-BuLi (2.0 mL, 5.0 mmol, 2.5 M), and **2** (0.301 g, 2.2 mmol) in THF (10 mL), **3h** was isolated as a colorless solid (0.203 g, 42%). Mp = 135 °C. IR (KBr): $\tilde{\nu}$ = 3405 (s), 3056 (w), 2933 (w) cm^{-1}. UV−vis (MeCN): λ_{max} (lg ϵ) = 237 (4.57), 274 (4.01), 284 (4.08) nm. ^{1}H NMR ($CDCl_3$, 300 MHz): δ = 1.64 (br. s, 1 H, OH), 1.97−2.13 (m, 2 H, CH_2), 2.71−2.88 (m, 2 H, CH_2), 3.77−4.01 (m, 3 H, CH_2, CH), 7.48−7.54 (m, 2 H, CH), 7.80−7.87 (m, 3 H, CH), 7.96 (dd, ^3J = 8 Hz, ^4J = 2 Hz, 1 H, CH), 8.01 (d, ^4J = 1 Hz, 1 H, CH). ^{13}C NMR (75 MHz, $CDCl_3$): δ = 20.5, 21.4, 64.4, 75.7, 122.8, 125.0, 126.4, 126.8, 127.7, 128.2, 128.5, 132.9, 133.0, 133.9, 155.0. MS (EI, 70 eV): *m*/*z* = 241 (M^+, 5), 210 (9), 167 (20), 148 (41), 28 (100). HRMS (FT-ICR): calcd for $C_{15}H_{16}NO_2$ *m*/*z* = 242.11756, found 242.117734 ± 2 ppm.

6-Hydroxymethyl[3,4]cyclohexyl-5,6-dihydro-4*H*-1,2-oxazine (3j). Starting with **1j** (0.226 g, 2.0 mmol), *n*-BuLi (2.0 mL, 5.0 mmol, 2.5 M), and **2** (0.301 g, 2.2 mmol) in THF (10 mL), **3j** was isolated as a yellow oil (0.127 g, 38%). IR (KBr): $\tilde{\nu}$ = 3376 (s), 2930 (s), 2859 (s), 1649 (w), 1624 (w), 1447 (m) cm^{-1}. ^{1}H NMR ($CDCl_3$, 300 MHz): δ = 1.10−1.26 (m, 1 H, CH_2), 1.37−1.53 (m, 3 H, CH_2), 1.80−2.11 (m, 5 H, CH_2), 2.23−2.35 (m, 1 H, CH_2), 2.46−2.55 (m, 1 H, CH), 3.12 (br. s, 1 H, OH), 3.63−3.80 (m, 3 H, CH, CH_2). ^{13}C NMR (75 MHz, $CDCl_3$): δ = 25.1, 25.7, 26.3, 27.6, 27.8, 29.6, 32.1, 32.3, 33.1, 33.4, 33.8, 35.3, 64.0, 64.4, 73.2, 75.8, 161.0, 161.1. MS (EI, 70 eV): *m*/*z* = 169 (M^+, 12), 120 (12), 94 (12), 68 (14), 28 (100). HRMS (FT-ICR): calcd for $C_9H_{16}NO_2$ *m*/*z* = 170.11756, found 170.11749 ± 2 ppm.

6-Hydroxymethyl[3,4]cycloheptyl-5,6-dihydro-4*H*-1,2-oxazine (3k). Starting with **1k** (0.254 g, 2.0 mmol), *n*-BuLi (2.0 mL, 5.0 mmol, 2.5 M), and **2** (0.301 g, 2.2 mmol) in THF (10 mL), **3k** was isolated as a yellow oil (0.190 g, 51%). IR (KBr): $\tilde{\nu}$ = 3367 (s), 2926 (s), 2857 (s), 1678 (w), 1644 (w), 1606 (w), 1451 (m) cm^{-1}. ^{1}H NMR ($CDCl_3$, 300 MHz): δ = 1.41−1.96 (m, 10 H, CH_2), 2.32−2.50 (m, 3 H, CH, CH_2), 3.36 (br. s, 1 H, OH), 3.61−3.82 (m, 2 H, CH_2), 3.99−4.01 (m, 1 H, CH). ^{13}C NMR (75 MHz, $CDCl_3$): δ = 25.9, 26.7, 27.1, 27.3, 28.6, 28.7, 29.1, 30.4, 31.0, 32.7, 33.5, 33.6, 33.7, 35.0, 63.9, 64.1, 73.3, 76.2, 164.2, 166.8. MS (EI, 70 eV): *m*/*z* = 183 (M^+, 6), 151 (7), 107 (13), 55 (11), 28 (100). HRMS (FT-ICR): calcd for $C_{10}H_{18}NO_2$ *m*/*z* = 184.13321, found 184.13313 ± 2 ppm.

6-Hydroxymethyl[3,4]cyclooctyl-5,6-dihydro-4*H*-1,2-oxazine (3l). Starting with **1l** (0.282 g, 2.0 mmol), *n*-BuLi (2.0 mL, 5.0 mmol, 2.5 M), and **2** (0.301 g, 2.2 mmol) in THF (10 mL), **3l** was isolated as a yellow oil (0.193 g, 49%). IR (KBr): $\tilde{\nu}$ = 3365 (s), 2926 (s), 2858 (s), 1687 (w), 1651 (w), 1606 (w), 1452 (s) cm^{-1}. ^{1}H NMR ($CDCl_3$, 300 MHz): δ = 1.26−1.48 (m, 12 H, CH_2), 1.62−1.91 (m, H, CH_2), 2.20−2.31 (m, 2 H, CH_2), 2.43−2.51 (m, 1 H, CH), 3.45 (br. s, 1 H, OH), 3.65−3.75 (m, 2 H, CH_2), 3.90−3.96 (m, 1 H, CH). ^{13}C NMR (75 MHz, $CDCl_3$): δ = 23.9, 24.4, 24.5, 25.2, 25.4, 25.5, 25.8, 25.9, 27.3, 27.5, 30.0, 31.0, 31.3, 31.8, 32.8, 33.8, 63.9, 64.3, 73.4, 76.2, 165.1, 165.5. MS (EI, 70 eV): *m*/*z* = 197 (M^+, 1), 166 (2), 122 (3), 32 (22), 28 (100). HRMS (FT-ICR): calcd for $C_{11}H_{20}NO_2$ *m*/*z* = 198.14886, found 198.14886 ± 2 ppm. Anal. Calcd for $C_{11}H_{19}NO_2$: C, 66.97; H, 9.71; N, 7.10. Found: C, 66.89; H, 9.32; N, 6.72.

6-Hydroxymethyl[3,4]cyclododecyl-5,6-dihydro-4*H*-1,2-oxazine (3m). Starting with **1m** (0.394 g, 2.0 mmol), *n*-BuLi (2.0 mL, 5.0 mmol, 2.5 M), and **2** (0.301 g, 2.2 mmol) in THF (10 mL), **3m** was isolated as a colorless solid (0.263 g, 52%). Mp = 73 °C. IR (KBr): $\tilde{\nu}$ = 3365 (s), 2933 (s), 2862 (s), 1467 (m), 1445 (w) cm^{-1}. ^{1}H NMR ($CDCl_3$, 300 MHz): δ = 1.24−1.95 (m, 20 H, CH_2), 2.16−2.52 (m, 3 H, CH_2, CH), 2.66 (br. s, 1 H, OH), 3.63−3.76 (m, 3 H, CH_2, CH). ^{13}C NMR (75 MHz, $CDCl_3$): δ = 22.0, 22.3, 22.3, 22.6, 23.0, 23.0, 23.2, 23.3, 23.5, 24.1, 24.5, 24.7, 25.0, 25.2, 25.57, 25.58, 27.7, 28.54 28.56 29.2 29.3, 29.8, 30.1, 32.7, 64.6, 64.7, 72.0, 76.1, 161.4, 164.2. MS (EI, 70 eV): *m*/*z* = 253 (M^+, 18), 222 (11), 142 (13), 129 (20), 28 (100). HRMS (FT-ICR): calcd for $C_{15}H_{18}NO_2$ *m*/*z* = 254.21146, found 254.21146 ± 2 ppm. Anal. Calcd for $C_{15}H_{27}NO_2$: C, 71.10; H, 10.74; N, 5.53. Found: C, 70.81; H, 10.67; N, 5.55.

