Tetrahedron 66 (2010) 7720–7725

Contents lists available at ScienceDirect

Tetrahedron

journal homepage: www.elsevier.com/locate/tet

# Stereoselective formation of tertiary and quaternary carbon centers via inverse conjugate addition of carbonucleophiles to allenic esters

Ana Lúcia Cardoso [a], Ana Matos Beja [b], Manuela Ramos Silva [b], Jesús M. de los Santos [c], Francisco Palacios [c], Paulo E. Abreu [a], Alberto A.C.C. Pais [a], Teresa M.V.D. Pinho e Melo [a,*]

[a] Department of Chemistry, University of Coimbra, 3004-535 Coimbra, Portugal
[b] Department of Physics, University of Coimbra, 3004-516 Coimbra, Portugal
[c] Department of Organic Chemistry I, Faculty of Pharmacy, University of the Basque Country, Apartado 450, 01080 Vitoria, Spain

ARTICLE INFO

*Article history:*
Received 23 March 2010
Received in revised form 23 July 2010
Accepted 1 August 2010
Available online 7 August 2010

*Keywords:*
Allenoates
Carbonucleophiles
Chiral α,β-unsaturated carboxylic esters
Chiral carbon centers
Stereoselective inverse conjugate addition

ABSTRACT

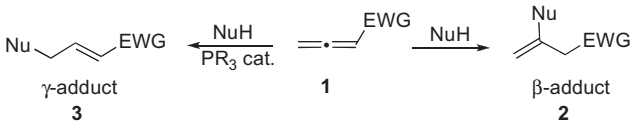
Stereoselective inverse conjugate addition of carbonucleophiles to allenoates bearing a chiral auxiliary in the ester moiety afforded optically active α,β-unsaturated carboxylic esters bearing a new stereocenter at the δ position. The rationalization of the observed selectivity was supported by semi-empirical molecular orbital calculations.



## 1. Introduction

The development of efficient asymmetric methods for carbon–carbon bond formation is an important target in modern organic synthesis. The formation of tertiary stereogenic centers has been widely studied and several efficient strategies are now available. In contrast, effective approaches to the production of quaternary stereocenters, which constitutes a challenging task, are limited. Furthermore, several biologically active molecules and natural compounds containing quaternary stereogenic centers are known.[1,2]

In recent years, electron-deficient allenes have emerged as attractive electrophiles for various synthetic purposes.[3] The addition of nucleophiles to electron-deficient allenes (**1**, Scheme 1), occurs at the electrophilic α,β-carbon–carbon double bond to give Michael type adducts[4] (**2**, Scheme 1) but reactivity inversion (umpolung) can be achieved when catalytic amounts of phosphines are added (**3**, Scheme 1). In fact, Cristau et al. observed that the presence of phosphines allows the nucleophilic attack at the γ-carbon of methyl 2,3-butadienoate (**1**, EWG=$CO_2$Me, Scheme 1) leading to γ-adducts (**3**, EWG=$CO_2$Me, Nu=OMe, Scheme 1).[5] On the other hand, Trost et al. reported the phosphine-catalyzed C–C bond formation at the γ-position of 2-butynoates with dimethyl malonate.[6] Lu et al. demonstrated that methyl 2,3-butadienoate undergoes similar addition with dimethyl malonate in the presence of 5 mol % triphenylphosphine giving adduct (**3**, EWG=$CO_2$Me, Nu=$MeO_2CCHCO_2$Me, Scheme 1) in good yield.[7] Asymmetric version of the γ-addition of carbonucleophiles to 2,3-butadienoates using chiral phosphines as catalysts for the construction of tertiary[8a] and quaternary centers has also been reported.[8b] However, as far as we know no examples of γ-addition of nucleophiles to chiral allenes have been reported.

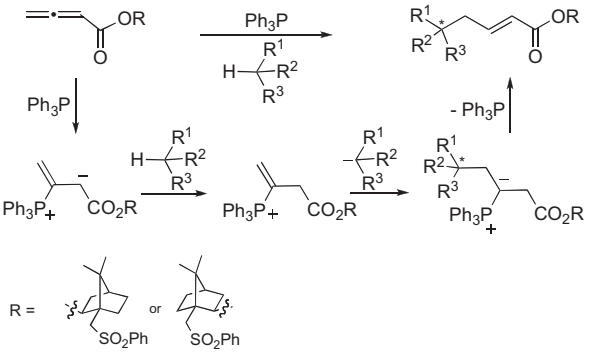



**Scheme 1.**

In connection with our interest in the synthesis of allenes and their use as building blocks in organic synthesis,[4a,b,9] we now describe a methodology to construct tertiary and quaternary stereocenters via stereoselective inverse conjugate addition of carbonucleophiles to allenoates bearing a chiral auxiliary in the ester moiety (Scheme 2).

