Stereoselective Preparation of (*E*)-α-Bromoacrylates from Mixtures of Brominated Ando Phosphonates

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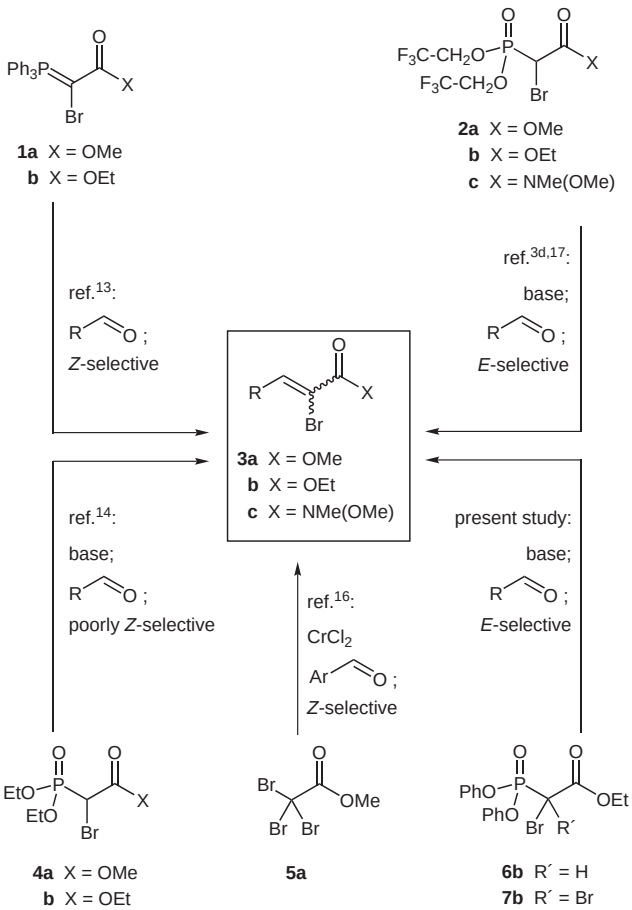
Abstract: We prepared 69:31–11:89 mixtures of phosphonates **6b** and **7b** containing two phenoxy substituents, a CO_2Et group, and 1 or 2 bromine atoms, respectively, at the interspersed methylene group. Deprotonating 64:36 mixtures of these reagents with NaH and adding a variety of aldehydes at 0 °C provided unsaturated α-bromoesters. Yields were typically 70–99% and *E*-selectivities (i.e. ester and β-substituent *cis*) 80:20–98:2. Similarly, we proceeded via the chlorinated phosphonate **49** to the unsaturated α-chloroester **51** with *E*:*Z* = 94:6 (80%).

Key words: α-bromoacrylates, brominated alkenes, α-chloroacrylates, chlorinated alkenes, Horner–Wadsworth–Emmons olefination, α,β-unsaturated esters

The stereoselective synthesis of olefins, especially of olefins with a trisubstituted double bond, is an area of ongoing interest.[1] α-Brominated α,β-unsaturated esters ('α-bromoacrylates') – besides many other compounds – turn out to be versatile precursors for the construction of such olefins. This is because their C_{sp2}–Br bond has been engaged in many transition metal-catalyzed C,C bond forming reactions[2] such as Stille couplings,[3] Suzuki couplings,[3b,d] Sonogashira couplings,[4] and copper-catalyzed trifluoromethylations.[3d,5] In addition, α-bromoacrylates were converted into 1,3-dienes by reduction of the ester moiety, further olefination, and C,C coupling.[6] Apart from that, α-bromoacrylates were used in Diels–Alder reactions,[7] tandem Michael additions/cyclizations (→ aziridines, cyclopropanes, benzotetrahydrofurans, pyroglutamates),[8] radical cyclizations,[9] dehydrobrominations (→ alkynoic acids[10]) as well as for carbapenem[11] and other natural product syntheses.[12]

Almost all applications of α-bromoacrylates hinge on their being stereopure. This makes accessing these compounds only worthwhile if stereocontrol is comprised. Arguably, the most important stereocontrolled syntheses of α-bromoacrylates **3a**,**b** – and other α-brominated derivatives of α,β-unsaturated carboxylic acids e. g. **3c** – constitute C_2-extensions of aldehydes (Scheme 1). Until recently, these transformations were effected by Wittig reactions of brominated phosphoranes **1a**,**b** if the α-bromoacrylates were to be *exclusively Z-configured* (i. e., ester and β-substituent *trans*).[13] When it sufficed that the α-bromoacrylates were *preponderantly Z-configured*, one could also employ the brominated phosphonates **4a**,**b** to conduct Horner–Wadsworth–Emmons ('HWE') reactions.[14] Takai's syntheses of *trans*-configured 1-iodoolefins from aldehydes and iodoform[15] were extended using methyl tribromoacetate (**5a**) in a similar fashion, which led to brominated cinnamic esters **3a** (R = anisyl, piperonyl) with very high *Z*-selectivity.[16]



Scheme 1 C_2-Elongating syntheses of α-bromoacrylates

The only *E-selective* syntheses of methyl α-bromoacrylates **3a** and the corresponding ethyl esters **3b** were reported by Kogen and Tago[3d,17a,b] and by Qing and Zhang,[17c] respectively. The *E*-configured Weinreb amide analogs **3c** were obtained in a similar manner by Deslongchamps et al.[17d] All three groups adopted the Still–Gennari variant of the HWE reaction – starting from bromine-*free*

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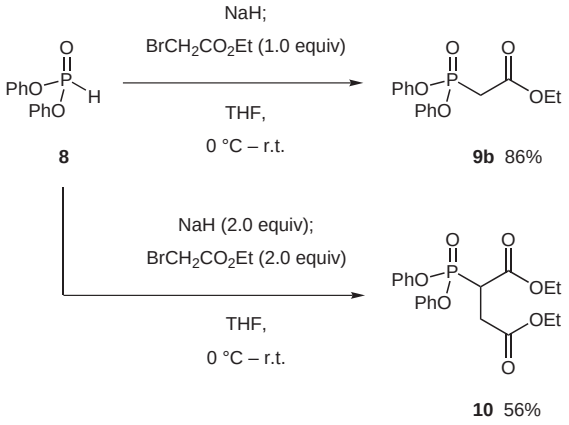
trifluoroethylphosphonates[18] – to using bromine-*containing* trifluoroethylphosphonates **2a**–**c**.

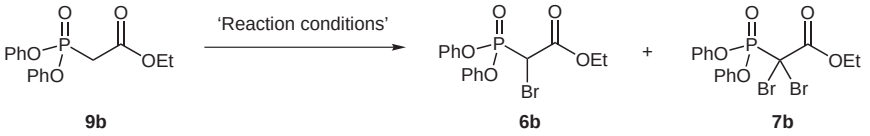
What we disclose here is an adoption of the Ando variant of the HWE reaction – which starts from bromine-*free* arylphosphonates[19] – to employing (a mixture of) phenylphosphonates **6b** and **7b** *containing* 1 and 2 bromine atoms, respectively. As we found, α-bromoacrylates **3b** are obtained from **6b**/**7b** and aldehydes almost as *E*-selectively as from **2a**,**c**. In turn, the preparation of **6b**/**7b** requires less labor than the preparation of **2a**,**c**. It costs less, is considerably higher yielding, and easily amenable to molar scale. Moreover, our phosphonates **6b**/**7b** could be stored without decomposition at room temperature whereas Kogen's reagent **2a** requires storage at –20 °C.[3d] All these should make our findings interesting for the synthetic community.

The reagent mixture **6b**/**7b** was obtained from diphenyl phosphite (**8**) in two steps: 1. deprotonation followed by alkylation with ethyl bromoacetate (Scheme 2); 2. deprotonation followed by bromination (Table 1).



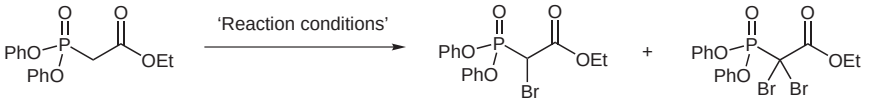
Scheme 2 Improved synthesis of Ando's reagent[19b,e] **9b**

Table 1 Obtaining Brominated HWE Reagents **6b**/**7b**[a]



Entry	Reaction Conditions	Yield Recovered **9b** (%)	Yield Monobromination **6b** (%)	Yield Dibromination **7b** (%)	Total Yield **9b** + **6b** + **7b** (%)	Monobromination:Dibromination (**6b**:**7b**)	Bromine Transfer from Reagent (%)[b]
1	NBS (1.1 equiv), benzoyl peroxide (0.1 equiv), CCl_4, 60 °C, 21 h	0	0	0	0	–	–
2	DBU (1.3 equiv), THF, –78 °C, 10 min; Br_2 (1.0 equiv), –78 °C, 30 min	33	22	43	98	34:66	110
3	DBU (1.3 equiv), THF, –78 °C, 10 min; CBr_4 (1.2 equiv), THF, –78 °C, 30 min	15	34	23	72	60:40	80
4	NaH (1.0 equiv), DME, 0 °C, 1 h; Br_2 (1.0 equiv), r.t., 4 h	5.4	32	57	94	36:64	146
5	NaH (1.0 equiv), THF, r.t., 20 min; Br_2 (1.07 equiv), r.t., 2 h	12	55	29	96	65:35	106
6	NaH (1.0 equiv), THF, –78 °C, 15 min; Br_2 (1.0 equiv), –78 °C, 30 min	78	1.2	ca. 1.5	81	–	–
7	NaH (1.0 equiv), THF, r.t., 20 min; Br_2 (2.03 equiv), r.t., 30 min	8.8	35	53	96	40:60	71
8	NaH (1.0 equiv), THF, 0 °C, 1 h; NBS (1.0 equiv), r.t., 24 h	22	45	27	94	62:38	99
9	NaH (1.0 equiv), THF, r.t., 20 min; NBS (1.86 equiv), r.t., 30 min	trace	12	87	99	11:89	100
10	NaH (1.0 equiv), THF, r.t., 20 min; CBr_4 (1.19 equiv), r.t.,70 min	12	5.2	12	46	31:69	25

Table 1 Obtaining Brominated HWE Reagents **6b**/**7b**[a] (continued)



9b **6b** **7b**

Entry	Reaction Conditions	Yield Recovered **9b** (%)	Yield Monobromination **6b** (%)	Yield Dibromination **7b** (%)	Total Yield **9b** + **6b** + **7b** (%)	Monobromination:Dibromination (**6b**:**7b**)	Bromine Transfer from Reagent (%)[b]
11	NaH (1.0 equiv), THF, r.t., 20 min; $Br_2(CH)_2Br_2$ (1.24 equiv), r.t., 2 h	100	0	0	100	–	–
12	NaH (1.0 equiv), THF, r.t., 20 min; $Br(CCl_2)_2Br$ (1.24 equiv), r.t., 1.5 h	11	59	26	95	69:31	96
13	NaH (1.0 equiv), THF, r.t., 20 min; $Br(CCl_2)_2Br$ (1.80 equiv), r.t., 1.5 h	11	58	27	97	69:31	61
14	NaH (1.0 equiv), THF, r.t., 20 min; $Br(CF_2)_2Br$ (1.24 equiv), r.t., 2 h	66	0	0	66	–	–
15	NaH (1.0 equiv), THF, r.t., 20 min; 2,4,4,6-tetrabromocyclohexa-2,5-dien-1-one (1.0 equiv)	11	48	39	98	55:45	124
16	LDA (1.2 equiv), –78 °C, 1 h; Br_2 (1.0 equiv), –78 °C, 60 min	11	50	26	87	66:34	102
17	LDA (1.2 equiv), r.t., 20 min; Br_2 (0.98 equiv), r.t., 30 min	21	47	29	97	62:38	109
18	LDA (1.2 equiv), TMSCl (1.0 equiv) –78 °C, 1 h; Br_2 (1.0 equiv), –78 °C, 60 min	4.4	51	30	85	63:37	111

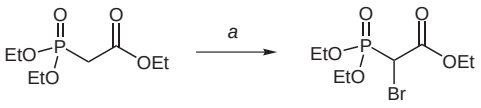
[a] For reasons unknown, the reactions presented in entries 2–10 and 16–18 provided also some monochlorophosphonate **49** (up to 3 mol%) and bromochlorophosphonate **52** (cf. Experimental Part; up to 11 mol%). These compounds could neither be separated nor readily (by ^1H NMR analysis) quantified. The formation of these contaminants reduces somewhat the precision of the respective numbers in Table 1. Only the preparations of entries 12, 13, and 15 provided **6b** and **7b** free from **49** and **52**.

[b] For values >100%, the combined yields of **6b** and **7b** surpassed the amount of electrophilic bromine present in the reagent used; hence, in these cases, some unaccounted-for oxidation must have occurred.

Step 1 afforded Ando's phosphonate **9b** in 86% yield when NaH in THF was used as the deprotonating agent and if one equivalent of ethyl bromoacetate were added to the reaction mixture very slowly (Scheme 2). This reaction was performed on a 300 g scale without any drop in the yield. If the same amount of ethyl bromoacetate was added too fast, the bisalkylation product **10** formed as a contaminant (while **10** resulted free from **9b** and in 56% yield using two equivalents both of the base and the alkylating agent). Ando's one-step synthesis **8** → **9b** had yielded trace amounts of **9b** using NaH/DMSO and 77% under the best conditions (Et_3N/CH_2Cl_2).[19e]

Step 2 of our synthesis, namely the bromination of phosphonate **9b**, failed to become the desired chemoselective monobromination (→ **6b**; Table 1). Invariably this transformation suffered from some accompanying if not dominating dibromination (→ **7b**) and possibly also from incomplete conversion of the starting material. This remained so irrespective of the base (no base, entry 1; DBU, entries 2–3; NaH, entries 4–15; LDA, entries 16–18), the brominating agent (NBS, entries 1,8,9; Br_2, entries 2, 4–7, 16–18; CBr_4, entries 3,10; dibromotetrachloroethane, entries 12–13; dibromotetrafluoroethane, entry 14; tetrabromocyclohexadieneone, entry 15) or the temperature (anywhere between –78 °C and r.t.). The best ratio favoring **6b** vs. **7b** was 69:31 (using 1.0 equiv of NaH and 1.80 equiv of dibromotetrachloroethane; 97% yield, entry 13). The optimum value in the opposite direction was 11:89 (using 1.0 equiv of NaH and 1.86 equiv of NBS; 99% yield, entry 9).

Our failure to realize the chemoselective monobromination of the phenyloxylated phosphonato ester **9b** contrasts with the facile monobromination of the ethoxylated phosphonato ester **11b** (→ **4b**; Scheme 3). On the other hand, it finds a parallel in the fact that we were unable to monobrominate the trifluoroethoxylated phosphonato ester **12a** (Scheme 4). There, too, was a competition of no, mono- (→ **2a**), and dibromination (→ **13a**). Clearly, the enhanced electron-withdrawal in Ando-type **6b** or Still–Gennari-type bromophosphonates **2a** versus the absence



11b **4b** 98%

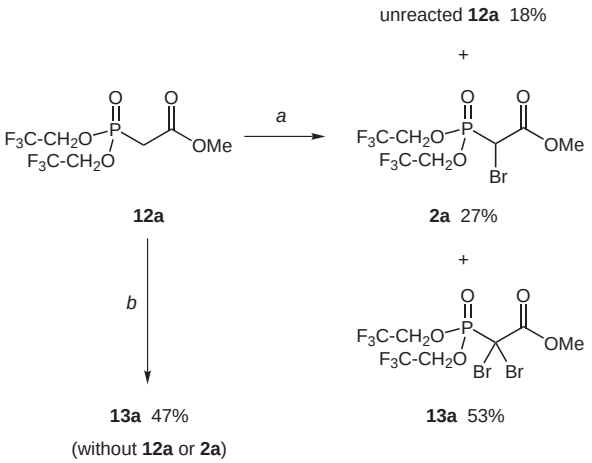
Scheme 3 a) NaH (1.1 equiv), DME, r.t., 1 h; Br_2 (1.0 equiv), 0 °C, 15 min; r.t., 2 h

of this effect in the 'standard' bromophosphonate **4b** makes the difference.

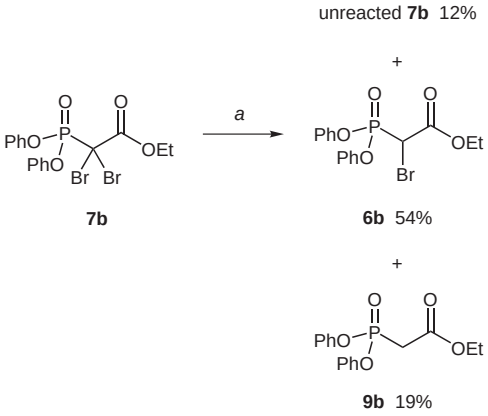
However, we encountered a notable difference between the Ando-type **7b** and Still–Gennari-type dibromophosphonates **13a**. The former did not form at all when **9b** was subjected to the dibromination conditions published[17a,b] for **12a** – and which we could reproduce (Scheme 4). Instead, **9b** decomposed completely.

Trying to get around these difficulties, we treated a pure sample of the Ando-type dibromophosphonate **7b** – separated from a 90:10 **7b**:**6b** mixture by careful flash chromatography on silica gel[20] – with stannous chloride (Scheme 5). We expected a selective reduction **7b** → **6b** because of the close similarity to the known[3d,17a,b] reduction of the analogous Still-Gennari-type dibromophosphonate **13a** (→ **2a**). However, our intended monoreduction (→ **6b**, 53%) was at the same time incomplete – we reisolated 12% **7b** – and overdone – we found 19% bis(debromination).