6-(Benzoyloxy)methyl-3-methyl-5,6-dihydro-4*H*-1,2-oxazine (3i). To a THF solution (10 mL) of **1i** (0.365 g, 5.0 mmol) was added *n*-BuLi (5.0 mL, 12.5 mmol, 2.5 M) at −78 °C, and the solution was stirred at this temperature for 45 min. Subsequently, the solution was stirred for 15 min at 20 °C. To the solution was added **2** (0.816 g, 6.0 mmol) at −78 °C. The solution was allowed to warm to 20 °C within 16 h; subsequently, benzoyl chloride (1.40 g, 10.0 mmol) was added. After the mixture was stirred for 2 h at 20 °C, a saturated aqueous solution of NH_4Cl (30 mL) was added. The organic and the aqueous layers were separated, and the latter was extracted with ethyl acetate (3 × 30 mL). The combined organic layers were dried (Na_2SO_4) and filtered, and the solvent of the filtrate was removed in vacuo. The residue was purified by chromatography (silica gel, hexane/EtOAc = 3:1) to give **3i** as a yellow oil (0.535 g, 45%). IR (KBr): $\tilde{\nu}$ = 3.423 (w), 3067 (w), 3037 (w), 2950 (m), 2925 (w), 2878 (w), 1778 (w), 1720 (s), 1654 (w), 1630 (w), 1604 (m), 1546 (w), 1527 (w), 1489 (w), 1448 (s) cm^{-1}. UV−vis (MeCN): λ_{max} (log ϵ) = 228 (4.11) nm. ^{1}H NMR ($CDCl_3$, 300 MHz): δ = 1.87 (m, 1 H, CH_2), 1.97 (s, 3 H, CH_3), 1.99 (m, 1 H, CH_2), 2.24 (dt, ^3J = 7 Hz, 2 H, CH_2), 3.97−4.05 (m, 1 H, CH), 4.43 (d, ^3J = 6 Hz, 1 H, CH_2), 4.45 (d, ^3J = 6 Hz, 1 H, CH_2), 7.43 (dt, ^3J = 7 Hz, ^4J = 2 Hz, 2 H, CH), 7.56 (ddd, ^3J = 7 Hz, ^4J = 2 Hz, 1 H, CH), 8.07 (dd, ^3J = 7 Hz, ^4J = 2 Hz, 2 H, CH). ^{13}C NMR (75 MHz, $CDCl_3$): δ = 21.2, 21.6, 24.2, 65.4, 71.8, 128.3, 129.6, 129.6, 133.0, 155.8, 166.3. MS (EI, 70 eV): *m*/*z* = 233 (M^+, 13), 110 (22), 105 (100), 98 (11), 78 (56). HRMS (FT-ICR): calcd for $C_{13}H_{16}NO_3$ *m*/*z* = 243.11247, found 234.11260 ± 2 ppm.

Typical Procedure for the Synthesis of 4a−e. To an Et_2O solution (20 mL) of **3a** (0.382 g, 2.0 mmol) was added PBr_3 (2.00 g) in excess, and the mixture was refluxed for 8 h. After the mixture was cooled to 20 °C, water (30 mL) was added to the solution. The organic and the aqueous layers were separated, and the latter was extracted with ethyl acetate (2 × 30 mL). The combined organic layers were dried (Na_2SO_4) and filtered, and the solvent of the filtrate was removed in vacuo. The residue was purified by chromatography (silica gel, hexane/EtOAc = 10:1) to give **4a** (0.097 g, 20%) as a colorless solid. ^{1}H NMR (300 MHz, $CDCl_3$): δ = 1.87−1.98 (m, 1 H, CH_2), 2.25−2.34 (m, 1 H, CH_2), 2.62−2.71 (m, 2 H, CH_2), 3.42−3.48 (m, 1 H, CH_2), 3.59−3.64 (m, 1 H, CH_2), 3.98−4.04 (m, 1 H, CH), 7.37−7.40 (m, 2 H, ArH), 7.67−7.77 (d, 2 H, ArH), 7.98 (m, 1 H, ArH). ^{13}C NMR (75 MHz, $CDCl_3$): δ =

21.2, 22.9, 32.4, 73.7, 126.3, 126.3, 129.2, 129.2, 130.7, 139.8, 154.8. MS (EI, 70 eV): $m/z = 253$ (M^+, 15).

4b. To an Et_2O solution (20 mL) of **3b** (0.410 g, 2.0 mmol) was added PBr_3 (2.00 g), and the mixture was refluxed for 8 h. Product **4b** was isolated as a colorless solid (0.113 g, 21%). ^1H NMR (300 MHz, $CDCl_3$): $\delta = 1.87-1.98$ (m, 1 H, CH_2), 2.25−2.34 (m, 1 H, CH_2), 2.39 (s, 3 H, CH_3), 2.62−2.71 (m, 2 H, CH_2), 3.42−3.48 (m, 1 H, CH_2), 3.59−3.64 (m, 1 H, CH_2), 3.98−4.02 (m, 1 H, CH), 7.17−7.29 (m, 3 H, ArH), 7.44−7.47 (m, 1 H, ArH). ^{13}C NMR (75 MHz, $CDCl_3$): $\delta = 21.3$, 21.4, 22.7, 32.3, 73.7, 122.5, 126.0, 128.3, 130.4, 135.2, 138.1, 155.0. MS (EI, 70 eV): $m/z = 270$ (M^+, 6), 269 (59), 267 (60), 174 (100), 158 (13), 146(25), 132 (21), 117 (42), 105(10), 91 (56), 65 (18), 55 (12). HRMS: calcd for $C_{12}H_{14}NOBr$ $m/z = 269.0233$, found 269.0231.

4c. To an Et_2O solution (20 mL) of **3c** (0.442 g, 2.0 mmol) was added PBr_3 (2.00 g), and the mixture was refluxed for 8 h. Product **4c** was isolated as a brownish solid (0.199 g, 35%). ^1H NMR (300 MHz, $CDCl_3$): $\delta = 1.87-1.98$ (m, 1 H,CH_2), 2.25−2.34 (m, 1 H, CH_2), 3.73 (s, 3 H, OCH_3), 2.62−2.71 (m, 2 H, CH_2), 3.42−3.48 (m, 1 H, CH_2), 3.59−3.64 (m, 1 H, CH_2), 3.98−4.04 (m, 1 H, CH), 6.87−6.91 (d, 2 H, ArH), 7.61−7.65 (d, 2 H, ArH). ^{13}C NMR (75 MHz, $CDCl_3$): $\delta = 21.2$, 22.9, 32.4, 55.3, 73.7, 113.85, 126.8, 126.8, 127.8, 154.5, 160.8. IR (KBr, cm^{-1}): $\tilde{\nu} = 2926$ (m), 2362 (w), 1847 (s), 1447 (m), 1252 (m), 1029 (m), 821 (m). MS (EI, 70 eV): $m/z = 283$ (M^+, 52), 190 (37), 133 (100), 90 (35), 77 (42), 63 (22), 39(15). HRMS: calcd for $C_{12}H_{14}NO_2Br$ $m/z = 283.0202$, found 283.0200.

4d. To an Et_2O solution (20 mL) of **3d** (0.442 g, 2.0 mmol) was added PBr_3 (2.00 g), and the mixture was refluxed for 8 h. Product **4d** was isolated as a brownish solid (0.182 g, 32%). ^1H NMR (300 MHz, $CDCl_3$): $\delta = 1.87-1.98$ (m, 1 H, CH_2), 2.25−2.34 (m, 1 H, CH_2), 3.73 (s, 3 H, OCH_3), 2.62−2.71 (m, 2 H, CH_2), 3.42−3.48 (m, 1 H, CH_2), 3.59−3.64(m, 1 H, CH_2), 3.98−4.02 (m, 1 H, CH), 6.91−6.94 (m, 1 H, ArH), 7.18−7.31 (m, 3 H, ArH). ^{13}C NMR (75 MHz, $CDCl_3$): $\delta = 21.1$, 21,7, 32.3, 55.2, 74.1, 111.2, 115.7, 117.7, 129.3, 136.6, 154.6, 159.5. IR (KBr, cm^{-1}): $\tilde{\nu} =$ 3191 (m), 2986 (w), 1842 (s), 1361 (m), 1293 (m), 1209 (m), 1135 (m), 911 (m), 864 (m). MS (EI, 70 eV): $m/z = 283$ (M^+, 18), 190 (17), 133 (100), 90 (24), 77 (32), 63 (46), 39(11). HRMS: calcd for $C_{12}H_{14}NO_2Br$ $m/z = 283.0202$, found 283.0205.

