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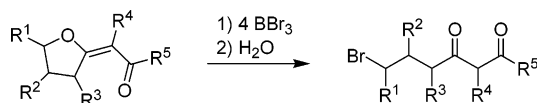
Convenient Synthesis of ϵ -Halo- β -ketoesters and γ,γ' -Dibromoalkanones by Regio- and Chemoselective Reaction of 2-Alkylidenetetrahydrofurans with Boron Trihalides: A “Ring-Closure/Ring-Cleavage” Strategy

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The reaction of boron tribromide and boron trichloride with 2-alkylidenetetrahydrofurans, readily available on the basis of cyclizations of free and masked dianions with 1,2-dielectrophiles, allowed an efficient synthesis of a variety of carbonyl compounds with remote halide functionality. This includes the chemo- and regioselective synthesis of 6-bromo- and 6-chloro-3-oxoalkanoates and 1,7-dibromoheptan-4-ones. The approach outlined herein can be regarded as a “ring-closure/ring-cleavage” strategy.

Introduction

Functionalized carbonyl compounds containing a halide group at a remote position represent versatile synthetic building blocks.^{1–4} 1,3-Dicarbonyl derivatives containing a halide group at a remote position are more rare. Despite their preparative usefulness, syntheses of 6-halo-3-oxoalkanoates (ϵ -halo- β -ketoesters) and the related 6-halo-1,3-diketones have only scarcely been reported in the literature. For example, 7-bromoheptane-2,4-dione has been prepared by reaction of 5-bromopent-1-yne with acetic anhydride.¹ The reaction of α -acetyl- γ -butyrolactone with HBr has been reported to give 5-bromopentan-2-one by ring-opening and subsequent decarboxylation.² The reaction of 3-oxoalkanoate dianions with 1-bromo-2-chloroethane has been reported to give 6-chloro-3-oxoalkanoates.³ In contrast, it has been reported that bis-1,3-diketones are not directly available by reaction of disodio 1,3-diketones with 1,2-dibromoethane.⁴

We have recently reported⁵ a convenient synthesis of 6-bromo-3-oxoalkanoates by reaction of BBr₃ with 2-alkylidenetetrahydrofurans. The starting materials, 2-alkylidenetetrahydrofurans, are readily available based on cyclizations of 1,2-dielectrophiles with 1,3-dicarbonyl dianions or 1,3-bis-silyl enol ethers (masked dianions)—reactions developed by us in the recent years.⁶ Thus, our approach to 6-bromo-3-oxoalkanoates can be regarded as a “ring-closure/ring-cleavage” strategy. Whereas the BBr₃-mediated cleavage of methylaryl ethers is well-known and broadly used,⁷ reactions of other ethers are more rare. Known examples include the formation of ω -bromoalkanols by ring-opening of cyclic ethers with BBr₃/MeOH⁸ or the transformation of lactones into ω -halocarboxylic acids.⁹ Herein, we wish to report full details of our “ring-closure/ring-cleavage” strategy and studies related to the preparative scope.

Results and Discussion

The reaction of 2-alkylidenetetrahydrofuran **2a**, prepared by cyclization of the dianion **1a** of ethyl aceto-

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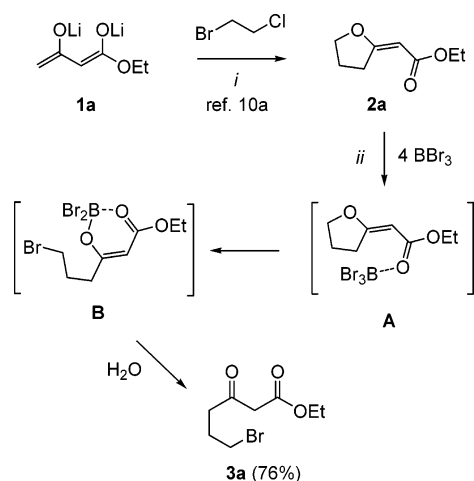
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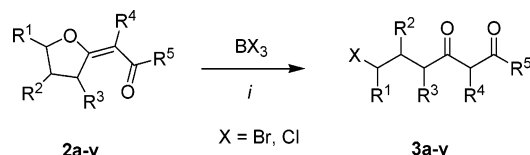
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SCHEME 1^a

^a Key: (i) (1) 2.3 equiv of LDA, THF, 0 °C, 1 h, (2) Br(CH₂)₂Cl, -78 → 20 °C, 14 h, then reflux, 12 h; (ii) (1) 4 equiv of BBr₃, CH₂Cl₂, 0 → 20 °C, 12 h, 20 °C, 6 h, (2) H₂O.

SCHEME 2. Synthesis of 3a–v^a

^a Key: (i) (1) 4 equiv of BX₃, CH₂Cl₂, 0 → 20 °C, 12 h, 20 °C, 6 h, (2) H₂O.

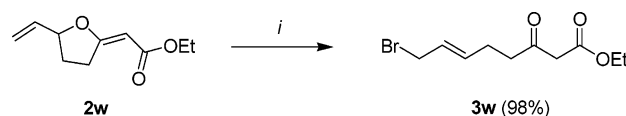
acetate with 1-bromo-2-chloroethane,¹⁰ with BBr₃ afforded ethyl 6-bromo-3-oxohexanoate (**3a**) in 76% yield (Scheme 1). The reaction presumably proceeds by activation of **2a** (intermediate **A**), ring-cleavage (intermediate **B**), and subsequent protonation of the enolate. During the optimization, the use of an excess of BBr₃ (4 equiv) proved to be important.

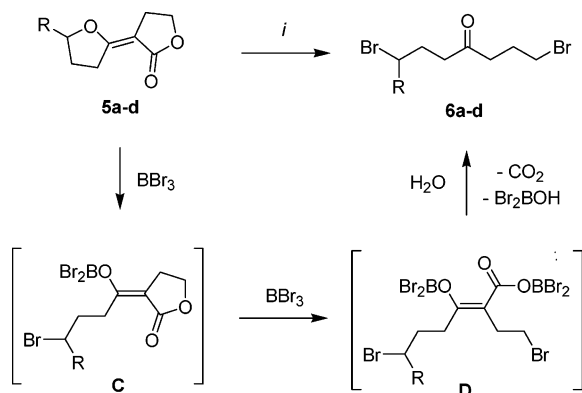
The preparative scope of our methodology was studied. The required starting materials were prepared by literature methods.^{10–12} The reaction of BBr₃ with 2-alkylidenetetrahydrofurans **2b–e** and **2g–i** afforded the 2-alkyl- and 2-aryl-6-bromo-3-oxoalkanoates **3b–e** and **3g–i** (Scheme 2, Table 1). During the formation of **3i**, the methylaryl ether of the starting material was cleaved. In addition to **3i** (72%), simple demethylation of methyl (dihydrofuran-2-ylidene)(4-methoxyphenyl)acetate (**2i**) and formation of methyl (dihydrofuran-2-ylidene)(4-hydroxyphenyl)acetate (**2i'**) was observed. Treatment of 2-alkylidenetetrahydrofuran **2f** with boron trichloride (BCl₃) afforded the 6-chloro-2-phenyl-3-oxoalkanoate **3f**. This experiment showed that not only a bromide but also a chloride function can be introduced in good yield. The reaction of BBr₃ with 2-alkylidenetetrahydrofurans **2j–v** afforded the 6-bromo-3-oxoalkanoates **3j–v** (Table 1). All

TABLE 1. Products and Yields

3	R ¹	R ²	R ³	R ⁴	R ⁵	X	% yield ^a
a	H	H	H	H	OEt	Br	76
b	H	H	H	Oct	OEt	Br	95
c	H	H	H	Dec	OEt	Br	81
d	H	H	H	(CH ₂) ₃ Cl	OMe	Br	84
e	H	H	H	Bn	OMe	Br	96
f	H	H	H	Ph	OMe	Cl	84
g	H	H	H	4-MeC ₆ H ₄	OMe	Br	89
h	H	H	H	4-ClC ₆ H ₄	OMe	Br	77
i	H	H	H	4-HOC ₆ H ₄	OMe	Br	72 ^b
j	H	H	Ph	Ph	OMe	Br	96
k	H	H	Et	H	OEt	Br	83
l	H	H	Pr	H	OEt	Br	96
m	H	H	(CH ₂) ₃ Cl	H	OMe	Br	86
n	H	H	–(CH ₂) ₉ –	H	OEt	Br	87
o	Me	H	H	H	OMe	Br	80
p	Et	H	H	H	OMe	Br	91
q	Bu	H	H	H	OMe	Br	75
r	CH ₂ Br	H	H	H	OEt	Br	93
s	CH ₂ Cl	H	H	H	OMe	Br	80
t	H	Et	H	H	OMe	Br	82
u	H	Ph	H	H	OEt	Br	83
v	H	H	H	H	Ph	Br	98

^a Yields of isolated products. ^b From **2i** (R⁴ = 4-(MeO)C₆H₄).

