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Percarboxylic Acid Oxidation of α-Hydroxy-Substituted Alkoxyallenes: The Unexpected Formation of Acyloxy-Substituted 1,2-Diketones and the Synthesis of Functionalized Quinoxalines

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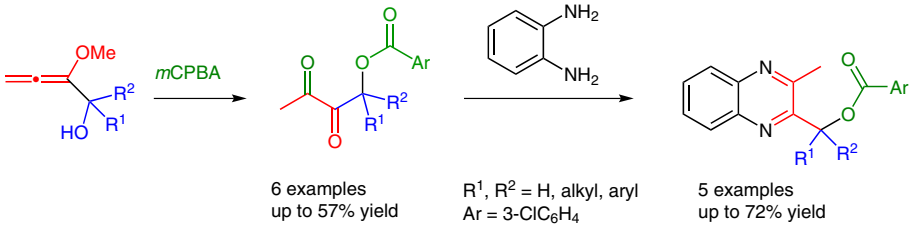
Dedicated to Professor Dieter Enders on the occasion of his 70th birthday



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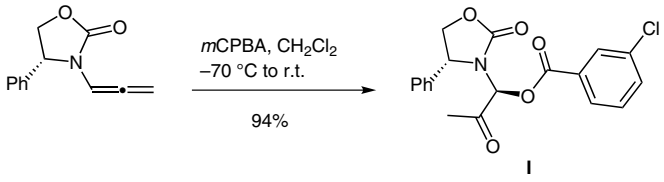
Abstract Treatment of α-hydroxy-substituted methoxyallene derivatives with *meta*-chloroperbenzoic acid provided acyloxy-substituted 1,2-diketones in moderate yields. A mechanism for the formation of these unexpected products is proposed. The configuration of the enantiopure compound (*S*)-1-(3-methylquinoxalin-2-yl)-1-(4-nitrobenzoyloxy)propan-2-yl 3-chlorobenzoate – determined by X-ray crystal structure analysis – indicates the intermediacy of a carbenium ion during formation of the 1,2-diketones. The functionalized 1,2-diketones are valuable starting materials for a variety of products as demonstrated by the synthesis of quinoxalines, an imidazole derivative, and electron-deficient alkenes.

Key words allenes, alkoxyallenes, quinoxalines, oxidation, peroxides, ring closure, rearrangement, 1,2-diketones

Donor-substituted allenes constitute a fascinating class of compounds that have notably contributed to organic synthesis as C_3-building blocks.[1] In particular, alkoxyallenes have been utilized in numerous synthetically useful reactions including hydrolysis, substitution and addition reactions, cross-couplings, multicomponent processes, cycloadditions, and cyclizations, transformations that lead to a variety of functionalized acyclic, carbocyclic, and heterocyclic products.[2] In contrast to the aforementioned reaction types, oxidations of alkoxyallenes are relatively little explored.[3] Whereas a few substituted alkoxyallenes have been subjected to ozonolyses providing carboxylic esters,[4] the epoxidation of electron-rich allenes using oxidizing reagents such as *meta*-chloroperbenzoic acid (*m*CPBA) or dimethyldioxirane (DMDO) has been rarely studied.[5] An interesting reaction outcome of the oxidation of allenyl amides with *m*CPBA was reported by Hsung and co-workers. They obtained the corresponding α-keto aminals of type **I** bearing a 3-chlorobenzoic ester moiety at the aminal moiety (Scheme 1).[6]

Stimulated by this result, we were interested to adopt these reaction conditions to α-hydroxy-substituted alkoxyallenes as substrates which might lead to 1,2-diketones bearing an α-oxy functionality. The motif of vicinal polycarbonyl groups, especially 1,2-diketone subunits, represents an important class of compounds.[7] 1,2-Diketone moieties are an integral part of numerous natural products and biologically active compounds.[8] Selected examples having embedded the 1,2-dicarbonyl moiety as an important structural element are shown in Figure 1, for instance, the antibiotic macrolide (–)-grahamimycin A_1 (**II**), the signaling molecule for bacterial interspecies communication AI-2



Scheme 1 Synthesis of **I** by oxidation of an allenamide with *m*CPBA

(**III**), and its precursor (*S*)-4,5-dihydroxypentane-2,3-dione (DPD, **IV**).

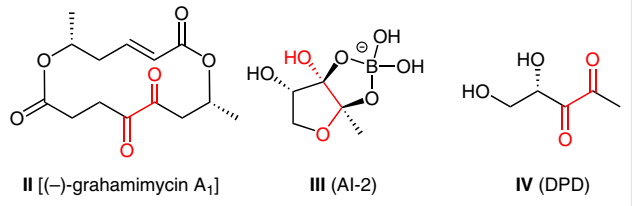
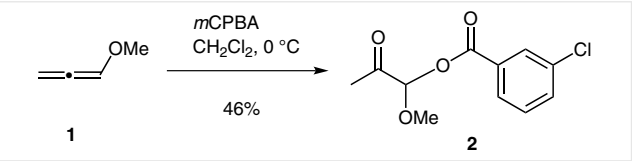


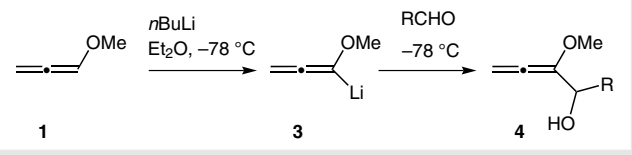
Figure 1 Examples of compounds bearing a 1,2-diketone moiety

First, before starting our investigation using C-1 substituted methoxyallene derivatives, we subjected the parent compound **1** to similar reaction conditions as reported by Hsung.[6] Oxidation of methoxyallene (**1**) using commercially available *m*CPBA at 0 °C in dichloromethane furnished the ketone **2** containing an adjacent acetal unit as a single product in 46% yield (Scheme 2). The oxidation of **1** apparently occurs in full analogy to that of the allenamide studied by Hsung.



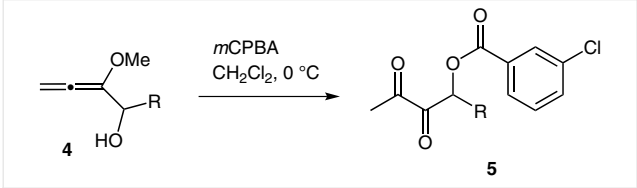
Scheme 2 Oxidation of methoxyallene (**1**) leading to acetal **2**

The α-hydroxy-substituted methoxyallene derivatives **4** required for this study were prepared from methoxyallene (**1**), which is easily converted into the lithiated species **3** and subsequently treated with the corresponding aldehyde using a well-known standard protocol (Scheme 3).[9]



Scheme 3 Synthesis of α-hydroxy-substituted methoxyallene derivatives **4**

We initiated our oxidation studies with the screening of the reaction conditions for the transformation of methoxyallene derivatives **4** using *m*CPBA (Scheme 4). In the first instance, the cyclohexyl-substituted methoxyallene derivative **4a** was treated at 0 °C with commercially available *m*CPBA (70%, containing water and *m*-chlorobenzoic acid)[10] in dichloromethane. These conditions furnished the 1,2-diketone derivative **5a** bearing a 3-chlorobenzoic ester unit, but the yield was only 20% (Table 1, entry 1). We noticed that a pre-treatment removing the *m*-chlorobenzoic acid and water from the commercially available *m*CPBA, as reported by Schwartz,[11] was quite beneficial. Applying the pre-treated reagent, the desired product **5a** was isolated in a significantly increased yield of 51% (Table 1, entry 2). To examine the scope of this oxidation, the reactions were also carried out with α-hydroxy-substituted methoxyallene derivatives **4b–d** under these optimized conditions and the expected products **5b–d** were obtained in moderate yields, ranging from 32 to 57% (Table 1, entries 3–5).



Scheme 4 Oxidation of aldehyde-derived α-hydroxy-substituted methoxyallenes **4a–d** with *m*CPBA leading to 1,2-diketone derivatives **5a–d**

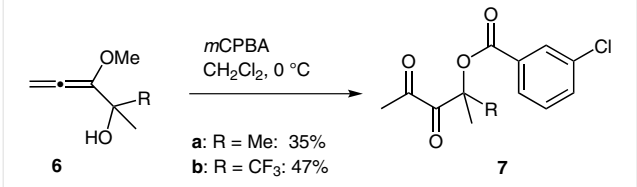
Table 1 Oxidation of α-Hydroxy-Substituted Methoxyallenes **4a–d** to 1,2-Diketones **5a–d**

Entry	R	4	Method[a]	5	Yield of 5
1	cyclohexyl	**4a**	A	**5a**	20%
2	cyclohexyl	**4a**	B	**5a**	51%
3	$(CH_2)_{10}Me$	**4b**	B	**5b**	57%
4	Ph	**4c**	B	**5c**	47%
5	CH_2OBn	**4d**	B	**5d**	32%

[a] Method A: commercial *m*CPBA was used without pre-treatment. Method B: *m*CBPA was pre-treated with a buffer solution[11] (see Supporting Information).