4e. To an Et_2O solution (20 mL) of **3e** (0.482 g, 2.0 mmol) was added PBr_3 (2.00 g), and the mixture was refluxed for 12 h. Product **4e** was isolated as a brownish solid (0.073 g, 12%). ^1H NMR (300 MHz, $CDCl_3$): $\delta = 1.87-1.98$ (m, 1 H, CH_2), 2.25−2.34 (m, 1 H, CH_2), 3.73 (s, 3 H, OCH_3), 2.62−2.71 (m, 2 H, CH_2), 3.42−3.48 (m, 1 H, CH_2), 3.59−3.64 (m, 1 H, CH_2), 3.98−4.04 (m, 1 H, CH), 7.49−7.52 (m, 2 H, ArH), 7.81−7.96 (m, 3 H, ArH), 7.98−8.01 (m, 2 H, ArH). ^{13}C NMR (75 MHz, $CDCl_3$): $\delta = 21.2$, 22.8, 32.3, 74.0, 122.8, 125.0, 126.4, 126.8, 127.7, 128.2, 128.5, 132.9, 133.9, 154.6. MS (EI, 70 eV): $m/z = 305$ (M^+, 60), 303 (62), 221 (16), 210 (82), 207 (78), 205 (20), 180 (22), 178 (18), 167(36), 165 (43), 153 (100), 127 (77), 81 (11), 55 (16). HRMS: calcd for $C_{15}H_{14}NO_2Br$ $m/z = 305.0233$, found 305.0232.

Typical Procedure for the Synthesis of Hydrazones 6a−n. To an acetic acid solution (10 mL, 50%) of the hydrazide (2.00 g, 19.2 mmol) were added water (15 mL) and ethanol (50 mL). To this solution was added an EtOH solution (5 mL) of **5a** (19.2 mmol), and the solution was stirred at 20 °C for 2 h. To the solution was added a saturated aqueous solution of sodium bicarbonate (100 mL); the organic and the aqueous layers were separated, and the latter was extracted with EtOAc (3 × 100 mL). The combined organic layers were dried (Na_2SO_4) and filtered, and the filtrate was concentrated in vacuo. The residue was purified by chromatography (silica gel, hexane/ EtOAc = 3:1) to give **6a** as a colorless solid (2.37 g, 60%). Mp = 120 °C (lit.[9,27,28] mp 119−120 °C). **6a.** IR (KBr, cm^{-1}): $\tilde{\nu} = 3431$ (m), 3206 (s), 2982 (m), 1748 (s), 1730 (s), 1704 (s), 1542 (s), 1420 (m). UV−vis (acetonitrile, nm): λ_{max} (log ϵ): 204.41 (4.2), 267.60 (4.2). IR (KBr, cm^{-1}): $\tilde{\nu} = 3431$ (m), 3206 (s), 2982 (m), 1748 (s), 1730 (s), 1704 (s), 1542 (s), 1420 (m). UV−Vis (acetonitrile, nm): λ_{max} (log ϵ): 204.41 (4.2), 267.60 (4.2). ^1H NMR (300 MHz, $CDCl_3$): $\delta = 1.33$ (t, $^3J = 7$ Hz, 3 H, OCH_2CH_3), 2.20 (s, 3 H, CH_3), 4.30 (q, $^3J = 7$ Hz, 2 H, CH_2), 7.21−7.37 (m, 3 H, Ar), 7.73−7.77 (m, 2 H, Ar), 8.15 (br s, 1 H, NH). ^{13}C NMR (75 MHz, $CDCl_3$): $\delta = 13.0$, 14.6, 61.9, 126.3, 128.3, 129.1, 138.1, 148.6, 154.4. MS (EI, 70 eV): $m/z = 206$ (M^+, 16), 133 (8), 92 (10), 77 (7), 28 (100). Anal. Calcd for $C_{11}H_{14}N_2O_2$: C, 64.06; H, 6.84; N, 13.58. Found: C, 63.88; H, 7.02; N, 13.20.

4-Methylacetophenone-ethoxycarbonylhydrazone (6b). Starting with ethyl carbazate (2.00 g, 19.2 mmol), dissolved in AcOH (10 mL, 50%), water (15 mL), and ethanol (50 mL), and an EtOH solution (5 mL, 20%) of 4-methylacetophenone (19.2 mmol), **6b** was isolated as a colorless solid (1.56 g, 37%). Mp: = 108 °C. IR (KBr, cm^{-1}): $\tilde{\nu} = 3204$ (s), 3035 (m), 2972 (m), 1724 (s), 1618 (m), 1538 (s), 1454 (m). UV−vis (acetonitrile, nm): λ_{max} (log ϵ) 207.23 (4.2), 270.54 (4.3). ^1H NMR (300 MHz, $CDCl_3$): $\delta = 1.35$ (t, $^3J = 7$ Hz, 3 H, OCH_2CH_3), 2.18 (s, 3 H, CH_3), 2.34 (s, 3 H, $ArCH_3$), 4.30 (q, $^3J = 7$ Hz, 2 H, CH_2), 7.14 (d, $^3J = 8$ Hz, 2 H, Ar), 7.65 (d, $^3J = 8$ Hz, 2 H, Ar), 8.06 (br s, 1 H, NH). ^{13}C NMR (75 MHz, $CDCl_3$): $\delta = 12.7$, 14.2, 20.8, 61.4, 125.9, 128.6, 135.0, 138.6, 148.5, 154.2. MS (EI, 70 eV) $m/z = 220$ (M^+, 100), 147 (85), 132 (53), 106 (73), 91 (49). Anal. Calcd for $C_{12}H_{16}N_2O_2$: C, 65.43; H, 7.32; N, 12.72. Found: C, 65.56; H, 7.69; N, 12.56.

4-Methoxyacetophenone-ethoxycarbonylhydrazone (6c). Starting with ethyl carbazate (2.00 g, 19.2 mmol), dissolved in AcOH (10 mL, 50%), water (15 mL), and ethanol (50 mL), and an EtOH solution (5 mL, 20%) of 4-methoxyacetophenone (19.2 mmol), **6c** was isolated as a colorless solid (1.46 g, 32%). Mp: = 131 °C. IR (KBr, cm^{-1}): $\tilde{\nu} = 3232$ (m), 2986 (m), 1702 (s), 1609 (m), 1511 (m), 1480 (s), 1424 (s). UV−vis (acetonitrile, nm): λ_{max} (log ϵ) 210.13 (4.1), 276.58 (4.2). ^1H NMR (300 MHz, $CDCl_3$): $\delta = 1.34$ (t, $^3J = 7$ Hz, 3 H, OCH_2CH_3), 2.18 (s, 3 H, CH_3), 3.79 (s, 3 H, OCH_3), 4.30 (q, $^3J = 7$ Hz, 2 H, CH_2), 6.86 (dt, $^3J = 10$ Hz, $^4J =$ 2 Hz, 2 H, Ar), 7.70 (dt, $^3J = 10$ Hz, $^4J = 2$ Hz, 2 H, Ar), 8.19 (br s, 1 H, NH). ^{13}C NMR (75 MHz, $CDCl_3$): $\delta = 12.7$, 14.3, 55.1, 61.2, 113.4, 127.5, 130.5, 148.3, 160.1, 160.2. MS (EI, 70 eV): $m/z = 236$ (M^+, 9), 163 (5), 134 (5), 104 (7), 28 (100).

3-Methylacetophenone-ethoxycarbonylhydrazone (6d). Starting with ethyl carbazate (2.00 g, 19.2 mmol), dissolved in AcOH (10 mL, 50%), water (15 mL), and ethanol (50 mL), and an EtOH solution (5 mL, 20%) of 3-methylacetophenone (19.2 mmol), **6d** was isolated as a yellow solid (1.43 g, 34%). Mp: = 81 °C. IR (KBr, cm^{-1}): $\tilde{\nu} = 3208$ (m), 3040 (w), 2982 (m), 1728 (s), 1704 (s), 1539 (s), 1479 (m), 1460 (m), 1444 (m), 1424 (m). UV−vis (acetonitrile, nm): λ_{max} (log ϵ) 206.98 (4.4), 268.61 (4.2). ^1H NMR (300 MHz, $CDCl_3$): $\delta = 1.35$ (t, $^3J = 7$ Hz, 3 H, OCH_2CH_3), 2.20 (s, 3 H, CH_3), 2.37 (s, 3 H, $ArCH_3$), 4.31 (q, $^3J = 7$ Hz, 2 H, CH_2), 7.14−7.27 (m, 2 H, Ar), 7.50−7.60 (m, 2 H, Ar), 8.02 (br s, 1 H, NH). ^{13}C NMR (75 MHz, $CDCl_3$): $\delta = 12.7$, 14.0, 20.8, 61.1, 122.9, 126.3, 127.5, 129.7, 137.2, 137.7, 148.6, 154.1. MS (EI, 70 eV): $m/z = 220$ (M^+, 100), 147 (97), 132 (54), 106 (72), 91 (50). Anal. Calcd for $C_{12}H_{16}N_2O_2$: C, 65.43; H, 7.32; N, 12.72. Found: C, 65.20; H, 6.77; N, 12.60.