SCHEME 3. Synthesis of 3w^a

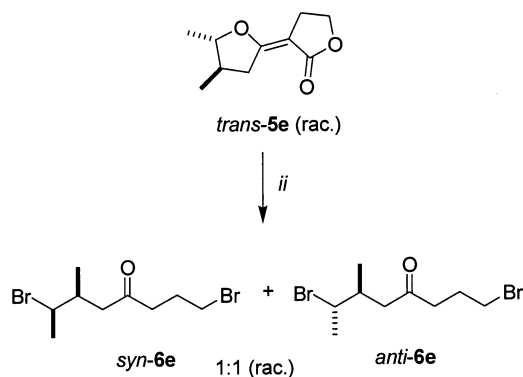
SCHEME 4. Synthesis of 6a-d^a

^a Key: (i) (1) 4 equiv of BBr₃, CH₂Cl₂, 0 → 20 °C, 12 h, 20 °C, 6 h, (2) H₂O.

TABLE 2. Products and Yields

6	R	% yield ^a
a	H	73
b	Me	88
c	Et	68
d	CH ₂ Cl	85

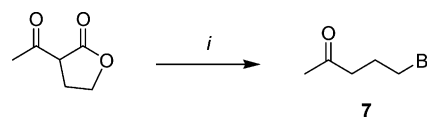
^a Yields of isolated products.

SCHEME 5. Synthesis of 6e^a

^a Key: (i) 2 equiv of TiCl₄, CH₂Cl₂, 4 Å molecular sieves, -78 → 20 °C, 37%; (ii) (1) 4 equiv of BBr₃, CH₂Cl₂, 0 → 20 °C, 12 h, 20 °C, 6 h, (2) H₂O, 87%.

s. 1,7-Dibromoheptan-4-ones represent versatile synthetic building blocks.¹⁴ For example, **6a** has been used for the synthesis of medium-sized carba- and heterocycles.^{14a,b} Notably, unsymmetrical 1,7-dibromoheptan-4-ones are not readily available by other methods.^{14f}

The reaction of 2-acetyl- γ -butyrolactone with HBr has been reported to give 1-bromopentan-4-one (**7**).² Treatment of α -acetyl- γ -butyrolactone with BBr₃ resulted in formation of **7** in 78% yield (Scheme 6). This result indicates that the employment of BBr₃ can be successfully employed for the synthesis of simple γ -bromoketones by cleavage of simple lactones.

SCHEME 6. Synthesis of 7^a

^a Key: (i) 1) 4 equiv of BBr₃, CH₂Cl₂, 0 → 20 °C, 12 h, 20 °C, 6 h, (2) H₂O, 78%.

Conclusions

In summary, the reaction of borontribromide with 2-alkylidenetetrahydrofurans allowed an efficient synthesis of a variety of 6-bromo- and 6-chloro-3-oxoalkanoates and 1,7-dibromoheptan-4-ones. The reactions proceeded with very good chemo- and regioselectivity.

Experimental Section

2-Alkylidenetetrahydrofurans. The required starting materials were prepared by published procedures: 2-Alkylidenetetrahydrofurans **2k–n** and **2v** were prepared in one step by cyclization of dilithiated 1,3-dicarbonyl compounds **1** with 1-bromo-2-chloroethane (Scheme 3).¹⁰ 2-Alkylidenetetrahydrofurans **2b–e**, containing an alkyl group located at the exocyclic double bond, were prepared in two steps by synthesis of 2-alkylidenetetrahydrofurans and subsequent lithiation and alkylation (Scheme 3).^{10b} The aryl-substituted 2-alkylidenetetrahydrofurans **2f–j** were prepared by bromination of 2-alkylidenetetrahydrofurans and subsequent Suzuki reaction.¹¹ 2-Alkylidenetetrahydrofurans **2o–u** were obtained in one step by cyclization of 1,3-bis-silyl enol ethers with epoxides.¹² Compound **5a** was prepared by cyclization of dilithiated α -acetyl- γ -butyrolactone with 1-bromo-2-chloroethane.¹⁰ Compounds **5b–d** are available by cyclization of the α -acetyl- γ -butyrolactone α -acetyl- γ -butyrolactone derived 1,3-bis-silyl enol ether with epoxides.^{12a}

General Procedure for the Reaction of 2-Alkylidenetetrahydrofurans with Boron Tribromide or Boron Trichloride. To a CH₂Cl₂ solution (10 mL/mmol) of the 2-alkylidenetetrahydrofuran (**2**, **5**) (1 equiv) was added BBr₃ (4 equiv) at 0 °C. The reaction mixture was allowed to warm to 20 °C over 12 h and was stirred for 6 h at 20 °C. Water (15 mL) was slowly added to the reaction mixture, and the organic layer was separated. The aqueous layer was extracted with CH₂Cl₂ (3 × 30 mL). The combined organic extracts were dried (Na₂SO₄) and filtered, and the filtrate was concentrated in vacuo. The residue was purified by chromatography (silica gel, *n*-hexane/EtOAc = 100:1 → 1:1) to give the 6-bromo-3-oxoalkanoate **3** or 1,7-dibromoheptan-4-one **6**.

6-Bromo-3-oxohexanoic Acid Ethyl Ester (3a). Starting with **2a** (0.200 g, 1.28 mmol) and BBr₃ (1.283 g, 5.12 mmol) in CH₂Cl₂ (10 mL), **3a** was isolated after chromatography (silica gel, *n*-hexane/EtOAc = 50:1 → 10:1) as a slightly yellow oil (0.229 g, 76%, 7% of enol form). ¹H NMR (CDCl₃, 300 MHz): δ = 1.29 (t, *J* = 7.2 Hz, 3 H), 2.16 (quint, *J* = 6.6 Hz, 2 H), 2.77 (t, *J* = 6.9 Hz, 2 H), 3.45 (t, *J* = 7.2 Hz, 2 H), 3.46 (s, 2 H), 4.21 (q, *J* = 7.2 Hz, 2 H), 5.03 (s, 1 H, CH of enol), 12.12 (s, 1 H, OH of enol). ¹³C NMR (CDCl₃, 150 MHz): δ = 14.1, 26.17, 32.9, 40.8, 49.3, 61.4, 90.0 (enol), 167.0, 172.5 (enol), 176.4 (enol), 201.6. IR (neat, cm⁻¹): $\tilde{\nu}$ = 2982 (w), 2937 (w), 1743 (s), 1716 (s), 1649 (w), 1440 (m), 1369 (m), 1320 (s), 1247 (s), 1184 (m), 1116 (m), 1096 (m), 1031 (m), 975 (w), 942 (w), 851 (w), 806 (w), 557 (w). MS (EI, 70 eV): *m/z* = 237 (M⁺, 1), 191 (5), 157 (14), 148 (63), 130 (100), 115 (35), 87 (18). The exact molecular mass *m/z* = 236.0048 ± 2 ppm [M⁺] for C₈H₁₃O₃Br was confirmed by HRMS (EI, 70 eV). Anal. Calcd for C₈H₁₃O₃Br (237.093): C, 40.53; H, 5.53. Found: C, 40.13; H, 6.11.

2-(4-Bromobutyl)decanoic Acid Ethyl Ester (3b). Starting with **2b** (0.070 g, 0.26 mmol) and BBr₃ (0.264 g, 1.04

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mmol) in CH_2Cl_2 (5 mL), **3b** was isolated after chromatography (silica gel, *n*-hexane/EtOAc = 75:1 \rightarrow 1:1) as a slightly yellow oil (0.086 g, 95%). ^1H NMR (CDCl_3 , 300 MHz): δ = 0.89 (t, J = 7.2 Hz, 3 H), 1.20–1.34 (m, 15 H), 1.80–1.87 (m, 2 H), 2.14 (quint, J = 6.6 Hz, 2 H), 2.62–2.82 (m, 2 H), 3.43 (t, J = 7.2 Hz, 1 H), 3.44 (t, J = 6.6 Hz, 2 H), 4.20 (q, J = 7.2 Hz, 2 H). ^{13}C NMR (CDCl_3 , 150 MHz): δ_{C} = 14.2, 14.3, 22.8, 26.4, 27.6, 28.4, 29.3, 29.4, 29.5, 32.0, 33.2, 40.0, 59.4, 61.5, 169.9, 204.5. IR (neat, cm^{-1}): $\tilde{\nu}$ = 2956 (m), 2927 (s), 2856 (w), 1744 (s), 1716 (s), 1462 (w), 1441 (w), 1406 (w), 1371 (w), 1298 (w), 1250 (w), 1186 (w), 1163 (w), 1123 (w), 1095 (w), 1028 (w). MS (EI, 70 eV): m/z = 349 (M^+ , 3), 304 (3), 251 (7), 236 (26), 227 (8), 200 (100), 197 (5), 159 (94), 135 (8), 123 (839), 121 (826), 115 (16). The exact molecular mass m/z = 348.1300 \pm 2 ppm [M^+] for $\text{C}_{16}\text{H}_{29}\text{O}_3\text{Br}$ was confirmed by HRMS (EI, 70 eV).

