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Stereochemistry and Mechanism of the Chemoselective Allylation of α-Substituted β-Keto Esters with Allyl Bromide Mediated by Zn in NH_4Cl(aq)–THF

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Six α-substituted β-keto esters were chemoselectively allylated at the keto group by a Zn-mediated reaction with allyl bromide in NH_4Cl(aq)–THF. The reactions gave diastereomeric homoallylic alcohols with d.e.s ranging from 28 to 74%. With ethyl 2-chloroacetoacetate, substitution of the chlorine atom by the allyl group took place. Similarly, on allylation of diethyl benzoylmalonate, diethyl malonate was eliminated. These reactions support a radical mechanism. The relative configurations of the formed diastereomers were determined by a combination of ^{1}H NMR spectroscopy and molecular modeling. The stereochemistry of the diastereomers supports a mechanism including strong association of the keto ester with the metal surface.

Allylation of carbonyl compounds with allyl halides mediated by metals in aqueous media has become an established method for the synthesis of homoallylic alcohols as shown in a comprehensive review by Li.[1] One of the main advantages of this method is that it can be used for the allylation of aldehydes and ketones containing acidic hydrogens. Moreover, Zn,[2,3] Sn[4] and In[4]-mediated allylations of esters containing aldehyde or keto groups show complete chemoselectivity to ketone and aldehyde vs. ester group allylation. Li *et al.* showed that when α-substituted β-keto esters were treated with allyl bromide or chloride in weakly acidic aqueous media in the presence of Sn or In, chemoselective allylation at the keto group gave mixtures of diastereomers with d.e.s ranging from 60 to 80%. The relative configurations of the diastereomers were, however, not determined and no suggestions on the stereochemical course of the reactions were presented. To our knowledge corresponding reactions of α-substituted β-keto esters in the presence of Zn have not been studied. Although some suggestions on the reaction mechanisms of metal mediated aqueous allylations have been presented,[1] the stereochemistry of these allylations has received little attention. α-Substituted β-keto esters are well suited to studies of the stereochemistry of these reactions as they give mixtures of diastereomers in reactions with allyl halides. To facilitate conclusions on the stereochemical course of the reaction to be drawn, the relative configurations of the diastereomers have to be determined. However, the determination is not straightforward as the configurations cannot be determined from the vicinal couplings between the α- and β-protons in the products. In this paper we report the results of Zn mediated allylation of selected α-substituted β-keto esters in NH_4Cl(aq)–THF. We also report a method for the determination of the relative configurations of the formed diastereomers based on a combination of ^{1}H NMR spectroscopy and molecular modeling. Based on the results we present some suggestions on the stereochemistry and the mechanism of the Zn-mediated allylation of α-substituted β-keto esters with allyl bromide in aqueous NH_4Cl.

Results and discussion

We reacted selected α-substituted β-keto esters (**1**, Scheme 1) with allyl bromide in NH_4Cl(aq)–THF in the presence of Zn dust, according to a previously described method,[3,5] in which a THF solution of the halide is added slowly to a stirred mixture of a saturated solution of NH_4Cl in H_2O, THF and Zn powder under an argon atmosphere. The reactions were completely keto-group selective. Owing to the presence of a diastereotopic keto carbonyl group in the substrates, the allylations resulted in the formation of two diastereomers (**2**) designated *syn* and *anti*, respectively, defined as they appear in Scheme 1.[6] The reactions gave fair to moderate yields and showed relatively high diastereoselectivities (Table 1). The reaction products were isolated by column

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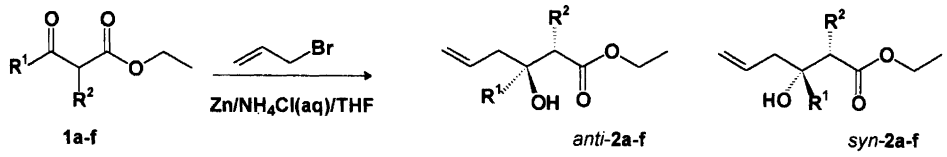


1a-f anti-2a-f syn-2a-f

a-d: $R^1 = CH_3$; a: $R^2 = CH_3$; b: $R^2 = CH_2CH_3$; c: $R^2 = CH_2COOCH_2CH_3$; d: $R^2 = Cl$;

e: $R^1, R^2 = -(CH_2)_3-$; f: $R^1, R^2 = -(CH_2)_4-$

Scheme 1.

Table 1. Total yields and isomer ratios of hydroxy esters (entries 1, 2, 4–7) and the substituted γ-lactones (entry 3) formed in the Zn-mediated reactions of allyl bromide with β-keto esters in THF–NH_4Cl(aq).

