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Synthesis of 2,5-dihydrobenzo[*b*]oxepines and 5,6-dihydro-2*H*-benzo[*b*]oxocines based on a '[3+3] cyclization-olefin-metathesis' strategy

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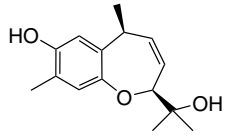
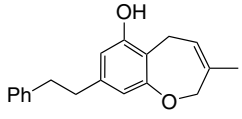
Abstract—Functionalized 2,5-dihydrobenzo[*b*]oxepines and 5,6-dihydro-2*H*-benzo[*b*]oxocines were prepared based on a '[3+3] cyclization-olefin-metathesis' strategy.

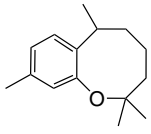
2,3,4,5-Tetrahydrobenzo[*b*]oxepines are of pharmacological relevance and occur in a number of natural products, such as heliannuol C and D[1] or plumbagic acid lactone.[2] Their eight-membered ring analogs, 3,4,5,6-tetrahydro-2*H*-benzo[*b*]oxocines, are found, for example, in heliannuol A and K,[1,3] helianane,[4] and protosappanine B.[5] 2,5-Dihydrobenzo[*b*]oxepines are present, for example, in heliannuol B[1] and in the radulanins A, H, and L isolated from *Haliclona fascigera* and *Radula variabilis*, respectively.[6] The 5,6-dihydro-2*H*-benzo[*b*]oxocine core structure occurs, for example, in heliannuol G and H,[4] specionine,[7] and sophoroside A.[7] Some years ago, Snieckus and co-worker reported the synthesis of benzene-fused oxygen heterocycles by application of a 'directed-ortho-metalation (DoM)-olefin-metathesis' strategy.[8] In recent years, a number of natural product syntheses based on RCM have been reported.[9] Herein, we report a new and convenient synthesis of 2,5-dihydrobenzo[*b*]oxepines and 5,6-dihydro-2*H*-benzo[*b*]-oxocines based on a '[3+3] cyclization-olefin-metathesis' strategy. Our approach relies on the regioselective assembly of the benzene moiety by [3+3] cyclizations of 1,3-bis(trimethylsilyloxy)hepta-1,3,6-trienes and 1,3-bis(trimethylsilyloxy)octa-1,3,7-trienes with 3-silyloxyalk-2-en-1-ones to give functionalized salicylates.[10,11] The latter were transformed into the desired products by O-allylation and subsequent ring-closing metathesis (RCM).



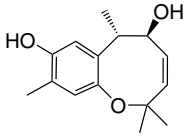
Heliannuol B



Radulanin A



Helianane



Heliannuol H

The 1,3-bis-silyl enol ethers **5a**,**b** were prepared according to a known procedure (Scheme 1).[12,13] The $TiCl_4$ mediated [3+3] cyclization of **5a** with 1,1,3,3-tetramethoxypropane afforded the allyl-substituted salicylate **6a** (Table 1). Allylation of the hydroxy group afforded the allylic ether **7a**, which was transformed into the desired 2,5-dihydrobenzo[*b*]oxepine **8a** by RCM using Grubbs' catalyst **9**.[14–16] Likewise, the 5,6-dihydro-2*H*-benzo[*b*]oxocine **8b** was prepared from 1,3-bis-silyl enol ether **5b**. Application of the Mitsunobu reaction for O-allylation was not successful.