2-(4-Bromobutryl)undecanoic Acid Ethyl Ester (3c). Starting with **2c** (0.100 g, 0.34 mmol) and BBr_3 (0.338 g, 1.35 mmol) in CH_2Cl_2 (5 mL), **3c** was isolated after chromatography (silica gel, *n*-hexane/EtOAc = 50:1 \rightarrow 20:1) as a slightly yellow oil (0.103 g, 81%). ^1H NMR (CDCl_3 , 300 MHz): δ = 0.88 (t, J = 6.9 Hz, 3 H), 1.19–1.13 (m, 19 H), 1.80–1.88 (m, 2 H), 2.14 (quint, J = 6.6 Hz, 2 H), 2.64–2.82 (m, 2 H), 3.42 (t, J = 7.5 Hz, 1 H), 3.44 (t, J = 6.6 Hz, 2 H), 4.20 (q, J = 7.2 Hz, 2 H). ^{13}C NMR (CDCl_3 , 150 MHz): δ_{C} = 14.30, 14.32, 22.9, 26.4, 27.6, 28.4, 29.49, 29.51, 29.70, 29.73, 32.1, 33.2, 39.8, 59.4, 61.6, 169.9, 204.5. IR (neat, cm^{-1}): $\tilde{\nu}$ = 2956 (m), 2927 (s), 2855 (m), 1744 (s), 1716 (s), 1645 (w), 1463 (m), 1407 (w), 1371 (w), 1300 (w), 1251 (m), 1184 (m), 1150 (m), 1128 (w), 1096 (w), 1031 (w). MS (EI, 70 eV): m/z = 377 (M^+ , 6), 256 (5), 252 (8), 229 (81), 199 (6), 183 (7), 150 (100), 121 (29). The exact molecular mass m/z = 376.1613 \pm 2 ppm [M^+] for $\text{C}_{18}\text{H}_{33}\text{O}_3\text{Br}$ was confirmed by HRMS (EI, 70 eV). Anal. Calcd for $\text{C}_{18}\text{H}_{33}\text{O}_3\text{Br}$ (377.361): C, 57.29; H, 8.81. Found: C, 56.92; H, 8.15.

6-Bromo-2-(3-chloropropyl)-3-oxohexanoic Acid Methyl Ester (3d). Starting with **2d** (0.100 g, 0.46 mmol) and BBr_3 (0.463 g, 1.83 mmol) in CH_2Cl_2 (10 mL), **3d** was isolated after chromatography (silica gel, *n*-hexane/EtOAc = 50:1 \rightarrow 1:1) as a slightly yellow oil (0.116 g, 84%). ^1H NMR (CDCl_3 , 300 MHz): δ = 1.74–1.83 (m, 2 H), 2.01 (quint, J = 7.5 Hz, 2 H), 2.10–2.19 (m, 2 H), 2.63–2.88 (m, 2 H), 3.42–3.57 (m, 5 H, CH), 3.76 (s, 3 H). ^{13}C NMR (CDCl_3 , 150 MHz): δ_{C} = 25.6, 26.3, 30.3, 33.1, 39.9, 44.4, 52.8, 58.2, 169.9, 203.7. IR (neat, cm^{-1}): $\tilde{\nu}$ = 2956 (m), 1745 (s), 1715 (s), 1639 (w), 1438 (m), 1406 (w), 1369 (w), 1273 (m), 1254 (m), 1203 (m), 1178 (m), 1150 (m), 1102 (w), 1078 (w), 1045 (w). MS (EI, 70 eV): m/z = 300 (M^+ , 1), 269 (2), 263 (3), 237 (2), 222 (3), 205 (2), 177 (5), 150 (98), 148 (100), 129 (2), 123 (26), 118 (5), 116 (11), 112 (6), 101 (4). The exact molecular mass m/z = 297.9971 \pm 2 ppm [M^+] for $\text{C}_{10}\text{H}_{16}\text{O}_3\text{BrCl}$ was confirmed by HRMS (EI, 70 eV). Anal. Calcd for $\text{C}_{10}\text{H}_{16}\text{O}_3\text{BrCl}$ (299.592): C, 40.09; H, 5.38. Found: C, 39.85; H, 5.95.

2-Benzyl-6-bromo-3-oxohexanoic Acid Methyl Ester (3e). Starting with **2e** (0.100 g, 0.43 mmol) and BBr_3 (0.436 g, 1.72 mmol) in CH_2Cl_2 (5 mL), **3e** was isolated after chromatography (silica gel, *n*-hexane/EtOAc = 50:1 \rightarrow 1:1) as a slightly yellow oil (0.130 g, 96%, 5% of enol form). ^1H NMR (CDCl_3 , 300 MHz): δ = 2.02–2.13 (m, 2 H), 2.48 (dt, J = 18.3, 6.6 Hz, 1 H), 2.77 (dt, J = 18.3, 6.6 Hz, 1 H), 3.18 (d, J = 7.5 Hz, 2 H), 3.35 (dt, J = 6.6, 1.4 Hz, 2 H), 3.71 (s, 3 H), 3.82 (t, J = 7.5 Hz), 7.15–7.30 (m, 5 H), 12.09 (s, 1 H, OH of enol). ^{13}C NMR (CDCl_3 , 150 MHz): δ_{C} = 26.2, 32.9, 34.2, 41.0, 52.7, 60.5, 102.0 (enol), 126.9, 128.8, 128.9, 138.1, 169.5, 172.0 (enol), 203.7. IR (neat, cm^{-1}): $\tilde{\nu}$ = 3029 (w), 3002 (w), 2953 (m), 1746 (s), 1715 (s), 1633 (m), 1604 (w), 1495 (w), 1437 (w), 1405 (w), 1369 (m), 1316 (m), 1255 (m), 1212 (s), 1170 (s), 1105 (m), 1078 (m), 1060 (m), 1031 (w), 983 (w), 751 (m), 701 (m). MS (EI, 70 eV): m/z = 313 (M^+ , 2), 283 (1), 255 (6), 232 (10), 200 (100), 172 (14), 163 (100), 148 (21), 131 (55), 103 (14), 91 (27), 77 (9). The exact molecular mass m/z = 312.0361 \pm 2 ppm [M^+] for $\text{C}_{14}\text{H}_{17}\text{O}_3\text{Br}$ was confirmed by HRMS (EI, 70 eV).

6-Chloro-3-oxo-2-phenylhexanoic Acid Methyl Ester (3f). Starting with **2f** (0.030 g, 0.14 mmol) and BCl_3 (0.55 mL,

1.0 M in heptane, 0.55 mmol) in CH_2Cl_2 (5 mL), **3f** was isolated after chromatography (silica gel, *n*-hexane/EtOAc = 50:1 \rightarrow 20:1) as a colorless oil (0.030 g, 84%). ^1H NMR (CDCl_3 , 300 MHz): δ = 2.01 (quint, J = 6.6 Hz, 2 H), 2.65 (t, J = 6.9 Hz, 2 H), 3.53 (t, J = 6.3 Hz, 2 H), 3.76 (s, 3 H), 4.74 (s, 1 H), 7.27–7.38 (m, 5 H). ^{13}C NMR (CDCl_3 , 150 MHz): δ_{C} = 26.5, 38.7, 44.5, 52.8, 65.1, 127.3, 128.7, 129.0, 134.2, 169.0, 207.4. IR (neat, cm^{-1}): $\tilde{\nu}$ = 3064 (w), 3031 (w), 2963 (m), 2926 (m), 2870 (w), 2857 (w), 1743 (s), 1717 (s), 1644 (w), 1603 (w), 1495 (w), 1450 (s), 1440 (s), 1408 (m), 1370 (m), 1350 (m), 1309 (m), 1260 (s), 1205 (s), 1158 (s), 1113 (s), 1095 (s), 1026 (s), 798 (w), 734 (w), 702 (s), 650 (w). MS (EI, 70 eV): m/z = 254 (M^+ , 3), 222 (13), 196 (4), 164 (43), 149 (71), 118 (55), 104 (100), 91 (38), 77 (40). The exact molecular mass m/z = 254.0710 \pm 2 ppm [M^+] for $\text{C}_{13}\text{H}_{15}\text{O}_3\text{Cl}$ was confirmed by HRMS (EI, 70 eV).

6-Bromo-3-oxo-2-*p*-tolylhexanoic Acid Methyl Ester (3g). Starting with **2g** (0.090 g, 0.39 mmol) and BBr_3 (0.388 g, 1.55 mmol) in CH_2Cl_2 (10 mL), **3g** was isolated after chromatography (silica gel, *n*-hex/EtOAc = 50:1 \rightarrow 5:1) as a colorless oil (0.109 g, 89%, 21% of enol form). ^1H NMR (CDCl_3 , 300 MHz): δ = 2.09 (quint, J = 6.6 Hz, 2 H), 2.36 (s, 3 H), 2.67 (t, J = 6.6 Hz, 2 H), 3.36 (t, J = 6.6 Hz, 2 H), 3.75 (s, 3 H), 4.69 (s, 1 H), 7.17–7.26 (m, 4 H), 13.06 (s, 1 H, OH of enol). ^{13}C NMR (CDCl_3 , 150 MHz): δ_{C} = 21.3 (CH_3), 26.7, 33.0, 39.6, 52.8, 64.8, 104.4 (enol), 129.4, 129.5, 129.9, 138.5, 169.2, 137.8 (enol), 175.6 (enol), 202.9. IR (neat, cm^{-1}): $\tilde{\nu}$ = 3132 (w), 3090 (w), 3026 (w), 3004 (w), 2954 (m), 2923 (m), 2862 (w), 1749 (s), 1717 (s), 1644 (w), 1609 (w), 1513 (w), 1437 (m), 1409 (w), 1338 (w), 1307 (w), 1262 (m), 1224 (m), 1205 (s), 1185 (m), 1159 (s), 1114 (w), 1076 (m), 1045 (w), 1020 (w), 814 (w). MS (EI, 70 eV): m/z = 313 (M^+ , 4), 280 (3), 253 (2), 232 (29), 201 (4), 174 (11), 164 (100), 148 (36), 132 (72). The exact molecular mass m/z = 312.0361 \pm 2 ppm [M^+] for $\text{C}_{14}\text{H}_{17}\text{O}_3\text{Br}$ was confirmed by HRMS (EI, 70 eV).