3-Methoxyacetophenone-ethoxycarbonylhydrazone (6e). Starting with ethyl carbazate (2.00 g, 19.2 mmol), dissolved in AcOH (10 mL, 50%), water (15 mL), and ethanol (50 mL), and an EtOH solution (5 mL, 20%) of 3-methoxyacetophenone (19.2 mmol), **6e** was isolated as a yellow solid (1.71 g, 38%). Mp = 92 °C. IR (KBr, cm^{-1}): $\tilde{\nu} = 3207$ (s), 3040 (m), 3000 (m), 2974 (m), 2941 (w), 1734 (s), 1704 (s), 1606 (m), 1578 (m), 1537 (s), 1485 (s), 1437 (m). UV−vis (acetonitrile, nm): λ_{max} (log ϵ) 213.51 (4.3), 268.07 (4.2). ^1H NMR (300 MHz, $CDCl_3$): $\delta = 1.35$ (t, $^3J = 7$ Hz, 3 H, OCH_2CH_3), 2.20 (s, 3 H, CH_3), 3.83 (s, 3 H, OCH_3), 4.31 (q, $^3J = 7$ Hz, 2 H, CH_2), 6.88−6.92 (m, 2 H, Ar), 7.24−7.34 (m, 2 H, Ar), 8.03 (br s, 1 H, NH). ^{13}C NMR (75 MHz, $CDCl_3$): $\delta =$ 13.0, 14.5, 55.3, 61.9, 111.5, 115.1, 118.9, 129.2, 139.5, 148.3, 154.2, 159.6. MS (EI, 70 eV): $m/z = 236$ (M^+, 6), 163 (4), 147

(4), 122 (2), 28 (100). Anal. Calcd for $C_{12}H_{16}N_2O_3$: C, 61.00; H, 6.83; N, 11.86. Found: C, 60.53; H, 6.22; N, 12.16.

2-Methylacetophenone-ethoxycarbonylhydrazone (6f). Starting with ethyl carbazate (2.00 g, 19.2 mmol), dissolved in AcOH (10 mL, 50%), water (15 mL), and ethanol (50 mL), and an EtOH solution (5 mL, 20%) of 2-methylacetophenone (19.2 mmol), **6f** was isolated as a colorless solid (1.82 g, 43%). Mp = 115 °C. IR (KBr, cm^{-1}): $\tilde{\nu}$ = 3433 (w), 3363 (w), 3212 (m), 3047 (w), 2984 (w), 1710 (s), 1621 (w), 1544 (s), 1492 (m), 1438 (m). UV−vis (acetonitrile, nm): λ_{max} (log ϵ) 241.39 (4.0). ^{1}H NMR (300 MHz, $CDCl_3$): δ = 1.23−1.36 (m, 3 H, OCH_2CH_3), 2.06 (s, 3 H, CH_3), 2.19−2.36 (m, 3 H, $ArCH_3$), 4.11−4.34 (m, 2 H, CH_2), 7.03 (dd, ^3J = 19 Hz, ^4J = 6 Hz, 2 H, Ar), 7.16−7.33 (m, 2 H, Ar), 8.4 (br s, 1 H, NH). ^{13}C NMR (75 MHz, $CDCl_3$): δ = 14.5, 18.8, 20.3, 62.0, 126.4, 127.0, 129.6, 131.1, 134.4, 139.5, 151.5, 152.3. MS (EI, 70 eV): *m*/*z* = 220 (M^+, 62), 205 (32), 132 (100), 117 (51), 91 (35). Anal. Calcd for $C_{12}H_{16}N_2O_2$: C, 65.43; H, 7.32; N, 12.72. Found: C, 64.71; H, 7.55; N, 12.63.

1-Acetonaphthone-ethoxycarbonylhydrazone (6g). Starting with ethyl carbazate (2.00 g, 19.2 mmol), dissolved in AcOH (10 mL, 50%), water (15 mL), and ethanol (50 mL), and an EtOH solution (5 mL, 20%) of 1-acetonaphthone (19.2 mmol), **6g** was isolated as a colorless solid (1.47 g, 30%). Mp = 144 °C. IR (KBr, cm^{-1}): $\tilde{\nu}$ = 3228 (m), 3049 (w), 2979 (w), 1733 (s), 1708 (s), 1540 (s), 1457 (w), 1438 (m). UV−vis (acetonitrile, nm): λ_{max} (log ϵ) 222.59 (4.7), 290.92 (4.0). ^{1}H NMR (300 MHz, $CDCl_3$): δ = 1.35 (t, ^3J = 7 Hz, 3 H, OCH_2CH_3), 2.32 (s, 3 H, CH_3), 4.33 (q, ^3J = 7 Hz, 2 H, CH_2), 7.40−7.51 (m, 3 H, Ar), 7.80−7.86 (m, 2 H, Ar), 8.00−8.03 (m, 2 H, Ar), 8.4 (br s, 1 H, NH). ^{13}C NMR (75 MHz, $CDCl_3$): δ = 14.5, 17.7, 62.0, 125.0, 125.2, 125.8, 126.1, 126.4, 128.4, 129.0, 130.5, 133.7, 137.3, 150.5, 154.2. MS (EI, 70 eV): *m*/*z* = 256 (M^+, 5), 168 (42), 152 (12), 114 (7), 28 (100). Anal. Calcd for $C_{15}H_{16}N_2O_2$: C, 70.29; H, 6.29; N, 10.93. Found: C, 70.01; H, 6.15; N, 11.16.

2-Acetonaphthone-ethoxycarbonylhydrazone (6h). Starting with ethyl carbazate (2.00 g, 19.2 mmol), dissolved in AcOH (10 mL, 50%), water (15 mL), and ethanol (50 mL), and an EtOH solution (5 mL, 20%) of 2-acetonaphthone (19.2 mmol), **6h** was isolated as a colorless solid (1.04 g, 21%). Mp = 129 °C. IR (KBr, cm^{-1}): $\tilde{\nu}$ = 3433 (w), 3240 (m), 3137 (w), 3060 (w), 2983 (w), 1697 (s), 1604 (w), 1534 (m), 1483 (m), 1421 (s). UV−vis (acetonitrile, nm): λ_{max} (log ϵ): 203.04 (4.6), 234.38 (4.4), 239.97 (4.4), 258.57 (4.5), 290.47 (4.4), 301.91 (4.3). ^{1}H NMR (300 MHz, $CDCl_3$): δ = 1.36 (t, ^3J = 7 Hz, 3 H, OCH_2CH_3), 2.27 (s, 3 H, CH_3), 4.33 (q, ^3J = 7 Hz, 2 H, CH_2), 7.42−7.48 (m, 2 H, Ar), 7.77−7.85 (m, 3 H, Ar), 8.03−8.09 (m, 2 H, Ar), 8.21 (br s, 1 H, NH). ^{13}C NMR (75 MHz, $CDCl_3$): δ = 12.7, 14.6, 62.0, 123.8, 125.9, 126.1, 127.6, 127.9, 128.5, 133.0, 133.6, 135.4, 148.4, 154.3. MS (EI, 70 eV): *m*/*z* = 256 (M^+, 14), 183 (8), 168 (42), 114 (6), 28 (100).

Cyclopentanone-ethoxycarbonylhydrazone (6i).[29] Starting with ethyl carbazate (2.00 g, 19.2 mmol), dissolved in AcOH (10 mL, 50%), water (15 mL), and ethanol (50 mL), and an EtOH solution (5 mL, 20%) of cyclopentanone (19.2 mmol), **6i** was isolated as a colorless solid (2.13 g, 65%). Mp = 83 °C (lit.[30] mp 101−102 °C). IR (KBr, cm^{-1}): $\tilde{\nu}$ = 3224 (s), 3178 (s), 2965 (s), 1719 (s), 1539 (s). UV−Vis (acetonitrile, nm): λ_{max} (log ϵ): 208.31 (4.0), 223.45 (4.0). ^{1}H NMR (300 MHz, $CDCl_3$): δ = 1.32 (t, ^3J = 7 Hz, 3 H, CH_3), 1.76 (dt, ^3J = 7 Hz, 2 H, CH_2), 1.87 (dt, ^3J = 7 Hz, 2 H, CH_2), 2.24 (t, ^3J = 7 Hz, 2 H, OCH_2CH_3), 2.42 (t, ^3J = 7 Hz, 2 H, CH_2), 4.28 (q, ^3J = 7 Hz, 2 H, CH_2), 7.74 (br s, 1 H, NH). ^{13}C NMR (75 MHz, $CDCl_3$): δ = 14.3, 24.5, 24.5, 27.0, 30.0, 61.1, 154.1, 163.0. MS (EI, 70 eV): *m*/*z* = 170 (M^+, 100), 124 (23), 97 (90), 82 (83), 68 (74).