Keywords: Cyclizations; Heterocycles; Medium-sized rings; Ring-closing metathesis; Silyl enol ethers.
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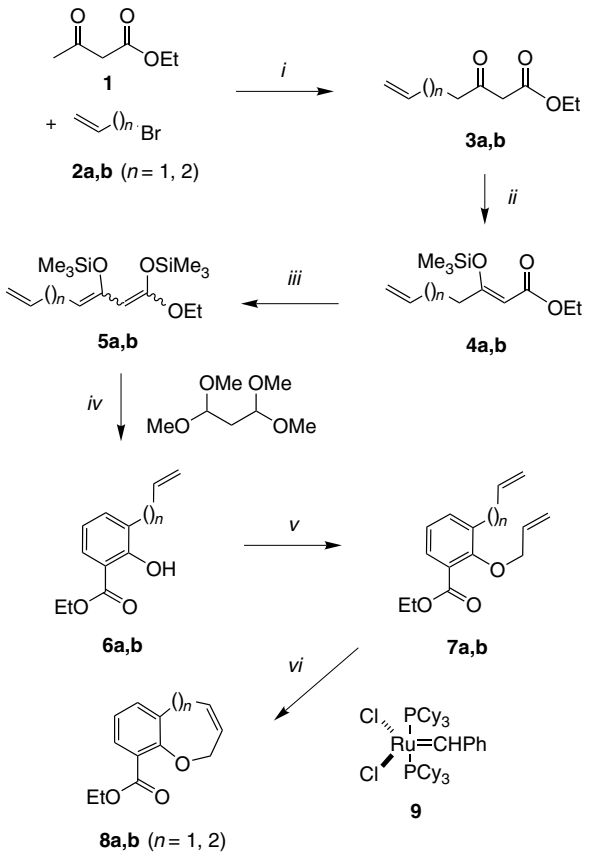


Scheme 1. Synthesis of **8a**,**b**. Reagents and conditions: (i) (1) LDA (2.3 equiv), THF, 0 °C, 1 h, (2) **2a**,**b**, −78 → 20 °C; (ii) Me_3SiCl, NEt_3, toluene, 20 °C, 24 h; (iii) (1) LDA, THF, −78 °C, 1 h, (2) Me_3SiCl, 20 °C, −78 → 20 °C; (iv) $TiCl_4$, CH_2Cl_2, −78 → 20 °C; (v) $H_2C{=}CH{-}CH_2Br$ (1.5 equiv), NaH (2.0 equiv), TBAI (2.0 equiv), THF, 0 °C, 24 h, 0 → 20 °C, 8–12 h; (vi) **9** (5 mol %), CH_2Cl_2 (1.5 equiv), 20 °C, 6–8 h.

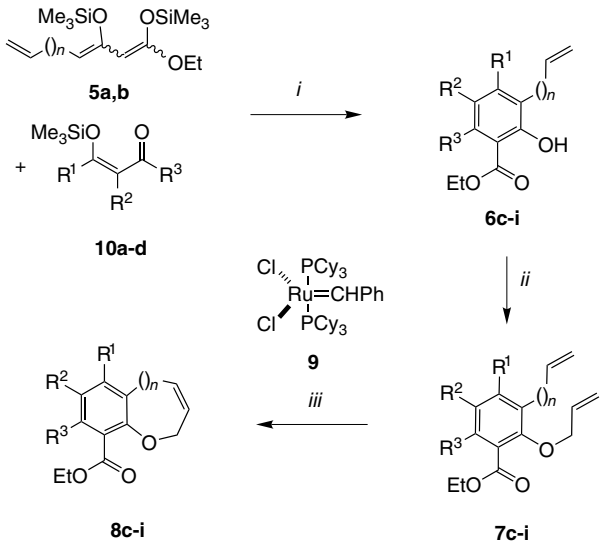
Table 1. Products and yields

6–8	*n*	% (**6**)[a]	% (**7**)[a]	% (**8**)[a]
a	1	45	86	99
b	2	53	84	75

[a] Yields of isolated products.

The $TiCl_4$ mediated [3+3] cyclization of **5a** with silyl enol ethers **10a**–**c**, prepared from pentane-2,4-dione, 3-methylpentane-2,4-dione, and heptane-3,5-dione, afforded the allyl-substituted salicylates **6c**–**e**, which were transformed into the 2,5-dihydrobenzo[*b*]oxepines **8c**–**e** (Scheme 2 and Table 2). The tetracyclic 2,5-dihydrobenzo[*b*]oxepine **8f** was prepared from **10d**, which is available from 2-acetyltetralone. The 5,6-dihydro-2*H*-benzo[*b*]oxocines **8g**–**i** were prepared from 1,3-bis-silyl enol ether **5b**.