* Corresponding author. Tel.: +351 239854475; e-mail address: tmelo@ci.uc.pt (T.M.V.D. Pinho e Melo).

0040-4020/$ – see front matter © 2010 Elsevier Ltd. All rights reserved.
doi:10.1016/j.tet.2010.08.002



Scheme 2.

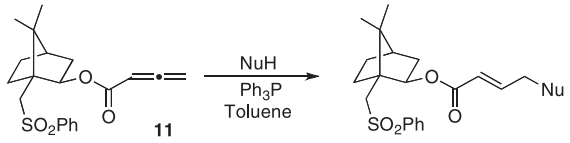
## 2. Results and discussion

First, the reactivity of benzyl but-2,3-dienoate (**4**)[10] toward pronucleophiles namely ethyl 3-oxobutanoate (**5**), ethyl 2-oxocyclohexanecarboxylate (**7**), and 2-acetylcyclohexanone (**9**) was examined (Table 1). It has been previously observed that the selection of the appropriated temperature, additives, and phosphine stoichiometry is important to optimize this C–C bond-forming reaction.[8b] Therefore, the inverse conjugate addition of ethyl 3-oxobutanoate (**5**) to allene **4** leading to compound **6** bearing a new tertiary center, was carried out under different reaction conditions (entries 1–6). The condensation performed at 70 °C for 5 h in the presence of 5 mol % of triphenylphosphine gave the desired product with trans selectivity in 40% yield (entry 1). A better yield (57%) was obtained carrying out the reaction at 110 °C for 24 h (entry 2). However, neither the use of additives (NaOAc/AcOH) nor the increase of phosphine stoichiometry led to improvement. Using the same reaction conditions compound **8** was prepared with trans selectivity in 42% yield from allene **4** and 2-oxocyclohexanecarboxylate **7** (entry 7). The triphenylphosphine (10 mol %) catalyzed addition of 2-acetylcyclohexanone (**9**) to allene **4** allowed the isolation of compounds **10**-*trans* in 62% yield (entry 8).

Then the behavior of optically active allene **11** was explored (Table 2). The reaction of (1*S*)-(+)-10-phenylsulfonylisobornyl buta-2,3-dienoate (**11**) with ethyl 3-oxobutanoate (**5**) carried out at 110 °C for 24 h in the presence of 5 mol % of triphenylphosphine gave the desired γ-addition product **12** in 85% yield but with moderate trans selectivity (entry 1). A similar result was obtained when the reaction was performed in the presence of polystyrene-supported triphenylphosphine (entry 2). However, the addition reaction in the presence of 10 mol % of triphenylphosphine carried out at 50 °C for 24 h gave **12** in 62% yield with high trans selectivity (entry 3). Using pronucleophile 2-oxocyclohexanecarboxylate **7** no reaction was observed at 50 °C (entry 4) whereas the inverse conjugate addition of allene **11** to ethyl 2-oxocyclohexanecarboxylate (**7**) at 110 °C gave compound **13** in 84% yield with trans selectivity (entry 5). Finally, the reaction of chiral allene **11** with 2-acetylcyclohexanone (**9**) allowed the synthesis of compound **14** in 75% yield in a selective fashion (entry 6). It should be emphasized that the $^1$H NMR spectra of α,β-unsaturated carbonyl compounds **12**–**14** showed signals for single diastereoisomers.

The triphenylphosphine catalyzed reaction of (1*R*)-(−)-10-phenylsulfonylisobornyl buta-2,3-dienoate **15**, enantiomer of allene **11**, with pronucleophiles **5**, **7**, and **9** was also studied (Table 3). Using 3-oxobutanoate **5** as pronucleophile the desired product **16** was obtained with higher trans selectivity when the reaction was

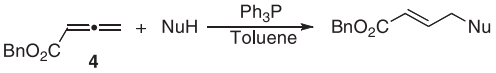
**Table 2**
Inverse conjugate addition of carbonucleophiles to chiral allenoate **11**



| Entry | NuH (5 equiv) | Conditions | Product | Yield % (*cis*:*trans*) |
|---|---|---|---|---|
| 1 | **5** | $PPh_3$ (5 mol %), 110 °C, 24 h | **12** | 85 (33:67) |
| 2 | **5** | $PPh_3$ (25 mol %),[a] 110 °C, 24 h | **12** | 89 (33:67) |
| 3 | **5** | $PPh_3$ (10 mol %), 50 °C, 24 h | **12** | 62 (>98% *trans*) |
| 4 | **7** | $PPh_3$ (10 mol %), 50 °C, 48 h | **13** | No reaction |
| 5 | **7** | $PPh_3$ (10 mol %), 110 °C, 24 h | **13** | 84 (*trans*) |
| 6 | **9** | $PPh_3$ (10 mol %), 110 °C, 24 h | **14** | 75 (*trans*) |

[a] Triphenylphosphine polystyrene-supported.