Starting to fear that, given these difficulties, we might have to quit our approach, we tested doing HWE chemistry with the (almost) best we possessed, namely with a 64:36 mixture of monobromophosphonate **6b** and dibromophosphonate **7b**, notwithstanding. In THF, **6b**/**7b** was deprotonated with potassium carbonate, DBU, Triton B, potassium *tert*-butoxide, KHMDS, LDA or NaH, added anisaldehyde, and in all instances observed formation of



Scheme 4 a) NaH (1.0 equiv), DME, r.t., 1 h; Br_2 (1.0 equiv), 0 °C, 15 min; r.t., 2 h; b) NaOH (7 equiv), Br_2 (3.5 equiv), H_2O, 0 °C, 30 min



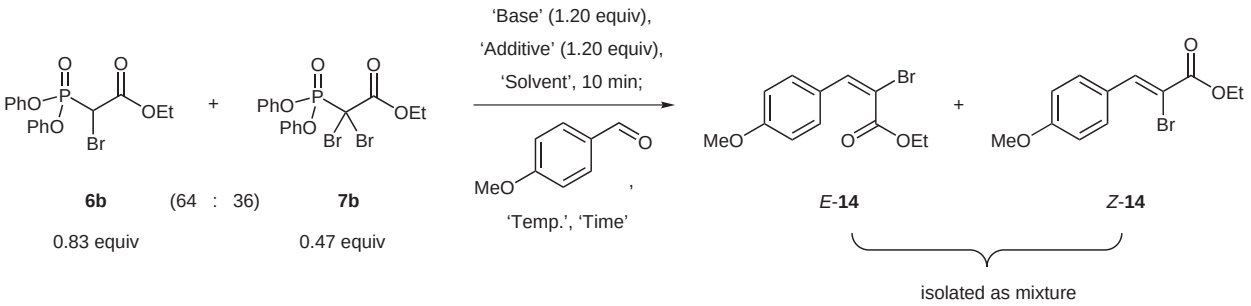
Scheme 5 a) $SnCl_2 \cdot 2\,H_2O$ (1.2 equiv), EtOH, –40 °C, 10 min

the olefination product **14** (Table 2). Surprisingly, the yields rose as high as 99% (entries 1, 23, 25–28, 33). This was entirely unexpected since the consumption of monobromophosphonate **6b** was just 0.83 equivalent which should have limited the maximum yield of **14** to 83%. That this was surpassed by up to 16 additional percents means that some dibromophosphonate **7b** must transform into deprotonated monobromophosphonate **6b** under the reaction conditions, thereby being channeled into the desired pathway, too. Responsible for this could be the diphenylphosphate by-product or a phenoxide ion expelled therefrom.

E:*Z* selectivities in the model study of Table 2 reached 92:8 (entry 33) at best and 90:10 under several conditions (entries 16, 23, 27). The temperature dependence of this selectivity was such that 0 °C/room temperature entailed the highest values (entries 9, 14, 23) with a slight drop-off towards 66 °C (cf. entries 10, 15, and 26, respectively) and a steep drop-off towards –78 °C (cf. entries 7, 12, and 19, respectively).

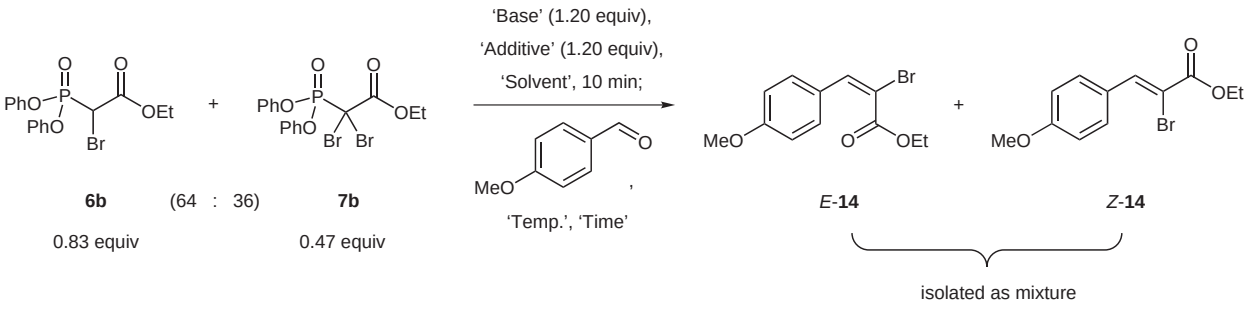
We applied the experimentally slightly more convenient conditions of entry 23 of Table 2 (→ *E*:*Z* = 90:10, 99% yield) to a variety of other aldehydes (Table 3) rather than the very best conditions of entry 33/Table 2 (→ *E*:*Z* = 92:8, 99% yield). We were pleased to find that other aromatic aldehydes (Table 3, entries 2,3), α,β-unsaturated aldehydes (entries 4–7), simple aliphatic aldehydes (entries 8–11), and α-oxygenated (entries 12–14) aldehydes as well as an α-amino- (entry 15) or a β-amino-substituted aldehyde (entry 16) were amenable to the bromoolefination protocol. Unless these aldehydes were sterically hindered, yields were 70–99%. Too hindered substrates were pivalaldehyde (entry 11; → 31%, the remainder of the aldehyde decomposing) and the trimethylated cyclohexadienecarbaldehyde of entry 7 (→ no conversion at all). In half of the cases the *E*:*Z* ratios were better than 90:10. The other ones were 80:20–90:10. The top result was *E*:*Z* = 98:2 observed starting from the α-oxygenated aldehyde of entry 14.

Table 2 HWE Reaction Between Phosphonates **6b**/**7b**[a] and Anisaldehyde: Optimizing the Reaction Conditions



Entry	Base	Additive	Solvent	Temp (°C)	Time (min)	Conversion of Anisaldehyde (%)	Yield after Chromatography (%)	*E*:*Z*-Selectivity[b]
1	K_2CO_3	–	THF	r. t.	23 h	100	99	79:21
2	DBU	–	THF	–78	80	76	–[c]	31:69
3	DBU	–	THF	r. t.	30	100	–[c]	37:63
4	DBU	NaBr	THF	0	4 h	90	–[c]	74:26
5	Triton B[d]	–	THF	–78	80	100	–[c]	32:68
6	Triton B[d]	–	THF	r. t.	30	90	60	64:36
7	*t*-BuOK	–	THF	–78	85	88	–[c]	44:56
8	*t*-BuOK	–	THF	0	30	95	92	80:20
9	*t*-BuOK	–	THF	r. t.	30	100	90	82:18
10	*t*-BuOK	–	THF	66	10	100	88	79:21
11	*t*-BuOK	18-crown-6	THF	r. t.	30	96	77	81:19
12	KHMDS (0.5 M in toluene)	–	THF	–78	75	51	–[c]	54:46
13	KHMDS (0.5 M in toluene)	–	THF	0	30	80	–[c]	82:18
14	KHMDS (0.5 M in toluene)	–	THF	r. t.	30	100	90	83:17
15	KHMDS (0.5 M in toluene)	–	THF	66	10	68	–[c]	78:22
16	KHMDS (0.5 M in toluene)	18-crown-6	THF	r. t.	30	100	81	90:10
17	LDA	–	THF	–78	75	100	79	69:31
18	LDA	–	THF	0	30	100	–[c]	53:47
19	NaH (60% in mineral oil)	–	THF	–78	80	63	–[c]	39:61
20	NaH (60% in mineral oil)	–	THF	–30	30	91	–[c]	76:24
21	NaH (60% in mineral oil)	–	THF	–20	30	79	66	87:13
22	NaH (60% in mineral oil)	–	THF	–10	30	92	78	89:11
23	NaH (60% in mineral oil)	–	THF	0	30	100	99	90:10
24	NaH (60% in mineral oil)	–	THF	10	30	100	–[c]	87:13
25	NaH (60% in mineral oil)	–	THF	r. t.	120	100	99	89:11
26	NaH (60% in mineral oil)	–	THF	66	10	100	99	83:19
27	NaH (60% in mineral oil)	–	Et_2O	0	30	100	99	90:10
28	NaH (60% in mineral oil)	–	CH_2Cl_2	0	30	100	99	71:29

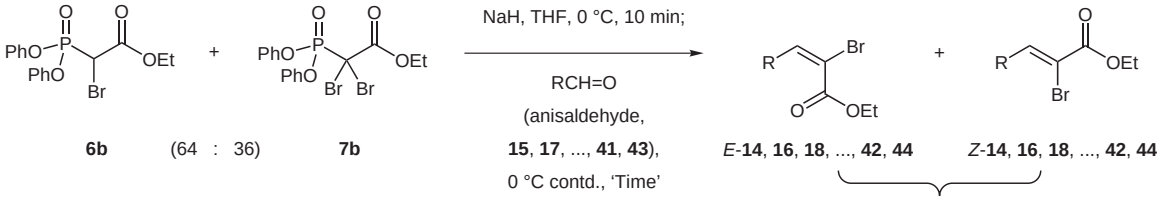
Table 2 HWE Reaction Between Phosphonates **6b**/**7b**[a] and Anisaldehyde: Optimizing the Reaction Conditions (continued)



Entry	Base	Additive	Solvent	Temp (°C)	Time (min)	Conversion of Anisaldehyde (%)	Yield after Chromatography (%)	*E*:*Z*-Selectivity[b]
29	NaH (60% in mineral oil)	–	DME	0	30	100	–[c]	63:37
30	NaH (60% in mineral oil)	–	dioxane	0	30	82	–[c]	52:48
31	NaH (60% in mineral oil)	15-crown-5	THF	0	30	47	–[c]	51.49
32	NaH (60% in mineral oil)	cryptand 222	THF	0	30	69	–[c]	69:31
33	NaH (60% in mineral oil)	NaBr	THF	0	30	100	99	92:8
34	NaH (60% in mineral oil)	LiBr	THF	0	30	90	–[c]	74:26

[a] These reactions were realized with a mixture of monobromophosphonate **6b** and dibromophosphonate **7b** which was contaminated with 1.7 mol% of the monochlorophosphonate **49** and 9.4 mol% of the analogous bromochlorophosphonate (**52**; cf. Experimental Part). As a consequence, the resulting bromoacrylates **14** were accompanied by some of the chloroacrylates **51** (cf. also Scheme 8 below). The numerical values given in Table 2 for conversion, yield, and *E*:*Z*-ratios are somewhat approximate since in our NMR-analysis we assumed that 1.7 + 9.4 = 11.1 mol% chloroacrylate **51** occurred in bromoacrylate **14** and that **51** resulted with the same conversion, yield, and *E*:*Z*-selectivity as **14**. Table 3, entry 1 shows a preparation of **14** free from **51** (99% yield) and Scheme 8 (see below) a preparation of **51** free from **14** (80% yield).
[b] The *E*/*Z*-ratio was determined by integration of the MeO signal in the ^{1}H NMR spectrum of the crude product ($\delta_{MeO,E}$ = 3.81, $\delta_{MeO,Z}$ = 3.85); the olefin protons could not be used for that purpose because $\delta_{=CH,Z}$ was superimposed by δ_{PhO} of unreacted reagent.
[c] Yield not determined because of unsatisfactory *E*/*Z*-ratio.
[d] Triton B = $BnNMe_3^+OH^-$.

Table 3 HWE Reactions Between Phosphonates **6b**/**7b** and Various Aldehydes



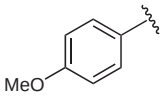
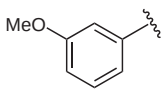
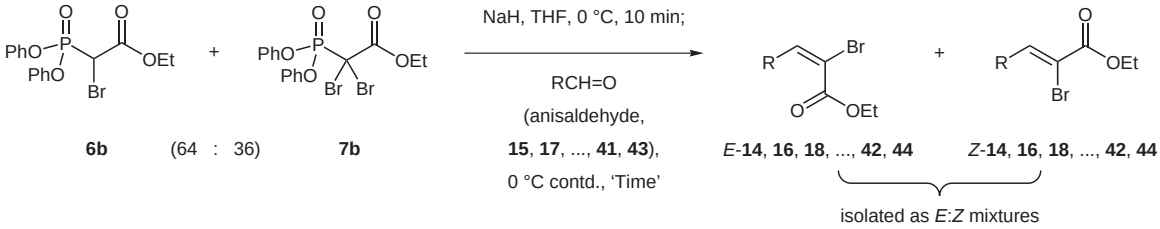
Entry	R	Aldehyde	**6b** (equiv)	**7b** (equiv)	NaH (equiv)	Time (min)	Product	Yield after Chromatography(%)	*E*:*Z* Selectivity	Separation
1		anisaldehyde	0.77	0.43	1.00	30	**14**	99	90:10	inseparable
2		**15**	0.83	0.46	1.00	90	**16**	97	86:14	inseparable

Table 3 HWE Reactions Between Phosphonates **6b**/**7b** and Various Aldehydes (continued)



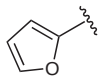
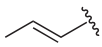
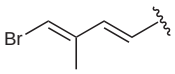
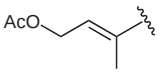
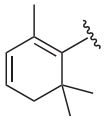
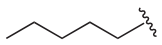
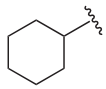
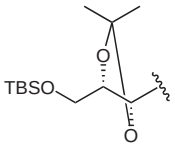
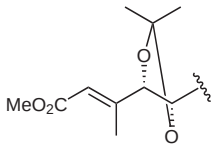
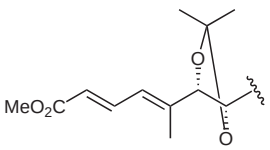
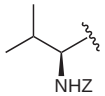
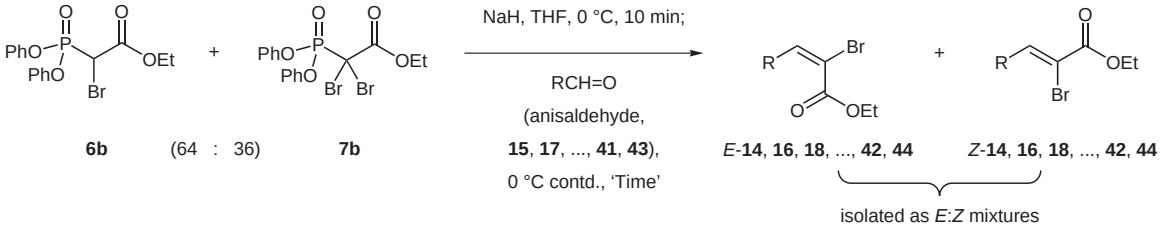
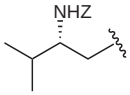
Entry	R	Aldehyde	**6b** (equiv)	**7b** (equiv)	NaH (equiv)	Time (min)	Prod-uct	Yield after Chromato-graphy(%)	*E*:*Z* Select-ivity	Separation
3		**17**	0.83	0.46	1.00	30	**18**	80	82:18	yes (difficult)
4		**19**	0.83	0.46	1.00	60	**20**	70	84:16	yes (difficult)
5		**21**	0.75	0.41	1.00	40	**22**	81	83:17	yes[a] (difficult)
6		**23**	0.84	0.47	1.00	30	**24**	72	80:20	inseparable
7		**25**	0.83	0.47	1.00	1320	**26**	0 (no reaction)	–	–
8		**27**	0.77	0.43	1.00	30	**28**	97	86:14	yes (difficult)
9		**29**	0.83	0.46	1.00	45	**30**	98	91:9	yes (difficult)
10		**31**	0.83	0.46	1.00	30	**32**	74	94:6	yes
11		**33**	0.83	0.46	1.00	420	**34**	31	97:3	inseparable
12		**35**	0.70	0.39	0.83	60	**36**	70	93:7	yes[a]
13		**37**	0.76	0.44	0.83	30	**38**	75	95:5	yes[a]
14		**39**	0.75	0.42	0.80	90	**40**	81	98:2	yes[a]
15		**41**	0.83	0.46	1.00	210	**42**	85	no *Z*-isomer detected	

Table 3 HWE Reactions Between Phosphonates **6b**/**7b** and Various Aldehydes (continued)



Entry	R	Aldehyde	**6b** (equiv)	**7b** (equiv)	NaH (equiv)	Time (min)	Product	Yield after Chromatography(%)	*E*:*Z* Selectivity	Separation
16		**43**	0.83	0.46	1.00	30	**44**	90	93:7	yes

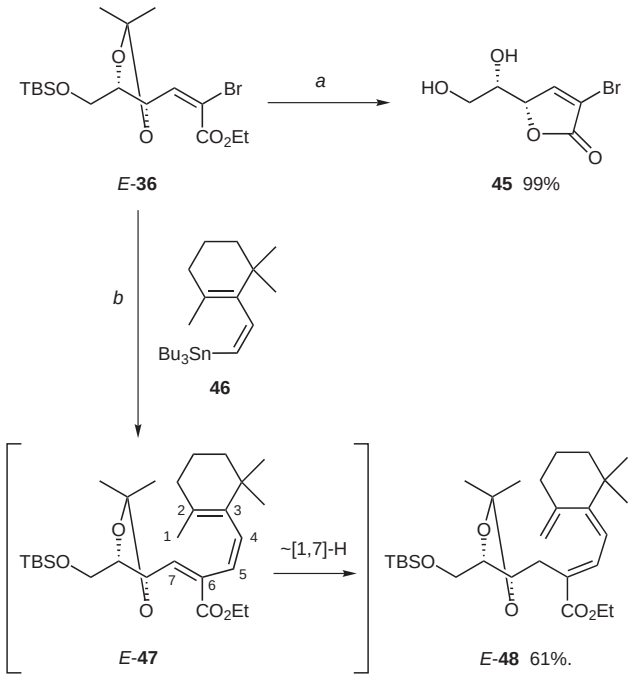
[a] This preparation was realized with a mixture of monobromophosphonate **6b** and dibromophosphonate **7b** which was contaminated with 1.7 mol% of the monochlorophosphonate **49** and 9.4 mol% of the analogous bromochlorophosphonate (**52**; cf. Experimental Part). As a consequence, the resulting bromoacrylate was accompanied by its chlorine analogue. The latter was inseparable by flash chromatography and therefore constituted 10, 4, 9, and 7 weight% of the isolated samples of **22**, **36**, **38**, and **40**, respectively. The yield of bromoacrylate and the equivalents of **6b** and **7b** in these cases refer to 'the amount of aldehyde used minus the amount of aldehyde incorporated into the chloroacrylate'. Obviously, using *pure* **6b**/**7b** would spare this complication.