The [3+3] cyclizations (to give salicylates **6a**–**i**) proceeded in 31–52% yield; the yields are similar to those reported for related cyclizations[11] and are not decreased by the presence of the additional alkenyl moiety in the 1,3-bis-silyl enol ether. Migration of the olefin functionality (to form cyclic enol ethers) was *not* observed during the ring-closing metathesis step.[17] The



Scheme 2. Synthesis of **8c**–**i**. Reagents and conditions: (i) $TiCl_4$ (1.0 equiv), CH_2Cl_2, −78 → 20 °C; (ii) $H_2C{=}CH{-}CH_2Br$ (1.5 equiv), NaH (2.0 equiv), TBAI (2.0 equiv), THF, 0 → 20 °C, 8–12 h; (iii) **9** (5 mol %), CH_2Cl_2 (1.5 equiv), 20 °C, 6–8 h.

Table 2. Products and yields

6–8	*n*	R^1	R^2	R^3	% (**6**)[a]	% (**7**)[a]	% (**8**)[a]
c	1	Me	H	Me	44	85	90
d	1	Me	Me	Me	52	95	93
e	1	Et	H	Et	31	78	91
f	1	$C_6H_4(CH_2)_2$		Me	43	77	80
g	2	Me	Me	Me	47	76	76
h	2	Et	H	Et	50	82	91
i	2	$C_6H_4(CH_2)_2$		Me	33	96	70

[a] Yields of isolated products.

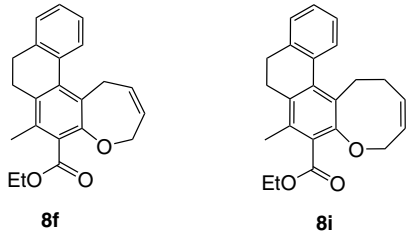


Figure 1.

structures of tetracyclic 2,5-dihydrobenzo[*b*]oxepine **8f** and 5,6-dihydro-2*H*-benzo[*b*]oxocine **8i** are given below for clarity (Fig. 1).

In summary, we have reported a new regioselective synthesis of functionalized 2,5-dihydrobenzo[*b*]oxepines and 5,6-dihydro-2*H*-benzo[*b*]oxocines based on a '[3+3] cyclization-ring-closing-metathesis' strategy.