Entry	R^1	R^2	Compd.	Diast. ratio major: minor[b]	Yield[a]
1	CH_3	CH_3	**2a**	74:26	72
2	CH_3	CH_2CH_3	**2b**	87:13	81
3	CH_3	$CH_2COOCH_2CH_3$	**3c**	71:29	69[c] (65)[d]
4[e]	CH_3	Cl	**2d**	64:36	37[b] (36)
5		$-(CH_2)_3-$	**2e**	83:17	50 (47)
6		$-(CH_2)_4-$	**2f**	71:29	23 (21)
7[f]		$-(CH_2)_4-$	**2f**	79:21	53 (49)

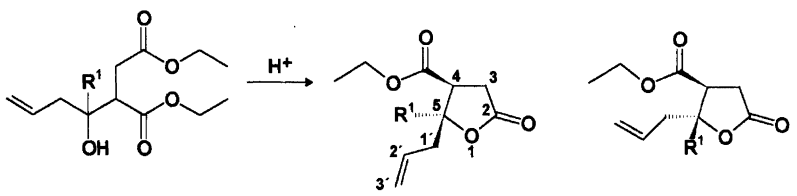
[a]By ^{1}H NMR. [b]By GC. [c]γ-Lactone. [d]Isolated yield. [e]Reversed-order addition. [f]C-18 silica instead of THF.

chromatography and identified by ^{1}H NMR spectroscopy and combined GC–MS of the diastereomer mixtures.

Ethyl 2-ethylacetoacetate (**1b**) displayed a higher diastereoselectivity than ethyl 2-methylacetoacetate (**1a**), showing the role of steric factors. The hydroxy esters (**2c**) formed in the allylation of diethyl acetosuccinate (**1c**), were quantitatively transformed into substituted γ-lactones (**3**, Scheme 2) on addition of dilute sulfuric acid to the reaction mixture after the allylation was complete. As lactonization occurred to some extent already during the reaction, no attempts were made to isolate the primarily formed homoallylic alcohols and the identification of the reaction products was based on the structures of the lactones.

The reaction of ethyl 2-chloroacetoacetate (**1d**) with allyl bromide gave a keto allylation product, ethyl 3-methyl-3-hydroxyhex-5-enoate lacking the chlorine atom on the α-carbon. The product, which was identified by comparison with an authentic sample,[3] could be formed by substitution of the chlorine atom in the keto ester by a hydrogen radical followed by allylation of the non-substituted β-keto ester, ethyl acetoacetate, which was identified in the reaction mixture in trace amounts. Hydrogen radicals can be formed at the Zn surface by the reactions of protons with electrons released by the metal. The presence of hydrogen radicals was evident from the evolution of H_2 during the reaction. The suggested mechanism is also supported by the fact that no chlorine substitution took place when an experimental procedure was applied in which the NH_4Cl(aq) was slowly added to a mixture of Zn, keto ester, allyl bromide and THF (reversed order addition). In this procedure the initial concentration of protons should be low and evolution of hydrogen was not observed. The only allylation products formed, the two diastereomers of ethyl 2-chloro-3-methyl-3-hydroxyhex-5-enoate (**2d**), contained a chlorine atom.

The allylations of cyclic β-keto esters (**1e** and **1f**) did not proceed as smoothly as those of the non-cyclic ones. However, when C-18 silica instead of THF was used as the organic phase (Table 1, entry 7), the yield of the reaction with ethyl 2-oxocyclohexanecarboxylate increased from 23 to 53% but the reaction was much slower than in THF. The keto–enol equilibrium ratio of ethyl 2-oxocyclohexanecarboxylate in the liquid state is 26:74,[7] and the allylation reaction probably occurs only to the keto form of the cyclic keto esters. The low yields could thus be explained by very slow tautomerization of the enol-form during the fast allylation reaction. The use of co-solvents like acetonitrile, methanol, 2-ethoxyethanol, ethanol and DMSO, instead of THF, slightly increased the yield. However, when the reaction time was increased from 2 to 12 h, the yield did not increase, but the keto ester was partly transformed – probably by reaction with free ammonia present in the NH_4Cl solu-



syn- and *anti*-**2c** *cis*-**3** (from *syn*-**2c**) *trans*-**3** (from *anti*-**2c**)

Scheme 2.

tion – to the corresponding imine which was identified as its enamino form, ethyl 2-amino-1-cyclohexene-carboxylate (Experimental, compd. **4**).