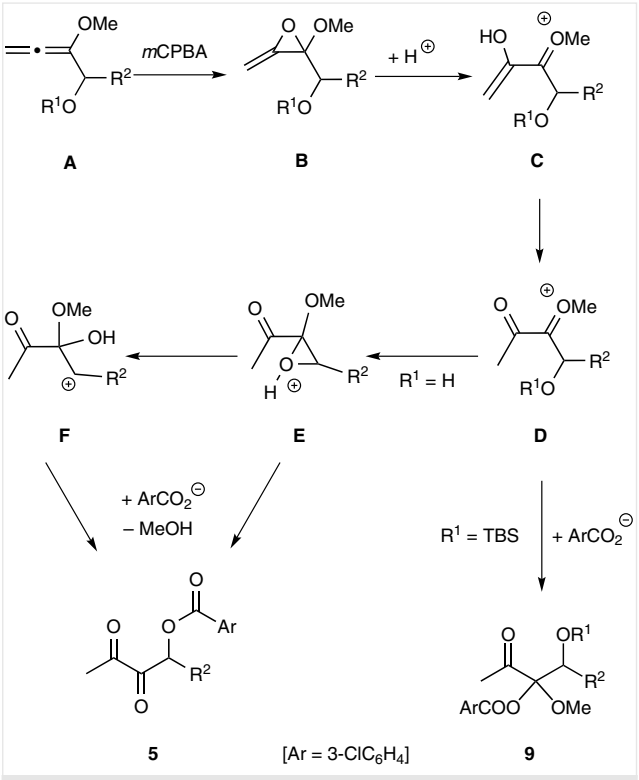
At this point, it should be mentioned that the moderate yields of products **5** may be attributed by some unavoidable side reactions, e.g. over-oxidation or hydrolysis, that could not completely suppressed despite the optimized reaction conditions. However, no side-products proving this assumption were isolated.

We briefly examined the oxidation protocol employing ketone-derived α-hydroxy-substituted methoxyallenes **6**. Treatment of **6a** (R = Me)[12] and **6b** (R = CF_3) with *m*CPBA by using the optimized reaction conditions furnished the expected 1,2-diketones **7a**,**b** bearing a quaternary center in moderate yields (Scheme 5).



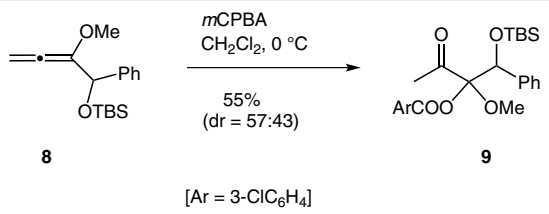
Scheme 5 Oxidation of ketone-derived α-hydroxyallenes **6**

The observed reactions of α-hydroxy-substituted methoxyallene derivatives **4** and **6** not only involve an oxidation, but also an unprecedented incorporation of *m*-chlorobenzoic acid into the product. A plausible mechanism of this transformation of **A** is shown in Scheme 6. The oxidation of **A** with *m*CPBA at the electron-rich double bond regioselectively forms the epoxide **B**[5c] that is ring-opened under the acidic reaction conditions to the enol **C**. Subsequent ring closing of its keto tautomer **D** leads to the protonated epoxide **E**. The nucleophilic attack of the carboxylate $ArCOO^-$ opens this highly reactive intermediate to deliver after elimination of methanol product **5**. Alternatively, the overall process may also be explained by ring opening of **E** to give carbenium ion **F** followed by its trapping by the carboxylate and release of methanol. A result presented below indicates that the pathway via carbenium ion **F** may be the preferred one. We cannot rigorously exclude an alternative route to **5** via compound **9** (R^1 = H) that may undergo an acyl transfer; however, this mechanism seems to be less likely under the acidic reaction conditions.



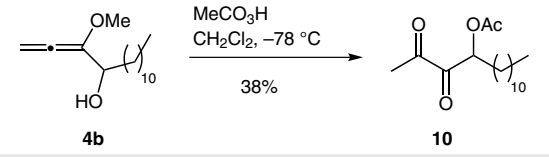
Scheme 6 Proposed mechanism for the formation of 1,2-diketones **5** or of compounds **9**

A control experiment was performed in order to confirm the mechanism proposed above. For this purpose, the *O*-silylated allene derivative **8** was subjected to the standard oxidation protocol with *m*CPBA (Scheme 7). Compound **9** (R^1 = TBS) bearing a ketal unit was formed in 55% yield as a mixture of two diastereomers (57:43). Due to the protected hydroxyl group of precursor **8** the mechanism as depicted in Scheme 6 is interrupted after formation of the *O*-silylated intermediate **D**. Due to the bulky silyl group the cyclization to intermediates analogous to **E** (and subsequently formation of **F**) is not possible, but *O*-silylated **D** directly reacts with the carboxylate to provide the isolated product **9**. The very low diastereoselectivity of this step is not surprising since no significant stereocontrol can be expected for the addition of the nucleophile to the corresponding oxocarbenium ion.[13]



Scheme 7 Oxidation of *O*-silylated methoxyallene derivative **8** leading to product **9**

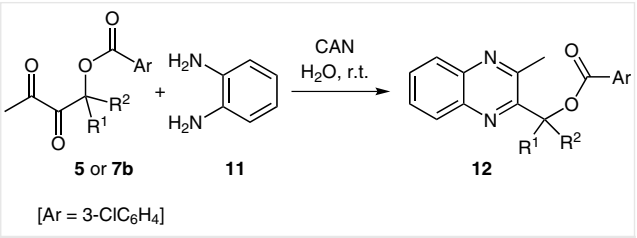
We attempted the oxidation of α-hydroxy-substituted methoxyallene derivative **4b** using other oxidation reagents instead of *m*CPBA. However, no clear reaction outcome was observed using MMPP (magnesium monoperoxyphthalate), $RuCl_3/NaIO_4$, or DMDO (dimethyldioxirane), only decomposition of the starting material occurred or hydrolysis of the enol ether unit of **4b** leading to the corresponding α,β-unsaturated ketone was observed. When the oxidation of **4b** was performed with peracetic acid (employed as a 35% aqueous solution) at –78 °C the 3-acetoxy-substituted 1,2-diketone **10** was obtained in 38% yield (Scheme 8). This example demonstrated that other peracids can also be applied furnishing the 1,2-diketones with the corresponding acid unit as substituent.



Scheme 8 Oxidation of **4b** using peracetic acid leading to 1,2-diketone derivative **10**

Having attained access to functionalized 1,2-diketones of type **5**, we turned our attention to their conversion into subsequent products by taking advantage of the 1,2-dicarbonyl unit. An obvious and useful application is the condensation of these compounds with aromatic 1,2-diamines leading to quinoxalines that are well known as biologically active heterocycles.[14] 1,2-Diketones **5a**–**c** and **7b** smoothly underwent the condensation reaction with *o*-phenylenediamine (**11**) in the presence of cerium ammonium nitrate

(CAN) in water at ambient temperature[15] affording the corresponding quinoxaline derivatives **12a–d** in 60–72% yield (Scheme 9, Table 2).



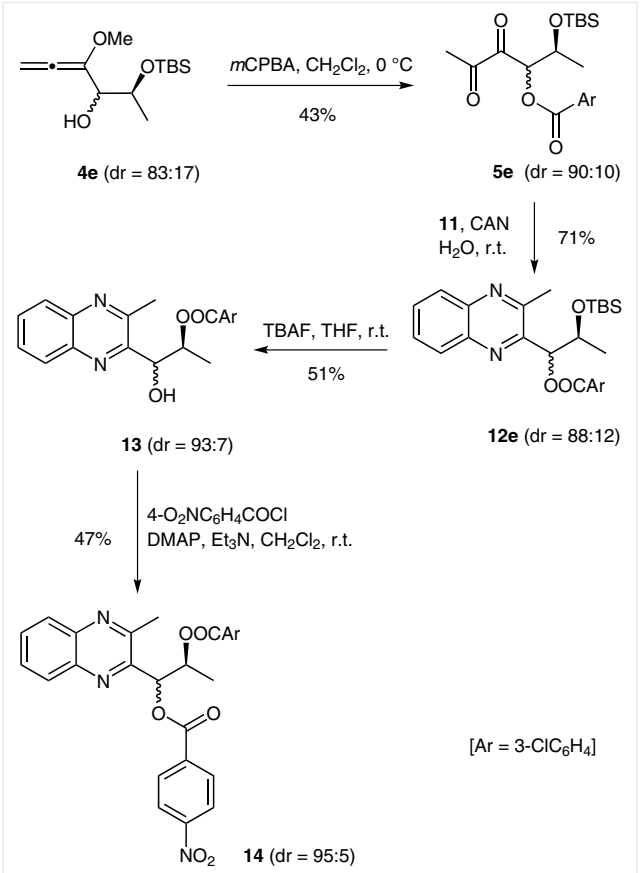
Scheme 9 Condensation reaction of functionalized 1,2-diketones **5a–c** and **7b** with *o*-phenylenediamine (**11**) leading to quinoxaline derivatives **12a–d**

Table 2 Preparation of Quinoxaline Derivatives **12a–d**

Entry	**5** or **7**	R^1	R^2	**12**	Yield of **12**
1	**5a**	cyclohexyl	H	**12a**	71%
2	**5b**	$(CH_2)_{10}Me$	H	**12b**	72%[a]
3	**5c**	Ph	H	**12c**	68%
4	**7b**	Me	CF_3	**12d**	60%

[a] Quinoxaline derivative **12b** was also obtained using an alternative protocol [NH_4Cl (50 mol%), MeOH, rt, 50 min][16] in 84% yield.

In order to gain additional insight into the mechanism of the oxidation reaction discussed in Scheme 6, we were interested to get an X-ray crystal structure analysis of one of the suitably functionalized 1,2-diketones or their derivatives. We therefore investigated the methoxyallene derivative **4e** obtained as an isomeric mixture (*anti*/*syn* = 83:17)[17] from enantiopure *O*-silylated (*S*)-lactaldehyde. As shown in Scheme 10, the oxidation of the α-hydroxy-substituted methoxyallene derivative **4e** afforded product **5e** in 43% yield with a similar ratio of diastereomers (*anti*/*syn* = 90:10). The conversion of **5e** into the corresponding quinoxaline derivative was achieved according to the procedure described above, leading to **12e** in reasonable yield with an *anti*/*syn* ratio of 88:12. To obtain a suitable crystalline compound, we tried to converted **12e** into the corresponding compound bearing a *p*-nitrobenzoic ester at C-1 of the side-chain. However, after desilylation of **12e** with TBAF by a standard procedure, esterification of the desilylated intermediate with *p*-nitrobenzoic chloride afforded the unexpected product **14** as a diastereomeric mixture (dr = 95:5). Apparently, during the first deprotection step an acyl group migration occurred, shifting the 3-ClC$_6$H$_4$CO substituent to the free hydroxyl group at C-2. The driving force for this (reversible) migration may be the lower repulsion of the bulky quinoxaline moiety and the arylcarbonyloxy group. The esterification in the next step then occurred at the remaining hydroxyl group at C-1. After chromatographic separation of both diastereomers, we were able to obtain suitable crystals of the major isomer of **14** for an X-ray crystal structure analysis (Figure 2). The crystal structure proves the constitution of the compound (and the unexpected acyl group migration) and the configurations at C-1 and C-2 as 1*R* and 2*S* revealing an *anti*-configuration of compound **14**. It is very likely that the acyl migration during the conversion of **12e** to **13** occurs under retention of configuration and therefore compound **12e** should also have 1*R* and 2*S* configurations at its stereogenic centers.