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References and notes

1. Macias, F. A.; Molinillo, J. M. G.; Varela, R. M.; Torres, A.; Fronczek, F. R. *J. Org. Chem.* **1994**, *59*, 8261.
2. Dinda, B.; Das, S. K.; Hajra, A. K.; Bhattacharya, A.; De, K.; Chel, G.; Achari, B. *Ind. J. Chem. Sect. B* **1999**, *38*, 577.
3. (a) Macias, F. A.; Varela, R. M.; Torres, A.; Molinillo, J. M. G.; Fronczek, F. R. *Tetrahedron Lett.* **1993**, *34*, 1999; (b) Takabatake, K.; Nishi, I.; Shindo, M.; Shishido, K. *J. Chem. Soc., Perkin Trans. 1* **2000**, 1807; (c) Macias, F. A.; Varela, R. M.; Torres, A.; Molinillo, J. M. G. *J. Nat. Prod.* **1999**, *62*, 1636.
4. Crews, P.; Harrison, B. *J. Org. Chem.* **1997**, *62*, 2646.
5. (a) Nagai, M.; Nagumo, S. *Chem. Pharm. Bull.* **1987**, *35*, 3002; (b) Oh, S. R.; Kim, D. S.; Lee, I. S.; Jung, K. Y.; Lee, J. J.; Lee, H.-K. *Planta Med.* **1998**, *64*, 456.
6. (a) Asakawa, Y.; Toyota, M.; Takemoto, T. *Phytochemistry* **1978**, *17*, 2005; (b) Asakawa, Y.; Takeda, R.; Toyota, M.; Tsunematsu, T. *Phytochemistry* **1981**, *20*, 858; (c) Asakawa, Y.; Hashimoto, T.; Takikawa, K.; Tori, M.; Ogawa, S. *Phytochemistry* **1991**, *30*, 235; (d) Yamaguchi, S.; Furihata, K.; Miyazawa, M.; Yokoyama, H.; Hirai, Y. *Tetrahedron Lett.* **2000**, *41*, 4787; (e) Breuer, M.; Leeder, G.; Proksch, P.; Budzikiewicz, H. *Phytochemistry* **1986**, *25*, 495; (f) McCormick, S.; Robson, K.; Bohm, B. *Phytochemistry* **1986**, *25*, 1723.
7. (a) Nohara, T.; Kinjo, J.; Furusawa, J.; Sakai, Y.; Inoue, M. *Phytochemistry* **1993**, *33*, 1207; (b) Shirataki, Y.; Tagaya, Y.; Yokoe, I.; Komatsu, M. *Chem. Pharm. Bull.* **1987**, *35*, 1637.
8. For the synthesis of 2,5-dihydrobenzo[*b*]oxepines and 5,6-dihydro-2*H*-benzo[*b*]oxocines based on a 'DOM–RCM' strategy, see: (a) Stefinovic, M.; Snieckus, V. *J. Org. Chem.* **1998**, *63*, 2808; (b) Fürstner, A.; Ackermann, L. *Chem. Commun.* **1999**, 95; see also: (c) Visser, M. S.; Heron, N. M.; Didiuk, M. T.; Sagal, J. F.; Hoveyda, A. H. *J. Am. Chem. Soc.* **1996**, *118*, 4291.
9. For the synthesis of heliannuol D, see: (a) Sabui, S. K.; Venkateswaran, R. V. *Tetrahedron Lett.* **2004**, *45*, 2047; for (−)-heliannuol C: (b) Kamei, T.; Shindo, M.; Shishido, K. *Tetrahedron Lett.* **2003**, *44*, 8505; for (−)-heliannuol A, see: (c) Kishuku, H.; Shindo, M.; Shishido, K. *Chem. Commun.* **2003**, 350; for pterulones, see: (d) Kahnberg, P.; Lee, C. W.; Grubbs, R. H.; Sterner, O. *Tetrahedron* **2002**, *58*, 5203; for the synthesis of pterulones, see: (e) Gruijters, B. W. T.; van Veldhuizen, A.; Weijers, C. A. G. M.; Wijnberg, J. B. P. A. *J. Nat. Prod.* **2002**, *65*, 558.
10. For a review of 1,3-bis-silyl enol ethers, see: Langer, P. *Synthesis* **2002**, 441.
11. For [3+3] cyclizations of 1,3-bis-silyl enol ethers, see: (a) Chan, T.-H.; Brownbridge, P. *J. Am. Chem. Soc.* **1980**, *102*, 3534; (b) Brownbridge, P.; Chan, T.-H.; Brook, M. A.; Kang, G. J. *Can. J. Chem.* **1983**, *61*, 688; for cyclizations with 2-acetyl-1-silyloxybut-1-en-3-one, see: (c) Dede, R.; Langer, P. *Tetrahedron Lett.* **2004**, *45*, 9177; for the synthesis of dibenzo[*b*,*d*]pyran-6-ones, see: (d) Nguyen, V. T. H.; Langer, P. *Tetrahedron Lett.* **2005**, *46*, 1013; for cyclizations with 1,1-diacylcyclopropanes, see: (e) Bose, G.; Nguyen, V. T. H.; Ullah, E.; Lahiri, S.; Görls, H.; Langer, P. *J. Org. Chem.* **2004**, *69*, 9128.
12. Molander, G. A.; Cameron, K. O. *J. Am. Chem. Soc.* **1993**, *115*, 830.
13. Langer, P.; Eckardt, T.; Saleh, N. N. R.; Karimé, I.; Müller, P. *Eur. J. Org. Chem.* **2001**, 3657.