6-Bromo-2-(4-chlorophenyl)-3-oxohexanoic Acid Methyl Ester (3h). Starting with **2h** (0.100 g, 0.40 mmol) and BBr_3 (0.398 g, 1.58 mmol) in CH_2Cl_2 (10 mL), **3h** was isolated after chromatography (silica gel, *n*-hexane/EtOAc = 50:1 \rightarrow 10:1) as a slightly yellow oil (0.102 g, 77%, 22% of enol form). ^1H NMR (CDCl_3 , 300 MHz): δ = 2.07–2.13 (m, 2 H), 2.64–2.73 (m, 2 H), 3.32–3.43 (m, 2 H), 3.76 (s, 3 H), 4.72 (s, 1 H), 7.27–7.38 (m, 4 H), 13.02 (s, 1 H, OH of enol). ^{13}C NMR (CDCl_3 , 150 MHz): δ_{C} = 26.5, 32.9, 39.9, 53.0, 64.2, 103.7 (enol), 129.3, 130.9, 133.5, 134.7, 168.6, 172.9 (enol), 175.4 (enol), 202.1. IR (neat, cm^{-1}): $\tilde{\nu}$ = 3003 (w), 2954 (m), 2921 (w), 1751 (s), 1717 (s), 1645 (s), 1610 (s), 1491 (s), 1438 (s), 1408 (s), 1491 (s), 1438 (s), 1335 (s), 1298 (s), 1272 (s), 1209 (s), 1162 (s), 1091 (s), 1047 (m), 1013 (s), 984 (w), 830 (s), 764 (w), 748 (w), 559 (w), 503 (w). MS (EI, 70 eV): m/z = 334 (M^+ , 6), 302 (21), 221 (5), 184 (89), 148 (100). The exact molecular mass m/z = 331.9815 \pm 2 ppm [M^+] for $\text{C}_{13}\text{H}_{14}\text{O}_3\text{BrCl}$ was confirmed by HRMS (EI, 70 eV).

6-Bromo-2-(4-hydroxyphenyl)-3-oxohexanoic Acid Methyl Ester (3i). Starting with **2i** (0.130 g, 0.5 mmol) and BBr_3 (0.525 g, 2.1 mmol) in CH_2Cl_2 (5 mL), **3i** and **2i'** were isolated after chromatography (silica gel, *n*-hexane/EtOAc = 30:1 \rightarrow 1:1) as brownish and white solids (**3i**: 0.118 g, 72%, 10% of enol-form; **2i'**: 0.027 g, 22%). ^1H NMR (CDCl_3 , 300 MHz): δ = 2.09 (quint, J = 6.9 Hz, 2 H), 2.68 (t, J = 6.9 Hz, 2 H), 3.35 (t, J = 6.9 Hz, 2 H), 3.76 (s, 3 H, OCH_3), 4.70 (s, 1 H), 5.65 (br, 1 H), 6.83 (d, J = 8.7 Hz, 2 H), 7.20 (d, J = 8.7 Hz, 2 H), 13.03 (br, 1 H, OH of enol). ^{13}C NMR (CDCl_3 , 75 MHz): δ_{C} = 26.3, 32.7, 39.4, 52.8, 63.9, 103.9 (enol), 116.0, 123.7, 130.6, 156.1, 169.6, 175.0 (enol), 203.6. IR (KBr, cm^{-1}): $\tilde{\nu}$ = 3396 (m), 3184 (w), 2957 (w), 1735 (s), 1703 (s), 1614 (w), 1594 (w), 1516 (s), 1439 (m), 1359 (m), 1335 (w), 1302 (w), 1274 (m), 1249 (m), 1213 (s), 1161 (m), 1095 (w), 991 (w), 832 (w), 557 (w), 528 (w). MS (EI, 70 eV): m/z = 315 (M^+ , 1), 284 (14), 234 (5), 203 (1), 175 (5), 165 (85), 150 (29), 118 (3), 109 (100), 106 (55). Anal. Calcd for $\text{C}_{13}\text{H}_{15}\text{O}_4\text{Br}$ (315.163): C, 49.54; H, 4.80. Found: C, 49.63; H, 5.03.

(Dihydrofuran-2-ylidene)(4-hydroxyphenyl)acetic Acid Methyl Ester (2i'). ^1H NMR (CDCl_3 , 300 MHz): δ = 1.97 (quint, J = 7.2 Hz, 2 H), 2.52 (t, J = 7.5 Hz, 2 H), 3.68 (s, 3 H), 4.47 (t, J = 6.9 Hz, 2 H), 5.43 (broad s, 1 H), 6.79 (dd, J = 6.6, 2.1 Hz, 2 H), 7.05 (dd, J = 6.6, 2.1 Hz, 2 H). ^{13}C NMR (CDCl_3 , 75 MHz): δ_{C} = 13.4, 32.1, 51.4, 74.2, 103.0, 115.2, 129.6, 131.8, 154.7, 167.2, 170.4. IR (KBr, cm^{-1}): $\tilde{\nu}$ = 3404 (br), 2955 (w), 2914 (w), 1684 (s), 1616 (s), 1515 (s), 1435 (m), 1338 (w), 1327 (w), 1305 (m), 1276 (s), 1243 (m), 1193 (s), 1170 (s), 1098 (w), 1051 (s), 1025 (w), 999 (m), 846 (m), 596 (w). MS (EI, 70 eV): m/z = 234 (M^+ , 100), 202 (56), 174 (18). The exact molecular mass m/z = 234.0892 \pm 2 ppm [M^+] for $\text{C}_{13}\text{H}_{14}\text{O}_4$ was confirmed by HRMS (EI, 70 eV).

6-Bromo-3-oxo-2,4-diphenylhexanoic Acid Methyl Ester (3j). Starting with **2j** (0.060 g, 0.20 mmol) and BBr_3 (0.204 g, 0.82 mmol) in CH_2Cl_2 (5 mL), **3j** was isolated after chromatography (silica gel, n -hexane/EtOAc = 75:1 \rightarrow 3:1) as a slightly yellow oil (0.072 g, 96%, 33% of enol-form). ^1H NMR (CDCl_3 , 300 MHz): δ = 2.10–2.33 (m, 1 H), 2.42–2.65 (m, 1 H), 3.03–3.20 (m, 1 H), 3.21–3.43 (m, 1 H), 3.65 (s, 3 H), 3.93 (t, J = 7.2 Hz, 1 H), 4.69 (s, 1 H), 7.00–7.38 (m, 10 H), 13.22 (s, 1 H). ^{13}C NMR (CDCl_3 , 150 MHz): δ_{C} = 29.9, 31.9, 34.9, 48.9, 55.9, 127.2, 128.0, 128.8, 128.9, 129.5, 129.7, 134.1, 137.3, 167.6, 206.8. IR (KBr, cm^{-1}): $\tilde{\nu}$ = 2956 (w), 2922 (w), 1750 (s), 1716 (s), 1494 (w), 1453 (m), 1436 (m), 1346 (w), 1308 (m), 1263 (m), 1206 (m), 1158 (m), 1114 (w), 1098 (w), 1078 (w), 1027 (w), 1013 (w), 704 (s). MS (EI, 70 eV): m/z = 375 (M^+ , 1), 344 (2), 294 (2), 236 (1), 235 (2), 225 (12), 197 (64), 177 (4), 149 (31), 117 (63), 91 (100), 77 (13). HRMS (ESI): calcd. for $\text{C}_{19}\text{H}_{20}\text{O}_3\text{Br}$ ($[\text{M} + 1]^+$) = 375.05959; found = 375.05880.

6-Bromo-3-oxo-4-ethylhexanoic Acid Ethyl Ester (3k). Starting with **2k** (0.100 g, 0.54 mmol) and BBr_3 (0.549 g, 2.17 mmol) in CH_2Cl_2 (10 mL), **3k** was isolated after chromatography (silica gel, n -hexane/EtOAc = 100:1 \rightarrow 1:1) as a yellow oil (0.118 g, 83%, 29% of enol-form). ^1H NMR (CDCl_3 , 300 MHz): δ = 0.92 (t, J = 7.2 Hz, 3 H), 1.29 (t, J = 7.2 Hz, 3 H), 1.51–1.63 (m, 1 H), 2.84–2.91 (m, 1 H), 3.29–3.38 (m, 1 H), 3.40–3.48 (m, 1 H), 3.51 (d, J = 3.3 Hz, 2 H), 4.20 (q, J = 7.2 Hz, 2 H), 5.06 (s, 1 H, enol), 12.09 (s, 1 H, OH of enol). ^{13}C NMR (CDCl_3 , 150 MHz): δ_{C} = 11.2, 14.2, 24.1, 31.5, 32.8, 48.9, 51.6, 61.5, 91.0 (enol), 167.0, 172.7 (enol), 178.6 (enol), 205.3. IR (neat, cm^{-1}): $\tilde{\nu}$ = 2968 (m), 2935 (w), 1745 (s), 1712 (s), 1648 (m), 1631 (m), 1461 (w), 1424 (w), 1386 (w), 1369 (w), 1352 (w), 1311 (m), 1234 (s), 1176 (w), 1153 (m), 1117 (w), 1095 (w), 1031 (m). MS (EI, 70 eV): m/z = 265 (M^+ , 2), 236 (1), 186 (5), 179 (8), 158 (59), 143 (7), 130 (5), 114 (55), 97 (5), 87 (42), 70 (100), 55 (30). The exact molecular mass m/z = 264.0361 \pm 2 ppm [M^+] for $\text{C}_{10}\text{H}_{17}\text{O}_3\text{Br}$ was confirmed by HRMS (EI, 70 eV).