Scheme 10 Preparation of quinoxaline derivative **14** starting from methoxyallene derivative **4e**

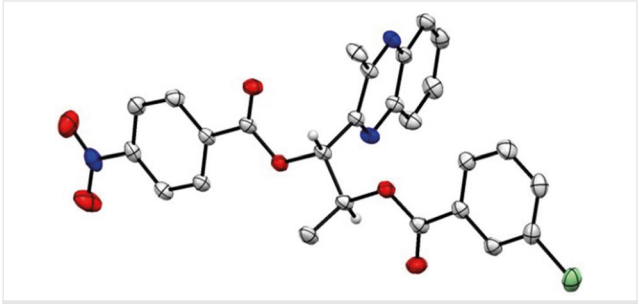
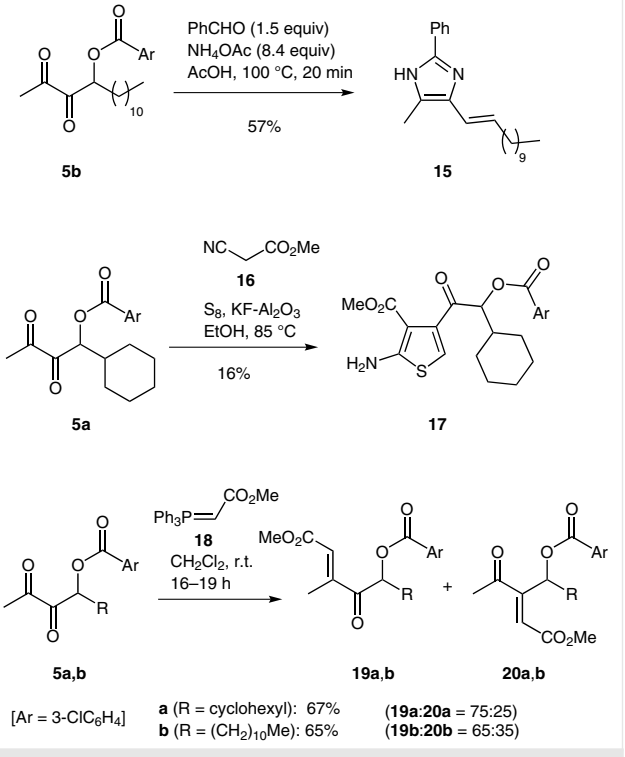


Figure 2 Molecular structure of the major diastereomer of compound **14** (thermal ellipsoid of 50% probability)

A nucleophilic attack of the *m*-chlorobenzoate anion to intermediate **E** (Scheme 6) requires an inversion of configuration of the attacked epoxide carbon atom and hence this center should have (*S*)-configuration for the major diastereomers of **12e** and **14**, respectively. However, this stereogenic center of quinoxaline **14** has (*R*)-configuration and hence a diastereoselective addition of the carboxylate to the acyclic intermediate **F** is more likely. Due to the neighboring stereogenic center the observed *anti*-configuration is induced with preference resulting mainly in overall retention of configuration at this carbon. The high diastereoselectivity of this step is nevertheless surprising.[13]

After the successful preparation of quinoxalines **12** we also checked the feasibility of converting 1,2-diketones **5** into functionalized imidazole and thiophene derivatives (Scheme 11). For example, according to a protocol described by Breslin et al.[18] the synthesis of the trisubstituted imidazole **15** was carried out by the condensation of 1,2-diketone **5b** with 1.5 equiv of benzaldehyde and 8.5 equiv of ammonium acetate in acetic acid at 100 °C. The formation of the additional C–C double bond is due to the elimination of *m*-chlorobenzoic acid under the relatively harsh conditions applied. No intermediate compound still bearing the $ArCO_2$ group was observed. A modified Gewald protocol[19] was applied to 1,2-diketone derivative **5a** with sulfur in the presence of KF-Al_2O_3 as base leading to the expected 2-amino-substituted thiophene derivative **17** although only in 16% yield. This sobering result shows that highly functionalized carbonyl compounds such as **5a** are not ideal precursors for the Gewald multicomponent reaction and probably give many (unidentified) side products.



Scheme 11 Synthesis of imidazole derivative **15**, thiophene derivative **17**, and 4-oxoalk-2-enoates **19** and **20** from 1,2-diketones **5a**,**b**

Since 4-oxoalk-2-enoates are interesting starting materials for the synthesis of complex molecular scaffolds we also examined their formation by Wittig olefination of 1,2-diketones **5**.[20] However it was not clear whether there will be any preference for one of the two ketone moieties present in these precursors. The Wittig reactions of 1,2-diketones **5a** or **5b** with one equiv of the stabilized phosphorane **18** took place under typical conditions[20] smoothly furnishing the two regioisomeric α,β-unsaturated carboxylic esters **19a**,**b** and **20a**,**b** in decent combined yields and exclusively as *E*-isomers. In both cases, the products could be separated by column chromatography or HPLC. The preferred olefinations of **5a** and **5b** at the sterically less hindered methyl ketone moiety was confirmed by the NMR data. In the ^{1}H NMR spectra of compounds **19** two sets of signals attributable to methyl group (δ = ~2.3) and the newly generated olefinic proton (δ = ~6.5) showing a small allylic coupling constant of ~1–1.5 Hz prove the proposed assignment for the major regioisomers.

In this report we demonstrate that a series of α-hydroxy-substituted methoxyallenes **4** and **6** can be easily oxidized with *m*CPBA to provide 3-acyloxy-substituted 1,2-diketone derivatives **5** and **7** in reasonable yields. These compounds are valuable starting materials for a quick access to synthetically important target molecules[21] as shown by the synthesis of numerous heterocycles, for instance quinoxalines **12**, imidazole **15**, and thiophene **17**, as well as by the regioselective preparation of 4-oxoalk-2-enoates **19** and **20**. The herein reported results again emphasize the versatility of alkoxyallenes as synthetically highly useful and flexible key compounds.

Reactions were generally performed under argon in flame-dried flasks. Solvents and reagents were added by syringe. Solvents were dried using standard procedures. Reagents were purchased and were used as received without further purification unless stated. The starting materials **4c**,[22] **4e**,[17] **6a**,[12] and **8**[23] were prepared according to literature procedures. Pre-treatment of *m*CPBA was performed according to ref.[11] Reactions were monitored by TLC. Products were purified by column chromatography on silica gel (32–63 μm). Unless otherwise stated, yields refer to chromatographically homogeneous and spectroscopically pure materials (^{1}H NMR spectroscopy). NMR spectra were recorded with JEOL (ECX 400, Eclipse 500) instruments. Chemical shifts are reported relative to TMS (^{1}H: δ = 0.00) and $CDCl_3$ (^{13}C: δ = 77.0). Integrals are in accordance with assignments. ^{13}C NMR spectra are ^{1}H-decoupled; signals marked with * correspond to 2 C atoms. MS and HRMS analyses were performed with a Varian Ionspec QFT-7 instrument (ESI-FT ICRMS). IR spectra were measured with a spectrophotometer 5 SXC Nicolet or a Nicolet Smart DuraSamplIR ATR spectrophotometer. Elemental analyses were carried out with a Vario EL Elemental Analyzer. Melting points were measured with a

Reichert apparatus (Thermovar) and are uncorrected. Optical rotations ($[\alpha]_D$) were determined with Perkin–Elmer 141 or Perkin–Elmer 241 polarimeter at the temperatures given.

1,2-Diketone Derivatives 5 and 7; General Procedure 1 (GP1)

The α-hydroxy-substituted methoxyallene **4** (or **6**) was dissolved in CH_2Cl_2 and cooled to 0 °C. After addition of *m*CPBA (1–1.5 equiv, used after pre-treatment, see above) the suspension was stirred for the required time (2–5 h). The mixture was quenched by addition of H_2O (1 mL/mmol of substrate) and extracted with CH_2Cl_2 (3 × 5 mL/mmol of substrate). The combined organic extracts were dried (Na_2SO_4) and concentrated. The residue was purified by column chromatography (silica gel, hexanes/EtOAc) to afford **5** (or **7**).

1-Methoxy-2-oxopropyl 3-Chlorobenzoate (2)

According to GP1, a solution of methoxyallene (**1**, 3.50 g, 50.0 mmol) and *m*CPBA (18.5 g, 75.0 mmol; commercially available *m*CPBA) dissolved in CH_2Cl_2 (100 mL) was stirred for 3 h at 0 °C. Work-up and column chromatography (hexanes/EtOAc 4:1) afforded **2** (5.60 g, 46%) as a colorless oil.

IR (neat): 3075–2845 (=C–H, C–H), 1735 (C=O), 1260 cm^{-1} (C–Cl).

^1H NMR ($CDCl_3$, 500 MHz): δ = 2.30 (s, 3 H, Me), 3.60 (s, 3 H, OMe), 5.97 (s, 1 H, CH), 7.38–7.43, 7.55–7.58, 7.92–7.97, 8.02–8.08 (4 m, 1 H each, Ar).