**Table 1**
Inverse conjugate addition of carbonucleophiles to benzyl buta-2,3-dienoate (**4**)



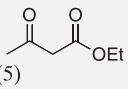
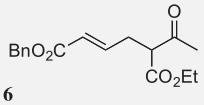
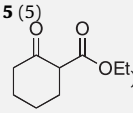
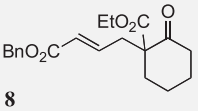
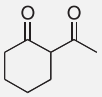
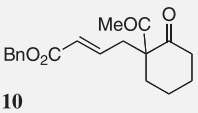
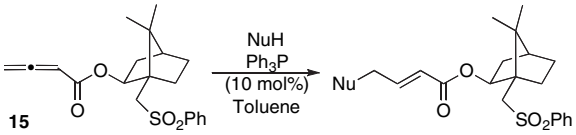
| Entry | NuH (equiv) | Conditions | Product | Yield % |
|---|---|---|---|---|
| 1 |  **5** (5) | $PPh_3$ (5 mol %), 70 °C, 5 h |  **6** | 40 *trans* |
| 2 | **5** (5) | $PPh_3$ (5 mol %), 110 °C, 24 h | **6** | 57 *trans* |
| 2 | **5** (5) | $PPh_3$ (5 mol %), NaOAc (0.5 equiv), AcOH (0.5 equiv), 110 °C, 5 h | **6** | 57 *trans* |
| 4 | **5** (5) | $PPh_3$ (5 mol %), NaOAc (0.5 equiv), AcOH (0.5 equiv), 110 °C, 24 h | **6** | 44 *trans* |
| 5 | **5** (5) | $PPh_3$ (10 mol %), 110 °C, 24 h | **6** | 47 *trans* |
| 6 | **5** (5) | $PPh_3$ (30 mol %), 110 °C, 5 h | **6** | 48 *trans* |
| 7 |  7 (1) | $PPh_3$ (10 mol %), 110 °C, 24 h |  **8** | 42 *trans* |
| 8 |  **9** (2) | $PPh_3$ (10 mol %), 110 °C, 24 h |  **10** | 62 *trans* 8 *cis* |

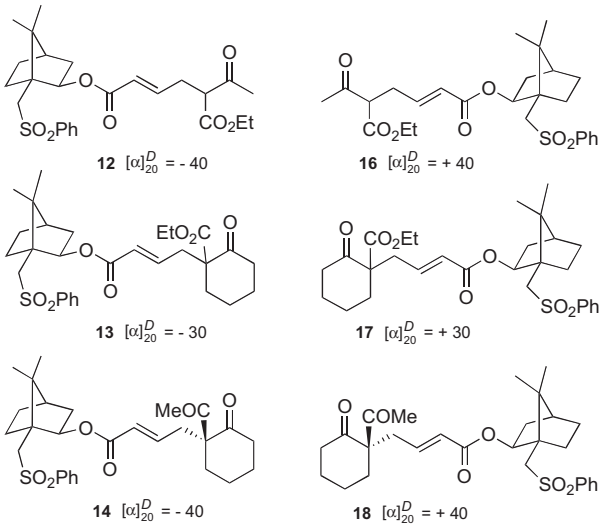
**Table 3**
Inverse conjugate addition of carbonucleophiles to chiral allenoate **15**




| Entry | NuH (5 equiv) | Conditions | Product | Yield % (*cis*:*trans*) |
|---|---|---|---|---|
| 1 | **5** | 70 °C, 24 h | **16** | 60 (9:91) |
| 2 | **5** | 110 °C, 24 h | **16** | 53 (29:71) |
| 3 | **5** | 50 °C, 48 h | **16** | 87 (>95 *trans*) |
| 4 | **7** | 70 °C, 24 h | **17** | 43 (*trans*) |
| 5 | **7** | 110 °C, 24 h | **17** | 83 (*trans*) |
| 6 | **9** | 110 °C, 24 h | **18** | 74 (*trans*) |

carried out a lower temperature (entries 1–3). Compound **17** was obtained in 43% yield carrying out the reaction of allene **15** with pronucleophile 2-oxocyclohexanecarboxylate **7** at 70 °C (entry 4) whereas at 110 °C compound **17** was isolated in 83% yield with trans selectivity (entry 5). The addition of 2-acetylcyclohexanone (**9**) to chiral allene **15** gave compound **18**-*trans* in 74% yield (entry 6). The $^1$H NMR spectra of α,β-unsaturated carbonyl compounds **16**–**18** showed also signals for single diastereoisomers.