Cyclohexanone-ethoxycarbonylhydrazone (6j).[29] Starting with ethyl carbazate (2.00 g, 19.2 mmol), dissolved in AcOH (10 mL, 50%), water (15 mL), and ethanol (50 mL), and an EtOH solution (5 mL, 20%) of cyclohexanone (19.2 mmol), **6j** was isolated as a colorless oil (0.64 g, 18%). IR (CAP, cm^{-1}): $\tilde{\nu}$ = 3590 (w), 3262 (s), 2981 (s), 2935 (s), 2882 (m), 2860 (s), 2363 (w), 2336 (w), 1718 (s), 1644 (m), 1525 (s), 1477 (s), 1448 (s), 1425 (s). ^{1}H NMR (300 MHz, $CDCl_3$): δ = 1.20−1.34 (m, 3 H, CH_3), 1.55−1.75 (m, 6 H, 3 × CH_2), 2.23−2.39 (m, 4 H, 2 × CH_2), 4.13−4.30 (m, 2 H, OCH_2CH_3), 7.94 (br s, 1 H, NH). ^{13}C NMR (75 MHz, $CDCl_3$): δ = 14.6, 25.6, 25.8, 26.2, 26.8, 35.4, 61.6, 154.6, 157.1. MS (EI, 70 eV): *m*/*z* = 184 (M^+, 85), 110 (37), 96 (100), 81 (54), 68 (76).

Cycloheptanone-ethoxycarbonylhydrazone (6k). Starting with ethyl carbazate (2.00 g, 19.2 mmol), dissolved in AcOH (10 mL, 50%), water (15 mL), and ethanol (50 mL), and an EtOH solution (5 mL, 20%) of cycloheptanone (19.2 mmol), **6k** was isolated as a colorless solid (1.36 g, 36%). Mp = 80 °C. IR (KBr, cm^{-1}): $\tilde{\nu}$ = 3252 (s), 2919 (s), 2853 (m), 1700 (s), 1481 (m), 1430 (s). UV−Vis (acetonitrile, nm): λ_{max} (log ϵ): 210.19 (4.0), 222.84 (4.1). ^{1}H NMR (300 MHz, $CDCl_3$): δ = 1.34 (t, ^3J = 7 Hz, 3 H, CH_3), 1.58−1.65 (m, 6 H, 3 x CH_2), 1.71−1.76 (m, 2 H, CH_2), 2.26−2.35 (m, 2 H, CH_2), 2.48−2.55 (m, 2 H, CH_2), 4.26 (q, ^3J = 7 Hz, 2 H, OCH_2CH_3), 7.78 (br s, 1 H, NH). ^{13}C NMR (75 MHz, $CDCl_3$): δ = 14.3, 24.1, 27.2, 29.6, 29.9, 30.0, 36.6, 61.4, 154.0, 159.0. MS (EI, 70 eV): *m*/*z* = 198 (M^+, 50), 170 (63), 95 (83), 68 (56), 29 (100). Anal. Calcd for $C_{10}H_{18}N_2O_2$: C, 60.58; H, 9.15; N, 14.13. Found: C, 60.51; H, 9.79; N, 14.33.

Cyclooctanone-ethoxycarbonylhydrazone (6l). Starting with ethyl carbazate (2.00 g, 19.2 mmol), dissolved in AcOH (10 mL, 50%), water (15 mL), and ethanol (50 mL), and an EtOH solution (5 mL, 20%) of cyclooctanone (19.2 mmol), **6l** was isolated as a colorless solid (0.89 g, 22%). Mp = 93 °C. IR (KBr, cm^{-1}): $\tilde{\nu}$ = 3215 (s), 3042 (m), 2981 (m), 2920 (s), 2862 (m), 1723 (s), 1699 (s), 1636 (w), 1540 (s), 1470 (s). UV−vis (acetonitrile, nm): λ_{max} (log ϵ): 225.78 (4.0). ^{1}H NMR (300 MHz, $CDCl_3$): δ = 1.32 (t, ^3J = 7 Hz, 3 H, CH_3), 1.40−1.58 (m, 4 H, 2 × CH_2), 1.70 − 1.81 (m, 4 H, 2 × CH_2), 2.32−3.45 (q, ^3J = 12 Hz, 2 H, CH_2), 2.42−2.46 (m, 4 H, 2 × CH_2), 4.28 (q, ^3J = 7 Hz, 2 H, OCH_2CH_3), 7.79 (br s, 1 H, NH). ^{13}C NMR (75 MHz, $CDCl_3$): δ = 14.5, 24.3, 24.3, 25.2, 27.1, 27.2, 36.2, 36.3, 61.6, 154.0, 159.0. MS (EI, 70 eV): *m*/*z* = 212 (M^+, 7), 184 (45), 144 (12), 108 (12), 28 (100). Anal. Calcd for $C_{11}H_{20}N_2O_2$: C, 61.99; H, 9.46; N, 13.14. Found: C, 61.98; H, 9.76; N, 13.28.

Cyclododecanone-ethoxycarbonylhydrazone (6m). Starting with ethyl carbazate (2.00 g, 19.2 mmol), dissolved in AcOH (10 mL, 50%), water (15 mL), and ethanol (50 mL), and an EtOH solution (5 mL, 20%) of cyclododecanone (19.2 mmol), **6m** was isolated as a colorless solid (1.01 g, 20%). Mp = 107 °C. IR (KBr, cm^{-1}): $\tilde{\nu}$ = 3205 (m), 2934 (s), 2860 (m), 1699 (s), 1541 (s). UV−vis (acetonitrile, nm): λ_{max} (log ϵ) 206.16 (4.0), 222.79 (4.0). ^{1}H NMR (300 MHz, $CDCl_3$): δ = 1.32 (t, ^3J = 7 Hz, 3 H, CH_3), 1.40−1.66 (m, 14 H, 7 x CH_2), 1.68−1.73 (m, 4 H, 2 x CH_2), 2.24 (t, ^3J = 7 Hz, 2 H, CH_2), 2.35 (t, ^3J = 7 Hz, 2 H, CH_2), 4.26 (q, ^3J = 7 Hz, 2 H, OCH_2CH_3), 7.74 (br s, 1 H, NH). ^{13}C NMR (75 MHz, $CDCl_3$): δ = 14.5, 22.2, 22.7, 23.2, 23.3, 23.6, 24.4, 24.5, 24.7, 25.1, 26.6, 33.1, 61.5, 154.3, 156.8. MS (EI, 70 eV): *m*/*z* = 268 (M^+, 3), 157 (34), 144 (100), 104 (43), 83 (52). Anal. Calcd for $C_{15}H_{28}N_2O_2$: C, 67.13; H, 10.51; N, 10.44. Found: C, 67.48; H, 10.28; N, 10.09.

α-Tetralone-ethoxycarbonylhydrazone (6n). Starting with ethyl carbazate (2.00 g, 19.2 mmol), dissolved in AcOH (10 mL, 50%), water (15 mL), and ethanol (50 mL), and an EtOH solution (5 mL, 20%) of α-tetralone (19.2 mmol), **6n** was isolated as a slightly yellow solid (1.36 g, 30%). Mp = 113 °C. IR (KBr, cm^{-1}): $\tilde{\nu}$ = 3434 (m), 3219 (m), 2986 (w), 2939 (m), 1732 (s), 1707 (s), 1615 (w), 1533 (s), 1480 (m), 1451 (m), 1418 (m). UV−vis (acetonitrile, nm): λ_{max} (log ϵ) 208.48 (4.3), 273.64 (4.2). ^{1}H NMR (300 MHz, $CDCl_3$): δ = 1.35 (t, ^3J = 7 Hz, 3 H, CH_3), 1.95 (dt, ^3J = 8 Hz, ^4J = 4 Hz, 2 H, CH_2), 2.49 (t, ^3J = 7 Hz, 2 H, CH_2), 2.72 (t, ^3J = 7 Hz, 2 H, CH_2), 4.30 (q, ^3J = 7 Hz, 2 H, OCH_2CH_3), 7.09−7.27 (m, 3 H, Ar), 8.03 (br s, 1 H, NH), 8.16 (dd, ^3J = 7 Hz, ^4J = 2 Hz, 1 H, Ar). ^{13}C NMR (75 MHz, $CDCl_3$): δ = 14.6, 21.5, 24.9, 29.4, 61.9, 125.2, 126.5, 128.2, 129.1, 132.2, 139.3, 148.3, 154.2. MS

(EI, 70 eV): m/z = 232 (M^+, 10), 143 (5), 131 (7), 115 (9), 28 (100). Anal. Calcd for $C_{13}H_{16}N_2O_2$: C, 67.22; H, 6.94; N, 12.06. Found: C, 66.99; H, 6.70; N, 12.03.