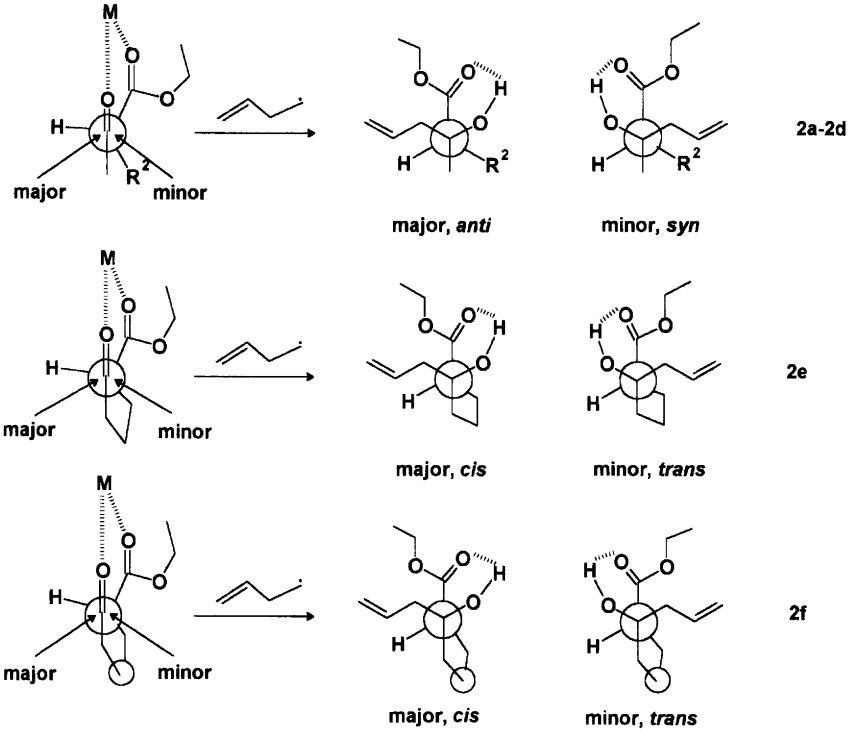
We also reacted allyl bromide with diethyl benzoylmalonate. However, no expected allylation products were detected. Instead, α,α-diallylbenzyl alcohol (Experimental, compd. **5**) was obtained as the main product, in addition to diethyl malonate, benzoic acid and 1-phenyl-3-buten-1-one (Experimental, compd. **6**). The formation of α,α-diallylbenzyl alcohol supports the mechanism suggested above and can be rationalised as follows. An allyl radical formed at the solid Zn surface by electron release from the metal, attacks the keto carbonyl group of the keto ester and substitutes an allyl group for the diethyl malonate group. The ketone formed is then allylated by an allyl radical. The formation of benzoic acid suggests that hydroxyl radicals may be present and that these also react at the keto carbonyl group by radical substitution.

The relatively high diastereoselectivities of the allylations (Table 1) suggest that the carbonyl groups of the keto esters do not move freely. Possibly, on mixing of the keto ester and Zn powder, the keto ester becomes associated to the metal surface in a way that resembles chelation. The next step, which takes place on addition of the allyl halide to the mixure, is the formation of an allyl radical on the metal surface. If the radical is strongly attached to the metal surface the complex may resemble an organometallic species, cf. the Grignard reagent. This would render the radical nucleophilic. After formation, the radical would then add to the keto carbonyl of the 'chelated' keto ester in which the ester and keto carbonyls are synclinal. Addition of the allyl radical to the less hindered side of the 'chelated' keto ester would thereby result in the formation of the major isomer. Allylation to the more hindered side of the 'chelated' keto ester would give the minor isomer. The suggested reaction path is presented schematically in Scheme 3. In a non-chelated system lower diastereoselectivity would be expected. The chelation model is also supported by the fact that the cyclic keto esters, in which the carbonyl groups are probably synclinal even without chelation, react by the same topology and similar stereoselectivities as the non-cyclic ones. To confirm the stereochemical course of the reactions the relative configurations of the diastereomers had to be determined. The assignment of the relative configurations was not straightforward. However, the reaction products constitute intramolecularly hydrogen bonded molecules (cf. Scheme 3) in which stereochemical assignments are easier to make than in systems containing only freely rotating bonds. We used a combination of ^{1}H NMR shifts, relative GC retention times[8] and molecular modeling to determine the relative configurations of the diastereomers. The relative configurations of the cyclic adducts, i.e., the lactones of **2c** and compounds **2e** and **2f** were more easily determined than those of the non-cyclic adducts owing to the structural rigidity of the former. The structural rigidity results in stronger intramolecular hydrogen bonds and larger proton shift differences in the ^{1}H NMR spectra of the cyclic isomers compared with the non-cyclic ones.