14. *General procedure for the synthesis of* **6a–i**: To a CH_2Cl_2 solution of **5a**,**b** and **10a–d** or 1,1,3,3-tetramethoxypropane was dropwise added $TiCl_4$ at −78 °C under argon atmosphere. The solution was stirred at −78 °C for 30 min and was subsequently allowed to warm to 20 °C during 18 h. To the solution was added a saturated aqueous solution of $NaHCO_3$. The organic layer was separated and aqueous layer was extracted with CH_2Cl_2 (4 × 100 mL). The combined organic layers were dried (Na_2SO_4), filtered, and the filtrate was concentrated in vacuo. The residue was purified by column chromatography (silica gel, *n*-hexane/EtOAc).
Synthesis of ethyl 3-allyl-2-hydroxybenzoate (**6a**): Starting with **5a** (1.570 g, 5.0 mmol), $TiCl_4$ (0.945 g, 5.0 mmol), 1,1,3,3-tetramethoxypropane (0.821 g, 5.0 mmol), and CH_2Cl_2 (10 mL), **6a** was isolated by column chromatography (*n*-hexane/EtOAc = 20:1) as a colorless oil (0.464 g, 45%). ^{1}H NMR ($CDCl_3$, 300 MHz): $\delta = 1.41$ (t, $J = 7.2$ Hz, 3H, OCH_2CH_3), 3.44 (d, 2H, CH_2=CHCH_2, $J = 6.6$ Hz), 4.42 (q, $J = 7.1$ Hz, 2H, OCH_2CH_3), 5.05–5.12 (m, 2H, CH_2=CHCH_2), 5.95–6.08 (m, 1H, CH_2=CHCH$_2$), 6.82 (*t*, $J = 7.8$ Hz, 1H, Ar), 7.31 (dd, $J = 6.0$ Hz, 1.5 Hz, 1H, Ar), 7.75 (dd, $J = 6.3$ Hz, 1.7 Hz, 1H, Ar), 11.14 (s, 1H, OH). ^{13}C NMR ($CDCl_3$, 75 MHz): $\delta = 14.2$ (CH_3), 33.6, 61.4 (CH_2), 112.2 (C), 115.8 (CH_2), 118.6, 127.9 (CH), 128.5 (C), 135.6, 136.2 (CH), 159.6, 170.6 (C). IR (KBr, cm^{-1}): $\tilde{\nu} = 3139$ (m, br), 2983 (m), 1672 (s), 1614 (m), 1149 (s), 1303 (s), 1248 (s), 1150 (s), 1025 (s), 760 (s). UV–vis (CH_3CN, nm): λ_{max} ($\log\varepsilon$) = 209.3 (4.47), 242.4 (3.92), 309.7 (3.63). MS (EI, 70 eV): *m*/*z* (%) = 206 (M^+, 38), 160 (43), 132 (100), 103 (34), 77 (41), 51 (16). Anal. Calcd for $C_{12}H_{14}O_3$: C, 69.88; H, 6.79. Found: C, 69.31; H, 7.04.
Synthesis of ethyl 3-allyl-2-hydroxy-4,6-dimethylbenzoate (**6c**): Starting with **5a** (1.257 g, 4.0 mmol), $TiCl_4$ (0.760 g, 4.0 mmol), **10a** (0.680 g, 4.0 mmol), and CH_2Cl_2 (10 mL), **6c** was isolated after chromatography (silica gel, *n*-hexane/EtOAc = 20:1) as a colorless oil (0.338 g, 44%). ^{1}H NMR ($CDCl_3$, 300 MHz): $\delta = 1.42$ (t, 3H, CH_3CH_2O, $J = 7.1$ Hz), 2.25 (s, 3H, CH_3), 2.49 (s, 3H, CH_3), 3.43 (m, 2H, CH_2=CHCH_2, $J = 1.5$ Hz), 4.42 (q, 2H, CH_3CH_2O, $J = 7.1$ Hz), 4.89–4.99 (m, 2H, CH_2=CHCH_2, $J = 15.5$, 10.4, 1.7 Hz), 5.93 (m, 1H, CH_2=CHCH$_2$, $J = 5.2$, 1.5 Hz), 6.55 (s, 1H, CH, Ar), 11.75 (s, 1H, OH). ^{13}C NMR ($CDCl_3$, 75 MHz): $\delta = 14.2$, 19.6, 23.9 (CH_3), 30.1, 61.4 (CH_2), 109.8 (C), 114.4 (CH_2), 123.8 (C), 124.7, 135.7 (CH), 138.5, 143.6, 160.8, 172.2 (C). IR (KBr, cm^{-1}): $\tilde{\nu} = 2979$ (m), 2934 (m), 1654 (s), 1616 (m), 1449 (m), 1396 (s), 1268 (s), 1173 (s), 1031 (m), 847 (m). UV–vis (CH_3CN, nm): λ_{max} ($\log\varepsilon$) = 216.7 (4.41), 253.2 (3.98), 315.6 (3.57). MS (EI, 70 eV): *m*/*z* (%) = 234 (M^+, 29), 188 (34), 173 (24), 160 (53), 145 (27), 114 (9), 91 (11), 28 (100). The exact molecular mass *m*/*z* = 234.1256 ± 2 ppm for $C_{14}H_{18}O_3$ was confirmed by HRMS (EI, 70 eV). All products gave correct spectroscopic data and correct elemental analyses and/or high resolution mass data.
15. *General procedure for the synthesis of* **7**: To a mixture of NaH and of nBu_4NI were simultaneously added a THF solution of **6** and of 3-bromoprop-1-ene at 0 °C under argon atmosphere. The pale yellow colored solution was stirred at 0 °C and was allowed to warm to 20 °C within 8–12 h. The solvent was removed in vacuo and the residue was purified by column chromatography (silica gel, *n*-hexane/EtOAc = 20:1) to give the product as a colorless oil. *Synthesis of ethyl 3-allyl-2-(allyloxy)-4,6-*