^{13}C NMR ($CDCl_3$, 125.8 MHz): δ = 25.2 (q, Me), 57.7 (q, OMe), 98.2 (d, CH), 128.0, 129.8*, 129.86, 129.89, 134.7 (2 d, 2 s, d, Ar), 164.5 (s, *C*O_2Ar), 199.6 (s, C=O).

Anal. Calcd for $C_{11}H_{11}ClO_4$ (242.7): C, 54.45, H 4.57. Found: C, 54.24; H, 4.12.

1-Cyclohexyl-2,3-dioxobutyl 3-Chlorobenzoate (5a)

According to GP1, a solution of methoxyallene derivative **4a** (0.710 g, 3.90 mmol) and *m*CPBA (1.44 g, 5.85 mmol) dissolved in CH_2Cl_2 (20 mL) was stirred for 3 h at 0 °C. Work-up and column chromatography (hexanes/EtOAc 4:1) afforded **5a** (0.638 g, 51%) as a yellow solid; mp 57–60 °C.

IR (KBr): 3070–2850 (=C–H, C–H), 1715, 1700 (C=O), 1250 cm^{-1} (C–Cl).

^1H NMR ($CDCl_3$, 250 MHz): δ = 1.10–2.10 (m, 11 H, CH, 5 CH_2), 2.40 (s, 3 H, Me), 5.57 (d, *J* = 5.9 Hz, 1 H, CH), 7.37–7.45, 7.54–7.60, 7.90–8.12 (3 m, 1 H, 1 H, 2 H, Ar).

^{13}C NMR ($CDCl_3$, 125.8 MHz): δ = 23.8 (q, Me), 25.7, 25.8, 25.9, 28.1, 28.2 (5 t, 5 CH_2), 39.0 (d, CH), 77.9 (d, CH), 127.9, 129.7, 129.8, 133.5, 134.6 (2 d, s, d, s, Ar), 165.2 (s, *C*O_2Ar), 194.2, 196.4 (2 s, C=O).

HRMS (80 eV): *m*/*z* $[M + Na]^+$ calcd for $C_{17}H_{19}ClNaO_4$: 345.0864; found: 345.0871.

UV-Vis ($CHCl_3$): λ (log ε) = 285 (3.2), 428 nm (1.7).

Anal. Calcd for $C_{17}H_{19}ClO_4$ (322.8): C, 63.26; H, 5.93. Found: C, 63.20; H, 5.95.

2,3-Dioxopentadecan-4-yl 3-Chlorobenzoate (5b)

According to GP1, a solution of methoxyallene derivative **4b** (1.21 g, 4.75 mmol) and *m*CPBA (1.75 g, 7.12 mmol) dissolved in CH_2Cl_2 (20 mL) was stirred for 3 h at 0 °C. Work-up and column chromatography (hexanes/EtOAc 4:1) afforded **5b** (1.99 g, 57%) as a yellow oil.

IR (neat): 3070–2880 (=C–H, C–H), 1710 (C=O), 1245 cm^{-1} (C–Cl).

^1H NMR ($CDCl_3$, 400 MHz): δ = 0.88 (t, *J* = 6.4 Hz, 3 H, Me), 1.15–1.60 (m, 18 H, 9 CH_2), 1.79–1.93 (m, 2 H, CH_2), 2.41 (s, 3 H, Me), 5.70 (dd, *J* = 5, 7.5 Hz, 1 H, CH), 7.49 (dd, *J* = 7.3, 8.2 Hz, 1 H, Ar), 7.57 (d, *J* = 8.2 Hz, 1 H, Ar), 7.94 (d, *J* = 7.3 Hz, 1 H, Ar), 8.02 (s, 1 H, Ar).

^{13}C NMR ($CDCl_3$, 125.8 MHz): δ = 14.1 (q, Me), 22.7 (t, CH_2), 24.3 (q, Me), 25.5, 29.3, 29.35, 29.43, 29.48, 29.57*, 30.1, 31.9 (9 t, 10 CH_2), 75.5 (d, CH), 128.0, 129.8, 129.85 (3 d, Ar), 130.5 (s, Ar), 133.5 (d, Ar), 134.7 (s, Ar), 165.1 (s, *C*O_2Ar), 193.9, 196.6 (2 s, C=O).

Anal. Calcd for $C_{22}H_{31}ClO_4$ (394.9): C, 66.91; H, 7.91. Found: C, 67.43; H, 8.45.

2,3-Dioxo-1-phenylbutyl 3-Chlorobenzoate (5c)

According to GP1, a solution of methoxyallene derivative **4c** (1.95 g, 11.0 mmol) and *m*CPBA (4.07 g, 16.5 mmol) dissolved in CH_2Cl_2 (30 mL) was stirred for 3 h at 0 °C. Work-up and column chromatography (hexanes/EtOAc 6:1) afforded **5c** (1.63 g, 47%) as a yellow oil.

IR (neat): 3070–2875 (=C–H, C–H), 1715 (C=O), 1245 cm^{-1} (C–Cl).

^1H NMR ($CDCl_3$, 250 MHz): δ = 2.33 (s, 3 H, Me), 6.89 (s, 1 H, CH), 7.37–7.46, 7.52–7.62 (2 m, 3 H, 2 H, Ph, Ar), 7.56 (m_c, 2 H, Ar), 7.97 (m_c, 1 H, Ar), 8.05 (s, 1 H, Ar).

^{13}C NMR ($CDCl_3$, 125.8 MHz): δ = 24.1 (q, Me), 77.3 (d, CH), 128.3, 128.9, 129.4, 130.06, 130.1, 130.15 (6 d, Ph, Ar), 130.8, 131.3 (2 s, Ph, Ar), 133.8 (d, Ar), 134.8 (s, Ar), 165.1 (s, *C*O_2Ar), 190.4, 196.0 (2 s, C=O).

HRMS (80 eV): *m*/*z* $[M + H]^+$ calcd for $C_{17}H_{14}ClO_4$: 317.0581; found: 317.0588.

1-(Benzyloxy)-3,4-dioxopentan-2-yl 3-Chlorobenzoate (5d)

According to GP1, a solution of methoxyallene derivative **4d** (0.706 g, 3.21 mmol) and *m*CPBA (0.790 g, 3.21 mmol) dissolved in CH_2Cl_2 (30 mL) was stirred for 3 h at 0 °C. Work-up and column chromatography (hexanes/EtOAc 4:1) afforded **5d** (0.370 g, 32%) as a yellow oil.

IR (neat): 3070–2870 (=C–H, C–H), 1720, 1700 (C=O), 1260 cm^{-1} (C–Cl).

^1H NMR ($CDCl_3$, 250 MHz): δ = 2.35 (s, 3 H, Me), 3.91 (dd, *J* = 3.5, 11.2 Hz, 1 H, CH_2O), 4.20 (dd, *J* = 5.2, 11.2 Hz, 1 H, CH_2O), 4.52, 4.59 (AB system, J_{AB} = 12.0 Hz, 1 H each, CH_2O), 6.07 (dd, *J* = 3.5, 5.2 Hz, 1 H, CHO), 7.22–7.43, 7.52–7.58 (2 m, 6 H, 1 H, Ar, Ph), 7.95 (br d, *J* ~ 6 Hz, 1 H, Ar), 8.05 (t, *J* = 1.7 Hz, 1 H, Ar).

^{13}C NMR ($CDCl_3$, 100.8 MHz): δ = 23.9 (q, Me), 68.4, 73.5 (2 t, 2 CH_2), 75.4 (d, CH), 127.8, 128.1, 128.2, 128.6, 129.9, 130.1, 130.6, 133.5, 134.6, 136.9 (7 d, 3 s, Ar, Ph), 164.9 (s, *C*O_2Ar), 191.3, 196.3 (2 s, C=O).

HRMS (ESI): *m*/*z* $[M + H]^+$ calcd for $C_{19}H_{18}ClO_5$: 361.0843; found: 361.0851.

(2*S*)-2-(*tert*-Butyldimethylsiloxy)-4,5-dioxohexan-3-yl 3-Chlorobenzoate (5e)

According to GP1, a solution of methoxyallene derivative **4e** (0.491 g, 1.90 mmol; *anti*/*syn* 83:17) and *m*CPBA (0.703 g, 2.85 mmol) dissolved in CH_2Cl_2 (20 mL) was stirred for 3 h at 0 °C. Work-up and column chromatography (hexanes/EtOAc 6:1) afforded **5e** (0.318 g, 43%, two diastereomers = 90:10) as a yellow solid; mp 159 °C.

IR (neat): 3060–2855 (=C–H, C–H), 1725, 1710 cm^{-1} (C=O).

^1H NMR ($CDCl_3$, 400 MHz): δ = 0.03, 0.09 (2 s, 3 H each, $OSiMe_2$), 0.83 (s, 9 H, Si*t*Bu), 1.38 (d, *J* = 6.4 Hz, 3 H, Me), 2.38 (s, 3 H, Me), 4.37 (m_c, 1 H, 2-H), 5.72 (d, *J* = 6.1 Hz, 1 H, 3-H), 7.40 (dd, *J* = 7.6, 8.3 Hz, 1 H, Ar), 7.52–7.58, 7.88–7.94 (2 m, 1 H each, Ar), 7.99 (t, *J* = 1.9 Hz, 1 H, Ar).

^{13}C NMR ($CDCl_3$, 100.8 MHz): δ = –5.1, –4.5 (2 q, $SiMe_2$), 17.9 (s, C–Si), 21.2, 23.7 (2 q, 2 Me), 25.7 (q, Si*t*Bu), 69.1, 77.1 (2 d, C-2, C-3), 128.0, 129.8, 129.9, 130.5, 133.5, 134.5 (3 d, s, d, s, Ar), 164.8 (s, CO_2Ar), 193.7, 195.4 (2 s, C=O).