Ando's bromine-free arylphosphonate **9b** could be improved with respect to the stereoselectivity of carbonyl olefinations upon replacement of the phenyloxy by certain other aryloxy groups, for example by α-naphthyloxy.[19b] One might expect a similar selectivity enhancement in the brominated reagent described here. However, we have not probed this yet.

The stereochemical assignments of Table 3 are mostly based upon ^{1}H NMR shift criteria (Table 4). In a pair of isomers, 3-H is deshielded when it is *cis* to the CO_2Et group (1st criterion), and 4-H is deshielded when it is *cis* to the CO_2Et group (2nd criterion). Exceptionally, we needed to take [**14** and (*E*)-**44**] – or additionally took [**22**, (*E*)-**28**, (*E*)-**34**, **36**, (*E*)-**42**] – recourse to a 3rd criterion. It is the magnitude of the 3-bond coupling between ^{13}C-1 and 3-^{1}H and was observed by gated-decoupled 1-dimensional ^{13}C NMR spectroscopy. These couplings are larger when the bonds between C-1 and 3-H possess a zigzag rather than U-shaped array.[21] 'Zigzag ^{13}C-1/3-^{1}H couplings' are 10.6–11.2 Hz in the *E*-isomers of **14**, **22**, **28**, **34**, **36**, **42**, and **44** as opposed to the 'U-shaped ^{13}C-1/3-^{1}H couplings' of 4.2–5.5 Hz in (*Z*)-**14**, (*Z*)-**22**, and (*Z*)-**36**.

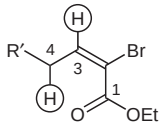
Scheme 6 shows the follow-up chemistry of an α-bromoacrylate. *It depends on its having been made accessible with the E configuration.* In the first reaction, pure α-bromoacrylate (*E*)-**36** was subjected to an acid-catalyzed transacetalization followed by an in situ lactonization. The result was a 99% yield of the γ-(α-hydroxyalkyl)-substituted butenolide **45**. Butenolides like this figure as key intermediates in the stereocontrolled synthesis of *Z*-configured γ-alkylidenebutenolides.[22] In the second follow-up reaction, the α-bromoacrylate (*E*)-**36** was Stille-coupled[2a] with dienylstannane **46**.[23] The primary product must have been (*E*)-**47**. This, however, underwent a sigmatropic 1,7-H shift, which provided the isomer (*E*)-**48**, i.e., a fully conjugated hexatrienoic ester.

Our early specimens of the bromophosphonate mixture **6b**/**7b** contained a small amount of the monochlorinated analogs of both compounds. Until we noticed we had wondered what the – quite minor – contaminants in the α-bromoacrylates subsequently obtained were. From then on it was clear that the contaminating chlorine analog of

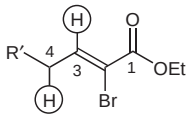


Scheme 6 a) *p*-TsOH (0.1 equiv), MeOH, reflux, 10 min; b) *E*-**36** (1.3 equiv), **46** (1.0 equiv), Pd_2dba_3·$CHCl_3$ (0.1 equiv), P(2-furyl)$_3$ (0.6 equiv), CuI (1.65 equiv), NMP, 25 °C, 27 h

Table 4 Elucidation of C=C bond Configurations by ^{1}H NMR (500 MHz, $CDCl_3$) and ^{13}C NMR (126 MHz) Spectroscopy (both in $CDCl_3$)



E-**14**, **16**, **18**, **20**, **22**, **22**, **24**, **26**, **28**, **30**, **32**, **34**, **36**, **38**, **40**, **42**, **44**



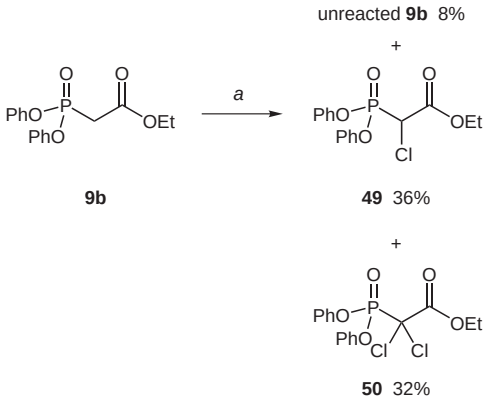
Z-**14**, **16**, **18**, **20**, **22**, **22**, **24**, **26**, **28**, **30**, **32**, **34**, **36**, **38**, **40**, **42**, **44**

Compound	^{1}H NMR $\delta_{3\text{-H}}$		$\delta_{4\text{-H}}$		^{13}C NMR $^3J_{\text{C-1,3-H}}$ (Hz)	
	E	*Z*	*E*	*Z*	*E*	*Z*
14	7.29	8.17	–	–	10.6	5.5
16	7.31	8.18	–	–	–[a]	–[a]
18	7.17	8.16	–	–	–[a]	–[a]
20	7.08	7.62	7.05	6.50	–[a]	–[a]
22	7.14	7.68	7.31	6.66	10.6	4.2
24	6.74	7.70	–	–	–[a]	–[a]
26	–	–	–	–	–	–
28	6.66	7.29	2.49	2.34	11.2	–[a]
30	6.47	7.09	2.93	2.57	–[a]	–[a]
32	6.44	7.08	3.23	2.86	–[a]	–[a]
34	6.17	7.45	–	–	11.1	–[a]
36	6.59	7.26	5.06	4.90	10.9	4.6
38	6.61	7.26	5.08	4.73	–[a]	–[a]
40	6.60	–[b]	5.11	4.73	–[a]	–[a]
42	6.48[c] 6.41	–[d]	4.86[c] 4.81	–[d]	10.9[e] –	–[d]
44	6.69	–[f]	2.55 and 2.73[g]	–[f]	11.2	–[f]

[a] Not determined.
[b] Amount of this compound in the mixture too small for identifying its 3-H resonance.
[c] ^{1}H NMR spectrum of isomer (*E*)-**42** showed line-broadening at +27 °C but sharp lines of two carbamate rotamers at –10 °C (80:20 ratio; data of major rotamer in top row, of minor rotamer below) and modified lines at +50 °C (e. g., *one* doublet for 3-H rather than two doublets at –10 °C, but not everywhere sharp lines of a rapidly interconverting mixture).
[d] Isomer (*Z*)-**42** was not detected.
[e] Value for major rotamer; the minor rotamer's resonances were too weak for determining $^3J_{\text{C,H}}$.
[f] (*Z*)-**44** could not be isolated in pure form which makes signal attributions risky.
[g] 4-H_A and 4-H_B resonances.

bromophosphonate **6b** had undertaken *its* share of the HWE chemistry and provided some α-chloroacrylate thereby. The origin of this stray chlorine has left us marvelling. It showed up when 'brominating' the deprotonated phosphonate **9b** with NBS, Br_2 or CBr_4. Zero chlorine was incorporated using dibromotetrachloroethane as the brominating agent following the procedure of entries 12–13/Table 1 or using 2,4,4,6-tetrabromo-2,5-cyclohexadien-1-one (Table 1, entry 15).

The mentioned chloroacrylate formation was an incentive, though, to briefly check it out in its own right. To that end, we chlorinated the deprotonated phosphonate **9b** arbitrarily, namely with NCS (Scheme 7). This furnished 76% of a 11:47:42 (mol:mol:mol) mixture of the non-, mono- and dichlorinated phosphonates **9b**, **49**, and **50**, respectively. The Ando-type monochlorophosphonate **49** could be separated from this mixture by repetitive flash chromatography on silica gel,[20] albeit not in analytically pure form due to the presence of a yet unidentified impurity.

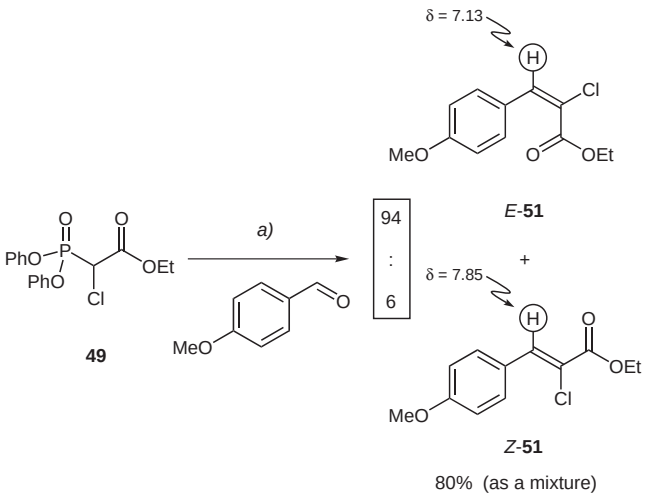


Scheme 7 a) NaH (1.2 equiv), NCS (1.2 equiv), THF, r.t., 40 min

When a THF solution of compound **49** was first treated with NaH and then combined with anisaldehyde, 80% of the chloroacrylates (*E*)- and (*Z*)-**51** resulted as a 94:6 mixture (Scheme 8). Their stereochemical assignments stem from the chemical shift of the respective olefin proton: 3-H is deshielded when it is *cis* to the CO_2Et group, i.e., when the double bond configuration is *Z*, i.e., in the minor isomer.

Reagent **49** should be as versatile to obtain *E*-configured chloroacrylates from aldehydes as, in the present study, reagents **6b**/**7b** were established to be for the preparation of *E*-configured bromoacrylates from aldehydes.

Products were purified by flash chromatography[20] on Macherey-Nagel silica gel 60 (details given in parentheses). ^{1}H [TMS (0.00 ppm) as internal standard in $CDCl_3$] and ^{13}C NMR [$CDCl_3$ (77.00 ppm) as internal standard in $CDCl_3$]: Bruker AM 400 or DRX 500; ^{31}P NMR [H_3PO_4 (0.00 ppm) as internal standard in $CDCl_3$]: Varian Mercury VX 300. Integrals are in accord with assignments; coupling constants are given in Hz. The assignments of ^{1}H and ^{13}C NMR resonances refer to the IUPAC nomenclature; primed num-



Scheme 8 a) **49** (1.2 equiv), NaH (1.2 equiv), THF, 0 °C, 50 min

bers belong to the side-chain. NMR: Dr. M. Keller, Institut für Organische Chemie und Biochemie, Universität Freiburg. Combustion analyses: E. Hickl, Institut für Organische Chemie und Biochemie, Universität Freiburg. MS: Dr. J. Wörth, Institut für Organische Chemie und Biochemie, Universität Freiburg. IR spectra: FTIR Perkin-Elmer Spectrum 1000 spectrophotometer. Optical rotations measured with a Perkin-Elmer polarimeter 341 at 589 nm and calculated according to the Drude equation $\{[\alpha]_v^\vartheta = (\alpha_{exp} \times 100)/(c \times d)\}$; rotational values are the average of 5 measurements of α in given solution of the respective sample. Melting points: Dr. Tottoli apparatus (Fa. Büchi), uncorrected.

Ethyl Bromo(diphenylphosphono)acetate (6b) in a 69:31 Mixture with Ethyl Dibromo(diphenylphosphono)acetate (7b)

Entry 12, *Table 1*: To a solution of phosphonate **9b** (5.94 g, 18.5 mmol) in THF (40 mL) was added NaH (60% in mineral oil, 741 mg, 18.5 mmol, 1.0 equiv) portionwise at r.t. during a period of 5 min. After 20 min at r. t., the gas evolution had ceased and 1,2-dibromotetrachloroethane (7.26 g, 22.3 mmol, 1.2 equiv) was added in one portion. A few seconds after the addition a white precipitate had formed. After 5 min reaction time, H_2O (40 mL) was added. The mixture was extracted with MTBE (3 × 150 mL). The combined organic layers were dried (Na_2SO_4) and evaporated under reduced pressure. The residue (8.59 g) was separated from the rest of the brominating reagent and H_2O by flash chromatography [∅ 10 cm, h 8 cm, cyclohexane–EtOAc, 5:1 (6 L), 1–50 (100 mL), fraction 1: 14–39, fraction 2: 40–47]. The mixtures of the products were obtained as hygroscopic colorless oils [fraction 1: 5.294 g, containing **9b**: 0.069 g, 1.2%; **6b**: 3.189 g, 43.1%; **7b**: 2.039 g, 23.0% (total 67% of a 1.8:64.0:34.2-mixture consisting of **9b**, **6b**, and **7b**); fraction 2: 1.946 g, containing **9b**: 0.805 g, 13.5%; **6b**: 1.004 g, 13.5%; **7b**: 0.137 g, 1.4%; (total 28% of a 47.5:47.5:5.0-mixture consisting of **9b**, **6b**, and **7b**); total yield: **9b**: 15%, **7b**: 57%, **6b**: 23%, total: 95%].

If the reaction was carried out on a small scale (1 mmol), the reaction time had little influence on the bromination ratio (Table 1). However, the scale described above required a very short reaction time to limit dibromination. The compositions of the above mixtures were determined by integration of the following ^{1}H NMR signals: 2-H for **6b**, 1′-CH_2 for **7b** and 2-CH_2 for **9b**. Only mixtures corresponding to fraction 1 above were employed for further olefination reactions. This fraction contained 2.3 mmol of the phosphonates **6b**/**7b** per g mixture. The amount of **9b** in these mixtures was neglected because in any cases no olefination byproducts of **9b** were detected. If instead of 1,2-dibromotetrachloroethane Br_2 was used (Table 1, entry 5) for bromination, small amounts of the chlorinated phosphonate **49** as well as ethyl bromochloro(diphenylphosphono)acetate (**52**) were formed.

6b

R_f = 0.49 (cyclohexane–EtOAc, 1:1).

IR (neat): 3070, 2980, 2940, 1740, 1590, 1490, 1460, 1290, 1205, 1185, 1160, 1025, 1010, 765, 685 cm^{-1}.

^{1}H NMR (500.0 MHz, $CDCl_3$): δ = 1.26 (t, 3 H, $J_{2',1'}$ = 7.1 Hz, 2′-CH_3), 4.27 (q, 2 H, $J_{1',2'}$ = 7.1 Hz, 1′-CH_2), 4.64 (d, 1 H, $^2J_{2,P}$ = 13.7 Hz, 2-H), 7.19–7.28 (m, 6 H, Ar-H), 7.32–7.37 (m, 4 H, Ar-H).

^{13}C NMR (125.7 MHz, $CDCl_3$): δ = 13.8 (C-2′), 34.9 (d, $^1J_{2,P}$ = 150.2 Hz, C-2), 63.5 (C-1′), 120.47 (d, $^3J_{2'',P}$ = 4.9 Hz) and 120.51 (d, $^3J_{2'',P}$ = 4.9 Hz; 2 × 2 × C-2″), 125.7 and 125.8 (2 × C-4″), 129.8 and 129.9 (2 × 2 × C-3″), 150.1 (d, $^2J_{1'',P}$ = 8.8 Hz) and 150.2 (d, $^2J_{1'',P}$ = 9.1 Hz, 2 × C-1″), 164.1 (C-1).

^{31}P NMR (121.5 MHz, $CDCl_3$): δ = 5.34.

MS (EI, 70 eV): *m*/*z* (%) = 398 (100, M^+), 320 (82), 305 (22).

Anal. Calcd for $C_{16}H_{16}BrO_5P$ (399.2): C, 48.14; H, 4.04. Found: C, 48.35; H, 4.13.

7b

R_f = 0.51 (cyclohexane–EtOAc, 1:1).

IR (neat): 3070, 2985, 2935, 1735, 1590, 1490, 1490, 1455, 1395, 1365, 1290, 1205, 1180, 1155, 1095, 1070, 1020, 955, 905, 835 cm^{-1}.

^{1}H NMR (500.0 MHz, $CDCl_3$): δ = 1.27 (t, 3 H, $J_{2',1'}$ = 7.1 Hz, 2′-CH_3), 4.31 (q, 2 H, $J_{1',2'}$ = 7.1 Hz, 1′-CH_2), 7.19–7.23 (m, 2 H, Ar-H), 7.26–7.30 (m, 4 H, Ar-H), 7.32–7.37 (m, 4 H, Ar-H).

^{13}C NMR (125.7 MHz, $CDCl_3$): δ = 13.6 (C-2′), 45.5 (d, $^1J_{2,P}$ = 167.1 Hz, C-2), 65.0 (C-1′), 120.4 (d, $^3J_{2'',P}$ = 4.5 Hz, 4 × C-2″), 125.7 (2 × C-4″), 129.7 (4 × C-3″), 150.9 (d, $^2J_{1'',P}$ = 9.4 Hz, 2 × C-1″), 163.0 (C-1).

^{31}P NMR (121.5 MHz, $CDCl_3$): δ = –0.97.

MS (EI, 70 eV): *m*/*z* (%) = 476 (46, M^+), 398 (42), 383 (10), 320 (21), 245 (100).

Anal. Calcd for $C_{16}H_{15}Br_2O_5P$ (478.1): C, 40.20; H, 3.16. Found: C, 40.25; H, 3.20.