General Procedure for the Cyclization of Dilithiated Hydrazones with Epibromohydrin. To a THF solution (40 mL) of **6** (4.0 mmol) was added *n*-butyllithium (9.0 mmol, 2.5 M) at −78 °C. After being stirred for 1 h at −78 °C, the mixture was stirred for 10 min at 20 °C. To the solution was added **2** (4.4 mmol) at −78 °C. The reaction mixture was allowed to warm to 20 °C over 16 h. Subsequently, a saturated aqueous solution of NH_4Cl was added. The organic and the aqueous layers were extracted with EtOAc (2 × 30 mL). The combined organic layers were dried (Na_2SO_4) and filtered, and the solvent of the filtrate was removed in vacuo. The residue was purified by chromatography (silica gel, *n*-heptane/ EtOAc, 4:1→ 1:1).

2-Phenyl-3,4,4a,5-tetrahydrooxazolo[3,4-*b*]pyridazin-7-one (7a). Starting with **6a** (0.41 g, 2.0 mmol), THF (10 mL), *n*-BuLi (2.0 mL, 5.0 mmol), and epibromohydrin (0.25 mL, 3.0 mmol), **7a** was isolated as a yellow solid (0.200 g, 46%). Mp = 199 °C. IR (KBr, cm^{-1}): $\tilde{\nu}$ = 2901 (w), 1757 (s), 1402 (s). UV−vis (acetonitrile, nm): λ_{max} (log ϵ) 206.92 (4.0), 218.22 (4.0), 281.41 (4.2). ^{1}H NMR (300 MHz, $CDCl_3$): δ = 1.78 (dddd, ^2J = 12 Hz, ^3J = 6 Hz, ^3J = 7 Hz, 1 H, CH_2), 2.35 (dddd, ^2J = 12 Hz, ^3J = 6 Hz, ^3J = 7 Hz, 1 H, CH_2), 2.60 (ddd, ^2J = 25 Hz, ^3J = 7 Hz, ^3J = 6 Hz, 1 H, CH_2), 2.88 (ddd, ^2J = 12 Hz, ^3J = 7 Hz, ^3J = 7 Hz, 1 H, CH), 3.95−4.04 (m, 2 H, CH, OCH_2), 4.58−4.62 (m, 1 H, CH_2), 7.34−7.39 (m, 3 H, Ar), 7.79−7.83 (m, 2 H, Ar). ^{13}C NMR (75 MHz, $CDCl_3$): δ = 22.2, 22.3, 50.4, 67.9, 125.7, 128.3, 129.7, 136.1, 150.5, 153.3. MS (EI, 70 eV): m/z = 216 (M^+, 40), 206 (23), 161 (100), 133 (24), 105 (20). Anal. Calcd for $C_{12}H_{12}N_2O_2$: C, 66.65; H, 5.59; N, 12.96. Found: C, 66.14; H, 5.68; N, 12.83.

2-(*p*-Tolyl)-3,4,4a,5-tetrahydrooxazolo[3,4-*b*]pyridazin-7-one (7b). Starting with **6b** (0.44 g, 2.0 mmol), *n*-BuLi (2.0 mL, 5.0 mmol), and epibromohydrin (0.25 mL, 3.0 mmol) in THF (10 mL), **7b** was isolated as a yellow solid (0.31 g, 56%): mp = 222 °C. IR (KBr, cm^{-1}): $\tilde{\nu}$ = 2361 (w), 2336 (w), 1755 (s), 1611 (w), 1467 (m), 1405 (s). UV−vis (acetonitrile, nm): λ_{max} (log ϵ) 209.24 (4.0), 214.60 (4.0), 220.28 (4.0), 283.68 (4.2). ^{1}H NMR (300 MHz, $CDCl_3$): δ = 1.73−1.84 (m, 1 H, CH_2), 2.29−2.38 (m, 4 H, CH_2, CH_3), 2.53−2.65 (m, 1 H, CH_2), 2.88 (dd, ^2J = 18 Hz, ^3J = 6 Hz, 1 H, CH), 3.96−4.04 (m, 2 H, CH, OCH_2), 4.56−4.63 (m, 1 H, CH_2), 7.17 (dd, ^3J = 8 Hz, ^4J = 2 Hz, 2 H, Ar), 7.71 (dd, ^3J = 8 Hz, ^4J = 2 Hz, 2 H, Ar). ^{13}C NMR (75 MHz, $CDCl_3$): δ = 21.2, 22.2, 22.9, 50.5, 67.9, 125.7, 129.0, 133.3, 139.9, 150.5, 153.4. MS (EI, 70 eV): m/z = 230 (M^+, 17), 160 (12), 143 (5), 91 (4), 28 (100).

2-(4-Methoxyphenyl)-3,4,4a,5-tetrahydrooxazolo[3,4-*b*]pyridazin-7-one (7c). Starting with **6c** (0.47 g, 2.0 mmol), *n*-BuLi (2.0 mL, 5.0 mmol), and epibromohydrin (0.25 mL, 3.0 mmol) in THF (10 mL), **7c** was isolated as a yellow solid (0.20 g, 41%). Mp = 209 °C. IR (KBr, cm^{-1}): $\tilde{\nu}$ = 3034 (w), 2963 (w), 2935 (w), 2911 (w), 2844 (w), 1750 (s), 1607 (s), 1513 (m), 1467 (m), 1407 (s). UV−vis (acetonitrile, nm): λ_{max} (log ϵ) 287.90 (4.3). ^{1}H NMR (300 MHz, $CDCl_3$): δ = 1.31 − 1.36 (m, 1 H, CH_2), 2.34 (m, 1 H, CH_2), 2.53−2.65 (m, 1 H, CH_2), 2.87 (dd, ^2J = 18 Hz, ^3J = 6 Hz, 1 H, CH), 3.81 (s, 3 H, OCH_3), 3.99−4.05 (m, 2 H, CH, OCH_2), 4.62 (m, 1 H, CH_2), 6.89 (dd, ^3J = 7 Hz, ^4J = 2 Hz, 2 H, Ar), 7.77 (dd, ^3J = 7 Hz, ^4J = 2 Hz, 2 H, Ar). ^{13}C NMR (75 MHz, $CDCl_3$): δ = 22.2, 23.1, 50.5, 55.3, 67.9, 113.7, 127.3, 128.8, 150.3, 153.4, 161.0. MS (EI, 70 eV): m/z = 246 (M^+, 65), 189 (34), 175 (21), 135 (65), 28 (100).

2-(*m*-Tolyl)-3,4,4a,5-tetrahydrooxazolo[3,4-*b*]pyridazin-7-one (7d). Starting with **6d** (0.44 g, 2.0 mmol), *n*-BuLi (2.0 mL, 5.0 mmol), and epibromohydrin (0.25 mL, 3.0 mmol) in THF (10 mL), **7d** was isolated as a yellow solid (0.25 g, 53%). Mp = 168 °C. IR (KBr, cm^{-1}): $\tilde{\nu}$ = 3495 (w), 3409 (w), 3038 (w), 2912 (m), 1756 (s), 1602 (m), 1464 (m). UV−vis (acetonitrile, nm): λ_{max} (log ϵ) 210.28 (4.2), 282.40 (4.2). ^{1}H NMR (300 MHz, $CDCl_3$): δ = 1.72−1.80 (m, 1 H, CH_2), 2.30−2.39 (m, 4 H, CH_2, CH_3), 2.53−2.65 (m, 1 H, CH_2), 2.88 (dd, ^2J = 15 Hz, ^3J = 7 Hz, 1 H, CH), 3.95−4.03 (m, 2 H, CH, OCH_2), 4.56−4.62 (m, 1 H, CH_2), 7.16−7.28 (m, 2 H, Ar), 7.56 (d, ^3J = 8 Hz, 1 H, Ar), 7.67 (br s, 1 H, Ar). ^{13}C NMR (75 MHz, $CDCl_3$): δ = 21.3, 22.3, 22.8, 50.5, 67.9, 122.9, 126.3, 128.2, 130.6, 136.0, 138.1, 150.7, 153.4. MS (EI, 70 eV): m/z = 230 (M^+, 100), 143 (78), 128 (51), 117 (40), 114 (42). Anal. Calcd for $C_{13}H_{14}N_2O_2$: C, 67.81; H, 6.13; N, 12.16. Found: C, 67.66; H, 6.27; N, 11.70.