The structure of (*E*)-(1*R*)-(−)-10-phenylsulfonylisobornyl 4-(2-acetyl-1-oxo-1,2,3,4-tetrahydronaphthalen-2-yl)but-2-enoate (**18**) was determined by X-ray crystallography (Fig. 1). This allowed us to establish the *S* configuration to the new chiral center. Compound **18**




**Scheme 3.**

subsequent elimination of the phosphine affording the target molecule **18**. We concentrated on the attack of **20** to intermediate **19** leading to **21**, the step where the new chiral center is generated (Scheme 4).

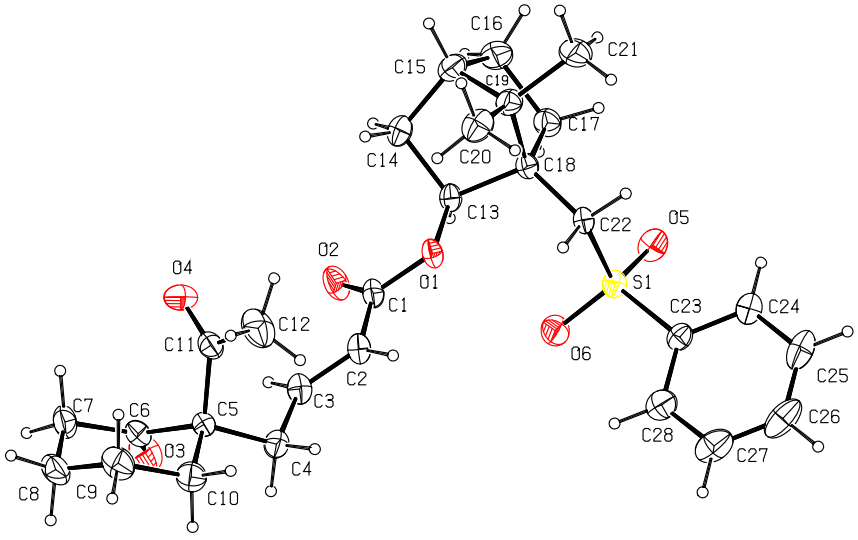


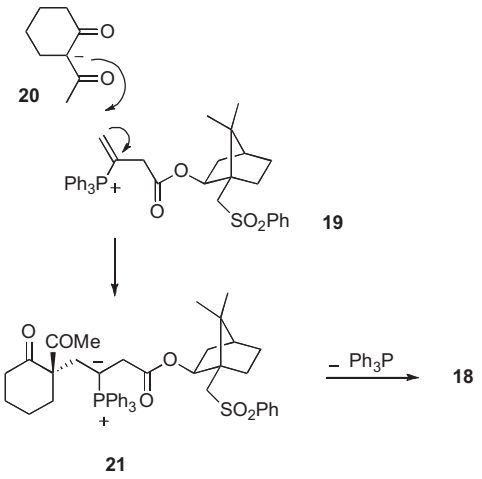

**Figure 1.** ORTEP diagram of the compound **18** with the ellipsoids drawn at the 20% probability level, for clarity reasons.

showed a positive value for the optical rotation (+40) and the same value with opposite sign (−40) was obtained for compound **14** indicating that these compounds are enantiomers (Scheme 3). Therefore, we could conclude that (1*R*)-(−)-10-phenylsulfonylisobornyl group induces selectivity leading to a new chiral center with *S* configuration whereas the enantiomeric chiral auxiliary affords a chiral center with *R* configuration. Furthermore, compounds **12**–**14** and **16**–**18** show the same physical properties but values for the optical rotation with opposite sign confirming that two sets of enantiomeric derivatives were obtained (Scheme 3).

In order to be able to rationalize the stereoselectivity observed in the synthesis of optically active α,β-unsaturated carboxylic ester **18** semi-empirical molecular orbital calculations have been carried out. This process involves the nucleophilic addition of triphenylphosphine to 2,3-allenoate **15** giving intermediate **19**, which reacts with nucleophile **20** to produce **21**, followed by proton transfer and

The supermolecular structure formed by these two compounds correspond to 105 atoms in total, and conformer generation was deemed a necessity. As such, for each of the reagents Marvin[13] was used as the generation step of the conformers. Each conformer was then subjected to geometry optimization using the PM6[14] Hamiltonian in MOPAC2009[15], resorting to the COSMO[16] approach to model the solvent. Scripts created by the authors ranked the conformers in terms of energy and automatically performed the calculations for all geometries.