Ethyl (Diphenylphosphono)acetate (9b)

A 2-L three-necked flask equipped with a 250-mL dropping funnel was charged with NaH (60% in mineral oil, 41.55 g, 1.039 mol, 1.0 equiv) and anhyd THF (800 mL). Diphenyl phosphite (**8**; 200.0 mL, 243.4 g, 1.039 mol) was added dropwise to the well-stirred suspension at 0 °C during a period of 3 h. After 1 h at 0 °C, the gas evolution had ceased and the reaction mixture became a clear orange solution. Subsequently ethyl bromoacetate (115.0 mL, 173.5 g, 1.039 mol, 1.0 equiv) was added dropwise over a period of 3 h, while a white solid started precipitating. The cooling bath was removed and the reaction mixture was stirred at r.t. for further 12 h. A sat. aq solution of NH_4Cl (100 mL) and H_2O (200 mL) were added to the mixture. The organic layer was separated and the aqueous layer was extracted with MTBE (3 × 500 mL). The combined organic layers were dried ($MgSO_4$) and the solvents were removed under reduced pressure. The orange oil (325 g) was purified by flash chromatography [∅ 10 cm, h 16 cm, cyclohexane–EtOAc, 4:1 (13 L), 1–25 (500 mL), **9b**: 4–20]. After removal of the solvents under reduced pressure (12 h, 1 mbar), the oil (301 g) was transferred to a separatory funnel. After 12 h, a film of H_2O had formed on the product. Separation from H_2O and further drying in vacuum (12 h, 1 mbar) gave **9b** (285.1 g, 86%) as a hygroscopic colorless oil.

If the reaction is carried out on a smaller scale (100 mmol) the drying procedure after the chromatography is not necessary. Alternatively the product can be purified by distillation; bp 174 °C, 3×10^{-4} mbar; R_f = 0.46 (cyclohexane–EtOAc, 1:1).

IR (neat): 3065, 2980, 2930, 1735, 1590, 1490, 1455, 1400, 1365, 1285, 1185, 1160, 1110, 1070, 1025, 1010, 940, 820, 760, 685 cm^{-1}.

^1H NMR (500.0 MHz, $CDCl_3$): δ = 1.25 (t, 3 H, $J_{2',1'}$ = 7.1 Hz, 2′-CH_3), 3.27 (d, 2 H, $^2J_{2,P}$ = 21.8 Hz, 2-CH_2), 4.21 (q, 2 H, $J_{1',2'}$ = 7.1, 1′-CH_2), 7.18 (ttd, 2 H, J_{ortho} = 7.4 Hz, $^4J_{meta}$ = $^6J_{H,P}$ = 1.1 Hz, Ar-H_{para}), 7.21–7.25 (m, 4 H, Ar-H_{ortho}), 7.30–7.34 (m, 4 H, Ar-H_{meta}).

^{13}C NMR (125.7 MHz, $CDCl_3$): δ = 14.0 (C-2′), 34.1 (d, $^1J_{2,P}$ = 137.2 Hz, C-2), 61.9 (C-1′), 120.6 (d, $^3J_{2'',P}$ = 4.5 Hz, 4 × C-2″), 125.5 (2 × C-4″), 129.8 (4 × C-3″), 150.0 (d, $^2J_{1'',P}$ = 8.5 Hz, 2 × C-1″), 164.7 (d, $^2J_{1,P}$ = 6.7 Hz, C-1).

^{31}P NMR (121.5 MHz, $CDCl_3$): δ = 12.99.

MS (EI, 70 eV): *m*/*z* (%) = 320 (46, M^+), 227 (32), 199 (100).

Anal. Calcd for $C_{16}H_{17}O_5P$ (320.3): C, 60.00; H, 5.35. Found: C, 59.73; H, 5.63.

Diethyl 2-(Diphenylphosphono)succinate (10)

To a suspension of NaH (60% in mineral oil, 2.88 g, 72.0 mmol, 2.0 equiv) in THF (100 mL) was added diphenyl phosphite (6.93 mL, 8.43 g, 36.0 mmol, 1.0 equiv) dropwise at 0 °C during a period of 20 min. After 35 min, the gas evolution had ceased and ethyl bromoacetate (7.97 mL, 12.0 g, 72.0 mmol, 2.0 equiv) was added dropwise over a period of 20 min. The cooling bath was removed and the reaction mixture was stirred at r.t. for 12 h. A sat. aq solution of NH_4Cl (200 mL) was added to the mixture. The organic layer was separated and the aqueous layer was extracted with MTBE (3 × 200 mL). The combined organic layers were dried ($MgSO_4$) and the solvents were removed under reduced pressure. The residue was purified by flash chromatography [∅ 10 cm, h 12 cm, cyclohexane–EtOAc, 4:1 (5 L), 1–45 (100 mL), **10**: 23–38] and the product (8.18 g, 56%) was obtained as a hygroscopic colorless oil; R_f = 0.47 (cyclohexane–EtOAc, 1:1).

IR (neat): 3065, 2985, 2935, 1770, 1735, 1590, 1490, 1455, 1410, 1375, 1280, 1185, 1095, 1070, 1025, 940, 845 cm^{-1}.

^1H NMR (499.9 MHz, $CDCl_3$): δ = 1.26 and 1.29 (2 t, 3 H each, $J_{2',1'}$ = $J_{2'',1''}$ = 7.1 Hz, 2′-CH_3, 2″-CH_3), AB signal (δ_A = 3.01, δ_B = 3.25, 2 H, $^2J_{AB}$ = 17.4 Hz, split by $^3J_{A,P}$ = 10.0 Hz, $J_{A,2}$ = 3.4 Hz and $J_{B,2}$ = 11.5 Hz, $^3J_{B,P}$ = 7.7 Hz, 3-CH_2), 3.80 (ddd, 1 H, $^2J_{2,P}$ = 24.7 Hz, $J_{2,3\text{-H(B)}}$ = 11.5 Hz, $J_{2,3\text{-H(A)}}$ = 3.4 Hz, 2-H), 4.17 and 4.28 (2 m_c, 2 H each, 1′-CH_2, 1″-CH_2), 7.17–7.22 (m, 6 H, Ar-H), 7.31–7.34 (m, 4 H, Ar-H).

^{13}C NMR (125.7 MHz, $CDCl_3$): δ = 14.0 and 14.1 (C-2′, C-2″), 31.4 (d, $^2J_{3,P}$ = 2.1 Hz, C-3), 41.5 (d, $^1J_{2,P}$ = 134.4 Hz, C-2), 61.3 and 62.2 (C-1′, C-1″), 120.4 and 120.5 (2 d, $^3J_{2''',P}$ = 4.5 Hz, 2 × 2 × C-2‴), 125.49 and 125.54 (2 × C-4‴), 129.79 and 129.82 (2 × 2 × C-3‴), 150.02 (d, $^2J_{1''',P}$ = 8.2) and 150.03 (d, $^2J_{1''',P}$ = 9.1 Hz, 2 × C-1‴), 167.3 (d, $J_{C,P}$ = 6.1 Hz) and 170.7 (d, $J_{C,P}$ = 20.3 Hz; C-1, C-4).

^{31}P NMR (121.4 MHz, $CDCl_3$): δ = 14.80.

MS (CI, 120 eV): *m*/*z* (%) = 407 (100, $[M + H]^+$).

Anal. Calcd for $C_{20}H_{23}O_7P$ (406.4): C, 59.11; H, 5.70. Found: C, 59.11; H, 5.84.

Olefination of 6b/7b; General Procedure

To a solution of a 64:36 (mol:mol) mixture of the phosphonates **6b**/**7b** (2.3 mmol of the phosphonates **6b**/**7b** per g mixture, 1.2 equiv) in THF (10–20 mL per g of phosphonate mixture) was added NaH (60% in mineral oil, 1.2 equiv) portionwise at 0 °C. After the gas evolution had ceased (10 min), the aldehyde (1 equiv, pure or as a solution in an appropriate amount of THF) was added. The reaction mixture was stirred at 0 °C until the TLC indicated the complete consumption of the aldehyde and a white precipitate had formed. H_2O was added and the mixture was extracted with MTBE (3 ×). The combined extracts were dried (Na_2SO_4) and the solvents were evaporated under reduced pressure. The residue was purified by flash chromatography.

Ethyl 2-Bromo-3-(4-methoxyphenyl)propenoate (14)

According to the general olefination procedure, a 64:36 mixture of **6b**/**7b** [753.5 mg, containing 60 wt% **6b**: 452.1 mg, 1.133 mmol, 0.77 equiv; 40 wt% **7b**: 301.4 mg, 630.4 μmol, 0.43 equiv (total: 1.2 equiv); 2.3 mmol **6b**/**7b** per g mixture], NaH (60% in mineral oil, 59.2 mg, 1.48 mmol, 1.0 equiv) and anisaldehyde (180 μL, 202 mg, 1.48 mmol) were reacted for 30 min in THF (20 mL). Flash chromatography [∅ 3 cm, h 21 cm, cyclohexane–EtOAc 6:1 (700 mL), 1–25 (20 mL), **14**: 9–13] provided the title compounds (*E*)-**14** and (*Z*)-**14** [(416.8 mg, 99%, (*E*)-**14**:(*Z*)-**14** = 90:10] as a colorless oil. The *E*:*Z* ratio of **14** prior to chromatography was 90:10 according to ^1H NMR spectroscopy; R_f = 0.41 (cyclohexane–EtOAc, 3:1).

IR (neat): 2980, 2935, 2900, 2835, 1735, 1600, 1570, 1515, 1490, 1465, 1440, 1420, 1370, 1335, 1305, 1235, 1165, 1115, 1090, 1020, 965, 885 cm^{-1}.

^1H NMR [500.0 MHz, $CDCl_3$; (*E*)-**14**:(*Z*)-**14** = 90:10]: (*E*)-**14**: δ = 1.24 (t, 3 H, $J_{2',1'}$ = 7.1 Hz, 2′-CH_3), 3.81 (s, 3 H, OCH_3), 4.24 (q, 2 H, $J_{1',2'}$ = 7.1 Hz, 1′-CH_2), 6.83–6.86 (m_c, 2 H_{arom}, 3″-CH), 7.25–7.29 (m_c, 2 H_{arom}, 2″-CH), 7.29 (s, 1 H, 3-CH); (*Z*)-**14**: δ = 1.38 (t, 3 H, $J_{2',1'}$ = 7.1 Hz, 2′-CH_3), 3.85 (s, 3 H, OCH_3), 4.34 (q, 2 H, $J_{1',2'}$ = 7.1 Hz, 1′-CH_2), 6.93–6.96 (m_c, 2 H_{arom}, 3″-CH), 7.87–7.92 (m_c, 2 H_{arom}, 2″-CH), 8.17 (s, 1 H, 3-H).

^{13}C NMR [125.7 MHz, $CDCl_3$; (*E*)-**14**:(*Z*)-**14** = 90:10]: (*E*)-**14**: δ = 13.8 (C-2′), 55.3 (OCH_3), 62.2 (C-1′), 109.4 (C-2), 113.8 (2 × C-3″), 127.3 (C-1″), 130.1 (2 × C-2″), 139.7 (C-3), 160.2 (C-4″), 164.6 (C-1); (*Z*)-**14**: δ = 14.2 (C-2′), 55.4 (OCH_3), 62.6 (C-1′), 110.3 (C-2), 113.9 (2 × C-3″), 126.2 (C-1″), 132.4 (2 × C-2″), 140.2 (C-3), 161.2 (C-4″), 163.6 (C-1).

MS (CI, 70 eV): *m*/*z* (%) = 285 (100, $[M + H]^+$).

Anal. Calcd for $C_{12}H_{13}BrO_3$ (285.1): C, 50.55; H, 4.60. Found: C, 50.51; H, 4.70.

Ethyl 2-Bromo-3-(3-methoxyphenyl)propenoate (16)

According to the general olefination procedure, a 64:36 mixture of **6b**/**7b** [586.4 mg, containing 60 wt% **6b**: 351.8 mg, 881.5 μmol, 0.83 equiv; 40 wt.-% **7b**: 234.6 mg, 490.6 μmol, 0.46 equiv (total: 1.3 equiv); 2.3 mmol **6b**/**7b** per g mixture], NaH (60% in mineral oil, 42.4 mg, 1.06 mmol, 1.0 equiv) and 3-methoxybenzaldehyde (**15**, 129 μL, 144 mg, 1.06 mmol) were reacted for 90 min in THF (15 mL). Flash chromatography [∅ 3 cm, h 21 cm, cyclohexane–EtOAc, 6:1 (700 mL), 1–25 (20 mL), **16**: 10–16] provided the title compound (294.0 mg, 97%, (*E*)-**16**:(*Z*)-**16** = 86:14) as a colorless oil. The *E*:*Z* ratio of **16** prior to chromatography was 86:14 according to ^1H NMR spectroscopy; R_f = 0.40 (cyclohexane–EtOAc, 3:1).

IR (neat): 2940, 1725, 1600, 1580, 1490, 1460, 1435, 1370, 1325, 1265, 1215, 1160, 1040, 670 cm^{-1}.

^1H NMR [499.9 MHz, $CDCl_3$; (*E*)-**16**:(*Z*)-**16** = 86:14]: (*E*)-**16**: δ = 1.20 (t, 3 H, $J_{2',1'}$ = 7.1 Hz, 2′-CH_3), 3.79 (s, 3 H, OCH_3), 4.22 (q, 2 H, $J_{1',2'}$ = 7.1 Hz, 1′-CH_2), 6.82–6.84 (m, 1 H, 2″-CH), 6.84–6.88 (m, 2 H_{arom}, Ar-H), 7.24 (dd, 1 H, $J_{5'',4''}$ = $J_{5'',6''}$ = 7.9 Hz, 5″-CH), 7.31 (s, 1 H, 3-H); (*Z*)-**16**: δ = 1.39 (t, 3 H, $J_{2',1'}$ = 7.1 Hz, 2′-CH_3), 3.84 (s, 3 H, OCH_3), 4.35 (q, 2 H, $J_{1',2'}$ = 7.1 Hz, 1′-CH_2), 6.98 (dm_c, 1 H_{arom}, $J_{Ar\text{-}H,5''}$ = 8.1 Hz, Ar-H), 7.34 (dd, 1 H_{arom}, $J_{5'',4''}$ = $J_{5'',6''}$ = 7.9 Hz, 5″-CH), 7.38 (dm_c, 1 H_{arom}, $J_{Ar\text{-}H,5''}$ = 7.7 Hz, Ar-H), 7.46–7.47 (m, 1 H_{arom}, 2″-CH), 8.18 (s, 1 H, 3-H).

^{13}C NMR [125.7 MHz, $CDCl_3$; (*E*)-**16**:(*Z*)-**16** = 86:14]: (*E*)-**16**: δ = 13.7 (C-2′), 55.2 (OCH_3), 62.3 (C-1′), 111.9 (C-2), 113.4, 114.6, 120.6 and 129.4 (4 × CH_{arom}), 136.1 (C-1″), 139.1 (C-3),

159.5 (C-3″), 164.4 (C-1); (*Z*)-**16**: δ = 14.2 (C-2′), 55.33 (OCH_3), 62.8 (C-1′), 115.0, 116.2, 123.1 (3 × CH_{arom}), 140.6 (C-3).

MS (EI, 70 eV): *m*/*z* (%) = 284 (28, M^+), 205 (72), 177 (100).

HRMS (EI): *m*/*z* calcd for $C_{12}H_{13}BrO_3$ (M^+): 284.0048; found: 284.0047.

Ethyl 2-Bromo-3-(2-furyl)propenoate (18)

According to the general olefination procedure, a 64:36 mixture of **6b**/**7b** [915.6 mg, containing 60 wt% **6b**: 549.4 mg, 1.377 mmol, 0.83 equiv; 40 wt% **7b**: 366.2 mg, 766.1 μmol, 0.46 equiv (total: 1.3 equiv); 2.3 mmol **6b**/**7b** per g mixture], NaH (60% in mineral oil, 66.3 mg, 1.66 mmol, 1.0 equiv) and furfural (**18**, 173 μL, 159 mg, 1.66 mmol) were reacted for 30 min in THF (15 mL). Flash chromatography [∅ 3.5 cm, h 22 cm, cyclohexane–EtOAc, 20:1 (630 mL), 1–20 (20 mL), cyclohexane–EtOAc, 10:1 (330 mL), 21–35 (20 mL), **18**: 13–25] provided the title compounds (*E*)-**18** and (*Z*)-**18** (366.4 mg, 80%, (*E*)-**18**:(*Z*)-**18** = 82:18) as a colorless oil, which became dark after several days. The *E*:*Z* ratio of **18** prior to chromatography was 82:18 according to ^{1}H NMR spectroscopy; R_f = 0.35 (cyclohexane–EtOAc, 10:1).

IR (neat): 3150, 2985, 2940, 2905, 1725, 1615, 1470, 1395, 1365, 1345, 1250, 1225, 1145, 1090, 1025, 885, 750, 710 cm^{-1}.

^{1}H NMR [499.9 MHz, $CDCl_3$; (*E*)-**18**:(*Z*)-**18** = 97:3]: (*E*)-**18**: δ = 1.36 (t, 3 H, $J_{2',1'}$ = 7.1 Hz, 2′-CH_3), 4.34 (q, 2 H, $J_{1',2'}$ = 7.1 Hz, 1′-CH_2), 6.45 (ddd, 1 H, $J_{4'',3''}$ = 3.6 Hz, $J_{4'',5''}$ = 1.8 Hz, $^5J_{4'',3}$ = 0.5 Hz, 4″-CH), 7.01 (ddd, 1 H, $J_{3'',4''}$ = 3.5 Hz, $^4J_{3'',5''}$ = $^4J_{3'',3}$ = 0.6 Hz, 3″-CH), 7.17 (s, 1 H, 3-H), 7.45 (dd, 1 H, $J_{5'',4''}$ = 1.8 Hz, $^4J_{5'',3''}$ = 0.7 Hz, 5″-CH).