2-(3-Methoxyphenyl)-3,4,4a,5-tetrahydrooxazolo[3,4-*b*]pyridazin-7-one (7e). Starting with **6e** (0.47 g, 2.0 mmol), *n*-BuLi (2.0 mL, 5.0 mmol), and epibromohydrin (0.25 mL, 3.0 mmol) in THF (10 mL), **7e** was isolated as a yellow solid (0.31 g, 62%). Mp = 157 °C. IR (KBr, cm^{-1}): $\tilde{\nu}$ = 3431 (w), 2951 (w), 2912 (w), 1759 (s), 1710 (w), 1604 (m), 1573 (m), 1464 (m), 1404 (s). UV−vis (acetonitrile, nm): λ_{max} (log ϵ): 216.76 (4.3), 282.04 (4.2). ^{1}H NMR (300 MHz, $CDCl_3$): δ = 1.77−1.78 (m, 1 H, CH_2), 2.33−2.34 (m, 1 H, CH_2), 2.52−2.65 (m, 1 H, CH_2), 2.86 (dd, ^2J = 18 Hz, ^3J = 7 Hz, 1 H, CH), 3.82 (s, 3 H, OCH_3), 3.99−4.04 (m, 2 H, CH, OCH_2), 4.61−4.63 (m, 1 H, CH_2), 6.92 (dd, ^3J = 8 Hz, ^4J = 2 Hz, 1 H, Ar), 7.27 (t, ^3J = 8 Hz, 1 H, Ar), 7.33−7.38 (m, 2 H, Ar). ^{13}C NMR (75 MHz, $CDCl_3$): δ = 22.3, 22.7, 50.5, 55.3, 67.9, 110.9, 115.7, 118.2, 129.2, 137.5, 150.3, 153.2, 159.6. MS (EI, 70 eV): m/z = 246 (M^+, 100), 159 (14), 144 (15), 133 (20), 77 (14). Anal. Calcd for $C_{13}H_{14}N_2O_3$: C, 63.40; H, 5.73; N, 11.38. Found: C, 63.31; H, 6.43; N, 11.06.

2-(*o*-Tolyl)-3,4,4a,5-tetrahydrooxazolo[3,4-*b*]pyridazin-7-one (7f). Starting with **6f** (0.44 g, 2.0 mmol), *n*-BuLi (2.0 mL, 5.0 mmol), and epibromohydrin (0.25 mL, 3.0 mmol) in THF (10 mL), **7f** was isolated as an orange oil (0.11 g, 24%). IR (KBr, cm^{-1}): $\tilde{\nu}$ = 3432 (s), 3124 (w), 3100 (w), 3061 (w), 2934 (s), 1761 (s), 1702 (s), 1601 (m), 1556 (m), 1456 (s). ^{1}H NMR (300 MHz, $CDCl_3$): δ = 1.29−1.34 (m, 1 H, CH_2), 2.29−2.42 (m, 4 H, CH_2, CH_3), 2.57−2.63 (m, 1 H, CH_2), 4.04−4.26 (m, 3 H, CH, OCH_2), 4.64 (m, 1 H, CH_2), 7.19−7.28 (m, 4 H, Ar). ^{13}C NMR (75 MHz, $CDCl_3$): δ = 20.2, 22.7, 26.0, 50.3, 67.9, 125.5, 127.6, 128.6, 130.7, 135.6, 137.2, 153.4, 154.2. MS (EI, 70 eV): m/z = 230 (M^+, 50), 144 (60), 130 (50), 91 (19), 28 (100).

2-(Naphth-1-yl)-3,4,4a,5-tetrahydrooxazolo[3,4-*b*]pyridazin-7-one (7g). Starting with **6g** (0.51 g, 2.0 mmol), *n*-BuLi (2.0 mL, 5.0 mmol), and epibromohydrin (0.25 mL, 3.0 mmol) in THF (10 mL), **7g** was isolated as an orange solid (0.27 g, 52%). Mp = 66 °C. IR (KBr, cm^{-1}): $\tilde{\nu}$ = 3437 (m), 3052 (w), 2928 (m), 2870 (m), 1774 (s), 1701 (s), 1600 (w), 1507 (m). UV−vis (acetonitrile, nm): λ_{max} (log ϵ) 221.72 (4.6). ^{1}H NMR (300 MHz, $CDCl_3$): δ = 1.80−1.97 (m, 1 H, CH_2), 2.26−2.34 (m, 1 H, CH_2), 2.67−2.79 (m, 1 H, CH_2), 4.04−4.17 (m, 2 H, CH, OCH_2), 4.63 (q, ^3J = 7 Hz, 2 H, CH_2), 7.43−7.54 (m, 4 H, Ar), 7.83−7.88 (m, 2 H, Ar), 8.12 (d, ^3J = 7 Hz, 1 H, Ar). ^{13}C NMR (75 MHz, $CDCl_3$): δ = 22.7, 26.7, 50.4, 68.0, 124.8, 125.1, 125.7, 125.9, 126.7, 128.3, 129.4, 130.5, 133.6, 135.2, 153.4, 153.5. MS (EI, 70 eV): m/z = 266 (M^+, 60), 194 (47), 180 (100), 167 (80), 152 (62).

2-(Naphth-2-yl)-3,4,4a,5-tetrahydrooxazolo[3,4-*b*]pyridazin-7-one (7h). Starting with **6h** (0.51 g, 2.0 mmol), *n*-BuLi (2.0 mL, 5.0 mmol), and epibromohydrin (0.25 mL, 3.0 mmol) in THF (10 mL), **7h** was isolated as an orange solid (0.17 g, 31%). Mp = 184 °C. IR (KBr, cm^{-1}): $\tilde{\nu}$ = 3432 (m), 2955 (m), 2928 (m), 1758 (s), 1504 (m), 1470 (m), 1405 (s). UV−vis (acetonitrile, nm): λ_{max} (log ϵ) 214.59 (4.3), 226.51 (4.3), 235.69 (4.3), 265.18 (4.2), 273.23 (4.2), 300.56 (4.2). ^{1}H NMR (300 MHz, $CDCl_3$): δ = 1.86−1.92 (m, 1 H, CH_2), 2.41−2.47 (m, 1 H, CH_2), 2.70−2.83 (m, 1 H, CH_2), 3.10 (dd, ^2J = 19 Hz, ^3J = 5 Hz, 1 H, CH_2), 4.04−4.14 (m, 2 H, CH, OCH_2), 4.66−4.70 (m, 1 H, CH_2), 7.47−7.54 (m, 3 H, Ar), 7.82 − 7.88 (m, 2 H, Ar), 8.13−8.18 (m, 2 H, Ar). ^{13}C NMR (75 MHz, $CDCl_3$): δ = 22.2, 23.0, 50.7, 68.0, 123.2, 125.5, 126.4, 127.0, 127.7, 128.1, 128.6, 132.9, 133.6, 134.0, 150.2, 153.3. MS (EI, 70 eV): m/z = 266 (M^+, 42), 209 (100), 180 (20), 152 (64), 127 (80).

7i. To a THF solution (40 mL) of **6i** (6.0 mmol, 1.02 g) was added *n*-butyllithium (6.0 mL, 2.5 M) at −78 °C. After being stirred

for 1 h at −78 °C, the mixture was stirred for 10 min at 20 °C. To the solution was added **2** (6.6 mmol) at −78 °C. The reaction mixture was allowed to warm to 20 °C over 16 h; **7i** was isolated as a colorless solid (0.407 g, 38%, dr > 98:2). Mp = 161 °C. IR (KBr, cm^{-1}): $\tilde{\nu}$ = 3433 (w), 2962 (s), 2922 (w), 1770 (s), 1407 (m), 1092 (w), 1072 (w), 987 (w), 753 (w). ^{1}H NMR (300 MHz, $CDCl_3$): δ = 1.21−1.43 (m, 3 H, CH_2), 1.85−2.04 (m, 2 H, CH_2), 2.08−2.21 (m, 1 H, CH), 2.38−2.86 (m, 3 H, CH_2), 2.95−4.17 (t, J = 8 Hz, 1 H, CH_2), 4.21−4.37 (m, 1 H, CH), 4.58−4.75 (t, J = 7.5 Hz, 1 H, CH_2). ^{13}C NMR (75 MHz, $CDCl_3$): δ = 22.0, 27.5, 30.0, 31.1, 37.3, 50.5, 68.1, 153.6, 164.4. MS (EI, 70 eV): m/z = 180 (M^+, 29), 169 (3), 135 (14), 123 (100), 109 (38), 93 (12), 86 (25), 81(34), 55 (59), 49 (44). HRMS (EI): calcd for $C_9H_{12}O_2N_2$ 180.0893, found 180.0892.