Geometry optimization for the intermediate **19** shows that the lowest energy conformers are not accessible from one of the sides. In fact, the substituents of the C–C double bond hinder one of the diastereofaces blocking the approach of the nucleophile (see Fig. 2 for an example of these conformers). This is consistent with the observed exclusive formation of (*E*)-(1*R*)-(−)-10-phenylsulfonylisobornyl (4*S*)-4-(2-acetyl-1-oxo-1,2,3,4-tetrahydronaphthalen-2-yl)but-2-enoate (**18**).




**Scheme 4.**

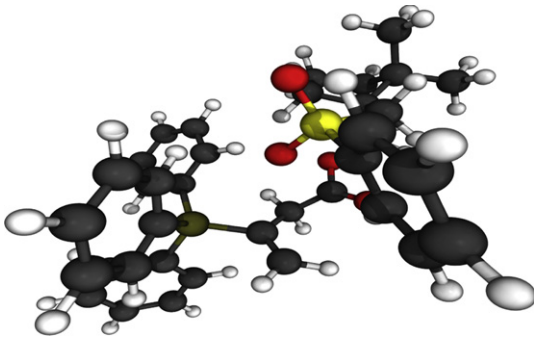


**Figure 2.** Example of a low energy conformer of **19**.

The minimum energy conformers were subsequently used to build tentative transition states, pertaining to the alternative approximation route. The search for this transition state was extensive, and most of the tryout geometries unsuccessful. The putative transition state is characterized by an imaginary frequency of 237 $cm^{-1}$, and this mode corresponds to the motion of the terminal carbon of the double bond (Fig. 3). It is located 21 kcal/mol above the optimized reactants in the gas phase. The calculation in the solvent is not possible, due to the fact that the Hessian calculation is not possible using the implicit solvent model and so the nature of a stationary point cannot be assessed. Nevertheless, the geometry of the transition state **22** is in agreement with the stereochemistry outcome of the formation of the final product **18** and corroborates the observed selectivity.

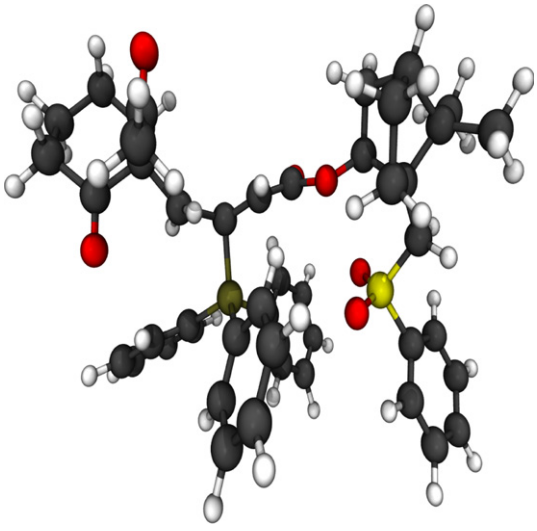


**Figure 3.** Geometry of the transition state **22** resulting from the attack of nucleophile **20** to intermediate **19** leading to **21**. Color code: gray is carbon, red is oxygen, white is hydrogen, yellow is sulfur and dark yellow is phosphorus.

## 3. Conclusion

The reaction of prochiral carbon pronucleophiles with allenoates bearing a chiral auxiliary in the ester moiety in the presence of triphenylphosphine is described. Stereoselective inverse conjugate addition was observed leading to optically active α,β-unsaturated carboxylic esters compounds bearing a new stereocenter at the δ position. The use of enantiomeric chiral auxiliaries led to the synthesis of two sets of enantiomeric derivatives.

The structure of (*E*)-(1*R*)-(−)-10-phenylsulfonylisobornyl 4-(2-acetyl-1-oxo-1,2,3,4-tetrahydronaphthalen-2-yl)but-2-enoate (**18**) was determined by X-ray crystallography allowing to establish the *S* configuration to the new chiral center whereas the enantiomeric chiral auxiliary, (1*S*)-(+)-10-phenylsulfonylisobornyl group, afforded a chiral center with *R* configuration. Computational studies corroborated the rationalization of the observed selectivity.