^{1}H NMR [400.1 MHz, $CDCl_3$; (*E*)-**18**:(*Z*)-**18** = 82:18]: (*Z*)-**18**: δ = 1.37 (t, 3 H, $J_{2',1'}$ = 7.3 Hz, 2′-CH_3), 4.33 (q, 2 H, $J_{1',2'}$ = 7.3 Hz, 1′-CH_2), 6.57 (dd, 1 H, $J_{4'',3''}$ = 3.9 Hz, $J_{4'',5''}$ = 1.7 Hz, 4″-CH), 7.60 (d, 1 H, $J_{5'',4''}$ = 1.7 Hz, 5″-CH), 8.16 (s, 1 H, 3-H).

^{13}C NMR [100.6 MHz, $CDCl_3$; (*E*)-**18**:(*Z*)-**18** = 82:18]: (*E*)-**18**: δ = 14.0 (C-2′), 62.3 (C-1′), 107.7 (C-2), 112.2 and 114.9 (C-3″, C-4″), 128.4 (C-5″), 144.1 (C-3), 149.4 (C-2″), 163.7 (C-1); (*Z*)-**18**: δ = 14.2 (C-2′), 62.6 (C-1′), 109.9 (C-2), 112.5 and 116.7 (C-3″, C-4″), 129.0 (C-5″), 144.9 (C-3), 150.0 (C-2″), 163.0 (C-1).

MS (EI, 70 eV): *m*/*z* (%) = 244 (94, M^+), 216 (18), 137 (100).

HRMS (EI): *m*/*z* calcd for $C_9H_9BrO_3$ (M^+), 243.9735; found: 243.9741.

Anal. Calcd for $C_9H_9BrO_3$ (245.1): C, 44.11; H, 3.70. Found: C, 43.77; H, 3.62.

Ethyl (2*E*,4*E*)-2-Bromohexa-2,4-dienoate (20)

According to the general olefination procedure, a 64:36 mixture of **6b**/**7b** [733.6 mg, containing 60 wt% **6b**: 440.2 mg, 1.103 mmol, 0.83 equiv; 40 wt% **7b**: 293.4 mg, 613.9 μmol, 0.46 equiv (total: 1.3 equiv); 2.3 mmol **6b**/**7b** per g mixture], NaH (60% in mineral oil, 45.6 mg, 1.33 mmol, 1.0 equiv) and *trans*-crotonaldehyde (**19**; 109 μL, 93.4 mg, 1.33 mmol, contains 3.4% *cis*-crotonaldehyde) were reacted for 60 min in THF (15 mL). Flash chromatography [∅ 3 cm, h 23 cm, cyclohexane–EtOAc, 100:1 (700 mL), 1–30 (20 mL), cyclohexane–EtOAc, 50:1 (400 mL), 31–50 (20 mL), **20**: 31–38] provided the title compounds (*E*)-**20** and (*Z*)-**20** [203.7 mg, 70%, (2*E*,4*E*)-**20**:(2*Z*,4*E*)-**20**:(2*E*,4*Z*)-**20**:(2*Z*,4*Z*)-**20** = 76.2:17.5:3.9:2.4] as a colorless oil. The *E*:*Z* ratio of **20** prior to chromatography was 84:16 according to ^{1}H NMR spectroscopy; R_f = 0.15 (cyclohexane–EtOAc, 20:1).

IR (neat): 2980, 2930, 1730, 1635, 1590, 1445, 1370, 1310, 1245, 1165, 1095, 1040, 970, 750 cm^{-1}.

^{1}H NMR [499.9 MHz, $CDCl_3$; (2*E*)-**20**:(2*Z*)-**20** = 84:16]: (2*E*)-**20**: δ = 1.36 (t, 3 H, $J_{2',1'}$ = 7.1 Hz, 2′-CH_3), 1.84 (dd, 3 H, $J_{6,5}$ = 6.8 Hz, $^4J_{6,4}$ = 1.5 Hz, 6-CH_3), 4.29 (q, 2 H, $J_{1',2'}$ = 7.1 Hz, 1′-CH_2), 6.08 (dq, 1 H, $J_{5,4}$ = 13.9 Hz, $J_{5,6}$ = 7.0 Hz, 5-H), AB signal (δ_A = 7.05, δ_B = 7.08, 1 H each, J_{AB} = 11.2 Hz, A branch split as dq, $^3J_{A,5}$ = 13.8 Hz, $^4J_{A,6}$ = 1.5 Hz, A: 4-H, B: 3-H); (2*Z*)-**20**: δ = 1.34 (t, 3 H, $J_{2',1'}$ = 7.1 Hz, 2′-CH_3), 1.91 (dd, 3 H, $J_{6,5}$ = 6.8 Hz, $^4J_{6,4}$ = 1.6 Hz, 6-CH_3), 4.28 (q, 2 H, $J_{1',2'}$ = 7.1 Hz, 1′-CH_2), 6.34 (dqd, 1 H, $J_{5,4}$ = 15.1 Hz, $J_{5,6}$ = 6.8 Hz, $^4J_{5,3}$ = 0.7 Hz, 5-H), 6.50 (ddq, 1 H, $J_{4,5}$ = 15.2 Hz, $J_{4,3}$ = 10.5 Hz, $^4J_{4,6}$ = 1.7 Hz, 4-H), 7.62 (d, 1 H, $J_{3,4}$ = 10.5 Hz, 3-H).

^{13}C NMR [125.7 MHz, $CDCl_3$; (2*E*)-**20**:(2*Z*)-**20** = 84:16]: (2*E*)-**20**: δ = 14.1 (C-2′), 18.7 (C-6), 62.1 (C-1′), 108.9 (C-2), 128.4 and 140.7 (C-4, C-5), 146.1 (C-3), 162.9 (C-1).

MS (CI, 250 eV): *m*/*z* (%) = 219 (100, $[M + H]^+$), 175 (20).

Ethyl (4*E*,6*E*)-2,7-Dibromo-6-methylhepta-2,4,6-trienoate (22)

According to the general olefination procedure, a 57:32:9:2 mixture of **6b**/**7b**/**52**/**49** [407.2 mg, containing 53.2 wt% **6b**: 218.2 mg, 546.9 μmol, 0.68 equiv; 35.7 wt% **7b**: 143.8 mg, 300.8 μmol, 0.38 equiv; 9.4 wt% **52**: 38.3 mg, 85.2 μmol, 0.11 equiv; 1.7 wt% **49**: 6.9 mg, 20 μmol, 0.024 equiv (total: 1.2 equiv); 2.2 mmol **6b**/**7b**/**52**/**49** per g mixture], NaH (60% in mineral oil, 32.0 mg, 800 μmol, 1.0 equiv) and (2*E*,4*E*)-5-bromo-4-methylpenta-2,4-dienal[24] (**21**; 140.0 mg, 799.9 μmol) were reacted for 40 min in THF (10 mL). Flash chromatography [∅ 3 cm, h 23 cm, cyclohexane–EtOAc, 6:1 (700 mL), 1–25 (20 mL), **22** and 2-chloro-2-debromo-**22**: 5–9] provided the title compounds (2*E*)-**22** and (2*Z*)-**22** (210.4 mg, 82%, (2*E*)-**22**:(2*Z*)-**22**:2-chloro-2-debromo-**22** = 75:15:10 mol:mol:mol) as a colorless oil. The *E*:*Z* ratio of **22** prior to chromatography was 83:17 according to ^{1}H NMR spectroscopy.

(2*E*)-**22**

R_f = 0.64 (cyclohexane–EtOAc, 5:1).

IR (neat): 3065, 2980, 2925, 1715, 1700, 1595, 1560, 1455, 1370, 1345, 1315, 1255, 1220, 1150, 1025, 970 cm^{-1}.

^{1}H NMR (500.0 MHz, $CDCl_3$): δ = 1.37 (t, 3 H, $J_{2',1'}$ = 7.2 Hz, 2′-CH_3), 1.99 (d, 3 H, $^4J_{6\text{-Me},7}$ = 1.2 Hz, 6-CH_3), 4.30 (q, 2 H, $J_{1',2'}$ = 7.2 Hz, 1′-CH_2), 6.46 (ddd, 1 H, $J_{5,4}$ = 15.1 Hz, $^4J_{5,7}$ = $^4J_{5,3}$ = 0.8 Hz, 5-H), 6.55 (hardly resolved qdd, 1 H, $^4J_{7,6\text{-Me}}$ = $^4J_{7,5}$ = $^5J_{7,4}$ = 0.8 Hz, 7-H), 7.14 (dd, 1 H, $J_{3,4}$ = 11.4 Hz, $^4J_{3,5}$ = 0.8 Hz, 3-H), 7.31 (ddd, 1 H, $J_{4,5}$ = 15.3 Hz, $J_{4,3}$ = 11.4 Hz, $^5J_{4,7}$ = 0.6 Hz, 4-H).

^{13}C NMR (125.7 MHz, $CDCl_3$): δ = 14.1 and 15.3 (C-2′, 6-CH_3), 62.2 (C-1′), 111.7 (C-2), 114.6 (C-7), 125.3, 140.9 and 145.5 (C-3, C-4, C-5), 139.9 (C-6), 162.8 (C-1).

MS (EI, 70 eV): *m*/*z* (%) = 322 (26, M^+), 215 (70), 91 (100).

HRMS (EI): *m*/*z* calcd for $C_{10}H_{12}Br_2O_2$ (M^+), 321.9204; found: 321.9206.

(2*Z*)-**22**

R_f = 0.56 (cyclohexane–EtOAc, 5:1).

IR (neat): 3080, 2980, 2920, 1700, 1600, 1560, 1455, 1365, 1320, 1260, 1235, 1155, 1045, 975 cm^{-1}.

^{1}H NMR (500.0 MHz, $CDCl_3$): δ = 1.35 (t, 3 H, $J_{2',1'}$ = 7.2 Hz, 2′-CH_3), 2.04 (d, 3 H, $^4J_{6\text{-Me},7}$ = 1.2 Hz, 6-CH_3), 4.30 (q, 2 H, $J_{1',2'}$ = 7.2 Hz, 1′-CH_2), 6.61 (m_c, 1 H, 7-H), AB signal (δ_A = 6.66, δ_B = 6.71, 1 H each, $^2J_{AB}$ = 15.3 Hz, split by $J_{A,3}$ = 9.6 Hz, A: 4-H, B: 5-H), 7.68 (d, 1 H, $J_{3,4}$ = 9.7 Hz, 3-H).

^{13}C NMR (125.7 MHz, $CDCl_3$): δ = 14.2 and 15.2 (C-2′, 6-CH_3), 62.5 (C-1′), 115.2 (C-2), 115.6 (C-7), 125.7, 140.7 and 142.2 (C-3, C-4, C-5), 139.9 (C-6), 162.9 (C-1).

Ethyl (4*E*)-6-Acetoxy-2-bromo-4-methylhexa-2,4-dienoate (24)

According to the general olefination procedure a 64:36 mixture of **6b**/**7b** [621.2 mg, containing 60 wt% **6b**: 372.7 mg, 934.1 μmol, 0.84 equiv; 40 wt% **7b**: 248.5 mg, 519.8 μmol, 0.47 equiv (total: 1.3 equiv); 2.3 mmol **6b**/**7b** per g mixture], NaH (60% in mineral oil,

44.4 mg, 1.11 mmol, 1.0 equiv) and (*E*)-4-acetoxy-2-methylbut-2-enal[25] (**23**; 158 mg, 1.11 mmol) were reacted for 30 min in THF (10 mL). Flash chromatography [∅ 3 cm, h 20 cm, cyclohexane–EtOAc, 5:1 (600 mL), 1–25 (20 mL), **24**: 10–15] provided the title compounds (*E*)-**24** and (*Z*)-**24** (232.1 mg, 72%, (*E*)-**24**:(*Z*)-**24** = 80:20) as a colorless oil. The *E*:*Z* ratio of **24** prior to chromatography was 80:20 according to ^{1}H NMR spectroscopy; R_f = 0.40 (cyclohexane–EtOAc, 1:1).

IR (neat): 2985, 2940, 1735, 1595, 1445, 1365, 1230, 1025, 960 cm^{-1}.

^{1}H NMR [400.1 MHz, $CDCl_3$; (2*E*)-**24**:(2*Z*)-**24** = 80:20]: (2*E*)-**24**: δ = 1.32 (t, 3 H, $J_{2',1'}$ = 7.3 Hz, 2′-CH_3), 1.81 (br s, 3 H, 4-CH_3), 2.06 (s, 3 H, 6-OCOCH_3), 4.26 (q, 2 H, $J_{1',2'}$ = 7.3 Hz, 1′-CH_2), 4.63 (d, 2 H, $J_{6,5}$ = 6.9 Hz, 6-CH_2), 5.65 (m_c, probably interpretable as tqd, 1 H, $J_{5,6}$ = 6.9 Hz, $^4J_{5,4\text{-Me}} = {}^4J_{5,3}$ = 1.3 Hz, 5-H), 6.74 (br s, 1 H, 3-H); (2*Z*)-**24**: δ = 1.34 (t, 3 H, $J_{2',1'}$ = 7.3 Hz, 2′-CH_3), 2.06 and 2.08 (2 s, 3 H each, 4-CH_3, 6-OCOCH_3), 4.29 (q, 2 H, $J_{1',2'}$ = 7.3 Hz, 1′-CH_2), 4.73 (d, 2 H, $J_{6,5}$ = 6.9 Hz, 6-CH_2), 6.07 (tm_c, 1 H, $J_{5,6}$ = ca. 6.9 Hz, 5-H), 7.70 (br s, 1 H, 3-H).

MS (EI, 70 eV): *m*/*z* (%) = 290 (3, M^+), 217 (26), 43 (100).

HRMS (EI): *m*/*z* calcd for $C_{11}H_{15}BrO_4$ (M^+), 290.0154; found: 290.0153.

Ethyl 2-Bromooct-2-enoate (28)

According to the general olefination procedure a 64:36 mixture of **6b**/**7b** [1.018 g, containing 60 wt% **6b**: 610.8 mg, 1.530 mmol, 0.77 equiv; 40 wt% **7b**: 407.2 mg, 851.7 μmol, 0.43 equiv (total: 1.3 equiv); 2.3 mmol **6b**/**7b** per g mixture], NaH (60% in mineral oil, 80.0 mg, 2.00 mmol, 1.0 equiv) and hexanal (**27**, 240 μL, 200 mg, 2.00 mmol) were reacted for 30 min in THF (20 mL). Flash chromatography [∅ 3 cm, h 19 cm, cyclohexane–EtOAc, 60:1 (600 mL), 1–25 (20 mL), **28**: 5–14] provided the title compounds (*E*)-**28** and (*Z*)-**28** (485.1 mg, 97%, (*E*)-**28**:(*Z*)-**28** = 86:14) as a colorless oil. The *E*:*Z* ratio of **28** prior to chromatography was 86:14 according to ^{1}H NMR spectroscopy; R_f = 0.58 (cyclohexane–EtOAc, 5:1).

IR (neat): 2930, 2860, 1735, 1625, 1455, 1370, 1255, 1135, 1095, 1045, 950, 865 cm^{-1}.

^{1}H NMR [500.0 MHz, $CDCl_3$; (*E*)-**28**:(*Z*)-**28** = 94:6]: (*E*)-**28**: δ = 0.89 (t, 3 H, $J_{8,7}$ = 7.1 Hz, 8-CH_3), 1.27–1.35 (m, 4 H, 6-CH_2, 7-CH_2), superimposed by 1.34 (t, 3 H, $J_{2',1'}$ = 7.2 Hz, 2′-CH_3), 1.46 (tt, 2 H, $J_{5,4} = J_{5,6}$ = 7.4 Hz, 5-CH_2), 2.49 (dt, 2 H, $J_{4,3} = J_{4,5}$ = 7.6 Hz, 4-CH_2), 4.270 (q, 2 H, $J_{1',2'}$ = 7.2 Hz, 1′-CH_2), 6.66 (t, 1 H, $J_{3,4}$ = 7.8 Hz, 3-H); (*Z*)-**28**: δ = 2.34 (dt, 2 H, $J_{4,3} = J_{4,5}$ = 7.4 Hz, 4-CH_2), 4.275 (q, 2 H, $J_{1',2'}$ = 7.2 Hz, 1′-CH_2), 7.29 (t, 1 H, $J_{3,4}$ = 7.2 Hz, 3-H).

^{13}C NMR [125.7 MHz, $CDCl_3$; (*E*)-**28**:(*Z*)-**28** = 94:6]: (*E*)-**28**: δ = 13.9 (C-8), 14.1 (C-2′), 22.4 (C-7), 28.4, 31.3 and 31.4 (C-4, C-5, C-6), 62.0 (C-1′), 111.0 (C-2), 148.7 (C-3), 163.0 (C-1); (*Z*)-**28**: δ = 14.2 (C-2′), 27.2, 31.4 and 32.1 (C-4, C-5, C-6), 62.3 (C-1′), 146.3 (C-3).

MS (CI, 250 eV): *m*/*z* (%) = 249 (100, $[M + H]^+$).

Anal. Calcd for $C_{10}H_{17}BrO_2$ (249.1): C, 48.21; H, 6.88. Found: C, 47.97; H, 6.91.