4-(2-Bromoethyl)-3-oxoheptanoic Acid Ethyl Ester (3l). Starting with **2l** (0.100 g, 0.50 mmol) and BBr_3 (0.505 g, 2.02 mmol) in CH_2Cl_2 (5 mL), **3l** was isolated after chromatography (silica gel, n -hex/EtOAc = 50:1 \rightarrow 20:1) as a slightly yellow oil (0.135 g, 96%, 12% of enol-form). ^1H NMR (CDCl_3 , 300 MHz): δ = 0.92 (t, J = 6.9 Hz, 3 H), 1.28 (t, J = 7.2 Hz, 3 H), 1.22–1.49 (m, 3 H), 1.58–1.68 (m, 1 H), 1.86–1.95 (m, 1 H), 2.24–2.33 (m, 1 H), 2.90–2.94 (m, 1 H), 3.29–3.37 (m, 1 H), 3.40–3.48 (m, 1 H), 3.51 (s, 2 H), 4.19 (q, J = 7.2 Hz, 2 H), 5.05 (s, 1 H, enol), 12.10 (s, 1 H, OH of enol). ^{13}C NMR (CDCl_3 , 150 MHz): δ_{C} = 14.18, 14.24, 20.2, 31.5, 33.3, 35.5, 43.9, 49.0, 61.6, 90.9 (enol), 167.0, 172.7 (enol), 178.9 (enol), 205.4. IR (neat, cm^{-1}): $\tilde{\nu}$ = 2962 (s), 2935 (s), 2873 (w), 1746 (s), 1712 (s), 1650 (s), 1629 (s), 1463 (m), 1446 (m), 1424 (m), 1382 (w), 1371 (w), 1311 (m), 1235 (s), 1153 (m), 1097 (w), 1034 (m), 842 (w), 808 (w). MS (EI, 70 eV): m/z = 279 (M^+ , 3), 264 (3), 250 (3), 236 (30), 200 (5), 172 (25), 165 (7), 163 (11), 157 (64), 143 (75), 130 (10), 115 (100), 101 (11), 87 (79). Anal. Calcd for $\text{C}_{11}\text{H}_{19}\text{O}_3\text{Br}$ (279.173): C, 47.33; H, 6.86. Found: C, 47.67; H, 6.54.

4-(2-Bromoethyl)-7-chloro-3-oxoheptanoic Acid Methyl Ester (3m). Starting with **2m** (0.070 g, 0.32 mmol) and BBr_3 (0.921 g, 1.28 mmol) in CH_2Cl_2 (5 mL), **3m** was isolated after chromatography (silica gel, n -hex/EtOAc = 50:1 \rightarrow 5:1)

as a slightly yellow oil (0.082 g, 86%, 33% of enol-form). ^1H NMR (CDCl_3 , 300 MHz): δ = 1.62–1.98 (m, 4 H), 2.16–2.33 (m, 2 H), 2.92–3.01 (m, 1 H), 3.31–3.54 (m, 4 H), 3.56 (s, 2 H), 3.75 (s, 3 H), 5.10 (s, 1 H, enol), 12.03 (s, 1 H, OH of enol). ^{13}C NMR (CDCl_3 , 150 MHz): δ_{C} = 27.9, 29.6, 31.2, 33.2, 35.36, 43.5, 44.6, 48.6, 52.6, 91.1 (enol), 167.4, 172.9 (enol), 177.8 (enol), 204.7. IR (neat, cm^{-1}): $\tilde{\nu}$ = 2997 (w), 2955 (s), 2868 (w), 1750 (s), 1711 (s), 1655 (s), 1629 (s), 1442 (s), 1404 (m), 1370 (m), 1317 (s), 1238 (s), 1155 (s), 1097 (m), 1050 (m), 1013 (m), 840 (w), 809 (m), 735 (w), 651 (m). MS (EI, 70 eV): m/z = 299 (M^+ , 2), 164 (2), 227 (s), 222 (4), 192 (18), 142 (15), 129 (18), 114 (3), 101 (100). The exact molecular mass m/z = 297.9971 \pm 2 ppm [M^+] for $\text{C}_{10}\text{H}_{16}\text{O}_3\text{BrCl}$ was confirmed by HRMS (EI, 70 eV).

3-(2-Bromoethyl)-2-oxocyclododecanecarboxylic Acid Ethyl ester (3n). Starting with **2n** (0.100 g, 0.36 mmol) and BBr_3 (0.357 g, 1.43 mmol) in CH_2Cl_2 (10 mL), **3n** was isolated after chromatography (silica gel, n -hex/EtOAc = 50:1 \rightarrow 15:1) as a yellow solid (0.113 g, 87%, 5% of enol-form). ^1H NMR (CDCl_3 , 300 MHz): δ = 0.95–1.40 (m, 15 H), 1.41–1.69 (m, 3 H), 1.72–1.85 (m, 1 H), 1.88–2.05 (m, 1 H), 2.09–2.18 (m, 1 H), 2.28–2.52 (m, 2 H), 3.21–3.42 (m, 2 H), 3.44–3.49 (m, 1 H), 4.03 (dd, J = 11.7, 3.0 Hz, 1 H), 4.17 (q, J = 7.2 Hz, 2 H), 13.01 (s, 1 H, OH of enol). ^{13}C NMR (CDCl_3 , 150 MHz): δ_{C} = 14.3, 20.4, 22.1, 22.2, 23.4, 23.5, 26.4, 26.6, 26.9, 27.9, 31.5, 32.4, 49.7, 53.7, 61.8, 102.0 (enol), 169.9, 174.5 (enol), 177.4 (enol), 206.7. IR (neat, cm^{-1}): $\tilde{\nu}$ = 2929 (s), 2855 (s), 1735 (s), 1701 (s), 1637 (w), 1629 (w), 1619 (w), 1465 (s), 1342 (s), 1371 (w), 1340 (w), 1235 (s), 1185 (m), 1156 (m), 1147 (m), 1125 (m), 1096 (m), 1064 (m), 1027 (m), 982 (w), 944 (w), 854 (w), 836 (w), 746 (w), 728 (w), 702 (w). MS (EI, 70 eV): m/z = 361 (M^+ , 53), 316 (77), 281 (68), 255 (60), 238 (80), 236 (100), 208 (57), 165 (61), 107 (59). The exact molecular mass m/z = 360.1300 \pm 2 ppm [M^+] for $\text{C}_{17}\text{H}_{29}\text{O}_3\text{Br}$ was confirmed by HRMS (EI, 70 eV).

6-Bromo-3-oxoheptanoic Acid Methyl Ester (3o). Starting with **2o** (0.060 g, 0.38 mmol) and BBr_3 (0.385 g, 1.54 mmol) in CH_2Cl_2 (5 mL), **3o** was isolated after chromatography (silica gel, n -hexane/EtOAc = 75:1 \rightarrow 3:1) as a slightly yellow oil (0.072 g, 80%, 8% of enol-form). ^1H NMR (CDCl_3 , 300 MHz): δ = 1.74 (dd, J = 6.6, 1.5 Hz, 3 H), 1.96–2.04 (m, 1 H), 2.11–2.20 (m, 1 H), 2.80 (dt, J = 1.5, 6.6 Hz, 2 H), 3.49 (s, 2 H), 3.75 (s, 3 H), 4.12–4.19 (m, 1 H), 5.07 (s, 1 H, enol), 12.04 (s, 1 H, OH of enol). ^{13}C NMR (CDCl_3 , 150 MHz): δ_{C} = 26.7, 34.4, 41.3, 49.2, 50.8, 52.6, 89.8 (enol), 167.6, 174.2 (enol), 178.1 (enol), 201.7. IR (neat, cm^{-1}): $\tilde{\nu}$ = 2957 (m), 2926 (m), 1750 (s), 1717 (s), 1652 (m), 1633 (m), 1439 (s), 1408 (s), 1378 (s), 1321 (s), 1257 (s), 1233 (s), 1194 (s), 1172 (s), 1152 (s), 1075 (m), 1012 (m), 963 (w), 887 (w), 840 (w), 655 (w), 587 (w), 530 (w). MS (EI, 70 eV): m/z = 221 (M^+ -Me, 16), 163 (18), 148 (12), 135 (14), 121 (21), 108 (21), 93 (17), 80 (100). HRMS (ESI): calcd for $\text{C}_8\text{H}_{14}\text{O}_3\text{Br}$ ($[\text{M} + 1]^+$) 237.01187, found 237.01187.