## 4. Experimental section

### 4.1. General

$^{1}H$ NMR spectra were recorded on a Bruker Avance III instrument operating at 400 MHz. $^{13}C$ NMR spectra were recorded on a Bruker Avance III instrument operating at 100 MHz. The solvent is deuterochloroform except where indicated otherwise. IR spectra were recorded on a Perkin–Elmer 1720X FTIR spectrometer. Mass spectra were recorded under chemical ionization (CI) or electrospray ionization (ESI). HRMS spectra were recorded on a Finnigan MAT95 S instrument. Optical rotations were measured on an Optical Activity AA-5 electrical polarimeter. Melting points were recorded on a Reichert hot stage and are uncorrected. Flash column chromatography was performed with Merck 9385 silica as the stationary phase.

### 4.2. General procedure

The appropriated allene (0.5 mmol) and $PPh_3$ (0.10 mmol %) were dissolved in dry toluene (10 mL) followed by the dropwise addition of the nucleophile (2.5 mmol). The reaction mixture was stirred overnight at the designed temperature. The solvent was evaporated off and the product purified by flash chromatography [ethyl acetate/hexane].

*4.2.1. (E)-1-Benzyl 6-ethyl 5-acetylhex-2-enedioate (**6**).* Obtained as an oil. IR (film) 1586, 1656, 1713 $cm^{-1}$; $^{1}H$ NMR 1.27 ($CH_3$, t, $J$=7.2 Hz), 2.26 ($CH_3$, s), 2.71–2.75 ($CH_2$, m), 3.58 (CH, t, $J$=7.3 Hz), 4.20 ($CH_2$, q, $J$=7.2 Hz), 5.16 ($CH_2$, s), 5.92 (CH=, d, $J$=15.6 Hz), 6.87–6.91 (CH=, m), 7.34–7.38 (5H, m, Ar–H); $^{13}C$ NMR 14.0, 29.2, 30.2, 58.0, 61.8, 66.2, 123.4, 128.2, 128.5, 135.9, 144.8, 165.8, 168.5, 201.2. MS (ESI) $m/z$ 304 ($MH^+$, 1), 213 (15), 91 (100), 68 (34); HRMS (ESI) $m/z$ 305.1383 ($C_{17}H_{21}O_5$ [$MH^+$], 305.1382).

*4.2.2. (E)-Benzyl 4-(1-ethoxycarbonyl-2-oxocyclohexyl)but-2-enoate (**8**).* Obtained as an oil. IR (film) 1497, 1654, 1714 $cm^{-1}$; $^{1}H$ NMR 1.21 ($CH_3$, t, $J$=7.2 Hz), 1.42–1.52 (1H, m), 1.60–1.80 (3H, m), 1.94–2.09 (2H, m), 2.45–2.51 (3H, m), 2.69–2.75 (1H, m), 4.18 ($CH_2$, q, $J$=7.3 Hz), 5.16 ($CH_2$, s), 5.87 (CH=, d, $J$=15.6 Hz), 6.92 (CH=, dt, $J$=7.6, 15.6 Hz), 7.32–7.36 (5H, m, Ar–H); $^{13}C$ NMR 14.1, 22.4, 27.4, 36.1, 37.6, 41.0, 60.6, 61.6, 66.1, 124.2, 128.2, 128.5, 136.0, 144.3, 165.7,

171.0, 206.8. MS (ESI) *m/z* 345 ($MH^+$, 100), 237 (66), 209 (27); HRMS (ESI) *m/z* 345.1697 ($C_{20}H_{25}O_5$ [$MH^+$], 345.1697).

*4.2.3. Benzyl 4-(1-acetyl-2-oxocyclohexyl)but-2-enoate (**10**).*

*4.2.3.1. (E)-Benzyl 4-(1-acetyl-2-oxocyclohexyl)but-2-enoate (**10**-trans).* Obtained as an oil. IR (film) 1653, 1700, 1718 $cm^{-1}$; $^1H$ NMR 1.46–1.51 (1H, m), 1.59–1.77 (3H, m), 1.98–2.05 (1H, m), 2.10 ($CH_3$, s), 2.25–2.33 (1H, m), 2.46–2.51 (2H, m), 2.57–2.70 (2H, m), 5.15 ($CH_2$, s), 5.88 (CH═, d, *J*=15.6 Hz), 6.78 (CH═, dt, *J*=7.6, 15.6 Hz), 7.35–7.36 (5H, m, Ar–H); $^{13}C$ NMR 22.1, 26.2, 27.0, 34.1, 36.9, 41.6, 66.2, 67.3, 124.6, 127.0, 128.3, 128.6, 135.9, 143.5, 165.5, 205.1, 208.8.