Ethyl 2-Bromo-3-cyclohexylpropenoate (30)

According to the general olefination procedure, a 64:36 mixture of **6b**/**7b** [1.004 g, containing 60 wt% **6b**: 602.4 mg, 1.510 mmol, 0.83 equiv; 40 wt% **7b**: 401.6 mg, 840.2 μmol, 0.46 equiv (total: 1.3 equiv); 2.3 mmol **6b**/**7b** per g mixture], NaH (60% in mineral oil, 72.8 mg, 1.82 mmol, 1.0 equiv) and cyclohexanecarboxaldehyde (**29**; 220 μL, 203 mg, 1.82 mmol) were reacted for 45 min in THF (20 mL). Flash chromatography [∅ 3 cm, h 24 cm, cyclohexane–EtOAc, 5:1 (600 mL), 1–20 (20 mL), **30**: 5–9] provided the title compounds (*E*)-**30** and (*Z*)-**30** (464.8 mg, 98%, (*E*)-**30**:(*Z*)-**30** = 91:9) as a colorless oil. The *E*:*Z* ratio of **30** prior to chromatography was 91:9 according to ^{1}H NMR spectroscopy.

(*E*)-**30**

R_f = 0.59 (cyclohexane–EtOAc, 3:1).

IR (neat): 2980, 2930, 2855, 1725, 1610, 1450, 1370, 1340, 1240, 1215, 1145, 1095, 1025, 980, 945, 905, 755 cm^{-1}.

^{1}H NMR [499.9 MHz, $CDCl_3$; (*E*)-**30**:(*Z*)-**30** = 89:11]: δ = 1.08–1.32 (m, 5 H, 5 × cyclohexyl-H), superimposed in part by 1.34 (t, 3 H, $J_{2',1'}$ = 7.1 Hz, 2′-CH_3), 1.64–1.68 (m, 1 H, 1 × cyclohexyl-H), 1.71–1.77 (m, 4 H, 4 × cyclohexyl-H), 2.93 (dtt, 1 H, $J_{1'',3} = J_{1'',2''\text{-H(ax)}}$ = 10.8 Hz, $J_{1'',2''\text{-H(eq)}}$ = 3.5 Hz, 1″-H), 4.27 (q, 2 H, $J_{1',2'}$ = 7.1 Hz, 1′-CH_2), 6.47 (d, 1 H, $J_{3,1''}$ = 10.0 Hz, 3-H).

^{13}C NMR [125.7 MHz, $CDCl_3$; (*E*)-**30**:(*Z*)-**30** = 89:11]: δ = 14.0 (C-2′), 25.4, 25.7 and 32.1 (2 × C-2″, 2 × C-3″, C-4″), 40.4 (C-1″), 62.0 (C-1′), 109.9 (C-2), 153.1 (C-3), 163.0 (C-1).

MS (EI, 70 eV): *m*/*z* (%) = 260 (28, M^+), 67 (100).

HRMS (EI): *m*/*z* calcd for $C_{11}H_{17}BrO_2$ (M^+): 260.0412; found: 260.0412.

(*Z*)-**30**

R_f = 0.59 (cyclohexane–EtOAc, 3:1).

^{1}H NMR (400.1 MHz, $CDCl_3$): δ = 1.16–1.41 (m, 5 H, 5 × cyclohexyl-H), 1.33 (t, 3 H, $J_{2',1'}$ = 7.1 Hz, 2′-CH_3), 1.67–1.76 (m, 5 H, 5 × cyclohexyl-H), 2.57 (dtt, 1 H, $J_{1'',3} = J_{1'',2''\text{-H(ax)}}$ = 9.5 Hz, $J_{1'',2''\text{-H(eq)}}$ = 3.4 Hz, 1″-CH), 4.27 (q, 2 H, $J_{1',2'}$ = 7.1 Hz, 1′-CH_2), 7.09 (d, 1 H, $J_{3,1''}$ = 9.5 Hz, 3-H).

^{13}C NMR (100.6 MHz, $CDCl_3$): δ = 14.1 (C-2′), 25.3 and 30.7 (2 × C-2″, 2 × C-3″), 25.8 (C-4″), 41.2 (C-1″), 62.3 (C-1′), 114.3 (C-2), 150.3 (C-3), 162.8 (C-1).

Ethyl 2-Bromo-4-methylpent-2-enoate (32)

According to the general olefination procedure, a 64:36 mixture of **6b**/**7b** [926.6 mg, containing 60 wt% **6b**: 556.0 mg, 1.393 mmol, 0.83 equiv; 40 wt% **7b**: 370.6 mg, 775.4 μmol, 0.46 equiv (total: 1.3 equiv); 2.3 mmol **6b**/**7b** per g mixture], NaH (60% in mineral oil, 67.3 mg, 1.68 mmol, 1.0 equiv) and 2-methylpropionaldehyde (**31**; 160 μL, 121 mg, 1.68 mmol) were reacted for 30 min in THF (15 mL). Flash chromatography [∅ 3.5 cm, h 20 cm, cyclohexane–EtOAc, 40:1 (400 mL), 1–10 (20 mL), cyclohexane–EtOAc, 20:1 (400 mL), 11–30 (20 mL), fraction 1: 9–19, fraction 2: 21–23] provided the title compounds (*E*)-**32** and (*Z*)-**32** (fraction 1: 261.9 mg, 71%, (*E*)-**32**:(*Z*)-**32** = 97:3, fraction 2: 10.1 mg, 2.8%, (*E*)-**32**:(*Z*)-**32** = 13:87, total yield: 74%) as colorless oils. The *E*:*Z* ratio of **32** prior to chromatography was 94:6 according to ^{1}H NMR spectroscopy.

(*E*)-**32**

R_f = 0.32 (cyclohexane–EtOAc, 20:1).

IR (neat): 2970, 2935, 2870, 1700, 1615, 1465, 1370, 1345, 1295, 1220, 1170, 1145, 1095, 1030, 935, 890, 805, 755 cm^{-1}.

^{1}H NMR (300.1 MHz, $CDCl_3$): δ = 1.05 (d, 6 H, $J_{5,4}/J_{4\text{-Me},4}$ = 6.6 Hz, 5-CH_3, 4-CH_3), 1.34 (t, 3 H, $J_{2',1'}$ = 7.1 Hz, 2′-CH_3), 3.23 (dqq, 1 H, $J_{4,3}$ = 10.2 Hz, $J_{4,5} = J_{4,4\text{-Me}}$ = 6.6 Hz, 4-H), 4.27 (q, 2 H, $J_{1',2'}$ = 7.1 Hz, 1′-CH_2), 6.44 (d, 1 H, $J_{3,4}$ = 10.1 Hz, 3-H).

^{13}C NMR (125.7 MHz, $CDCl_3$): δ = 14.0 (C-2′), 22.1 (C-5, 4-CH_3), 30.8 (C-4), 62.0 (C-1′), 109.5 (C-2), 154.3 (C-3), 163.0 (C-1).

MS (EI, 70 eV): *m*/*z* (%) = 220 (42, M^+), 192 (44), 59 (100).

Anal. Calcd for $C_8H_{13}BrO_2$ (221.1): C, 43.46; H, 5.93. Found: C, 43.15; H, 5.81.

(*Z*)-**32**

R_f = 0.27 (cyclohexane–EtOAc, 20:1).

^{1}H NMR (499.9 MHz, $CDCl_3$): δ = 1.09 (d, 6 H, $J_{5,4}/J_{4\text{-Me},4}$ = 6.7 Hz, 5-CH_3, 4-CH_3), 1.34 (t, 3 H, $J_{2',1'}$ = 7.1 Hz, 2′-CH_3), 2.86 (dqq, 1 H, $J_{4,3}$ = 9.3 Hz, $J_{4,5}$ = $J_{4,4\text{-Me}}$ = 6.7 Hz, 4-H), 4.27 (q, 2 H, $J_{1',2'}$ = 7.1 Hz, 1′-CH_2), 7.08 (d, 1 H, $J_{3,4}$ = 9.4 Hz, 3-H).

^{13}C NMR (125.7 MHz, $CDCl_3$): δ = 14.2 (C-2′), 20.9 (C-5, 4-CH_3), 31.7 (C-4), 62.4 (C-1′), 114.2 (C-2), 151.9 (C-3), 162.7 (C-1).

Ethyl 2-Bromo-4,4-dimethylpent-2-enoate (34)

According to the general olefination procedure, a 64:36 mixture of **6b**/**7b** [911.8 mg, containing 60 wt% **6b**: 547.1 mg, 1.371 mmol, 0.83 equiv; 40 wt% **7b**: 364.7 mg, 763.0 μmol, 0.46 equiv (total: 1.3 equiv); 2.3 mmol **6b**/**7b** per g mixture], NaH (60% in mineral oil, 66.1 mg, 1.65 mmol, 1.0 equiv) and pivalaldehyde (**33**; 180 μL, 142 mg, 1.65 mmol) were reacted for 7 h in THF (15 mL). Flash chromatography [∅ 3.5 cm, h 21 cm, cyclohexane–EtOAc, 40:1 (500 mL), 1–15 (20 mL), cyclohexane–EtOAc, 20:1 (400 mL), 16–30 (20 mL), **34**: 10–18] provided the title compounds (*E*)-**34** and (*Z*)-**34** [119.5 mg, 31%, (*E*)-**34**:(*Z*)-**34** = 97:3] as a colorless oil. The *E*:*Z* ratio of **34** prior to chromatography was 97:3 according to ^{1}H NMR spectroscopy; R_f = 0.30 (cyclohexane–EtOAc, 20:1).

IR (neat): 2965, 2910, 2870, 1730, 1635, 1480, 1465, 1370, 1340, 1225, 1195, 1095, 1040, 1025, 895, 695 cm^{-1}.

^{1}H NMR [499.9 MHz, $CDCl_3$; (*E*)-**34**:(*Z*)-**34** = 97:3]: (*E*)-**34**: δ = 1.12 (s, 9 H, 5-CH_3, 2 × 4-CH_3), 1.34 (t, 3 H, $J_{2',1'}$ = 7.1 Hz, 2′-CH_3), 4.26 (q, 2 H, $J_{1',2'}$ = 7.1 Hz, 1′-CH_2), 6.17 (s, 1 H, 3-H); (*Z*)-**34**: δ = 1.27 (s, 9 H, 5-CH_3, 2 × 4-CH_3), 1.33 (t, 3 H, $J_{2',1'}$ = 7.1 Hz, 2′-CH_3), 4.43 (q, 2 H, $J_{1',2'}$ = 7.1 Hz, 1′-CH_2), 7.45 (s, 1 H, 3-H).

^{13}C NMR [125.7 MHz, $CDCl_3$; (*E*)-**34**:(*Z*)-**34** = 97:3]: (*E*)-**34**: δ = 13.8 (C-2′), 29.2 (C-5, 2 × 4-CH_3), 36.1 (C-4), 62.0 (C-1′), 107.3 (C-2), 147.3 (C-3), 165.2 (C-1); (*Z*)-**34**: δ = 28.8 (C-5, 2 × 4-CH_3), 62.5 (C-1′), 153.7 (C-3).

MS (EI, 70 eV): *m*/*z* (%) = 234 (27, M^+), 219 (16), 109 (100).

Anal. Calcd for $C_9H_{15}BrO_2$ (235.1): C, 45.98; H, 6.43. Found: C, 45.76; H, 6.41.

Ethyl (4*S*,5*S*)-2-Bromo-6-(*tert*-butyldimethylsiloxy)-4,5-dihydroxy-4,5-*O*,*O*-isopropylidenehex-2-enoate (36)

According to the general olefination procedure, a 57:32:9:2 mixture of **6b**/**7b**/**52**/**49** [2.226 g, containing 53.2 wt% **6b**: 1.184 g, 2.967 mmol, 0.68 equiv; 35.7 wt% **7b**: 794.7 mg, 1.663 mmol, 0.38 equiv; 9.4 wt% **52**: 209.5 mg, 466.0 μmol, 0.11 equiv; 1.7 wt% **49**: 37.8 mg, 107 μmol, 0.024 equiv (total: 1.2 equiv); 2.2 mmol **6b**/**7b**/**52**/**49** per g mixture], NaH (60% in mineral oil, 145.1 mg, 3.629 mmol, 0.83 equiv) and (2*R*,3*S*)-4-(*tert*-butyldimethylsiloxy)-2,3-dihydroxy-2,3-*O*,*O*-isopropylidenebutanal[26] (**35**; 1.200 g, 4.373 mmol) were reacted for 60 min in THF (30 mL). Flash chromatography [∅ 6 cm, h 22 cm, cyclohexane–EtOAc, 33:1 (3090 mL), 1–18 (120 mL), cyclohexane–EtOAc, 20:1 (2100 mL), 19–38 (120 mL), (*E*)-**36** and 2-chloro-2-debromo-**36**: 15–23] provided the title compound (*E*)-**36** and its chlorine analogue (1.295 g, 70%, (*E*)-**36**:2-chloro-2-debromo-**36** = 96:4 mol:mol) as a colorless oil. The *E*:*Z* ratio of **36** prior to chromatography was 93:7 according to ^{1}H NMR spectroscopy.

A specimen of pure (*Z*)-**36** (for comparison) and a chlorine-free specimen of (*E*)-**36** (for the subsequent conversion into lactone **45**) were prepared as follows: To a solution of phosphonate **4b** (298 mg, 984 μmol, 1.5 equiv) in THF (5 mL) NaH (60% in mineral oil, 44.6 mg, 1.12 mmol, 1.7 equiv) was added portionwise at 0 °C during a period of 5 min. After 10 min at 0 °C, the gas evolution had ceased and (2*R*,3*S*)-4-(*tert*-butyldimethylsiloxy)-2,3-dihydroxy-2,3-*O*,*O*-isopropylidenebutanal[26] (**35**; 180 mg, 656 mol) in THF (2 mL) was added. The reaction mixture was stirred for 90 min, while a white precipitate was formed. H_2O (5 mL) was added and the mixture was extracted with MTBE (3 × 10 mL). The combined extracts were dried (Na_2SO_4) and the solvents were evaporated under reduced pressure. The residue was purified by flash chromatography [∅ 4 cm, h 25 cm, cyclohexane–EtOAc, 20:1 (1050 mL), 1–11 (50 mL), cyclohexane–EtOAc, 10:1 (1100 mL), 12–36 (50 mL), (*E*)-**36**: 9–17, (*Z*)-**36**: 23–27]. The products [(*E*)-**36**: 74.5 mg, 27%; (*Z*)-**36**: 145.4 mg, 52%, total: 79%] were obtained as colorless oils. The *E*:*Z* ratio of **36** prior to chromatography was 36:64 according to ^{1}H NMR spectroscopy.

(*E*)-**36**

R_f = 0.42 (cyclohexane:EtOAc 5:1); $[\alpha]_D^{20}$ –5.9 (*c* = 1.17, $CHCl_3$).

IR (neat): 2985, 2960, 2930, 2860, 1720, 1625, 1460, 1370, 1300, 1255, 1215, 1170, 1145, 1100, 1025, 945, 835, 785 cm^{-1}.

^{1}H NMR (500.0 MHz, $CDCl_3$): δ = 0.06 and 0.07 [2 s, 3 H each, $Si(CH_3)_2$], 0.89 [s, 9 H, $SiC(CH_3)_3$], 1.34 (t, 3 H, $J_{2',1'}$ = 7.1 Hz, 2′-CH_3), 1.42 and 1.43 [2 s, 6 H, $C(CH_3)_2$], AB signal (δ_A = 3.78, δ_B = 3.80, 2 H, $^2J_{AB}$ = 11.1 Hz, split by $J_{A,5}$ = 5.1 Hz, $J_{B,5}$ = 4.2 Hz, 6-CH_2), 3.85 (ddd, 1 H, $J_{5,4}$ = 7.7 Hz, $J_{5,6(A)}$ = $J_{5,6(B)}$ = 4.5 Hz, 5-H), 4.27 (q, 2 H, $J_{1',2'}$ = 7.1 Hz, 1′-CH_2), 5.06 (dd, 1 H, $J_{4,3}$ = $J_{4,5}$ = 8.2 Hz, 4-H), 6.59 (d, 1 H, $J_{3,4}$ = 8.8 Hz, 3-H).

^{13}C NMR (125.7 MHz, $CDCl_3$): δ = –5.39 and –5.37 [$Si(CH_3)_2$], 14.0 (C-2′), 18.3 [Si*C*$(CH_3)_3$], 25.9 [SiC(*C*$H_3)_3$], 26.98 and 27.02 [C(*C*$H_3)_2$], 62.5 (C-1′), 63.0 (C-6), 75.3 (C-4), 81.5 (C-5), 110.2 [*C*$(CH_3)_2$], 115.3 (C-2), 143.3 (C-3), 162.3 (C-1).

MS (APCI): *m*/*z* (%) = 440 (42, $[M + H_2O]^+$), 423 (72, $[M + H]^+$), 365 (100).

Anal. Calcd for $C_{17}H_{31}BrO_5Si$ (423.4): C, 48.22; H, 7.38. Found: C, 48.46; H, 7.28.

(*Z*)-**36**

R_f = 0.32 (cyclohexane–EtOAc, 5:1); $[\alpha]_D^{20}$ –5.0 (*c* = 1.17, $CHCl_3$).

IR (neat): 2980, 2935, 2850, 1730, 1635, 1600, 1465, 1370, 1255, 1170, 1140, 1085, 1030, 840, 780 cm^{-1}.

^{1}H NMR (500.0 MHz, $CDCl_3$): δ = 0.07 and 0.08 [2 s, 3 H each, $Si(CH_3)_2$], 0.90 [s, 9 H, $SiC(CH_3)_3$], 1.34 (t, 3 H, $J_{2',1'}$ = 7.1 Hz, 2′-CH_3), 1.45 [s, 6 H, $C(CH_3)_2$], AB signal (δ_A = 3.76, δ_B = 3.84, 2 H, $^2J_{AB}$ = 11.1 Hz, split by $J_{A,5}$ = 4.0 Hz, $J_{B,5}$ = 4.0 Hz, 6-CH_2), 3.91 (ddd, 1 H, $J_{5,4}$ = 7.8 Hz, $J_{5,6(A)}$ = $J_{5,6(B)}$ = 3.9 Hz, 5-H), 4.30 (m_c, 2 H, 1′-CH_2), 4.90 (dd, 1 H, $J_{4,3}$ = $J_{4,5}$ = 8.1 Hz, 4-H), 7.26 (d, 1 H, $J_{3,4}$ = 8.3 Hz, 3-H).