The following NMR signals could be assigned to the minor diastereomer:

^{1}H NMR ($CDCl_3$, 400 MHz): δ = 0.05, 0.11 (2 s, 3 H each, $OSiMe_2$), 0.85 (s, 9 H, Si*t*Bu), 1.28 (d, *J* = 6.4 Hz, 3 H, Me), 2.37 (s, 3 H, Me), 4.49–4.60 (m, 1 H, 2-H), 5.90 (d, *J* = 4.8 Hz, 1 H, 3-H), 8.02 (m_c, 1 H, Ar).

^{13}C NMR ($CDCl_3$, 100.8 MHz): δ = 68.0, 77.4 (2 d, C-2, C-3).

HRMS (ESI): *m*/*z* [M + H]$^+$ calcd for $C_{19}H_{28}ClO_5Si$: 399.1394; found: 399.1393.

2-Methyl-3,4-dioxopentan-2-yl 3-Chlorobenzoate (7a)

According to GP1, a solution of methoxyallene derivative **6a** (1.20 g, 10.7 mmol) and *m*CPBA (3.05 g, 12.4 mmol) dissolved in CH_2Cl_2 (25 mL) was stirred for 3 h at 0 °C. Work-up and column chromatography (hexanes/EtOAc 6:1) afforded **7a** (1.00 g, 35%) as a yellow oil.

IR (neat): 3075–2945 (=C–H, C–H), 1715, 1700 (C=O), 1265 cm^{-1} (C–Cl).

^{1}H NMR ($CDCl_3$, 500 MHz): δ = 1.72 (s, 6 H, 2 Me), 2.36 (s, 3 H, Me), 7.36–7.43, 7.54–7.60, 7.87–7.94, 7.98–8.03 (4 m, 1 H each, Ar).

^{13}C NMR ($CDCl_3$, 125.8 MHz): δ = 24.2, 24.3 (2 q, Me), 30.7 (q, Me), 83.0 (s, CO), 127.8, 129.7*, 130.1, 133.8, 134.4 (2 d, 2 s, d, Ar), 166.0 (s, CO_2Ar), 196.7, 197.0 (2 s, C=O).

Anal. Calcd for $C_{13}H_{13}ClO_4$ (268.7): C, 58.11; H, 4.88. Found: C, 57.75; H, 4.74.

1,1,1-Trifluoro-2-methyl-3,4-dioxopentan-2-yl 3-Chlorobenzoate (7b)

According to GP1, a solution of methoxyallene derivative **6b** (1.00 g, 5.50 mmol) and *m*CPBA (2.03 g, 8.25 mmol) dissolved in CH_2Cl_2 (25 mL) was stirred for 3 h at 0 °C. Work-up and column chromatography (hexanes/EtOAc 4:1) afforded **7b** (0.673 g, 47%) as a yellow wax.

IR (ATR): 3075–2885 (=C–H, C–H), 1720, 1700 (C=O), 1260 cm^{-1} (C–Cl).

^{1}H NMR ($CDCl_3$, 400 MHz): δ = 1.93 (s, 3 H, Me), 2.38 (s, 3 H, Me), 7.41 (dd, *J* = 9.6, 6.3 Hz, 1 H, Ar), 7.60 (ddd, *J* = 8.0, 2.0, 1.0 Hz, 1 H, Ar), 7.88 – 7.92 (m, 1 H, Ar), 7.96 – 8.00 (m, 1 H, Ar).

^{13}C NMR ($CDCl_3$, 100.8 MHz): δ = 17.7, 24.3 (2 q, 2 Me), 82.3 (q, $^2J_{CF}$ = 29.1 Hz, C–O), 122.2 (q, $^1J_{CF}$ = 285 Hz, CF_3), 128.3, 129.3, 130.0, 130.1, 134.5, 134.9 (d, s, 3 d, s, Ar), 165.1 (s, CO_2Ar), 188.4, 193.9 (2 s, C=O).

Anal. Calcd for $C_{13}H_{10}ClF_3O_4$ (322.7): C, 48.39; H, 3.12. Found: C, 48.45; H, 2.98.

1-(*tert*-Butyldimethylsiloxy)-2-methoxy-3-oxo-1-phenylbutan-2-yl 3-Chlorobenzoate (9)

According to GP1, a solution of methoxyallene derivative **8** (3.20 g, 11.0 mmol) and *m*CPBA (4.06 g, 16.5 mmol) dissolved in CH_2Cl_2 (30 mL) was stirred for 3 h at 0 °C. Work-up and column chromatography (hexanes/EtOAc 6:1) afforded **9** (2.79 g, 55%; two diastereomers = 57:43) as a colorless oil.

IR (neat): 3070–2845 (=C–H, C–H), 1720, 1700 cm^{-1} (C=O).

^{1}H NMR ($CDCl_3$, 250 MHz): δ = –0.24 (s, 1.7 H, $SiMe_2$), –0.17 (s, 1.3 H, $SiMe_2$), –0.01 (s, 1.7 H, $SiMe_2$), 0.19 (s, 1.3 H, $SiMe_2$), 0.88 (s, 5.1 H, Si*t*Bu), 0.94 (s, 3.9 H, Si*t*Bu), 1.92 (s, 1.3 H, Me), 2.48 (s, 1.7 H, Me), 2.97 (s, 1.7 H, OMe), 3.76 (s, 1.3 H, OMe), 5.166 (s, 0.45 H, CH), 5.174 (s, 0.55 H, CH), 7.30–7.44, 7.52–7.64, 7.84–7.94, 7.97, 8.05 (3 m, 2 m_c, 9 H, Ph).

^{13}C NMR ($CDCl_3$, 125.8 MHz): δ = –7.2, –6.8, –6.3 (3 q, $SiMe_2$), 16.4, 25.2 (s, q, Si*t*Bu), 26.0, 26.6 (2 q, Me), 51.4, 51.5 (2 q, OMe), 75.3, 77.8 (2 d, CH), 100.7, 101.0 (2 s, COO), 126.1, 126.3, 126.34, 126.8, 126.9, 128.2 (6 d, Ph, Ar), 130.7, 131.0 (2 s, Ph, Ar), 133.6, 133.9 (2 d, Ar), 135.3, 135.9 (2 s, Ar), 161.5, 161.53 (2 s, CO_2Ar), 203.5, 204.1 (2 s, C=O).

HRMS (80 eV): *m*/*z* [M + Na]$^+$ calcd for $C_{24}H_{31}ClNaO_5Si$: 485.1527; found: 485.1525.

Anal. Calcd for $C_{24}H_{31}ClO_5Si$ (463.0): C, 62.25; H, 6.75. Found: C, 62.91; H, 7.02.

2,3-Dioxopentadecan-4-yl Acetate (10)

A solution of methoxyallene derivative **4b** (1.14 g, 4.48 mmol) in CH_2Cl_2 (25 mL) was cooled to –78 °C. After the addition of 35% aq peracetic acid solution (1.50 mL, 6.72 mmol), the mixture was stirred for 3 h at this temperature. Water (5 mL) was added, the aqueous phase was extracted with CH_2Cl_2 (2 × 10 mL), and the combined organic phases were dried (Na_2SO_4). After removal of the solvent, the residue was purified by column chromatography (hexanes/EtOAc 6:1) to yield **10** (0.508 g, 38%) as a yellow oil.

IR (ATR): 2930–2855 (=C–H, C–H), 1745, 1725, 1715 (C=O), 1235 cm^{-1} (C–Cl).

^{1}H NMR ($CDCl_3$, 250 MHz): δ = 0.88 (t, *J* = 7.0 Hz, 3 H, Me), 1.09–1.44, 1.56–1.85 (2 m, 18 H, 2 H, 10 CH_2), 2.11, 2.36 (2 s, 3 H each, Me), 5.43 (dd, *J* = 4.5, 8.3 Hz, 1 H, CH).

^{13}C NMR ($CDCl_3$, 100.8 MHz): δ = 14.1 (q, Me), 20.3 (t, CH_2), 22.6, 24.0 (2 q, 2 Me), 25.3, 29.1, 29.3, 29.5, 29.6*, 30.1, 31.9* (7 t, CH_2), 74.3 (d, CH), 170.9 (s, CO_2Ar), 194.4, 196.7 (2 s, C=O).

HRMS (80 eV): *m*/*z* [M + K]$^+$ calcd for $C_{17}H_{30}KO_4$: 337.1784; found: 337.1806.

UV-Vis ($CHCl_3$): λ (log ε) = 281 (0.7), 427 nm (1.9).

Quinoxaline Derivatives 12; General Procedure 2 (GP2)

A mixture of 1,2-diketone **5** (or **7**) (1 equiv), *o*-phenylenediamine (**11**, 1.25–2 equiv), and CAN (0.05–0.15 equiv) in water (3–10 mL/mmol of substrate) was vigorously stirred at room temperature for the time indicated. The mixture was then diluted with EtOAc (10–30 mL/mmol of substrate) and washed with water (3 × 10 mL/mmol of substrate). The organic layer was dried (Na_2SO_4) and filtered, and the filtrate was evaporated under reduced pressure. The residue was purified by flash chromatography (hexanes/EtOAc).

Cyclohexyl(3-methylquinoxalin-2-yl)methyl 3-Chlorobenzoate (12a)

According to GP2, a mixture of 1,2-diketone derivative **5a** (0.118 g, 0.365 mmol), diamine **11** (0.050 g, 0.460 mmol), and CAN (0.010 g, 0.018 mmol) dissolved in water (1 mL) was stirred for 30 min at room temperature. Work-up and column chromatography (hexanes/EtOAc 4:1) afforded **12a** (0.103 g, 71%) as a viscous orange oil.

IR (neat): 3065–2850 (=C–H, C–H), 1720 cm^{-1} (C=O).

^{1}H NMR ($CDCl_3$, 250 MHz): δ = 1.15–1.35, 1.65–1.90 (2 m, 11 H, CH, CH_2), 2.97 (s, 3 H, Me), 5.96 (d, *J* = 8.9 Hz, 1 H, CH), 7.34–7.40, 7.50–7.55, 7.65–7.70, 7.93–8.08 (4 m, 1 H, 1 H, 3 H, 3 H, Ar).