*4.2.3.2. (Z)-Benzyl 4-(1-acetyl-2-oxocyclohexyl)but-2-enoate (**10**-cis).* Obtained as an oil. IR (film) 1653, 1700, 1718 $cm^{-1}$; $^1H$ NMR 1.26–1.37 (1H, m), 1.45–1.78 (3H, m), 1.94–2.03 (1H, m), 2.11 ($CH_3$, s), 2.31–2.51 (3H, m), 3.12 (1H, dd, *J*=7.6, 15.6 Hz), 3.25 (1H, dd, *J*=7.6, 15.6 Hz), 5.15 ($CH_2$, s), 5.89 (CH═, d, *J*=11.6 Hz), 6.13 (CH═, dt, *J*=7.6, 11.6 Hz), 7.26–7.36 (5H, m, Ar–H); $^{13}C$ NMR 22.1, 26.1, 27.0, 32.6, 36.9, 41.3, 65.9, 67.3, 121.7, 128.3, 128.6, 135.9, 145.0, 165.9, 207.2, 209.5.

*4.2.4. 1-[10-Phenylsulfonylisobornyl] 6-ethyl 5-acetylhex-2-enedioate **12** and **16**.* IR (film) 1586, 1656, 1713 $cm^{-1}$; $^1H$ NMR 0.87 ($CH_3$, s), 0.96 ($CH_3$, s), 1.19–1.23 (1H, m), 1.28 ($CH_3$, t, *J*=7.1 Hz), 1.73–2.05 (6H, m), 2.29 ($CH_3$, s), 2.75 (2H, approx. t, *J*=7.1 Hz), 3.00 (1H, d, *J*=14.0 Hz), 3.56 (1H, d, *J*=14.0 Hz), 3.63 (CH, t, *J*=7.3 Hz), 4.22 ($CH_2$, q, *J*=7.1 Hz), 4.80–4.83 (1H, m), 5.82 (CH═, d, *J*=15.5 Hz), 6.77 (CH═, dt, *J*=7.1, 15.5 Hz), 7.53–7.63 (3H, m, Ar–H), 7.85–7.88 (2H, m, Ar–H); $^{13}C$ NMR 14.1, 19.9, 20.3, 21.1, 29.3, 29.4, 29.7, 30.2, 39.5, 44.1, 49.4, 49.9, 55.2, 58.1, 61.8, 77.6, 123.9, 127.7, 129.3, 133.6, 141.3, 144.0, 164.3, 168.6, 201.3.

*4.2.4.1. (E)-1-[(1S)-(+)-10-Phenylsulfonylisobornyl] 6-ethyl 5-acetylhex-2-enedioate (**12**).* Obtained as an oil. MS (ESI) *m/z* 491 ($MH^+$, 10), 277 (100), 135 (55); HRMS (ESI) *m/z* 491.2098 ($C_{26}H_{35}O_7S$ [$MH^+$], 491.2103). $[\alpha]_D^{20}$ −40 (*c* 1, $CH_2Cl_2$).

*4.2.4.2. (E)-1-[(1R)-(−)-10-Phenylsulfonylisobornyl] 6-ethyl 5-acetylhex-2-enedioate (**16**).* Obtained as an oil. MS (ESI) *m/z* 491 ($MH^+$, 63), 277 (22); HRMS (ESI) *m/z* 491.2098 ($C_{26}H_{35}O_7S$ [$MH^+$], 491.2104). $[\alpha]_D^{20}$ +40 (*c* 1, $CH_2Cl_2$).

*4.2.5. 10-Phenylsulfonylisobornyl 4-(1-ethoxycarbonyl-2-oxocyclohexyl)but-2-enoate **13** and **17**.* IR (film) 1447, 1653, 1711 $cm^{-1}$; $^1H$ NMR 0.87 ($CH_3$, s), 0.96 ($CH_3$, s), 1.17–1.27 (3+1H, m), 1.48–2.20 (12H, m), 2.45–2.55 (3H, m), 2.70–2.76 (1H, m), 2.99 (1H, d, *J*=14.0 Hz), 3.57 (1H, d, *J*=14.0 Hz), 4.21 ($CH_2$, q, *J*=7.2 Hz), 4.75–4.78 (1H, m), 5.75 (CH═, d, *J*=16.0 Hz), 6.75–6.83 (CH═, m), 7.49–7.64 (3H, m, Ar–H), 7.86–7.90 (2H, m, Ar–H); $^{13}C$ NMR 14.2, 19.9, 20.3, 22.5, 27.1, 27.4, 29.6, 30.9, 36.2, 37.6, 39.6, 41.0, 44.0, 49.3, 49.9, 55.1, 61.6, 77.4, 124.6, 127.7, 129.3, 133.5, 141.1, 143.5, 164.2, 171.1, 206.8.