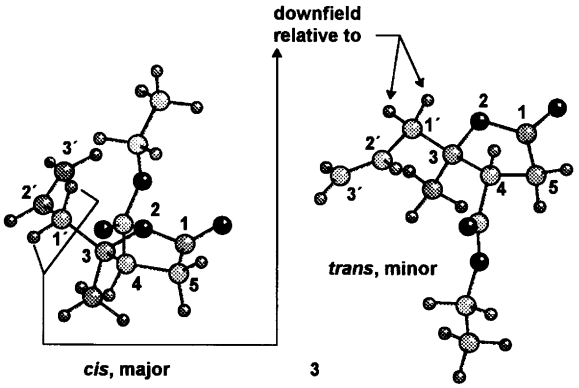
In the lactones (**3**, Scheme 2) a *cis* arrangement of the allyl and the ethoxycarbonyl group in the major isomer is supported by NMR data. The protons at C-1′ in the major isomer are deshielded by 0.16 and 0.28 ppm, respectively, relative to the minor isomer due to the through-space deshielding effect of the ester carbonyl group. This effect is possible only in the isomer where the allyl and the ethoxycarbonyl group have a *cis* relationship as shown by molecular modeling (Scheme 4). The major isomer of compound **2c** then would have the *R**,*R** configuration and the minor one would have the *R**,*S** configuration.

Indications of the relative configurations of the homoallylic alcohols (**2e** and **2f**) formed in the allylations of ethyl 2-oxocyclopentanecarboxylate and ethyl 2-oxocyclohexanecarboxylate, respectively, could be obtained from the relative retention times of the major and minor isomers on a weakly polar gas chromatography column. In both cases the major isomer had the shorter retention time. This might be due to a stronger intramolecular hydrogen bond in the major isomer.[8] Molecular modeling showed that both in the cyclopentyl (**2e**) and in the cyclohexyl (**2f**) adducts the intramolecular hydrogen bond was stronger in the isomers with the ethoxycarbonyl and hydroxy groups in a *cis* relationship than in the *trans* isomers (Scheme 5). In the ^{1}H NMR spectra the shifts of the hydroxy groups of the major isomers were downfield of those of the minor isomers also indicating a stronger intramolecular hydrogen bond in the former. The downfield shifts of H-1 in the minor isomers relative to those in the major ones are probably due to deshielding by the van der Waals effect of the hydroxy group. This can be effective only in the *trans* isomers. The larger ax–ax couplings between the H-1 and the *vicinal* methylene protons in the spectra of the major isomers also supported a *cis* configuration and a more rigidly hydrogen-bonded system for the major than for the minor isomers. Thus the major isomers of **2e** and **2f** would have the *cis* (*R**,*R**) relative configuration while the minor ones would have the *trans* (*R**,*S**) configuration as shown in Scheme 5. For the non-cyclic adducts (**2a**, **2b** and **2d**) the GC retention times of the minor isomers were shorter than for the major isomers. For all three adducts the shifts of the hydroxy protons of the minor isomers were downfield of those of the major ones. Based on this and the arguments above the *anti* (*R**,*R**) configuration was assigned to the major and the *syn* (*R**,*S**) configuration to the minor isomers of **2a**, **2b** and **2c**.

In conclusion, Zn-mediated allylations of α-substituted β-keto esters with allyl bromide proceed with complete keto selectivity and with fair to good yields. The diastereoselectivities in most reactions are quite high, which could be ascribed to the formation of a chelate-like complex of the keto ester with the metal surface.

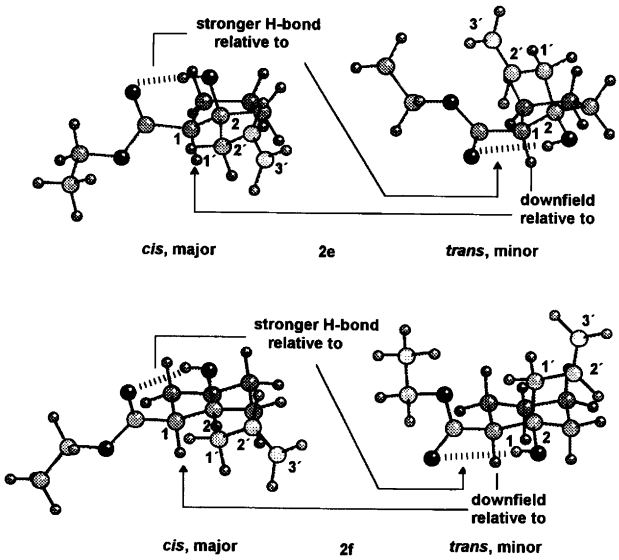


Scheme 3.