dimethylbenzoate (**7c**): Starting with **6c** (0.285 g, 1.22 mmol), NaH (0.059 g, 2.44 mmol), nBu$_4$NI (0.797 g, 2.44 mmol), 3-bromoprop-1-ene (0.220 g, 1.83 mmol), and THF (15 mL), **7c** was isolated as a colorless oil (0.285 g, 85%). ^{1}H NMR ($CDCl_3$, 300 MHz): $\delta = 1.37$ (t, 3H, CH_3CH$_2$O, $J = 7.1$ Hz), 2.24 (s, 3H, CH_3), 2.26 (s, 3H, CH_3), 3.42 (m, 2H, CH$_2$=CHCH_2Ar, $J = 1.8$ Hz), 4.37 (q, 2H, CH$_3$CH_2O, $J = 7.1$ Hz), 4.39 (m, 2H, CH$_2$=CHCH_2O, $J = 1.5$ Hz), 4.86–4.93 (m, 2H, CH_2=CHCH$_2$Ar, $J = 15.3$, 10.2, 1.8 Hz), 5.34–5.41 (m, 2H, CH_2=CHCH$_2$O, $J = 10.4$, 15.5, 1.6 Hz), 5.88–5.93 (m, 1H, CH$_2$=CHCH$_2$Ar, $J = 5.4$ Hz), 5.99–6.04 (s, 1H, CH$_2$=CHCH$_2$O, $J = 5.3$ Hz), 6.80 (s, 2H, Ar). ^{13}C NMR ($CDCl_3$, 75 MHz): $\delta = 14.3$, 19.0, 19.4 (CH_3), 30.5, 61.1, 76.0, 115.2, 116.8 (CH_2), 126.8 (C), 127.8 (CH), 128.9 (C), 133.9 (CH), 134.0 (C), 136.1 (CH), 140.1, 154.4, 168.6 (C). IR (KBr, cm^{-1}): $\tilde{\nu} = 3081$ (m), 2981 (s), 2928 (s), 2870 (m), 1726 (s), 1642 (m), 1609 (m), 1666 (m), 1453 (s), 1411 (s), 1297 (s), 1270 (s), 1150 (s), 1108 (s), 1067 (s), 1041 (s), 992 (s), 918 (s), 864 (m). UV–vis (CH_3CN, nm): λ_{max} ($\log\varepsilon$) = 202.9 (4.59), 276.4 (3.89). MS (EI, 70 eV): m/z (%) = 275.5 ([M+1]$^+$, 11), 274.5 (M$^+$, 62), 233 (24), 232 (26), 229 (36), 228 (17), 201 (12), 188 (19), 187 (100), 173 (20), 161 (34), 160 (36), 159 (31), 145 (18), 91 (16), 41 (20), 29 (11). Anal. Calcd for $C_{17}H_{22}O_3$ (274.355): C, 74.42; H, 8.08. Found: C, 74.41; H, 7.91.