^{13}C NMR ($CDCl_3$, 100.8 MHz): δ = 22.8 (q, Me), 25.6, 25.8, 26.2, 28.8, 29.4 (5 t, 5 CH_2), 41.9 (d, CH), 78.3 (d, CH), 127.9, 128.4, 129.0, 129.1, 129.7, 129.8, 129.9 (7 d, Ar), 131.6 (s, Ar), 133.1 (d, Ar), 134.5 (s, Ar), 141.0, 141.3 (2 s, Ar), 152.8, 153.5 (2 s, C=N), 165.2 (s, CO_2Ar).

HRMS (80 eV): *m*/*z* [M + Na]$^+$ calcd for $C_{23}H_{23}ClN_2NaO_2$: 417.1340; found: 417.1351.

1-(3-Methylquinoxalin-2-yl)dodecyl 3-Chlorobenzoate (12b)

According to GP2, a mixture of 1,2-diketone derivative **5b** (0.464 g, 1.17 mmol), diamine **11** (0.136 g, 1.26 mmol), and CAN (0.053 g, 0.10 mmol) dissolved in water (10 mL) was stirred for 30 min at room temperature. Work-up and column chromatography (hexanes/EtOAc 8:1) afforded **12b** (0.391 g, 72%) as a colorless oil.

IR (neat): 3090–2850 (=C–H, C–H), 1720 cm^{-1} (C=O).

^{1}H NMR ($CDCl_3$, 250 MHz): δ = 0.86 (t, *J* = 7.1 Hz, 3 H, Me), 1.15–1.65 (m, 18 H, CH_2), 2.09–2.18, 2.22–2.30 (2 m, 1 H each, CH_2), 2.90 (s, 3 H, Me), 6.26 (dd, *J* = 5.5, 8.3 Hz, 1 H, CH), 7.37 (t, *J* = 7.9 Hz, 1 H, Ar), 7.51–7.53, 7.63–7.71, 7.96–8.04 (3 m, 1 H, 2 H, 3 H, Ar), 7.68 (t, *J* = 1.9 Hz, 1 H, Ar).

^{13}C NMR ($CDCl_3$, 125.8 MHz): δ = 14.1 (q, Me), 22.5 (q, Me), 22.6 (t, CH_2), 25.7, 29.3, 29.32, 29.36, 29.47, 29.54, 29.55, 29.56, 31.8, 33.5 (10 t, 10 CH_2), 74.6 (d, CH), 127.9, 128.3, 129.0, 129.1, 129.7, 129.72, 129.8 (6 d, Ar), 131.6 (s, Ar), 133.1 (d, Ar), 134.5 (s, Ar), 140.9, 141.5 (2 s, Ar), 152.0, 153.3 (2 s, C=N), 165.1 (s, *C*O_2Ar).

HRMS (80 eV): *m*/*z* [M + Na]$^+$ calcd for $C_{28}H_{35}ClN_2NaO_2$: 489.2279; found: 489.2290.

Anal. Calcd for $C_{28}H_{35}ClN_2O_2$ (467.0): C, 72.01; H, 7.55; N, 6.00. Found: C, 72.39; H, 7.86; N, 5.95.

(3-Methylquinoxalin-2-yl)(phenyl)methyl 3-Chlorobenzoate (12c)

According to GP2, a mixture of 1,2-diketone derivative **5c** (0.160 g, 0.505 mmol), diamine **11** (0.068 g, 0.628 mmol), and CAN (0.014 g, 0.027 mmol) dissolved in water (3 mL) was stirred for 30 min at room temperature. Work-up and column chromatography (hexanes/EtOAc 4:1) afforded **12c** (0.134 g, 68%) as a colorless oil.

IR (neat): 3090–2850 (=C–H, C–H), 1725 cm^{-1} (C=O).

^{1}H NMR ($CDCl_3$, 400 MHz): δ = 2.77 (s, 3 H, Me), 7.30 (s, 1 H, CH), 7.35–7.45, 7.49–7.58, 7.63–7.76, 7.95–8.11 (4 m, 4 H, 3 H, 2 H, 3 H, Ph, Ar), 8.14 (dd, *J* = 1.3, 1.9 Hz, 1 H, Ar).

^{13}C NMR ($CDCl_3$, 100.8 MHz): δ = 22.7 (q, Me), 77.3 (d, CH), 128.0, 128.2, 128.3, 128.8, 128.9, 129.2, 129.4, 129.7, 129.9, 129.94 (10 d, Ph, Ar), 131.5 (s, Ph), 133.0 (d, Ar), 135.0, 136.5, 141.0, 141.5 (4 s, Ar), 151.9, 152.1 (2 s, C=N), 164.8 (s, *C*O_2Ar).

HRMS (80 eV): *m*/*z* [M + H]$^+$ calcd for $C_{23}H_{17}ClN_2O_2$: 389.1051; found: 389.1057.

Anal. Calcd for $C_{23}H_{16}ClN_2O_2$ (387.9): C, 71.04; H, 4.41; N, 7.20. Found: C, 70.65; H, 4.69; N, 7.08.

1,1,1-Trifluoro-2-(3-methylquinoxalin-2-yl)propan-2-yl 3-Chlorobenzoate (12d)

According to GP2, a mixture of 1,2-diketone derivative **7b** (0.226 g, 0.570 mmol), diamine **11** (0.123 g, 1.18 mmol), and CAN (0.021 g, 0.052 mmol) dissolved in water (3 mL) was stirred for 30 min at room temperature. Work-up and column chromatography (hexanes/EtOAc 4:1) afforded **12d** (0.134 g, 60%) as a colorless oil.

IR (ATR): 3070–2890 (=C–H, C–H), 1735 (C=O), 1195 cm^{-1} (C–F).

^{1}H NMR ($CDCl_3$, 500 MHz,): δ = 2.39 (d, *J* = 0.9 Hz, 3 H, Me), 2.73 (s, 3 H, Me), 7.44 (t, *J* = 7.9 Hz, 1 H, Ar), 7.61 (ddd, *J* = 1.1, 2.1, 8.0 Hz, 1 H, Ar), 7.70–7.78 (m, 2 H, Ar), 7.97–8.02 (m, 2 H, Ar), 8.06 (t, *J* = 1.9 Hz, 1 H, Ar), 8.08–8.11 (m, 1 H, Ar).

^{13}C NMR ($CDCl_3$, 125.8 MHz): δ = 20.0 (q, C-9), 24.2 (qq, $^3J_{CF}$ = 3.0 Hz, C-11), 85.1 (q, $^2J_{CF}$ = 29.2 Hz, C-10), 124.6 (q, $^1J_{CF}$ = 284.9 Hz, C-12), 128.2, 128.3, 129.5, 130.1, 130.3, 130.7, 130.9 (7 d, C-1–C-4, C-15–C-17), 134.0 (d, C-19), 134.2, 135.1 (2 s, C-14, C-18), 139.8, 141.3 (2 s, C-5, C-6), 148.3, 151.9 (2 s, C-7, C-8), 162.9 (s, C-13).

HRMS (ESI): *m*/*z* [M + H]$^+$ calcd for $C_{19}H_{15}ClF_3N_2O_2$: 395.0696; found: 395.0771.

(2*S*)-2-(*tert*-Butyldimethylsiloxy)-1-(3-methylquinoxalin-2-yl)propyl 3-Chlorobenzoate (12e)

According to GP2, a mixture of 1,2-diketone derivative **5e** (0.087 g, 0.220 mmol), diamine **11** (0.030 g, 0.280 mmol), and CAN (0.008 g, 0.015 mmol) dissolved in water (1 mL) was stirred for 30 min at room temperature. Work-up and column chromatography (hexanes/EtOAc 4:1) afforded **12e** (0.073 g, 71%; two diastereomers = 88:12) as a viscous orange oil.

Major diastereomer

$[\alpha]_D^{22}$ +104.2 (*c* 0.5, $CHCl_3$).

IR (ATR): 3065–2855 (=C–H, C–H), 1725 cm^{-1} (C=O).

^{1}H NMR ($CDCl_3$, 400 MHz): δ = –0.72, –0.09 (2 s, 3 H each, $OSiMe_2$), 0.61 (s, 9 H, Si*t*Bu), 1.51 (d, *J* = 6.4 Hz, 3 H, Me), 3.02 (s, 3 H, Me), 4.65 (m_c, 1 H, 2-H), 5.92 (d, *J* = 9.5 Hz, 1 H, 1-H), 7.40 (dd, *J* = 7.6, 8.3 Hz, 1 H, Ar), 7.51 (td, *J* = 1.3, 8.3 Hz, 1 H, Ar), 7.60–7.74 (m, 2 H, Ar), 7.93 (d, *J* = 7.6 Hz, 1 H, Ar), 7.96–8.10 (m, 3 H, Ar).

^{13}C NMR ($CDCl_3$, 100.8 MHz): δ = –5.7, –4.9 (2 q, $SiMe_2$), 17.5 (s, C–Si), 21.7, 22.9 (2 q, 2 Me), 25.7 (q, Si*t*Bu), 71.0, 76.6 (2 d, C-1, C-2), 127.9, 128.4, 128.8, 129.0, 129.7, 129.8, 129.9 (7 d, Ar), 131.3 (s, Ar), 133.2 (d, Ar), 134.6 (s, Ar), 141.0, 141.3 (2 s, Ar), 153.9, 154.1 (2 s, C=N), 164.8 (s, *C*O_2Ar).

HRMS (80 eV): *m*/*z* [M + H]$^+$ calcd for $C_{25}H_{32}ClN_2O_3Si$: 471.1865; found: 471.1878.

Minor diastereomer

$[\alpha]_D^{22}$ +42.8 (*c* 0.22, $CHCl_3$).