6-Bromo-3-oxooctanoic Acid Methyl Ester (3p). Starting with **2p** (0.150 g, 0.88 mmol) and BBr_3 (0.883 g, 3.53 mmol) in CH_2Cl_2 (15 mL), **3p** was isolated after chromatography (silica gel, n -hexane/EtOAc = 75:1 \rightarrow 1:1) as a slightly yellow oil (0.200 g, 91%, 8% of enol-form). ^1H NMR (CDCl_3 , 300 MHz): δ = 1.05 (t, J = 7.2 Hz, 3 H), 1.82–1.92 (m, 2 H), 1.94–2.06 (m, 1 H), 2.15–2.24 (m, 1 H), 2.80–2.87 (m, 2 H), 3.49 (s, 2 H), 3.75 (s, 3 H), 3.95–4.07 (m, 1 H), 5.07 (s, 1 H, enol), 12.08 (s, 1 H, OH of enol). ^{13}C NMR (CDCl_3 , 75 MHz): δ_{C} = 10.5, 27.7, 32.4, 41.1, 49.1, 52.3, 59.1, 89.8 (enol), 166.5, 201.3. IR (neat, cm^{-1}): $\tilde{\nu}$ = 2971 (m), 2940 (m), 2881 (w), 1750 (s), 1717 (s), 1646 (w), 1639 (w), 1456 (m), 1439 (m), 1409 (m), 1378 (m), 1322 (s), 1262 (s), 1247 (s), 1216 (s), 1171 (m), 1116 (w), 1077 (w), 1051 (w), 1015 (w). MS (EI, 70 eV): m/z = 249 (M^+ , 6), 219 (3), 192 (37), 177 (21), 171 (3), 157 (26), 139 (25), 116 (9), 110 (7), 102 (95), 97 (86), 87 (20), 84 (24), 70 (100), 55 (95). Anal. Calcd for $\text{C}_9\text{H}_{15}\text{O}_3\text{Br}$ (251.120): C, 43.05; H, 6.02. Found: C, 43.89; H, 6.54.

6-Bromo-3-oxodecanoic Acid Methyl Ester (3q). Starting with **2q** (0.150 g, 0.76 mmol) and BBr_3 (0.766 g, 3.03 mmol)

in CH_2Cl_2 (15 mL), **3q** was isolated after chromatography (silica gel, *n*-hexane/EtOAc = 75:1 \rightarrow 1:1) as a slightly yellow oil (0.158 g, 75%, 24% of enol-form). ^1H NMR (CDCl_3 , 300 MHz): δ = 0.89 (t, J = 6.9 Hz, 3 H), 1.29–1.57 (m, 4 H), 1.77–1.88 (m, 2 H), 1.91–2.04 (m, 1 H), 2.16–2.27 (m, 1 H), 2.83 (t, J = 7.2 Hz, 2 H), 3.48 (s, 2 H), 3.75 (s, 3 H), 3.99–4.08 (m, 1 H), 5.04 (s, 1 H, enol), 12.06 (s, 1 H, OH of enol). ^{13}C NMR (CDCl_3 , 150 MHz): δ_{C} = 14.1, 22.2, 29.8, 32.5, 39.3, 41.2, 49.3, 52.5, 57.6, 89.7 (enol), 167.6, 173.8 (enol), 177.8 (enol), 201.8. IR (neat, cm^{-1}): $\tilde{\nu}$ = 2958 (m), 2933 (m), 2868 (w, C–H), 1750 (s, O=C–O), 1719 (s, C=O), 1654 (w), 1633 (w), 1438 (m), 1409 (m), 1377 (w), 1361 (w), 1320 (m), 1241 (m), 1197 (m), 1173 (m), 1151 (m), 1101 (w), 1081 (w), 1026 (w). MS (EI, 70 eV): m/z = 279 (M^+ , 2), 205 (5), 199 (35), 167 (7), 139 (2), 129 (15), 116 (100), 101 (49), 85 (34), 60 (45). Anal. Calcd for $\text{C}_{11}\text{H}_{19}\text{O}_3\text{Br}$ (279.173): C, 47.33; H, 6.86. Found: C, 47.25; H, 7.34.

6,7-Dibromo-3-oxoheptanoic Acid Ethyl Ester (3r). Starting with **2r** (0.100 g, 0.40 mmol) and BBr_3 (0.402 g, 1.61 mmol) in CH_2Cl_2 (10 mL), **3r** was isolated after chromatography (silica gel, *n*-hexane/EtOAc = 50:1 \rightarrow 10:1) as a slightly yellow oil (0.123 g, 93%, 7% of enol-form). ^1H NMR (CDCl_3 , 300 MHz): δ = 1.29 (t, J = 7.2 Hz, 3 H), 1.93–2.05 (m, 1 H), 2.51–2.62 (m, 1 H), 2.80–2.86 (m, 2 H), 3.48 (s, 2 H), 3.62 (dd, J = 7.5, 6.6 Hz, 1 H), 3.86 (dd, J = 7.5, 4.5 Hz, 1 H), 4.21 (q, J = 7.2 Hz, 2 H), 4.19–4.27 (m, 1 H), 5.06 (s, 1 H, enol), 12.10 (s, 1 H, OH of enol). ^{13}C NMR (CDCl_3 , 150 MHz): δ_{C} = 14.3, 30.2, 36.2, 40.5, 49.5, 51.9, 61.9, 90.2 (enol), 167.1, 201.4. IR (neat, cm^{-1}): $\tilde{\nu}$ = 2983 (w), 2935 (w), 1743 (s), 1716 (s), 1651 (w), 1467 (w), 1436 (w), 1410 (m), 1370 (m), 1318 (s), 1258 (s), 1239 (s), 1177 (m), 1157 (m), 1095 (w), 1029 (m), 566 (w). MS (EI, 70 eV): m/z = 330 (M^+ , 1), 251 (11), 243 (20), 215 (3), 205 (4), 169 (100), 163 (16), 143 (5), 135 (26), 115 (28), 97 (5), 95 (32), 87 (13). Anal. Calcd for $\text{C}_9\text{H}_{14}\text{O}_3\text{Br}_2$ (330.016): C, 32.76; H, 4.28. Found: C, 33.36; H, 4.01.

6-Bromo-7-chloro-3-oxoheptanoic Acid Methyl Ester (3s). Starting with **2s** (0.100 g, 0.52 mmol) and BBr_3 (0.531 g, 2.10 mmol) in CH_2Cl_2 (10 mL), **3s** was isolated after chromatography (silica gel, *n*-hexane/EtOAc = 75:1 \rightarrow 1:1) as a slightly yellow oil (0.113 g, 80%, 8% of enol-form). ^1H NMR (CDCl_3 , 300 MHz): δ = 1.94–2.06 (m, 1 H), 2.44–2.57 (m, 1 H), 2.80–2.86 (m, 2 H), 3.50 (s, 2 H), 3.74 (dd, J = 11.4, 8.4 Hz, 1 H), 3.76 (s, 3 H), 3.93 (dd, J = 11.4, 4.8 Hz, 1 H), 4.13–4.22 (m, 1 H), 5.07 (s, 1 H, enol), 12.07 (s, 1 H, OH of enol). ^{13}C NMR (CDCl_3 , 150 MHz): δ_{C} = 29.3, 40.4, 48.3, 49.1, 52.3, 52.6, 167.5, 201.2. IR (neat, cm^{-1}): $\tilde{\nu}$ = 2955 (w), 2929 (w, C–H), 1747 (s, O=C–O), 1717 (s, C=O), 1653 (w), 1633 (w), 1438 (s), 1408 (m), 1375 (w), 1322 (m), 1260 (m), 1165 (m), 1125 (w), 1087 (w), 1013 (w). MS (EI, 70 eV): m/z = 271 (M^+ , 2), 241 (7), 199 (35), 191 (9), 171 (5), 155 (100), 129 (6), 117 (18), 101 (71), 84 (6). The exact molecular mass m/z = 269.9658 \pm 2 ppm [M^+] for $\text{C}_8\text{H}_{12}\text{O}_3\text{BrCl}$ was confirmed by HRMS (EI, 70 eV).