16. *General procedure for the synthesis of* **8**: To a CH_2Cl_2 solution of **7** was added a CH_2Cl_2 solution of **9** under argon atmosphere. After stirring for 6–8 h at 20 °C under argon, the solution was exposed to air, and concentrated in vacuo. The residue was purified by column chromatography (silica gel, n-hexane/EtOAc = 25:1) to give the product as a colorless oil. The product should be stored at ca 0 °C. *Synthesis of ethyl 8,6-dimethyl-2,5-dihydrobenzo[b]oxepine-9-carboxylate* (**8c**): Starting with **7c** (0.260 g, 0.95 mmol), **9** (0.039 g, 0.047 mmol, 5 mol %, dissolved in 2 mL of CH_2Cl_2) and CH_2Cl_2 (18 mL), **8c** was isolated as a colorless oil (0.210 g, 90%). ^{1}H NMR ($CDCl_3$, 300 MHz): $\delta = 1.38$ (t, 3H, CH_3CH$_2$O, $J = 7.1$ Hz), 2.26 (s, 3H, CH_3), 2.27 (s, 3H, CH_3), 3.44 (m, 2H, CH_2, $J = 1.9$ Hz), 4.39 (q, 2H, CH$_3$CH_2O, $J = 7.1$ Hz), 4.63 (m, 2H, CH_2, $J = 1.5$ Hz), 5.46 (m, 1H, CH, $J = 5.2$ Hz, 1.4 Hz), 5.83 (m, 1H, CH), 6.76 (s, 1H, Ar). ^{13}C NMR ($CDCl_3$, 75 MHz): $\delta = 14.3$, 18.9, 19.8 (CH_3), 25.7, 60.9, 71.4 (CH_2), 124.9 (CH), 126.1 (C), 127.5, 127.8 (CH), 133.5 (2C), 136.6, 152.2, 168.1 (C). IR (KBr, cm^{-1}): $\tilde{\nu} = 3438$ (w), 2979 (s), 2930 (s), 1726 (s), 1609 (s), 1456 (s), 1387 (m), 1293 (s), 1270 (s), 1223 (m), 1149 (s), 1091 (s), 1046 (s), 862 (m), 653 (w). UV–vis (CH_3CN, nm): λ_{max} ($\log\varepsilon$) = 205.8 (4.25), 263.1 (3.62), 301.8 (3.27). MS (EI, 70 eV): m/z (%) = 247 ([M+1]$^+$, 9), 246 (M$^+$, 77), 201 (92), 200 (100), 199 (47), 183 (35), 173 (23), 172 (63), 171 (24), 157 (53), 129 (41), 128 (31), 114 (21), 45 (18), 31 (41). Anal. Calcd for $C_{15}H_{18}O_3$ (246.302): C, 73.15; H, 7.36. Found: C, 73.03; H, 6.96.

17. For the combination of RCM with isomerizations to give enol ethers, see: Sutton, A. E.; Seigal, B. A.; Finnegan, D. F.; Snapper, M. L. *J. Am. Chem. Soc.* **2002**, *124*, 13390.