^{1}H NMR ($CDCl_3$, 400 MHz): δ = 0.01, 0.12 (2 s, 3 H each, $OSiMe_2$), 0.83 (s, 9 H, Si*t*Bu), 1.11 (d, *J* = 6.3 Hz, 3 H, Me), 2.97 (s, 3 H, Me), 4.72 (qd, *J* = 6.3, 7.6 Hz, 1 H, 2-H), 6.19 (d, *J* = 7.6 Hz, 1 H, 1-H), 7.36 (t, *J* = 7.9 Hz, 1 H, Ar), 7.51 (ddd, *J* = 8.0, 2.1, 1.1 Hz, 1 H, Ar), 7.64–7.73 (m, 2 H, Ar), 7.94–8.00 (m, 2 H, Ar), 8.03–8.08 (m, 2 H, Ar).

The following ^{13}C NMR signals could be assigned ($CDCl_3$, 100.8 MHz): δ = –4.7, –4.5 (2 q, $SiMe_2$), 25.78 (q, Si*t*Bu), 70.0, 78.2 (2 d, C-1, C-2).

HRMS (80 eV): *m*/*z* [M + H]$^+$ calcd for $C_{25}H_{32}ClN_2O_3Si$: 471.1865; found: 471.1876.

(2*S*)-1-Hydroxy-(3-methylquinoxalin-2-yl)propan-2-yl 3-Chlorobenzoate (13)

To a solution of **12e** (0.68 g, 0.145 mmol; two diastereomers = 88:12) in THF (1 mL) was added 1 M TBAF in THF (0.29 mL, 0.29 mmol). The mixture was stirred for 1 h at room temperature. Then, the mixture was filtered through a pad of silica gel (hexanes/EtOAc 1:1) and concentrated under reduced pressure. The crude product was purified by column chromatography (hexanes/EtOAc 2:1) to yield **13** (0.026 g, 51%, two diastereomers = 93:7) as a yellow oil.

^{1}H NMR ($CDCl_3$, 400 MHz): δ = 1.28 (d, *J* = 6.4 Hz, 3 H, Me), 2.94 (s, 3 H, Me), 4.74 (s, 1 H, OH), 5.39–5.42 (m, 1 H, 1-H), 5.46 (dq, *J* = 3.2, 6.4 Hz, 1 H, 2-H), 7.39 (t, *J* = 7.9 Hz, 1 H, Ar), 7.54 (ddd, *J* = 0.9, 2.0, 8.0 Hz, 1 H, Ar), 7.71–7.79, 7.95–7.98, 8.02–8.09 (3 m, 2 H, 1 H, 3 H, Ar).

The following ^{1}H NMR signals could be assigned to the minor diastereomer ($CDCl_3$, 400 MHz): δ = 1.62 (d, *J* = 6.4 Hz, 3 H, Me), 2.82 (s, 3 H, Me), 5.14 (d, *J* = 2.5 Hz, 1 H, 1-H).

(1*R*,2*S*)-1-(3-Methylquinoxalin-2-yl)-1-(4-nitrobenzoyloxy)propan-2-yl 3-Chlorobenzoate (14)

Quinoxaline derivative **13** (0.026 g, 0.073 mmol, two diastereomers = 93:7), *p*-nitrobenzoyl chloride (0.015 g, 0.078 mmol), and DMAP (0.007 g, 0.055 mmol) were dissolved in CH_2Cl_2 (1 mL). After addition of Et_3N (0.008 g, 0.080 mmol) the mixture was stirred under an argon atmosphere at room temperature for 16 h. Then, water (2 mL) and CH_2Cl_2 (3 mL) were added to the mixture and the aqueous phase was extracted with CH_2Cl_2 (3 × 5 mL). The combined organic layers were dried (Na_2SO_4) and filtered, and the filtrate was evaporated under reduced pressure. The residue was purified by column chromatography (neutral alumina, hexanes/EtOAc 1:1) to give diester **14** (0.017 g, 47%, two diastereomers = 95:5) as a pale yellow solid.

Another reaction starting from configurationally pure major isomer of precursor **12e** (0.072 g, 0.153 mmol) gave after desilylation and esterification as described above the pure major diastereomer of **14** (0.008 g, 12% yield after two steps) as a pale yellow solid; mp 141 °C; $[\alpha]_D^{22}$ +5.0 (*c* 0.01, $CHCl_3$).

IR (ATR): 3075–2845 (=C–H, C–H), 1720 cm^{-1} (C=O).

^{1}H NMR ($CDCl_3$, 700 MHz): δ = 1.71 (d, *J* = 6.5 Hz, 3 H, Me), 3.05 (s, 3 H, Me), 5.92 (dq, *J* = 5.2, 6.5 Hz, 1 H, 2-H), 6.61 (d, *J* = 5.1 Hz, 1 H, 1-H), 7.37 (t, *J* = 7.8 Hz, 1 H, Ar), 7.54 (ddd, *J* = 1.1, 2.2, 8.0 Hz, 1 H, Ar), 7.70 (ddd, *J* = 1.4, 6.9, 8.2 Hz, 1 H, Ar), 7.75 (ddd, *J* = 1.4, 6.9, 8.4 Hz, 1 H, Ar), 7.85 (ddd, *J* = 1.1, 1.5, 7.8 Hz, 1 H, Ar), 7.95–7.96 (m, 1 H, Ar), 8.02–8.04 (m, 2 H, Ar), 8.31–8.36 (m, 4 H, Ar).

^{13}C NMR ($CDCl_3$, 176.0 MHz): δ = 15.6, 22.5 (2 q, 2 Me), 71.8, 75.1 (2 d, C-1, C-2), 123.7, 127.7, 128.5, 129.29, 129.32, 129.75, 129.79, 130.5, 131.1, 131.5 (10 d, Ar), 133.3, 134.7, 134.9 (3 s, Ar), 140.8, 141.7, 149.9 (3 s, Ar), 150.9, 152.4 (2 s, C=N), 164.1, 164.4 (2 s, *C*O$_2$Ar).

The following ^{1}H NMR signals could be assigned to the minor diastereomer ($CDCl_3$, 700 MHz): δ = 1.43 (d, *J* = 6.5 Hz, 3 H, Me), 3.03 (s, 3 H, Me), 6.30 (m$_c$, 1 H, 2-H), 7.52 (ddd, *J* = 1.1, 2.2, 8.0 Hz, 1 H, Ar), 7.77–7.80 (m, 1 H, Ar), 7.99–8.00 (m, 1 H, Ar), 8.18–8.24 (m, 2 H, Ar), 8.21–8.24 (m, 2 H, Ar).

HRMS (ESI): *m*/*z* [M + H]$^+$ calcd for $C_{26}H_{21}ClN_3O_6$: 506.1113; found: 506.1146; *m*/*z* [M + Na]$^+$ calcd for $C_{26}H_{20}ClN_3NaO_6$: 528.0933; found: 528.0962.

Crystal Data

$C_{26}H_{20}ClN_3O_6$, M_r = 505.90, triclinic, *P*1, *a* = 8.6386(13), *b* = 9.2367(14), *c* = 15.275(2) Å, α = 85.791(3)°, β = 74.646(4)°, γ = 85.096(3)°, V = 1169.4(3) Å^3, *Z* = 2, ρ_c = 1.437 g cm^{-3}, μ = 0.213 mm^{-1} Mo$_{K\alpha}$, λ = 0.71073 Å, *T* = 123 K, 15878 measured reflections, 9728 unique reflections, and 9033 observed reflections with $I > 2\sigma(I)$, R_{int} = 0.0211, The structure was solved by direct methods, a final refinement on F^2 with 653 parameters converged at $wR(F^2)$ = 0.0960, $R(F)$ = 0.0363, Flack parameter 0.05(3).[24] CCDC 1445384 (**14**) contains the supplementary crystallographic data for this paper. These data can be obtained free of charge from The Cambridge Crystallographic Data Centre via www.ccdc.cam.ac.uk/data_request/cif.

(*E*)-4-(Dodec-1-enyl)-5-methyl-2-phenyl-1*H*-imidazole (15)

1,2-Diketone **5b** (0.395 g, 1.00 mmol) and NH_4OAc (0.648 g, 8.40 mmol) were added to a solution of benzaldehyde (0.158 g, 1.50 mmol) in AcOH (1.2 mL) and the mixture was heated at 100 °C for 20 min. After cooling to room temperature, ice water (20 g) and concd NH_3 (reaching pH ~ 8–9) were added and the mixture was extracted with Et_2O (2 × 8 mL). The combined organic layers were dried (Na_2SO_4) and filtered, and the filtrate was evaporated under reduced pressure. The residue was purified by flash chromatography (hexanes/EtOAc 6:1) to afford imidazole derivative **15** (0.183 g, 57%) as a colorless oil.

IR (ATR): 3070–2950 (=C–H, C–H), 1600 cm^{-1} (C=C).

^{1}H NMR ($CDCl_3$, 500 MHz,): δ = 0.86 (t, *J* = 7.1 Hz, 3 H, Me), 1.05–1.50, 2.10–2.20 (2 m, 18 H, 2 H, 10 CH_2), 2.25 (s, 3 H, Me), 5.85–6.08 (m, 1 H, =CH), 6.25 (d, *J* = 16.0 Hz, 1 H, =CH), 7.23–7.37, 7.74–7.82 (2 m, 3 H, 2 H, Ph).

^{13}C NMR ($CDCl_3$, 125.8 MHz): δ = 11.5 (q, Me), 14.1, 16.5, 22.7, 24.7, 29.2, 29.3, 29.5, 29.6, 33.2 (9 t, 9 CH_2), 31.9 (q, Me), 118.1 (d, =CH), 125.1, 128.2, 128.6, 128.7, 130.2, 145.2 (4 d, 2 s, =CH, Ph, imidazole-C).

HRMS (ESI): *m*/*z* [M + H]$^+$ calcd for $C_{22}H_{33}N_2$: 325.2638; found: 325.2657.