5-Bromomethyl-3-oxoheptanoic Acid Methyl Ester (3t). Starting with **2t** (0.100 g, 0.59 mmol) and BBr_3 (0.589 g, 2.35 mmol) in CH_2Cl_2 (10 mL), **3t** was isolated after chromatography (silica gel, *n*-hexane/EtOAc = 75:1 \rightarrow 5:1) as a slightly yellow oil (0.122 g, 82%, 12% of enol-form). ^1H NMR (CDCl_3 , 300 MHz): δ = 0.91 (t, J = 7.2 Hz, 3 H), 1.03–1.09 (m, 2 H), 2.18–2.21 (m, 1 H), 2.56 (dd, J = 18, 5.4 Hz, 1 H), 2.78 (dd, J = 18, 7.2 Hz, 1 H), 3.47 (s, 2 H), 3.50–3.58 (m, 2 H), 3.75 (s, 3 H), 5.07 (s, 1 H, enol), 12.05 (s, 1 H, OH of enol). ^{13}C NMR (CDCl_3 , 150 MHz): δ_{C} = 11.2, 25.5, 36.4, 38.6, 46.9, 49.6, 52.6, 90.8 (enol), 167.6, 201.7. IR (neat, cm^{-1}): $\tilde{\nu}$ = 2966 (m), 2936 (w), 2879 (w), 1749 (s), 1717 (s), 1654 (w), 1633 (w), 1454 (m), 1439 (m), 1407 (m), 1377 (w), 1322 (m), 1245 (m), 1156 (m), 1128 (w), 1076 (w), 1012 (w). MS (EI, 70 eV): m/z = 249 (M^+ , 10), 219 (5), 192 (43), 177 (27), 171 (3), 157 (38), 139 (30), 116 (3), 110 (8), 102 (91), 87 (89), 87 (21), 84 (20), 70 (97), 55 (100). Anal. Calcd for $\text{C}_9\text{H}_{15}\text{O}_3\text{Br}$ (251.120): C, 43.05; H, 6.02. Found: C, 43.11; H, 6.08.

6-Bromo-3-oxo-5-phenylhexanoic Acid Ethyl Ester (3u). Starting with **2u** (0.200 g, 0.86 mmol) and BBr_3 (0.862 g, 3.44 mmol) in CH_2Cl_2 (15 mL), **3u** was isolated after chromatog-

raphy (silica gel, *n*-hexane/EtOAc = 75:1 \rightarrow 1:1) as a slightly yellow oil (0.223 g, 83%, 9% of enol-form). ^1H NMR (CDCl_3 , 300 MHz): δ = 1.25 (t, J = 7.2 Hz, 3 H), 3.01 (dd, J = 17.7, 7.2 Hz, 1 H), 3.24 (dd, J = 17.7, 5.7 Hz, 1 H), 3.88 (s, 2 H), 3.56–3.66 (m, 3 H), 4.16 (q, J = 7.2 Hz, 2 H), 4.93 (s, 1 H, enol), 7.19–7.32 (m, 5 H), 12.09 (s, 1 H, OH of enol). ^{13}C NMR (CDCl_3 , 150 MHz): δ_{C} = 14.3, 38.1, 42.4, 46.9, 49.9, 61.6, 91.9 (enol), 127.6, 127.9, 128.9, 141.2, 166.9, 173.8 (enol), 176.7 (enol), 200.7. IR (neat, cm^{-1}): $\tilde{\nu}$ = 3105 (w), 3086 (w), 3063 (w), 3030 (w), 2983 (m), 2934 (w), 2907 (w, C–H), 1743 (s), 1717 (s), 1650 (m), 1606 (w), 1495 (w), 1470 (w), 1451 (m), 1408 (m), 1369 (m), 1318 (s), 1247 (s), 1197 (m), 1157 (m), 1096 (m), 1075 (m), 1030 (s), 942 (w), 851 (w), 760 (m), 702 (s), 652 (w), 542 (w). MS (EI, 70 eV): m/z = 313 (M^+ , 1), 267 (1), 232 (88), 225 (9), 203 (6), 199 (2), 187 (6), 185 (26), 158 (15), 145 (100), 141 (4), 129 (2), 114 (69), 103 (74), 87 (11). Anal. Calcd for $\text{C}_{14}\text{H}_{17}\text{O}_3\text{Br}$ (313.191): C, 53.69; H, 5.47. Found: C, 54.10; H, 5.68.

6-Bromo-1-phenylhexane-1,3-dione (3v). Starting with **2v** (0.100 g, 0.53 mmol) and BBr_3 (0.532 g, 2.13 mmol) in CH_2Cl_2 (10 mL), **3v** was isolated after chromatography (silica gel, *n*-hexane/EtOAc = 100:1 \rightarrow 50:1) as a yellow solid (0.140 g, 98%, 84% of enol-form, data are listed for enol). ^1H NMR (CDCl_3 , 300 MHz): δ = 2.25 (quint, J = 6.9 Hz, 2 H), 2.64 (t, J = 7.2 Hz, 2 H), 3.50 (t, J = 6.6 Hz, 2 H), 6.21 (s, 1 H), 7.43–7.56 (m, 3 H), 7.87–7.90 (m, 2 H), 16.02 (s, 1 H, OH). ^{13}C NMR (CDCl_3 , 150 MHz): δ_{C} = 28.4, 33.2, 37.6, 96.7, 127.2, 128.8, 132.6, 135.0, 183.1, 195.7. IR (neat, cm^{-1}): $\tilde{\nu}$ = 3439 (br), 1617 (s), 1573 (s), 1490 (m), 1458 (m), 1433 (m), 1359 (w), 1298 (w), 1264 (m), 767 (m), 694 (m). MS (EI, 70 eV): m/z = 269 (M^+ , 15), 189 (3), 175 (5), 162 (53), 147 (100), 120 (3), 105 (58), 77 (48). The exact molecular mass m/z = 268.0099 \pm 2 ppm [M^+] for $\text{C}_{12}\text{H}_{13}\text{O}_2\text{Br}$ was confirmed by HRMS (EI, 70 eV).

8-Bromo-3-oxooct-6-enoic Acid Ethyl Ester (3w). Starting with **2w** (0.150 g, 0.82 mmol) and BBr_3 (0.833 g, 3.29 mmol) in CH_2Cl_2 (15 mL), **3w** was isolated after chromatography (silica gel, *n*-hexane/EtOAc = 50:1 \rightarrow 1:1) as a slightly yellow oil (0.211 g, 98%, 10% of enol-form). ^1H NMR (CDCl_3 , 300 MHz): δ = 1.29 (t, J = 7.2 Hz, 2 H), 3.44 (s, 2 H), 3.92 (d, J = 6.0 Hz, 2 H), 4.20 (q, J = 7.2 Hz, 2 H), 4.98 (s, 1 H, enol), 5.72–5.77 (m, 2 H), 12.10 (s, 1 H, OH of enol). ^{13}C NMR (CDCl_3 , 150 MHz): δ_{C} = 14.2, 25.8, 33.0, 41.9, 49.4, 61.5, 89.9 (enol), 127.6, 134.0, 167.1, 201.7. IR (neat, cm^{-1}): $\tilde{\nu}$ = 2983 (w), 2935 (w), 1742 (s), 1716 (s), 1654 (w), 1438 (w), 1410 (w), 1369 (w), 1316 (m), 1247 (m), 1206 (m), 1160 (w), 1113 (w), 1100 (w), 1031 (m), 968 (w). MS (EI, 70 eV): m/z = 263 (M^+ , 3), 218 (1), 183 (100), 176 (7), 148 (2), 137 (42), 135 (1), 130 (9), 119 (6), 114 (19), 110 (6), 95 (61), 87 (23).

1,7-Dibromoheptan-4-one (6a).^{14a} Starting with **5a** (0.300 g, 1.95 mmol) and BBr_3 (1.950 g, 7.8 mmol) in CH_2Cl_2 (15 mL), **6a** was isolated after chromatography (silica gel, *n*-hexane/EtOAc = 50:1 \rightarrow 1:1) as a slightly yellow oil (0.365 g, 73%). ^1H NMR (CDCl_3 , 300 MHz): δ = 2.14 (quint, J = 6.6 Hz, 4 H), 2.65 (t, J = 6.6 Hz, 4 H), 3.45 (t, J = 6.6 Hz, 4 H). ^{13}C NMR (CDCl_3 , 75 MHz): δ_{C} = 26.4, 33.4, 40.8, 208.1. IR (neat, cm^{-1}): $\tilde{\nu}$ = 2964 (m), 2918 (w), 1714 (s), 1436 (m), 1409 (m), 1375 (m), 1296 (w), 1282 (w), 1253 (m), 1197 (w), 1151 (w), 1091 (w), 1046 (w), 558 (w). MS (EI, 70 eV): m/z = 272 (M^+ , 1), 193 (4), 164 (24), 150 (100), 121 (38), 106 (3), 93 (7).

1,7-Dibromooctan-4-one (6b). Starting with **5b** (0.020 g, 0.12 mmol) and BBr_3 (0.119 g, 0.48 mmol) in CH_2Cl_2 (3 mL), **6b** was isolated after chromatography (silica gel, *n*-hexane/EtOAc = 100:1 \rightarrow 50:1), as a colorless oil (0.030 g, 88%). ^1H NMR (CDCl_3 , 300 MHz): δ = 1.73 (d, J = 6.6 Hz, 3 H), 1.92–2.03 (m, 1 H), 2.08–2.18 (m, 1 H), 2.18 (quint, J = 6.6 Hz, 2 H), 2.65 (t, J = 6.6 Hz, 2 H), 2.66–2.70 (m, 2 H), 3.45 (t, J = 6.6 Hz, 2 H), 4.12–4.18 (m, 1 H). ^{13}C NMR (CDCl_3 , 75 MHz): δ_{C} = 26.3, 26.6, 33.2, 34.4, 40.8, 40.9, 51.0, 208.4. IR (neat, cm^{-1}): $\tilde{\nu}$ = 2965 (m), 2923 (m), 1714 (s), 1637 (w), 1439 (m), 1410 (m), 1377 (m), 1336 (w), 1283 (w), 1250 (m), 1215 (w), 1182 (m), 1142 (m), 1079 (m). MS (EI, 70 eV): m/z = 286 (M^+ , 3), 205 (4), 178 (1), 166 (45), 164 (45), 148 (49), 121 (16), 83

(30), 55 (100). HRMS (ESI): calcd. for $C_8H_{14}OBr$ ($[M - Br]^+$) = 205.02281, found = 205.02196.