^{13}C NMR (125.7 MHz, $CDCl_3$): δ = –5.5 and –5.4 [$Si(CH_3)_2$], 14.1 (C-2′), 18.3 [Si*C*$(CH_3)_3$], 25.9 [SiC(*C*$H_3)_3$], 26.9 and 27.0 [C(*C*$H_3)_2$], 62.3 (C-6), 62.8 (C-1′), 76.8 (C-4), 81.3 (C-5), 110.5 [*C*$(CH_3)_2$], 118.5 (C-2), 142.0 (C-3), 161.9 (C-1).

MS (APCI): *m*/*z* (%) = 440 (100, $[M + H_2O]^+$), 423 (30, $[M + H]^+$), 365 (14).

Anal. Calcd for $C_{17}H_{31}BrO_5Si$ (423.4): C, 48.22; H, 7.38. Found: C, 48.79; H, 7.45.

Ethyl (4*S*,5*S*,6*E*)-2-Bromo-4,5-dihydroxy-4,5-*O*,*O*-isopropylidene-7-(methoxycarbonyl)-6-methylhepta-2,6-dienoate (38)

According to the general olefination procedure, a 57:32:9:2 mixture of **6b**/**7b**/**52**/**49** [1.740 g, containing 53.2 wt% **6b**: 925.7 mg, 2.230 mmol, 0.71 equiv; 35.7 wt% **7b**: 621.2 mg, 1.280 mmol, 0.41 equiv; 9.4 wt% **52**: 163.6 mg, 364.3 μmol, 0.12 equiv; 1.7 wt% **49**: 29.6 mg, 83.6 μmol, 0.026 equiv (total: 1.2 equiv); 2.2 mmol **6b**/**7b**/**52**/**49** per g mixture], NaH (60% in mineral oil, 105.0 mg, 2.625 mmol, 0.83 equiv) and methyl (2*E*,4*S*,5*R*)-4,5-dihydroxy-4,5-*O*,*O*-isopropylidene-3-methyl-6-oxohex-2-enoate[27] (**37**; 720.0 mg, 3.155 mmol) were reacted for 30 min in THF (30 mL). Flash chromatography [∅ 5 cm, h 22 cm, cyclohexane–EtOAc, 15:1 (3200 mL), 1–19 (120 mL), cyclohexane–EtOAc, 12:1 (975 mL), 20–27 (120 mL), **38** and 2-chloro-2-debromo-**38**: 12–19] provided the title compounds (2*E*)-**38** and (2*Z*)-**38** and their chlorine analogue (888.9 mg, 75%, (2*E*)-**38**:2-chloro-2-debromo-**38**:(2*Z*)-**38** = 87:10:3

mol:mol:mol) as a colorless oil. The *E*:*Z* ratio of **38** prior to chromatography was 95:5 according to ^{1}H NMR spectroscopy.

A specimen of pure (*Z*)-**38** and a chlorine-free specimen of (*E*)-**38** were prepared in analogy to the second procedure described for preparing compound **36**.

(2*E*)-**38**

R_f = 0.31 (cyclohexane–EtOAc, 5:1); $[\alpha]_D^{20}$ –30.6 (*c* = 0.75, $CHCl_3$).

IR (neat): 2990, 2950, 1720, 1660, 1630, 1435, 1370, 1295, 1225, 1160, 1080, 1045, 895, 865, 830 cm^{-1}.

^{1}H NMR (500.0 MHz, $CDCl_3$): δ = 1.29 (t, 3 H, $J_{2',1'}$ = 7.1 Hz, 2′-CH_3), 1.46 and 1.47 [2 s, 3 H each, $C(CH_3)_2$], 2.15 (d, 3 H, $^4J_{6\text{-Me},7}$ = 1.4 Hz, 6-CH_3), 3.70 (s, 3 H, OCH_3), 4.15 (hardly resolved dd, 1 H, $J_{5,4}$ = 8.2 Hz, $^4J_{5,7}$ = 0.8 Hz, 5-H), 4.22 (q, 2 H, $J_{1',2'}$ = 7.1 Hz, 1′-CH_2), 5.08 (dd, 1 H, $J_{4,5}$ = $J_{4,3}$ = 8.5 Hz, 4-H), 5.96 (qd, 1 H, $^4J_{7,6\text{-Me}}$ = $^4J_{7,5}$ = 1.3 Hz, 7-H), 6.61 (d, 1 H, $J_{3,4}$ = 8.8 Hz, 3-H).

^{13}C NMR (125.7 MHz, $CDCl_3$): δ = 13.9 (C-2′), 14.5 (6-CH_3), 26.7 and 27.0 [C(*C*H_3)$_2$], 51.1 (OCH_3), 62.8 (C-1′), 76.9 (C-4), 84.3 (C-5), 110.7 [*C*(CH_3)$_2$], 116.3 (C-2), 117.1 (C-7), 142.1 (C-3), 153.0 (C-6), 162.0 (C-1), 166.5 (7-C=O).

MS (CI, 40 eV): *m*/*z* (%) = 377 (28, $[M + H]^+$), 318 (100).

Anal. Calcd for $C_{15}H_{21}BrO_6$ (377.2): C, 47.76; H, 5.61. Found: C, 47.81; H, 5.76.

(2*Z*)-**38**

R_f = 0.25 (cyclohexane–EtOAc, 5:1).

IR (neat): 2980, 2925, 2855, 1730, 1715, 1650, 1560, 1535, 1495, 1455, 1370, 1260, 1220, 1160, 1080, 1045, 1035, 875, 820 cm^{-1}.

^{1}H NMR (500.0 MHz, $CDCl_3$): δ = 1.35 (t, 3 H, $J_{2',1'}$ = 7.2 Hz, 2-CH_3), 1.49 and 1.51 [2 s, 3 H each, $C(CH_3)_2$], 2.19 (d, 3 H, $^4J_{6\text{-Me},7}$ = 1.4 Hz, 6-CH_3), 3.72 (s, 3 H, OCH_3), 4.26 (dd, 1 H, $J_{5,4}$ = 8.2 Hz, $^4J_{5,7}$ = 0.8 Hz, 5-H), 4.31 (m_c, 2 H, 1′-CH_2), 4.73 (dd, 1 H, $J_{4,5}$ = $J_{4,3}$ = 8.2 Hz, 4-H), 6.01 (qd, 1 H, $^4J_{7,6\text{-Me}}$ = $^4J_{7,5}$ = 1.3 Hz, 7-H), 7.26 (d, 1 H, $J_{3,4}$ = 8.8 Hz, 3-H).

^{13}C NMR (125.7 MHz, $CDCl_3$): δ = 14.1 (C-2′), 14.4 (6-CH_3), 26.7 and 26.9 [C(*C*H_3)$_2$], 51.2 (OCH_3), 63.0 (C-1′), 78.9 (C-4), 84.0 (C-5), 111.2 [*C*(CH_3)$_2$], 117.6 (C-7), 120.0 (C-2), 140.4 (C-3), 152.6 (C-6), 161.6 (C-1), 166.4 (7-C=O).

MS (CI, 40 eV): *m*/*z* (%) = 394 (100, $[M + NH_4]^+$), 377 (24, $[M + H]^+$).

HRMS (EI): *m*/*z* calcd for $C_{14}H_{18}BrO_6$ ($[M - CH_3]^+$): 361.0287; found: 361.0288.

Ethyl (2*E*,4*S*,5*S*,6*E*,8*E*)-2-Bromo-4,5-dihydroxy-4,5-*O*,*O*-isopropylidene-9-(methoxycarbonyl)-6-methylnona-2,6,8-trienoate (40)

According to the general olefination procedure, a 57:32:9:2 mixture of **6b**/**7b**/**52**/**49** [1.057 g, containing 53.2 wt% **6b**: 562.3 mg, 1.409 mmol, 0.71 equiv; 35.7 wt% **7b** : 377.3 mg, 789.4 μmol, 0.40 equiv; 9.4 wt% **52**: 99.4 mg, 221 μmol, 0.11 equiv; 1.7 wt% **49**: 18.0 mg, 50.7 μmol, 0.025 equiv (total: 1.2 equiv); 2.2 mmol **6b**/**7b**/**52**/**49** per g mixture], NaH (60% in mineral oil, 63.8 mg, 1.59 mmol, 0.80 equiv) and methyl (2*E*,4*E*,6*S*,7*R*)-6,7-dihydroxy-6,7-*O*,*O*-isopropylidene-5-methyl-8-oxoocta-2,4-dienoate[27] (**39**; 506.8 mg, 1.993 mmol) were reacted for 90 min in THF (25 mL). Flash chromatography [∅ 5.5 cm, h 20 cm, cyclohexane–EtOAc, 10:1 (3300 mL), 1–26 (100 mL), **40** and 2-chloro-2-debromo-**40**: 11–22] provided the title compound **40** and its chlorine analogue (651.1 mg, 81%, **40**:2-chloro-2-debromo-**40** = 93:7 mol:mol) as a colorless oil. The *E*:*Z* ratio of **40** prior to chromatography was 98:2 according to ^{1}H NMR spectroscopy; R_f = 0.65 (cyclohexane–EtOAc, 1:1); $[\alpha]_D^{20}$ –17.4 (*c* = 0.96, $CHCl_3$).

IR (neat): 2985, 2940, 1715, 1645, 1615, 1435, 1370, 1310, 1275, 1220, 1165, 1040, 1025, 980, 825, 665 cm^{-1}.

^{1}H NMR (500.0 MHz, $CDCl_3$): δ = 1.27 (t, 3 H, $J_{2',1'}$ = 7.1 Hz, 2′-CH_3), 1.46 and 1.48 [2 s, 3 H each, $C(CH_3)_2$], 1.93 (d, 3 H, $^4J_{6\text{-Me},7}$ = 1.2 Hz, 6-CH_3), 3.75 (s, 3 H, OCH_3), 4.18 (br d, 1 H, $J_{5,4}$ = 8.2 Hz, 5-H), 4.19 (q, 2 H, $J_{1',2'}$ = 7.1 Hz, 1′-CH_2), 5.11 (dd, 1 H, $J_{4,5}$ = $J_{4,3}$ = 8.4 Hz, 4-H), 5.90 (d, 1 H, $^3J_{9,8}$ = 15.2 Hz, 9-H), 6.22 (dm_c, 1 H, $J_{7,8}$ = ca. 11.7 Hz, 7-H), 6.60 (d, 1 H, $J_{3,4}$ = 8.5 Hz, 3-H), 7.56 (dd, 1 H, $J_{8,9}$ = 15.2 Hz, $J_{8,7}$ = 11.5 Hz, 8-H).

^{13}C NMR (125.7 MHz, $CDCl_3$): δ = 12.9 (6-CH_3), 13.9 (C-2′), 26.8 and 27.0 [C(*C*H_3)$_2$], 51.6 (OCH_3), 62.7 (C-1′), 76.5 (C-4), 84.9 (C-5), 110.4 [*C*(CH_3)$_2$], 115.6 (C-2), 121.8 (C-9), 125.5 (C-7), 139.5 (C-8), 142.5 (C-6), 142.7 (C-3), 162.0 (C-1), 167.5 (9-C=O).

MS (EI, 70 eV): *m*/*z* (%) = 387 (10, $[M - CH_3]^+$), 192 (100).

Anal. Calcd for $C_{17}H_{23}BrO_6$ (403.3): C, 50.63; H, 5.75. Found: C, 50.62; H, 5.81.

Ethyl (2*E*,4*S*)-4-[(Benzyloxy)carbonylamino]-2-bromo-5-methylhex-2-enoate (42)

According to the general olefination procedure, a 64:36 mixture of **6b**/**7b** [360.3 mg, containing 60 wt% **6b**: 216.2 mg, 542.6 μmol, 0.83 equiv; 40 wt% **7b**: 144.1 mg, 301.5 μmol, 0.46 equiv (total: 1.3 equiv); 2.3 mmol **6b**/**7b** per g mixture], NaH (60% in mineral oil, 26.1 mg, 653 μmol, 1.0 equiv) and (*S*)-2-(benzyloxycarbonylamino)-3-methylbutanal[28] (**41**; 153.1 mg, 653.3 μmol) were reacted for 3.5 h in THF (10 mL). Flash chromatography [∅ 2.5 cm, h 18 cm, cyclohexane–EtOAc 5:1 (500 mL), 1–15 (20 mL), cyclohexane–EtOAc 4:1 (500 mL), 16–40 (20 mL), (*E*)-**42**: 10–17, unreacted **6b**/**7b**: 18–21] provided the title compound (*E*)-**42** (212.5 mg, 85%) as a colorless oil. (*Z*)-**42** was not detected; R_f = 0.65 (cyclohexane–EtOAc 1:1); $[\alpha]_D^{20}$ +18.6 (*c* = 0.81, $CHCl_3$).

IR (neat): 3330, 2965, 2875, 1720, 1615, 1530, 1455, 1390, 1370, 1300, 1215, 1100, 1020, 905, 775, 740, 700 cm^{-1}.

^{1}H NMR (499.9 MHz, 263 K, $CDCl_3$, major:minor rotamer = 80:20): major rotamer: δ = 0.96 and 0.965 (2 d, 3 H each, $J_{5\text{-Me},5}$/$J_{6,5}$ = 6.8/6.9 Hz, 5-CH_3, 6-CH_3), 1.37 (t, 3 H, $J_{2',1'}$ = 7.1 Hz, 2′-CH_3), 1.90 (dqq, 1 H, $J_{5,4}$ = $J_{5,5\text{-Me}}$ = $J_{5,6}$ = 6.8 Hz, 5-H), 4.31 (q, 2 H, $J_{1',2'}$ = 7.1 Hz, 1′-CH_2), 4.86 (ddd, 1 H, $J_{4,3}$ = $J_{4,NH}$ = 9.1 Hz, $J_{4,5}$ = 6.6 Hz, 4-H), 4.99 (d, 1 H, $J_{NH,4}$ = 8.8 Hz, NH), 5.08 (s, 2 H, benzyl-CH_2), 6.48 (d, 1 H, $J_{3,4}$ = 9.5 Hz, 3-H), 7.30–7.41 (m, 5 H, Ar-H); minor rotamer: δ = 0.94 and 0.972 (2 d, 3 H each, $J_{5\text{-Me},5}$/$J_{6,5}$ = ca. 7.0 Hz, 6-CH_3, 5-CH_3), 1.16 (t, 3 H, $J_{2',1'}$ = 7.1 Hz, 2′-CH_3), 1.76 (dqq, 1 H, $J_{5,4}$ = $J_{5,5\text{-Me}}$ = $J_{5,6}$ = 6.8 Hz, 5-H), 3.97–4.03 (m, 2 H, 1′-H_2), 4.79–4.84 (m, 1 H, 4-H), 4.94 (d, 1 H, $J_{NH,4}$ = 8.8 Hz, NH), 5.09 (s, 2 H, benzyl-CH_2), 6.41 (d, 1 H, $J_{3,4}$ = 9.7 Hz, 3-H), 7.30–7.41 (m, 5 H, Ar-H).

^{13}C NMR (125.7 MHz, 263 K, $CDCl_3$, major:minor rotamer = 80:20): major rotamer: δ = 14.0 (C-2′), 18.1 and 19.0 (5-CH_3, C-6), 32.2 (C-5), 56.0 (C-4), 62.6 (C-1′), 66.9 (benzyl-CH_2), 113.3 (C-2), 128.3 (3 × CH_{arom}), 128.5 (2 × CH_{arom}), 135.9 (C_{ipso}), 146.3 (C-3), 155.6 (carbamate-CO), 162.4 (C-1); minor rotamer: δ = 13.8 (C-2′), 18.3 and 18.9 (5-CH_3, 6-C), 32.1 (C-5), 56.6 (C-4), 62.4 (C-1′), 67.1 (benzyl-CH_2), 112.9 (C-2), 127.8 (2 × CH_{arom}), 128.0 (C_{para}), 128.4 (2 × CH_{arom}), 135.8 (C_{ipso}), 146.9 (C-3), 156.1 (carbamate-CO), 162.2 (C-1).

MS (EI, 70 eV): *m*/*z* (%) = 383 (7, M^+), 340 (16), 91 (100).

Anal. Calcd for $C_{17}H_{22}BrNO_4$ (384.2): C, 53.14; H, 5.77; N, 3.65. Found: C, 53.16; H, 5.77; N, 3.56.

Ethyl (2*E*,5*S*)-5-[(Benzyloxy)carbonylamino]-2-bromo-6-methylhept-2-enoate (44)

According to the general olefination procedure, a 64:36 mixture of **6b**/**7b** [336.7 mg, containing 60 wt% **6b**: 202.0 mg, 506.3 μmol, 0.83 equiv; 40 wt% **7b**: 134.7 mg, 281.8 μmol, 0.46 equiv (total: 1.3

equiv); 2.3 mmol **6b**/**7b** per g mixture], NaH (60% in mineral oil, 24.4 mg, 611 μmol, 1.0 equiv) and (*R*)-3-(benzyloxycarbonylamino)-4-methylpentanal[29] (**43**; 152.2 mg, 610.5 μmol) were reacted for 30 min in THF (10 mL). Flash chromatography [∅ 2.5 cm, h 17 cm, cyclohexane–EtOAc 4:1 (600 mL), 1–20 (20 mL), cyclohexane–EtOAc 3:1 (200 mL), 21–30 (20 mL), (*E*)-**44**: 9–13, (*Z*)-**44** and unreacted **7b**: 14–18, unreacted **6b**: 22–25] provided the title compound (*E*)-**44** (204.9 mg, 84%) as a white solid. The *E*:*Z* ratio of **44** prior to chromatography was 93:7 according to ^{1}H NMR spectroscopy; R_f = 0.59 (cyclohexane–EtOAc, 1:1); mp 60–62 °C; $[\alpha]_D^{20}$ –54.5 (*c* = 1.17, $CHCl_3$).