Scheme 4.

The chelation model is supported by the stereochemistry of the products. Products formed by substitution reactions point towards allyl radical formation on the Zn surface as the initiation step of the allylations.



Scheme 5.

Experimental

All chemicals were either commercially available or were synthesised by standard methods. The allylation reactions were performed by the addition of a solution of allyl bromide (12.5 mmol) in THF (5 ml) to a stirred mixture of saturated NH_4Cl(aq) (20 ml), THF (5 ml), Zn powder (12.5 mmol) and the keto ester (5.0 mmol). In entry 4 of Table 1, however, the expected allylation products were obtained only when saturated NH_4Cl(aq) was slowly added to a stirred mixture of allyl bromide (12.5 mmol), ethyl 2-chloroacetoacetate (5.0 mmol) and zinc (12.5 mmol) in 20 ml THF. All reactions were performed under an argon atmosphere. The diastereomer mixtures were isolated by column chromatography on silica using diethyl ether–pentane (2:8 or 3:7 v/v) as the eluent. The isolation of pure compounds **2a** and **2b** was not successful and only NMR yields are given. The NMR signals of the diastereomers were well separated and shifts and couplings could be obtained from spectra of the mixtures. Gas chromatographic analyses were

performed on an HP-5 capillary column (0.32 mm ID × 25 m). The mass spectra were recorded with a gas chromatograph provided with a mass selective detector. ^{1}H NMR spectra were recorded at 500 MHz in $CDCl_3$ with TMS as an internal standard. Quantitative GC analyses were performed using 1-nonanol as an internal standard. In the quantitative NMR analyses naphthalene was used as an internal standard. Construction of molecular models and optimisations of structures were performed with the NEMESIS program for PC[9] using the COSMIC[10] force field.

(2R,3R*)-Ethyl 2,3-dimethyl-3-hydroxyhex-5-enoate* (**2a**, major). ^{1}H NMR: δ 1.21 (s, 3 H, 3-Me), 1.22 (d, 3 H, J=7.2 Hz, 2-Me), 1.28 (t, 3 H, J=7.1 Hz, O-CH_2CH_3), 2.23 (dd, 1 H, J=13.8 and 8.4 Hz, H-4), 2.31 (ddt, 1 H, J=13.8, 6.6 and 1.3 Hz, H-4), 2.51 (q, 1 H, J=7.2 Hz, H-2), 3.19 (s, 1 H, 3-OH) 4.16 (ABq, 1 H, J=10.8 and 7.1 Hz, OCH_2CH_3), 4.19 (ABq, 1 H, J=10.8 and 7.1 Hz, OCH_2CH_3), 5.09–5.14 (m, 2 H, H-6), 5.83 (dddd, 1 H, J=17.0, 11.0, 8.4 and 6.6 Hz, H-5). MS: 186 (M^+, 0), 145 (73), 141 (7), 102 (36), 99 (100), 85 (24), 74 (32), 69 (11), 57 (22), 56 (8), 55 (6).

(2R,3S*)-Ethyl 2,3-dimethyl-3-hydroxyhex-5-enoate* (**2a**, minor). ^{1}H NMR: δ 1.15 (s, 3 H, 3-Me), 1.20 (d, 3 H, J=7.2 Hz, 2-Me), 1.29 (t, 3 H, J=7.1 Hz, OCH_2CH_3), 2.20–2.28 (m, 2 H, H-4), 2.54 (q, 1 H, J= 7.2 Hz, H-2), 3.39 (s, 1 H, 3-OH), 4.12–4.23 (m, 2 H, OCH_2CH_3), 5.05–5.14 (m, 2 H, H-6), 5.90 (ddt, 1 H, J=17.5, 10.5 and 7.5 Hz, H-5). MS: 186 (M^+, 0), 145 (89), 141 (8), 102 (35), 99 (100), 95 (9), 85 (26), 74 (31), 69 (9), 57 (28), 56 (8).