7j. To a THF solution (40 mL) of **6j** (6.0 mmol, 1.104 g) was added *n*-butyllithium (6.0 mL, 2.5 M) at −78 °C. After being stirred for 1 h at −78 °C, the mixture was stirred for 10 min at 20 °C. To the solution was added **2** (6.6 mmol) at −78 °C. The reaction mixture was allowed to warm to 20 °C over 16 h; **7j** was isolated as a colorless solid (0.338 g, 29%, dr = 1:1). Mp = 163 °C. IR (KBr, cm^{-1}): $\tilde{\nu}$ = 3441 (w), 2932 (s), 2863 (m), 1766 (s), 1409 (s), 1296 (w), 1264 (w), 1074 (w), 982 (w), 753 (w). ^{1}H NMR (300 MHz, $CDCl_3$): δ = 1.20−1.77 (m, 4 H, CH_2), 1.82−2.58 (m, 6 H, CH, CH_2), 2.62−2.77 (m, 2 H, CH_2), 3.83−4.17 (m, 2H, CH, CH_2), 4.52−4.67 (m, 1 H, CH_2). ^{13}C NMR (75 MHz, $CDCl_3$): δ = 25.1, 26.0, 26.1, 28.4, 30.2, 32.3, 33.3, 34.4, 35.5, 36.4, 34.5, 34.5, 48.0, 50.6, 67.8, 68.0, 153.6, 153.7, 159.8, 162.6. MS (EI, 70 eV): m/z = 194 (M^+, 100), 168 (5), 135 (3), 137 (8), 123 (4), 109 (7), 93 (15), 86 (22), 81 (63), 55 (19), 41 (40). HRMS (EI): calcd for $C_{10}H_{14}O_2N_2$ 194.1050, found 194.1055.

7k. To a THF solution (40 mL) of **6k** (6.0 mmol, 1.188 g) was added *n*-butyllithium (6.0 mL, 2.5 M) at −78 °C. After being stirred for 1 h at −78 °C, the mixture was stirred for 10 min at 20 °C. To the solution was added **2** (4.4 mmol) at −78 °C. The reaction mixture was allowed to warm to 20 °C over 16 h; **7k** was isolated as a colorless solid (0.553 g, 44%, dr = 3:1). Mp = 169 °C. IR (KBr, cm^{-1}): $\tilde{\nu}$ = 3441 (w), 2932 (s), 2855 (m), 1762 (s), 1405 (s), 1297(w), 1265 (w), 1078 (w), 1001 (w), 985 (w), 760 (w). ^{1}H NMR (300 MHz, $CDCl_3$): δ = 1.23−1.97 (m, 9 H, CH_2), 2.05−2.18 (m, 1 H, CH), 2.41−3.74 (m, 3 H, CH_2), 3.93−4.12 (m, 1 H, CH_2), 4.17−4.31 (m, 1 H, CH), 4.58−4.67 (m, 1 H, CH_2). ^{13}C NMR (75 MHz, $CDCl_3$): δ = 24.7, 26.8, 27.0, 27.4, 27.9, 29.5, 29.9, 30.6, 30.8, 35.9, 36.0, 36.0, 34.1, 36.3, 47.0, 51.3, 68.0, 68.4, 153.5, 153.5, 159.5, 160.4. MS (EI, 70 eV): m/z = 208 (M^+, 100), 163 (10), 149 (24), 137 (8), 123 (10), 109 (12), 95 (37), 86 (14), 67 (50), 55 (48), 49 (13). HRMS (EI): calcd for $C_{11}H_{16}O_2N_2$ 208.1206, found 208.1206.

7l. To a THF solution (40 mL) of **6l** (4.0 mmol, 0.848 g) was added *n*-butyllithium (4.0 mL, 2.5 M) at −78 °C. After being stirred for 1 h at −78 °C, the mixture was stirred for 10 min at 20 °C. To the solution was added **2** (4.4 mmol) at −78 °C. The reaction mixture was allowed to warm to 20 °C over 16 h; **7l** was isolated as a colorless solid (0.535 g, 60%, dr = 3:2). Mp = 165 °C. IR (KBr, cm^{-1}): $\tilde{\nu}$ = 3435 (w), 2920 (s), 2854 (m), 1758 (s), 1411 (s), 1300 (w), 1271 (w), 1076 (w), 1004 (w), 976 (w), 748 (w). ^{1}H NMR (300 MHz, $CDCl_3$): δ = 1.13−2.01 (m, 10 H, CH_2), 2.03−2.17 (m, 1 H, CH), 2.29−2.83 (m, 4 H, CH_2), 3.93−4.07 (m, 1 H, CH_2), 4.07−4.25 (m, 1 H, CH), 4.57−4.68 (m, 1 H, CH_2). ^{13}C NMR (75 MHz, $CDCl_3$): δ = 24.1, 24.9, 25.1, 25.3, 25.8, 26.0, 26.1, 26.4, 27.6, 29.9, 31.3, 33.0, 34.8, 36.1, 34.1, 35.0, 47.6, 51.6, 67.9, 68.6, 153.6, 154.0, 160.6, 162.7. MS (EI, 70 eV): m/z = 222 (M^+, 96), 194 (100), 167 (19), 137 (5), 123 (5), 109 (13), 95 (14), 86 (13), 67 (41), 55 (29), 49 (11). HRMS (EI): calcd for $C_{12}H_{18}O_2N_2$ 222.1363, found 222.1360.

7m. To a THF solution (40 mL) of **6m** (4.0 mmol, 1.072 g) was added *n*-butyllithium (4.0 mL, 2.5 M) at −78 °C. After being stirred for 1 h at −78 °C, the mixture was stirred for 10 min at 20 °C. To the solution was added **2** (4.4 mmol) at −78 °C. The reaction mixture was allowed to warm to 20 °C over 16 h; **7m** was isolated as a colorless solid (0.414 g, 37%, dr = 1:1). Mp = 125 °C. IR (KBr, cm^{-1}): $\tilde{\nu}$ = 3433 (w), 2930 (s), 2863 (m), 1769 (s), 1469 (m), 1410 (s), 1264 (w), 1076 (w), 996 (w), 747 (w). ^{1}H NMR (300 MHz, $CDCl_3$): δ = 1.22−1.61 (m, 18 H, CH_2), 2.22−2.58 (m, 4 H, CH_2), 3.86−3.95 (m, 2 H, CH, CH_2), 4.52−4.68 (m, 1 H, CH_2). ^{13}C NMR (75 MHz, $CDCl_3$): δ = 21.8, 22.0, 22.3, 22.9, 23.1, 23.1, 23.1, 23.2, 23.5, 24.3, 24.6, 25.3, 25.5, 25.6, 26.9, 28.9, 29.0, 30.9, 31.0, 31.6, 33.7, 29.7, 36.6, 47.0, 51.1, 67.8, 68.0, 153.3, 153.7, 159.8, 161.6. MS (EI, 70 eV): m/z = 278 (M^+, 79), 263 (6), 208 (10), 179 (11), 167 (94), 154 (100), 135 (4), 123 (4), 109 (9), 93 (5), 86 (10), 55 (20), 43 (96), 40 (11). HRMS (EI): calcd for $C_{16}H_{26}O_2N_2$ 278.1989, found 278.1990.

7n. To a THF solution (40 mL) of **6n** (4.0 mmol) was added *n*-butyllithium (4.0 mL, 2.5 M) at −78 °C. After being stirred for 1 h at −78 °C, the mixture was stirred for 10 min at 20 °C. To the solution was added **2** (4.4 mmol) at −78 °C. The reaction mixture was allowed to warm to 20 °C over 16 h; **7n** was isolated as a brownish solid (0.232 g, 24%, dr = 4:1). Mp = 184 °C. IR (KBr, cm^{-1}): $\tilde{\nu}$ = 3435 (w), 2925 (m), 1760 (s), 1402 (s), 1277 (m), 1244 (m), 1106 (m), 1093 (m), 997 (m), 768 (m), 748 (m), 733 (w), 565 (w). ^{1}H NMR (300 MHz, $CDCl_3$): δ = 1.23−2.78 (m, 2 H, CH_2), 1.82−2.38 (m, 2 H, CH_2), 2.42−2.62 (m, 1 H, CH), 3.91−4.07 (m, 1 H, CH_2), 4.12−4.27 (m, 1 H, CH), 4.51−4.63 (m, 1 H, CH_2), 7.07−7.38 (m, 3 H, CH, Ar), 8.21−8.35 (m, 1 H, CH, ArH). ^{13}C NMR (75 MHz, $CDCl_3$): δ = 29.1, 29.3, 29.7, 30.2, 31.8, 32.4, 31.6, 33.2, 49.4, 51.4, 68.0, 68.4, 125.0, 125.3, 126.4, 126.4, 128.9, 128.9, 129.8, 130.0, 130.9, 132.2, 138.5, 138.9, 150.2, 153.5, 154.3, 157.4. MS (EI, 70 eV): m/z = 242 (M^+, 100), 183 (4), 170 (5), 155 (13), 149 (11), 141 (18), 129 (26), 115 (20), 97 (9), 83 (10), 71 (15), 63 (4). HRMS (EI): calcd for $C_{14}H_{14}O_2N_2$ 242.1055, found 242.1050.

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