IR (neat): 3310, 2960, 1705, 1690, 1540, 1365, 1340, 1310, 1230, 1115, 1025, 915, 750, 695 cm^{-1}.

^{1}H NMR (499.9 MHz, $CDCl_3$): δ = 0.91 and 0.93 (2 d, 3 H each, $J_{6\text{-Me},6}/J_{7,6}$ = 6.8/6.9 Hz, 6-CH_3, 7-CH_3), 1.32 (t, 3 H, $J_{2',1'}$ = 7.1 Hz, 2′-CH_3), 1.79 (dqq, 1 H, $J_{6,5} = J_{6,6\text{-Me}} = J_{6,7}$ = 6.6 Hz, 6-H), AB signal (δ_A = 2.55, δ_B = 2.73, 2 H, $^2J_{AB}$ = 15.1 Hz, split by $J_{A,3}$ = 7.1 Hz, $J_{A,5}$ = 4.3 Hz, $J_{B,5} = J_{B,3}$ = 9.5 Hz, 4-CH_2), 3.67 (dddd, 1 H, $J_{5,4\text{-H(B)}} = J_{5,NH}$ = 9.5 Hz, $J_{5,6} = J_{5,4\text{-H(A)}}$ = 4.8 Hz, 5-H), 4.24 (q, 2 H, $J_{1',2'}$ = 7.1 Hz, 1′-CH_2), 4.92 (br d, 1 H, $J_{NH,5}$ = 9.5 Hz, NH), AB signal (δ_A = 5.07, δ_B = 5.12, 2 H, $^2J_{AB}$ = 12.4 Hz, benzyl-CH_2), 6.69 (dd, 1 H, $J_{3,\ 4\text{-H(B)}}$ = 8.7 Hz, $J_{3,\ 4\text{-H(A)}}$ = 7.3 Hz, 3-H), 7.29–7.38 (m, 5 H, Ar-H).

^{13}C NMR (125.7 MHz, $CDCl_3$): δ = 14.0 (C-2′), 17.8 and 18.9 (C-7, 6-CH_3), 32.4 (C-6), 33.9 (C-4), 55.7 (C-5), 62.3 (C-1′), 66.6 (benzyl-CH_2), 112.8 (C-2), 127.9, 128.0 and 128.5 (5 × CH_{arom}), 136.6 (C_{ipso}), 145.1 (C-3), 156.4 (carbamate-CO), 163.1 (C-1).

MS (EI, 70 eV): *m*/*z* (%) = 397 (0.1, M^+), 354 (1), 91 (100).

Anal. Calcd for $C_{18}H_{24}BrNO_4$ (398.3): C, 54.28; H, 6.07; N, 3.52. Found: C, 54.23; H, 6.02; N, 3.62.

(5*S*)-3-Bromo-5-[(1*S*)-1,2-dihydroxyethyl]-2(5*H*)-furanone (45)

To a solution of bromoacrylate (*E*)-**36** (isomerically pure, chlorine-free; 219.5 mg, 518.4 μmol) in MeOH (10 mL) was added *p*-toluenesulfonic acid monohydrate (20.0 mg, 105 μmol, 20 mol%) was added. The mixture was refluxed for 10 min. After cooling to r.t., the mixture was evaporated under reduced pressure. The crude product was separated from the catalyst by flash chromatography [∅ 2.5 cm, h 17 cm, cyclohexane–EtOAc, 1:2 (600 mL), 1–20 (20 mL), cyclohexane–EtOAc, 1:3 (600 mL), 21–40 (20 mL), **45**: 21–36] and the product (115.5 mg, 99%) was obtained as a white solid; R_f = 0.25 (EtOAc); mp 107–109 °C; $[\alpha]_D^{20}$ –20.5 (*c* = 1.12, $CHCl_3$).

IR (neat): 3420, 3090, 2930, 2885, 1770, 1605, 1560, 1455, 1260, 1160, 1105, 1025, 980, 880 cm^{-1}.

^{1}H NMR (500.0 MHz, $CDCl_3$): δ = 1.82 (br s, 2 H, 2 × OH), AB signal (δ_A = 3.79, δ_B = 3.84, 2 H, $^2J_{AB}$ = 11.4 Hz, split by $J_{A,1'}$ = 5.1 Hz, $J_{B,1'}$ = 4.5 Hz, 2′-CH_2), 3.91 (ddd, 1 H, $J_{1',2''\text{-H(A)}} = J_{1',2''\text{-H(B)}} = J_{1',5}$ = 4.8 Hz, 1′-H), 5.11 (dd, 1 H, $J_{5,1'}$ = 4.7 Hz, $J_{5,4}$ = 1.7 Hz, 5-H), 7.58 (d, 1 H, $J_{4,5}$ = 1.9 Hz, 4-H).

^{13}C NMR (125.7 MHz, $CDCl_3$): δ = 62.8 (C-2′), 71.6 (C-1′), 83.4 (C-5), 113.9 (C-3), 149.8 (C-4), 168.0 (C-2).

MS (CI, 120 eV): *m*/*z* (%) = 223 (64, $[M + H]^+$), 205 (9), 69 (100).

Anal. Calcd for $C_6H_7BrO_4$ (223.0): C, 32.31; H, 3.16. Found: C, 33.06; H, 3.32.

Ethyl (2*E*,4*S*,5*S*)-6-(*tert*-Butyldimethylsiloxy)-2-[(2*Z*)-2-(2,2-dimethyl-6-methylenecyclohexylidene)ethylidene]-4,5-dihydroxy-4,5-*O*,*O*-isopropylidenehexanoate (*E*-48)

A suspension of $Pd_2dba_3{\cdot}CHCl_3$ (28.1 mg, 27.2 μmol, 10 mol%) and tri(2-furyl)phosphine (37.8 mg, 163 μmol, 60 mol%) in NMP (4 mL) was stirred under argon at r.t. for 30 min. After a clear yellow solution had formed, dienylstannane **46**[23] (155.1 mg, 353.1 μmol, 1.3 equiv) in NMP (4 mL) and bromoacrylate (*E*)-**36** (115.0 mg, 271.6 μmol) in NMP (4 mL) were added. The reaction mixture was then degassed by freezing with liquid nitrogen under vacuum and thawing under argon. After 3 degassing cycles, CuI (85.3 mg, 448 μmol, 1.65 equiv) was added and the mixture was stirred at r.t. for 27 h. The mixture was poured onto a sat. aq solution of NH_4Cl (20 mL) and extracted with EtOAc (3 × 60 mL). The combined extracts were washed with water (5 × 150 mL) to remove the high boiling solvent. The organic layer was dried (Na_2SO_4) and the solvent was evaporated under reduced pressure. After flash chromatography [∅ 4 cm, h 34 cm, cyclohexane–EtOAc, 25:1 (1040 mL), 1–25 (20 mL), cyclohexane–EtOAc, 20:1 (1575 mL), 26–85 (20 mL), (*E*)-**48**: 46–60, dba and P(2-furyl)$_3$: 74–85] compound (*E*)-**48** (90.4 mg, 68%) was obtained as a colorless oil; R_f = 0.21 (cyclohexane–EtOAc, 10:1); $[\alpha]_D^{20}$+45.2 (*c* = 1.05, $CHCl_3$).

IR (neat): 2955, 2930, 2860, 1700, 1620, 1460, 1380, 1370, 1250, 1200, 1170, 1145, 1095, 1010, 905, 840, 780 cm^{-1}.

^{1}H NMR (500.0 MHz, $CDCl_3$): δ = 0.05 and 0.06 [2 s, 3 H each, $Si(CH_3)_2$], 0.89 [s, 9 H, $SiC(CH_3)_3$], 1.10 and 1.12 [2 s, 6 H, 2″-$(CH_3)_2$], 1.29 (t, 3 H, $J_{2''',1'''}$ = 7.1 Hz, 2‴-CH_3), 1.36 and 1.41 [2 s, 3 H each, $C(CH_3)_2$], 1.51–1.54 (m, 2 H, 3″-CH_2), 1.68–1.74 (m, 2 H, 4″-CH_2), 2.21–2.30 (m, 2 H, 5″-CH_2), 2.78–2.80 (m, 2 H, 3-CH_2), AB signal (δ_A = 3.65, δ_B = 3.74, 2 H, $^2J_{AB}$ = 11.0 Hz, split by $J_{A,5}$ = 4.5 Hz, $J_{B,5}$ = 3.8 Hz, 6-CH_2), 3.78 (ddd, 1 H, $J_{5,4}$ = 7.9 Hz, $J_{5,6\text{-H(A)}} = J_{5,6\text{-H(B)}}$ = 4.0 Hz, 5-H), 4.07 (hardly resolved dt, 1 H, $J_{4,5}$ = 7.8 Hz, $J_{4,3}$ = 6.3 Hz, 4-H), 4.19 (q, 2 H, $J_{1''',2'''}$ = 7.1 Hz, 1‴-CH_2), 4.68 (d, 1 H, $^2J_{6''\ =CH(Z),6''\ =CH(E)}$ = 2.5 Hz, 6″ =CH^Z), 5.14 (dt, 1 H, $^2J_{6''\ =CH(E),6''\ =CH(Z)}$ = 2.5 Hz, $^4J_{6''\ =CH(E),5''}$ = 1.2 Hz, 6″ =CH^E), 6.34 (d, 1 H, $J_{2',1'}$ = 11.5 Hz, 2′-H), 7.72 (d, 1 H, $J_{1',2'}$ = 11.4 Hz, 1′-H).

^{13}C NMR (125.7 MHz, $CDCl_3$): δ = –5.4 and –5.3 (2 × $SiCH_3$), 14.3 (C-2‴), 18.4 [$SiC(CH_3)_3$], 23.1 (C-4″), 25.9 [$SiC(CH_3)_3$], 27.0 and 27.4 [$C(CH_3)_2$], 27.6 and 27.7 [2″-$(CH_3)_2$], 31.0 (C-3), 37.0 (C-5″), 38.9 (C-2″), 41.3 (C-3″), 60.4 (C-1‴), 63.3 (C-6), 76.9 (C-4), 81.6 (C-5), 108.6 [$C(CH_3)_2$], 115.0 (6″ =CH_2), 116.3 (C-2′), 125.4 (C-2), 139.3 (C-1′), 145.3, 160.9 and 168.4 (C-1, C-1″, C-6″).

MS (ESI): *m*/*z* (%) = 1007 (100, $[2 M + Na]^+$), 515 (58, $[M + Na]^+$).

HRMS (EI): *m*/*z* calcd for $C_{27}H_{45}O_5Si$ ($[M - CH_3]^+$): 477.3036; found: 477.3040.

Anal. Calcd for $C_{28}H_{48}O_5Si$ (492.8): C, 68.25; H, 9.82. Found: C, 67.70; H, 9.57.

Ethyl Chloro(diphenylphosphono)acetate (49) Separated from a 11:47:42 Mixture with Ethyl (Diphenylphosphono)acetate (9b) and Ethyl Dichloro(diphenylphosphono)acetate (50)

To a solution of phosphonate **9b** (642 mg, 2.00 mmol) in THF (10 mL) was added NaH (60% in mineral oil, 96.0 mg, 2.40 mmol, 1.2 equiv) portionwise at r.t. during a period of 5 min. After 10 min at r.t., the gas evolution had ceased and *N*-chlorosuccinimide (320 mg, 2.40 mmol, 1.2 equiv) was added in one portion. After 40 min, H_2O (20 mL) was added and the resulting mixture was extracted with MTBE (3 × 20 mL). The combined organic extracts were dried (Na_2SO_4) and evaporated under reduced pressure. The residue (712 mg) was separated by flash chromatography [∅ 3 cm, h 20 cm, cyclohexane–EtOAc, 5:1 (600 mL), 1–25 (20 mL), cyclohexane–EtOAc, 1:1 (300 mL), 26–40 (20 mL), **49**: 11–17, **50**: 21–26, **9b**: 28–30]. The products [**49**: 256.3 mg, 36%; **50**: 250.9 mg, 32%; recovered **9b**: 47.9 mg, 7.5%; total yield: 76%] were obtained as hygroscopic colorless oils.

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R_f = 0.53 (cyclohexane–EtOAc, 1:1).

IR (neat): 3070, 2985, 2940, 1760, 1590, 1495, 1370, 1285, 1180, 1025, 965, 760, 690 cm^{-1}.

^{1}H NMR (400.1 MHz, $CDCl_3$): δ = 1.28 (t, 3 H, $J_{2',1'}$ = 7.3 Hz, 2′-CH_3), 4.29 (q, 2 H, $J_{1',2'}$ = 7.3 Hz, 1′-CH_2), 4.79 (d, 1 H, $^2J_{2,P}$ = 15.9 Hz, 2-H), 7.19–7.30 (m, 6 H, Ar-H), 7.31–7.37 (m, 4 H, Ar-H).

^{13}C NMR (100.1 MHz, $CDCl_3$): δ = 13.9 (C-2′), 49.8 (d, $^1J_{2,P}$ = 149.7 Hz, C-2), 63.5 (C-1′), 120.48 and 120.51 (2 d, $^3J_{2'',P}$ = 3.6 Hz, 2 × 2 × C-2″), 125.76 and 125.82 (2 × C-4″), 129.8 and 129.9 (2 × 2 × C-3″), 150.0 and 150.1 (2 d, $^2J_{1'',P}$ = 8.7 Hz, 2 × C-1″), 163.9 (C-1).

^{31}P NMR (121.5 MHz, $CDCl_3$): δ = 4.96.

MS (EI, 70 eV): *m*/*z* (%) = 353 (100, M^+).

HRMS (EI): *m*/*z* calcd for $C_{16}H_{16}ClO_5P$ (M^+): 354.0424; found: 354.0434.

Ethyl 2-Chloro-3-(4-methoxyphenyl)propenoate (51)

To a solution of phosphonate **49** (204.2 mg, 575.7 μmol, 1.2 equiv) in THF (10 mL) was added NaH (60% in mineral oil, 96.0 mg, 2.40 mmol, 1.2 equiv) portionwise at 0 °C during a period of 5 min. After 10 min at 0 °C, the gas evolution had ceased and 4-methoxybenzaldehyde (58.1 μL, 65.3 mg, 480 μmol) was added. The reaction mixture was stirred for 50 min, while a white precipitate was formed. H_2O (10 mL) was added and the mixture was extracted with MTBE (3 × 20 mL). The combined extracts were dried (Na_2SO_4) and the solvents were evaporated under reduced pressure. The residue was purified by flash chromatography [∅ 3.5 cm, h 20 cm, cyclohexane–EtOAc, 12.5:1 (500 mL), 1–15 (20 mL), cyclohexane–EtOAc, 8:1 (340 mL), 16–35 (20 mL), **51**: 23–30], while the isomers could not be separated. The products [92.3 mg, 80%, (*E*)-**51**:(*Z*)-**51** = 94:6] were obtained as a colorless oil; R_f = 0.31 (cyclohexane–EtOAc, 5:1).

IR (neat): 2980, 1725, 1605, 1510, 1460, 1370, 1300, 1260, 1220, 1180, 1115, 1030, 830 cm^{-1}.

^{1}H NMR [499.9 MHz, $CDCl_3$; (*E*)-**51**:(*Z*)-**51** = 94:6]: (*E*)-**51**: δ = 1.24 (t, 3 H, $J_{2',1'}$ = 7.1 Hz, 2′-CH_3), 3.81 (s, 3 H, OCH_3), 4.24 (q, 2 H, $J_{1',2'}$ = 7.1 Hz, 1′-CH_2), 6.84–6.89 (m, 2 H, 2 × 3″-H), 7.13 (s, 1 H, 3-H), 7.29–7.32 (m, 2 H, 2 × 2″-H); (*Z*)-**51**: δ = 1.38 (t, 3 H, $J_{2',1'}$ = 7.1 Hz, 2′-CH_3), 3.85 (s, 3 H, OCH_3), 4.34 (q, 2 H, $J_{1',2'}$ = 7.1 Hz, 1′-CH_2), 6.93–6.96 (m_c, 2 H, 2 × 3″-H), 7.84–7.87 (m_c, 2 H, 2 × 2″-H), superimposed by 7.85 (s, 1 H, 3-H).

^{13}C NMR [125.7 MHz, $CDCl_3$; (*E*)-**51**:(*Z*)-**51** = 94:6]: (*E*)-**51**: δ = 13.8 (C-2′), 55.3 (OCH_3), 62.1 (C-1′), 113.7 (2 × C-3″), 120.8 (C-2), 126.2 (C-1″), 130.5 (2 × C-2″), 137.2 (C-3), 160.2 and 163.7 (C-4″, C-1); (*Z*)-**51**: δ = 14.2 (C-2′), 55.3 (OCH_3), 62.4 (C-1′), 114.0 (2 × C-3″), 132.7 (2 × C-2″), 136.4 (C-3), 161.1 (C-4″ or C-1).

MS (EI, 70 eV): *m*/*z* (%) = 240 (100, M^+).

Anal. Calcd for $C_{12}H_{13}ClO_3$ (240.7): C, 59.88; H, 5.44. Found: C, 59.83; H, 5.58.

Ethyl Bromochloro(diphenylphosphono)acetate (52)

This compound arose as a contaminant in some preparations of ethyl bromo(diphenylphosphono)acetate (**6b**)/dibromo(diphenylphosphono)acetate (**7b**) (as mentioned above).

MS (EI, 70 eV): *m*/*z* (%) = 432 (26, M^+), 240 (100).

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