(2R,3R*)-Ethyl 2-ethyl-3-methyl-3-hydroxyhex-5-enoate* (**2b**, major). ^{1}H NMR: δ 0.89 (t, 3 H, J=7.4 Hz, $CHCH_2CH_3$), 1,19 (s, 3 H, 3-Me), 1.28 (t, 3 H, J= 7.1 Hz, OCH_2CH_3), 1.71 (ABdq, 1 H, J= 13.5, 4.1 and 7.4 Hz, $CHCH_2CH_3$), 1.77 (ABdq, 1 H, J=13.5, 11.1 and 7.4 Hz, $CHCH_2CH_3$), 2.24 (dd, 1 H, J=13.3 and 8.2 Hz, H-4), 2.33 (dd, 1 H, J=13.3 and 7.6 Hz, H-4), 2.33 (dd, 1 H, J=11.1 and 4.1 Hz, H-2), 2.87 (s, 1 H, 3-OH), 4.16 (ABq, 2 H, J=10.9 and 7.1 Hz, OCH_2CH_3), 4.19 (ABq, 2 H, J=10.9 and 7.1 Hz, OCH_2CH_3), 5.05–5.08 (m, 2 H, H-6), 5.82 (dddd, 1 H, J=16.9, 10.2, 8.2 and 7.6 Hz, H-5). The isomers of **2b** were not completely separated on GC and the mass spectrum represents the mixture. MS: 200 (M^+, 0), 159 (72), 116 (34), 113 (100), 101 (32), 88 (10), 85 (20), 73 (27), 71 (44), 69 (18), 55 (11).

(2R,3S*)-Ethyl 2-ethyl-3-methyl-3-hydroxyhex-5-enoate* (**2b**, minor). ^{1}H NMR: δ 0.90 (t, 3 H, J=7.5 Hz, $CHCH_2CH_3$), 1,17 (s, 3 H, 3-Me), 1.28 (t, 3 H, J= 7.1 Hz, OCH_2CH_3), 1.65 (dq, 1 H, J= 13.5, 3.8 and 7.5 Hz, $CHCH_2CH_3$), 1.75 (dq, 1 H, J=13.5, 11.1 and 7.5 Hz, $CHCH_2CH_3$), 2.22 (ddt, 1 H, J= 13.7, 7.5 and 1.1 Hz, H-4), 2.28 (dd, 1 H, J=13.7 and 7.2 Hz, H-4), 2.36 (dd, 1 H, J=11.1 and 3.8 Hz, H-2), 3.01 (s, 1 H, 3-OH), 4.15 (ABq, 2 H, J=11.2 and 7.1 Hz, OCH_2CH_3), 4.20 (ABq, 2 H, J=11.2 and 7.1 Hz, OCH_2CH_3), 5.01–5.05 (m, 2 H, H-6), 5.85 (dddd, 1 H, J=17.0, 10.2, 7.5 and 7.2 Hz, H-5).

(4R,5R*)-5-Allyl-5-methyl-4-ethoxycarbonyl-tetrahydro-2-furanone* (**3c**, major). ^{1}H NMR: δ 1.29 (t, 3 H, J=7.2 Hz, OCH_2CH_3), 1,30 (s, 3 H, 5-Me), 2.51 (dd, 1 H, J=14.4 and 7.8 Hz, H-1′), 2.63 (ddt, 1 H, J=14.4, 6.7 and 1.2 Hz, H-1′), 2.65 (dd, 1 H, J=18.0 and 9.1 Hz, H-3), 3.08 (dd, 1 H, J=18.0 and 9.6 Hz, H-3), 3.30 (dd, 1 H, J=9.6 and 9.1 Hz, H-4), 4.21 (q, 2 H, J=7.2 Hz, OCH_2CH_3), 5.21 (dm, 1 H, J=18.2 Hz, H-3′), 5.25 (dm, 1 H, J=10.2 Hz, H-3′), 5.82 (dddd, 1 H, J=18.2, 10.2, 7.9 and 6.7 Hz, H-2′). MS: 212 (M^+, 0), 171 (83), 143 (100), 128 (10), 125 (19), 115 (17), 101 (44), 100 (11), 97 (20), 69 (16), 55 (86).

(2R,3S*)-5-Allyl-5-methyl-4-ethoxycarbonyl-tetrahydro-2-furanone* (**3c**, minor). ^{1}H NMR: δ 1.29 (s, 3 H, 5-Me), 1.30 (t, 3 H, J=7.2 Hz, OCH_2CH_3), 2.23 (ddt, 1 H, J=14.3, 8.3 and 1.0 Hz, H-1′), 2.47 (dd, 1 H, J= 14.3 and 6.3 Hz, H-1′), 2.69 (dd, 1 H, J=18.0 and 9.0 Hz, H-3), 3.06 (dd, 1 H, J=18.0 and 9.9 Hz, H-3), 3.19 (dd, 1 H, J=9.9 and 9.0 Hz, H-4), 4.20 (q, 2 H, J=7.2 Hz, OCH_2CH_3), 5.13 (dm, 1 H, J=17.0 Hz, H-3′), 5.18 (dm, 1 H, J=10.3 Hz, H-3′), 5.78 (dddd, 1 H, J=17.0, 10.3, 8.3 and 6.3 Hz, H-2′). MS: 212 (M^+, 0), 171 (89), 143 (100), 125 (22), 115 (20), 101 (49), 100 (11), 97 (24), 73 (13), 69 (31), 55 (87).