Methyl 2-Amino-4-[2-(3-chlorobenzoyloxy)-2-cyclohexylacetyl]thiophene-3-carboxylate (17)

A mixture of 1,2-diketone derivative **5a** (0.200 g, 0.820 mmol), methyl cyanoacetate (**16**, 0.062 g, 0.620 mmol), sulfur (0.020 g, 0.620 mmol), and KF-Al_2O_3 (0.124 g) in EtOH (2 mL) was heated to 85 °C in a sealed tube for 2.5 h. The mixture was allowed to cool to room temperature and diluted with CH_2Cl_2 (10 mL). The resulting precipitate was removed by filtration and the solution was concentrated under reduced pressure. The residue was purified by column chromatography (hexanes/EtOAc 4:1) to give **17** (0.044 g, 16%) as a pale yellow oil.

IR (ATR): 3440–3250 (N–H), 3070–2850 (=C–H, C–H), 1740, 1710 cm^{-1} (C=O).

^{1}H NMR ($CDCl_3$, 250 MHz): δ = 0.80–1.40, 1.55–1.89, 1.95–2.15 (3 m, 5 H, 5 H, 1 H, CH, 5 CH_2), 3.78 (s, 3 H, OMe), 5.51 (d, *J* = 6.1 Hz, 1 H, CH), 6.10 (br s, 2 H, NH_2), 6.80 (s, 1 H, =CH), 7.37–7.44, 7.53–7.58, 7.92–7.96 (3 m, 1 H, 1 H, 2 H, Ar).

^{13}C NMR ($CDCl_3$, 100.8 MHz): δ = 26.0, 26.1, 26.2, 27.1, 30.1 (5 t, 5 CH_2), 39.6 (d, CH), 51.2 (q, OMe), 82.2 (d, CH), 104.5, 112.1, 122.7 (s, d, s, thienyl), 127.9, 129.74, 129.77, 131.5, 133.2, 134.6, 139.8 (3 d, s, d, 2 s, Ar, thienyl), 164.6, 164.9 (2 s, *C*O$_2$Ar, *C*O$_2$Me), 194.9 (s, C=O).

HRMS (80 eV): *m*/*z* [M + Na]$^+$ calcd for $C_{21}H_{22}ClNNaO_5S$: 458.0804; found: 458.0776.

(*E*)-1-Cyclohexyl-5-methoxy-3-methyl-2,5-dioxopent-3-enyl 3-Chlorobenzoate (19a) and (*E*)-2-Acetyl-1-cyclohexyl-4-methoxy-4-oxobut-2-enyl 3-Chlorobenzoate (20a)

Phosphorane **18** (0.598 g, 1.70 mmol) was added to a solution of 1,2-diketone **5a** (0.550 g, 1.70 mmol) in CH_2Cl_2 (10 mL) and the mixture was stirred at room temperature for 16 h. After removal of the solvent, the residue was purified by column chromatography (hexanes/EtOAc 15:1 to 9:1) to yield **19a** and **20a** (0.250 g of **19a**; 0.177 g as a mixture of both products; combined yield 67%) as colorless oils. A sample (0.090 g) of **19a** and **20a** could be separated by HPLC (hexanes/*i*-PrOH 98:2) to afford pure **20a**.

Compound 19a

IR (ATR): 3070–2855 (=C–H, C–H), 1715, 1695 (C=O), 1575 (C=C), 1250 cm^{-1} (C–Cl).

^{1}H NMR ($CDCl_3$, 500 MHz): δ = 1.10–1.40, 1.55–2.10 (2 m, 6 H, 5 H, CH, 5 CH_2), 2.31 (d, *J* = 1.6 Hz, 3 H, Me), 3.80 (s, 3 H, CO_2Me), 5.57 (d, *J* = 5.2 Hz, 1 H, CH), 6.65 (q, *J* = 1.6 Hz, 1 H, =CH), 7.35–7.45, 7.52–7.60, 7.90–8.05 (3 m, 1 H, 1 H, 2 H, Ar).

^{13}C NMR ($CDCl_3$, 125.8 MHz): δ = 13.9 (q, Me), 25.80, 25.84, 26.0, 28.0, 29.6 (5 t, 5 CH_2), 39.8 (d, CH), 51.8 (q, OMe), 79.5 (d, CH), 125.3, 127.9, 129.75, 129.77, 131.1, 133.4, 134.6, 149.9 (4 d, s, d, 2 s, Ar, C=CH), 165.0, 166.2 (2 s, CO_2Ar, CO_2Me), 198.9 (s, C=O).

Anal. Calcd for $C_{20}H_{23}ClO_5$ (378.9): C, 63.41; H, 6.12. Found: C, 62.99; H, 5.46.

Compound 20a

IR (ATR): 3070–2880 (=C–H, C–H), 1715, 1690 (C=O), 1575 (C=C), 1250 cm^{-1} (C–Cl).

^{1}H NMR ($CDCl_3$, 500 MHz): δ = 1.02–1.40, 1.63–1.95 (2 m, 6 H, 5 H, CH, 5 CH_2), 2.41 (s, 3 H, Me), 3.72 (s, 3 H, CO_2Me), 5.37 (d, *J* = 6.6 Hz, 1 H, CH), 5.85 (s, 1 H, =CH), 7.39–7.46, 7.56–7.61, 7.93–8.04 (3 m, 1 H, 1 H, 2 H, Ar).

^{13}C NMR ($CDCl_3$, 100.5 MHz): δ = 25.6, 25.7, 26.0, 27.6, 29.6 (5 t, 5 CH_2), 30.7 (q, Me), 39.6 (d, CH), 52.0 (q, OMe), 78.4 (d, CH), 118.1, 127.8, 129.6, 130.0, 131.1, 133.6, 134.8, 156.9 (4 d, s, d, 2 s, Ar, C=CH), 164.3, 165.1 (2 s, CO_2Ar, CO_2Me), 203.3 (s, C=O).

HRMS (ESI): *m*/*z* [M + Na]$^+$ calcd for $C_{20}H_{23}ClNaO_5$: 401.1126; found: 401.1122.

(*E*)-1-Methoxy-3-methyl-1,4-dioxohexadeca-2-en-5-yl 3-Chlorobenzoate (19b) and (*E*)-3-Acetyl-1-methoxy-1-oxopentadeca-2-en-4-yl 3-Chlorobenzoate (20b)

Phosphorane **18** (0.267 g, 0.79 mmol) was added to a solution of 1,2-diketone **5b** (0.310 g, 0.79 mmol) in CH_2Cl_2 (10 mL) and the mixture was stirred at room temperature for 19 h. After removal of the solvent, the residue was purified by column chromatography (hexanes/EtOAc 9:1 to 4:1) to yield **19b** and **20b** (0.145 g **19b**, 0.051 g of **20b**, 0.034 g mixture of both products; combined yield 65%) as colorless oils.

Compound 19b

IR (ATR): 3070–2860 (=C–H, C–H), 1715, 1700 (C=O), 1570 (C=C), 1250 cm^{-1} (C–Cl).

^{1}H NMR ($CDCl_3$, 500 MHz): δ = 0.88 (t, *J* = 7.1 Hz, 3 H, Me), 1.18–1.40, 1.45–1.55, 1.86–1.93 (3 m, 16 H, 2 H, 2 H, 10 CH_2), 2.30 (d, *J* = 1.0 Hz, 3 H, Me), 3.80 (s, 3 H, OMe), 5.71 (t, *J* = 6.4 Hz, 1 H, OCH), 6.62 (q, *J* = 1.0 Hz, 1 H, =CH), 7.40 (t, *J* = 8.0 Hz, 1 H, Ar), 7.52–7.59, 7.94–7.97, 8.04 (2 m, m_c, 1 H each, Ar).

^{13}C NMR ($CDCl_3$, 125.8 MHz): δ = 13.9, 14.1 (2 q, 2 Me), 22.7, 25.5, 29.4, 29.42*, 29.6, 29.7*, 31.3, 32.0 (8 t, 10 CH_2), 51.8 (q, OMe), 76.0 (d, CH), 125.3, 128.0, 129.8, 129.84, 129.87, 130.5, 133.4, 134.6, 149.1 (4 d, s, d, 2 s, Ar, C=CH), 165.0, 166.1 (2 s, CO_2Ar, CO_2Me), 198.6 (s, C=O).

HRMS (ESI): *m*/*z* [M + H]$^+$ calcd for $C_{25}H_{36}ClO_5$: 450.2173; found: 450.2186.

Compound 20b

IR (ATR): 3075–2865 (=C–H, C–H), 1715, 1695 (C=O), 1570 (C=C), 1250 cm^{-1} (C–Cl).

^{1}H NMR ($CDCl_3$, 500 MHz): δ = 0.87 (t, *J* = 6.9 Hz, 3 H, Me), 1.20–1.50, 1.81–1.93 (2 m, 18 H, 2 H, 10 CH_2), 2.43 (s, 3 H, Me), 3.73 (s, 3 H, OMe), 5.52 (dd, *J* = 5.2, 7.7 Hz, 1 H, OCH), 5.89 (br s, 1 H, =CH), 7.43 (t, *J* = 8.0 Hz, 1 H, Ar), 7.57–7.59, 7.93–7.95, 8.01 (2 m, m_c, 1 H each, Ar).

^{13}C NMR ($CDCl_3$, 125.8 MHz): δ = 14.2 (q, Me), 22.7, 23.5, 29.2*, 29.4*, 29.5*, 29.6 (6 t, 9 CH_2), 29.7 (q, Me), 32.0 (t, CH_2), 52.1 (q, OMe), 74.3 (d, CH), 116.9 (d, =CH), 127.9, 129.8, 130.1, 131.3, 132.5, 133.7 (3 d, s, d, s, Ar), 158.3 (s, =C), 164.3, 164.9 (2 s, CO_2Ar, CO_2Me), 203.5 (s, C=O).

HRMS (ESI): *m*/*z* [M + H]$^+$ calcd for $C_{25}H_{36}ClO_5$: 450.2173; found: 450.2179.

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Supporting Information

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