1,7-Dibromononan-4-one (6c). Starting with **5c** (0.600 g, 3.29 mmol) and BBr_3 (3.300 g, 13.2 mmol) in CH_2Cl_2 (20 mL), **6c** was isolated after chromatography (silica gel, *n*-hex/EtOAc = 100:1 \rightarrow 50:1) as a colorless oil (0.668 g, 68%). 1H NMR ($CDCl_3$, 300 MHz): δ = 1.05 (t, J = 7.2 Hz, 3 H), 1.40–1.51 (m, 2 H), 1.82–1.92 (m, 2 H), 2.14 (quint, J = 6.6 Hz, 2 H), 2.65 (t, J = 6.6 Hz, 2 H), 2.68–2.73 (m, 2 H), 3.45 (t, J = 6.6 Hz, 2 H), 3.94–4.03 (m, 1 H). ^{13}C NMR ($CDCl_3$, 75 MHz): δ_C = 12.1, 26.3, 32.2, 32.5, 33.2, 40.7, 40.8, 59.5, 208.4. IR (neat, cm^{-1}): $\tilde{\nu}$ = 2965 (s), 2935 (m), 2879 (w), 1717 (s), 1604 (w), 1440 (s), 1410 (w), 1375 (m), 1312 (s), 1261 (m), 1227 (m), 1199 (s), 1154 (s), 1100 (m), 1066 (m), 1034 (m), 942 (w), 795 (w), 750 (w). MS (EI, 70 eV): m/z = 300 (M^+ , 1), 219 (6), 177 (19), 164 (10), 150 (24), 139 (18), 135 (7), 121 (15), 108 (12), 95 (15), 70 (61), 55 (63), 41 (100). HRMS (ESI): calcd for $C_9H_{16}OBr$ ($[M - Br]^+$) = 219.03846, found = 219.03779.

1,7-Dibromo-8-chlorooctan-4-one (6d). Starting with **5d** (0.200 g, 0.99 mmol) and BBr_3 (0.999 g, 3.95 mmol) in CH_2Cl_2 (15 mL), **6d** was isolated after chromatography (silica gel, *n*-hexane/EtOAc = 75:1 \rightarrow 1:1) as a colorless oil (0.269 g, 85%). 1H NMR ($CDCl_3$, 300 MHz): δ = 1.92–2.05 (m, 1 H), 2.15 (quint, J = 6.6 Hz, 2 H), 2.42–2.53 (m, 1 H), 2.66 (t, J = 6.6 Hz, 2 H), 2.61–2.74 (m, 2 H), 3.46 (t, J = 6.6 Hz, 2 H), 3.73 (dd, J = 11.4, 8.7 Hz, 1 H), 3.91 (dd, J = 11.4, 4.8 Hz, 1 H), 4.13–4.22 (m, 1 H). ^{13}C NMR ($CDCl_3$, 150 MHz): δ_C = 26.5, 29.6, 33.4, 40.5, 40.9, 48.4, 52.7, 208.0. IR (neat, cm^{-1}): $\tilde{\nu}$ = 2963 (w), 1714 (s), 1435 (m), 1410 (m), 1375 (m), 1287 (w), 1249 (w), 1180 (w), 1158 (w), 1093 (w), 774 (w). MS (EI, 70 eV): m/z = 321 (M^+ , 4), 285 (5), 241 (16), 213 (11), 199 (47), 171 (10), 164 (12), 161 (6), 150 (100), 133 (32), 121 (35). HRMS (ESI): calcd for $C_8H_{13}OBrCl$ ($[M - Br]^+$) = 238.98384, found = 238.98305. Anal. Calcd for $C_8H_{13}OBr_2Cl$ (320.451): C, 29.99; H, 4.09. Found: C, 29.95; H, 4.74.

1,7-Dibromo-6-methyloctan-4-one (6e). Starting with *trans*-**5e** (0.100 g, 0.55 mmol) and BBr_3 (0.550 g, 2.2 mmol) in CH_2Cl_2 (5 mL), **6e** was isolated after chromatography (silica gel, *n*-hex/EtOAc = 100:1 \rightarrow 5:1) as a colorless oil (0.144 g, 87%). The product was obtained as a 1:1 mixture of diastereomers. The analytical data are given for a separated sample of a pure diastereomer. 1H NMR ($CDCl_3$, 300 MHz): δ = 0.98 (d, J = 6.6 Hz, 3 H), 1.68 (d, J = 6.9 Hz, 3 H), 2.13 (quint, J = 6.6 Hz, 2 H), 2.17–2.24 (m, 1 H), 2.41 (dd, J = 17.4, 7.0 Hz, 1 H), 2.62 (t, J = 6.6 Hz, 2 H), 2.69 (dd, J = 17.4, 6.1 Hz, 1 H), 3.45 (t, J = 6.6 Hz, 2 H), 4.31 (dq, J = 6.9, 2.8 Hz, 1 H). ^{13}C NMR ($CDCl_3$, 150 MHz): δ_C = 15.1, 23.9, 26.5, 33.4, 35.9, 41.5, 48.7, 57.8, 208.6. IR (neat, cm^{-1}): $\tilde{\nu}$ = 2969

(s), 2927 (m), 1713 (s), 1444 (m), 1409 (m), 1376 (s), 1328 (m), 1273 (m), 1257 (m), 1208 (m), 1143 (m), 1081 (m), 1014 (w), 970 (w), 602 (w). MS (EI, 70 eV): m/z = 300 (M^+ , 6), 219 (7), 177 (21), 164 (66), 150 (65), 148 (74), 121 (26), 97 (31), 85 (7), 70 (100). HRMS (ESI): calcd for $C_9H_{16}OBr$ ($[M - Br]^+$) = 219.03846, found = 219.03767.

5-Bromopentan-2-one (7).² Starting with α -acetyl- γ -butyrolactone (0.25 mL, 2.34 mmol) and BBr_3 (2.346 g, 9.37 mmol) in CH_2Cl_2 (15 mL), **7** was isolated after chromatography (silica gel, *n*-hex/EtOAc = 50:1 \rightarrow 1:1) as a slightly yellow oil (0.206 g, 59%). 1H NMR ($CDCl_3$, 300 MHz): δ = 2.12 (quint, J = 6.6 Hz, 2 H), 2.17 (s, 3 H), 2.65 (t, J = 6.9 Hz, 2 H), 3.45 (t, J = 6.3 Hz, 2 H). IR (neat, cm^{-1}): $\tilde{\nu}$ = 2965 (w), 1715 (s), 1432 (m), 1413 (m), 1367 (m), 1302 (w), 1282 (w), 1248 (m), 1217 (w), 1196 (w), 1179 (m), 1185 (m).

Synthesis of *trans*-4,5-Dimethyltetrahydro[2,3']bifuranylidene-2'-one (5e). The synthesis was carried out according to a known procedure for related products.¹¹ Starting with the 1,3-bis-silyl enol ether of α -acetyl- γ -butyrolactone (2.725 g, 10 mmol), *cis*-2,3-epoxybutane (0.883 g, 12 mmol), and $TiCl_4$ (2.2 mL, 20 mmol) in CH_2Cl_2 (75 mL), **5e** was isolated after chromatography (silica gel, *n*-hexane/EtOAc = 75:1 \rightarrow 5:1) as a colorless oil (0.669 g, 37%). 1H NMR ($CDCl_3$, 300 MHz): δ = 1.11 (d, J = 6.7 Hz, 3 H), 1.38 (d, J = 6.2 Hz, 3 H), 1.92–2.03 (m, 1 H), 2.54 (ddt, J = 18.0, 9.9, 3.0 Hz, 1 H), 2.83–2.90 (m, 2 H), 3.55 (ddt, J = 18.0, 7.7, 1.7 Hz, 1 H), 4.01–4.10 (m, 1 H), 4.30 (t, J = 7.7 Hz, 2 H). ^{13}C NMR ($CDCl_3$, 150 MHz): δ_C = 16.1, 18.8, 25.0, 37.7, 39.5, 65.3, 86.7, 92.8, 168.7, 173.3. IR (neat, cm^{-1}): $\tilde{\nu}$ = 2975 (w), 2930 (w), 1733 (s), 1680 (s), 1454 (w), 1389 (w), 1377 (w), 1306 (m), 1262 (m), 1164 (w), 1057 (s), 1023 (s), 1001 (s), 851 (w). MS (EI, 70 eV): m/z = 182 (M^+ , 46), 167 (100), 152 (6), 139 (4), 124 (10), 111 (52), 95 (17). HRMS (ESI): calcd. for $C_{10}H_{15}O_3$ ($[M + 1]^+$) = 183.10212, found = 183.10127.

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Supporting Information Available: Experimental procedures, spectroscopic data, copies of NMR spectra, and details of crystal structure analyses. This material is available free of charge via the Internet at <http://pubs.acs.org>.

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