(2R,3R*)-Ethyl 2-chloro-3-methyl-3-hydroxyhex-5-enoate* (**2d**, major). ^{1}H NMR: δ 1.33 (t, 3 H, J=7.2 Hz, OCH_2CH_3), 1.35 (s, 3 H, 3-Me), 2.43 (ABdt, 1 H, J= 14.2, 7.1 and 1.3 Hz, H-4), 2.45 (ABd, 1 H, J=14.2 and 8.8 Hz, H-4), 3.00 (s, 1 H, 3-OH), 4.23 (s, 1 H, H-2), 4.27 (q, 2 H, J=7.2 Hz, OCH_2CH_3), 5.14–5.21 (m, 2 H, H-6), 5.82 (dddd, 1 H, J=18.2, 9.6, 8.0 and 7.0 Hz, H-5). MS: 206/208 (M^+, 0), 165/167 (67/27), 137/139 (100/28), 122 (21), 119/121 (68/24), 94 (30), 85 (39), 69 (35).

(2R,3S*)-Ethyl 2-chloro-3-methyl-3-hydroxyhex-5-enoate* (**2d**, minor). ^{1}H NMR: δ 1.32 (s, 3 H, 3-Me), 1.33 (t, 3 H, J=7.2 Hz, OCH_2CH_3), 2.33 (ddt, 1 H, J=14.1, 7.6 and 1.0 Hz, H-4), 2.48 (dd, 1 H, J=14.1 and 7.3 Hz, H-4), 2.03 (s, 1 H, 3-OH), 4.22 (s, 1 H, H-2), 4.28 (q, 2 H, J=7.2 Hz, OCH_2CH_3), 5.14–5.21 (m, 2 H, H-6), 5.88 (ddt, 1 H, J=17.5, 10.2, and 7.4 Hz, H-5). MS: 206/208 (M^+, 0), 165/167 (79/24), 137/139 (100/30), 122 (20), 119/121 (64/21), 94 (38), 85 (40), 69 (37).

(1R,2R*)-Ethyl 2-allyl-2-hydroxycyclopentane-1-carboxylate* (**2e**, major). ^{1}H NMR: δ 1.28 (t, 3 H, J=7.2 Hz, OCH_2CH_3), 1.55–2.32 (m, 6 H, H-3, H-4 and H-5), 2.36 (ddt,1 H, J=13.7, 7.4 and 1.1 Hz, H-1′), 2.45 (ddt, 1 H, J=13.7, 7.2 and 1.2 Hz, H-1′), 2.56 (dd, 1 H, J=10.3

and 8.8 Hz, H-1), 3.53 (s, 1 H, 3-OH), 4.16 (ABq, 2 H, J=9.2 and 7.2 Hz, OCH_2CH_3), 4.18 (ABq, 2 H, J=9.2 and 7.2 Hz, OCH_2CH_3), 5.07–5.13 (m, 2 H, H-3′), 5.88 (ddt, 1 H, J=16.3, 11.0 and 7.4 Hz, H-2′). MS: 198 (M^+, 0), 157 (33), 124 (4), 112 (6), 111 (100), 107 (8), 83 (18), 73 (10), 69 (5), 68 (6), 55 (23).

(1R,2S*)-Ethyl 2-allyl-2-hydroxycyclopentane-1-carboxylate* (**2e**, minor). ^{1}H NMR: δ 1.28 (t, 3 H, J=7.2 Hz, OCH_2CH_3), 1.55–2.32 (m, 6-H, H-3, H-4 and H-5), 2.25 (ddt, 1 H, J=13.9, 7.8 and 1.1 Hz, H-1′), 2.33 (dd, 1 H, J=13.9 and 7.2 Hz, H-1′), 2.78 (dd, 1 H, J=8.4 and 6.8 Hz, H-1), 2.05 (s, 1 H, 3-OH), 4.16 (q, 2 H, J= 7.2 Hz, OCH_2CH_3), 5.12–5.20 (m, 2 H, H-3′), 5.91 (dddd, 1 H, J=17.2, 10.0, 7.8 and 7.2 Hz, H-2′). MS: 198 (M^+, 0), 157 (26), 124 (4), 112 (8), 111 (100), 107 (10), 101 (8), 83 (16), 73 (16), 69 (8), 68 (10), 55 (25).

(1R,2R*)-Ethyl 2-allyl-2-hydroxycyclohexane-1-carboxylate* (**2f**, major). ^{1}H NMR: δ 1.26 (t, 3 H, J=7.2 Hz, OCH_2CH_3), 1.44–2.29 (m, 8 H, H-3, H-4, H-5 and H-6), 2.19 (ABd, 1 H, J=14.5 and 7.0 Hz, H-1′), 2.24 (ABd, 1 H, J=14.5 and 7.9 Hz, H-1′), 2.34 (dd, 1 H, J=12.5 and 4.0 Hz, H-1), 3.78 (s, 1 H, 3-OH), 4.14 (ABq, 2 H, J=10.8 and 7.2 Hz, OCH_2CH_3), 4.16 (ABq, 2 H, J= 10.8 and 7.2 Hz, OCH_2CH_3), 5.03 (dm, 1 H, J=17.2 Hz, H-3′), 5.07 (dm, 1 H, J=10.2 Hz, H-3′), 5.83 (dddd, 1 H, J=17.2, 10.2, 7.9 and 7.0 Hz, H-2′). MS: 212 (M^+, 0), 172 (5), 171 (54), 125 (100), 121 (9), 97 (11), 81 (6), 79 (9), 73 (5), 69 (24), 55 (17).

(1R,2S*)-Ethyl 2-allyl-2-hydroxycyclohexane-1-carboxylate* (**2f**, minor). ^{1}H NMR: δ 1.27 (t, 3 H, J=7.2 Hz, OCH_2CH_3), 1.44–2.29 (m, 8 H, H-3, H-4, H-5 and H-6), 2.26 (dd, 1 H, J=14.2 and 6.3 Hz, H-1′), 2.38 (dd, 1 H, J=14.2 and 8.2 Hz, H-1′), 2.48 (dd, 1 H, J=9.9 and 3.6 Hz, H-1), 3.34 (s, 1 H, 3-OH), 4.19 (ABq, 2 H, J= 10.8 and 7.2 Hz, OCH_2CH_3), 4.22 (ABq, 2 H, J=10.8 and 7.2 Hz, OCH_2CH_3), 5.08 (dm, 1 H, J=17.1 Hz, H-3′), 5.12 (dm, 1 H, J=10.2 Hz, H-3′), 5.90 (dddd, 1 H, J=17.1, 10.2, 8.2 and 6.3 Hz, H-2′). MS: 212 (M^+, 0), 171 (48), 125 (100), 121 (9), 97 (13), 81 (6), 79 (10), 73 (5), 69 (26), 55 (17).

Ethyl 2-amino-1-cyclohexenecarboxylate (**4**). ^{1}H NMR: δ 1.27 (t, 3 H, J=7.2 Hz, OCH_2CH_3), 1.56–1.66 (m, 4 H, H-4 and H-5), 2.21 (t, 2 H, J=6.1 Hz, H-6), 2.25 (t, 2 H, J=6.1 Hz, H-3), 4.14 (q, 2 H, J=7.2 Hz, OCH_2CH_3), 6.01 (br s, 2 H, NH_2). MS: 169 (M^+, 61), 140 (68), 124 (53), 122 (69), 96 (100), 95 (57), 94 (34), 69 (45), 67 (40) 54 (40).

4-Phenylhepta-1,6-dien-4-ol (**5**). ^{1}H NMR: δ 2.52 (ddt, 2 H, J=13.8, 8.3 and 1.0 Hz, H-3, H-5, H-5), 2.70 (dddd, 2 H, J=13.8, 6.2, 1.5 and 1.1 Hz, H-3, H-5), 5.07–5.13 (m, 4 H, H-1, H-7), 5.61 (dddd, 2 H, J=17.1, 10.2, 8.3 and 6.2 Hz, H-2, H-6), 7.2–7.4 (m, 5 H, ArH). MS: 188 (M^+, 0), 170 (1), 147 (17), 128 (2), 115 (2), 106 (7), 105 (100), 91 (2), 77 (22), 69 (1), 51 (4).

1-Phenyl-3-buten-1-one (**6**). ^{1}H NMR: δ 3.77 (dt, 2 H, J=6.8 and 1.5 Hz, H-2), 5.21 (dq, 1 H, J=17.1 and 1.5 Hz, H-4), 5.25 (dq, 1 H, J=10.3 and 1.5 Hz, H-4), 6.10 (ddt, 1 H, J=17.0, 10.3 and 6.8 Hz, H-4), 7.3–7.9 (m, 5 H, ArH). MS: 146 (M^+, 1), 107 (2), 106 (8), 105 (100), 78 (3), 77 (40), 51 (8).

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