*4.2.5.1. (E)-(1S)-(+)-10-Phenylsulfonylisobornyl 4-(1-ethoxycarbonyl-2-oxocyclohexyl)but-2-enoate (**13**).* Obtained as an oil. MS (ESI) *m/z* 531 ($MH^+$, 34), 277 (20), 254 (4); HRMS (ESI) *m/z* 531.2411 ($C_{29}H_{35}O_7S$ [$MH^+$], 531.2414). $[\alpha]_D^{20}$ −30 (*c* 1, $CH_2Cl_2$).

*4.2.5.2. (E)-(1R)-(−)-10-Phenylsulfonylisobornyl 4-(1-ethoxycarbonyl-2-oxocyclohexyl)but-2-enoate (**17**).* Obtained as an oil. MS (ESI) *m/z* 531 ($MH^+$, 100), 277 (63), 254 (12); HRMS (ESI) *m/z* 531.2411 ($C_{29}H_{35}O_7S$ [$MH^+$], 531.2409). $[\alpha]_D^{20}$ ±30 (*c* 1, $CH_2Cl_2$).

*4.2.6. 10-Phenylsulfonylisobornyl 4-(2-acetyl-1-oxo-1,2,3,4-tetrahydronaphthalen-2-yl)but-2-enoate **14** and **18**.* IR (film) 1559, 1653, 1700, 1717 $cm^{-1}$; $^1H$ NMR (DMSO-$d_6$) 0.87 ($CH_3$, s), 0.96 ($CH_3$, s), 1.17–1.26 (1H, m), 1.48–2.04 (12H, m), 2.11 ($CH_3$, s), 2.47–2.52 (2H, m), 2.56–2.71 (2H, m), 2.99 (1H, d, *J*=14.4 Hz), 3.56 (1H, d, *J*=14.4 Hz), 4.74–4.78 (1H, m), 5.76 (CH═, d, *J*=15.6 Hz), 6.61–6.69 (CH═, m), 7.52–7.62 (3H, m, Ar–H), 7.87–7.88 (2H, m, Ar–H); $^{13}C$ NMR 19.9, 20.3, 21.5, 22.1, 26.3, 27.1, 29.7, 34.2, 36.8, 39.6, 41.6, 44.1, 49.4, 50.0, 55.2, 67.3, 77.6, 125.3, 127.8, 129.3, 133.5, 141.2, 142.7, 164.0, 205.3, 208.8.

*4.2.6.1. (E)-(1S)-(+)-10-Phenylsulfonylisobornyl 4-(2-acetyl-1-oxo-1,2,3,4-tetrahydronaphthalen-2-yl)but-2-enoate (**14**).* Obtained as a white solid. Mp 169.4–171.0 °C (from ethyl acetate/hexane). MS (ESI) *m/z* 501 ($MH^+$, 58), 328 (4), 277 (53); HRMS (ESI) *m/z* 501.2306 ($C_{28}H_{37}O_6S$ [$MH^+$], 501.2310). $[\alpha]_D^{20}$ −40 (*c* 1, $CH_2Cl_2$).

*4.2.6.2. (E)-(1R)-(−)-10-Phenylsulfonylisobornyl 4-(2-acetyl-1-oxo-1,2,3,4-tetrahydronaphthalen-2-yl)but-2-enoate (**18**).* Obtained as a white solid. Mp 168.7–170.1 °C (from ethyl acetate/hexane). MS (ESI) *m/z* 501 ($MH^+$, 64), 277 (100), 233 (4); HRMS (ESI) *m/z* 501.2305 ($C_{28}H_{37}O_6S$ [$MH^+$], 501.2310). $[\alpha]_D^{20}$ +40 (*c* 1, $CH_2Cl_2$).

### 4.3. Crystal data for (*E*)-(1*R*)-(−)-10-phenylsulfonylisobornyl 4-(2-acetyl-1-oxo-1,2,3,4-tetrahydronaphthalen-2-yl)but-2-enoate (18)

$C_{28}H_{36}O_6S$, *M*=500.63, crystal dimensions 0.36×0.21×0.19 $mm^3$, orthorhombic, $P2_12_12_1$, *a*=8.1873(2) Å, *b*=17.3020(5) Å, *c*=18.8325 (5) Å, *V*=2667.75(12) $Å^3$, *Z*=4, $\rho_{calcd}$=1.246 g $cm^{-3}$, $\mu$=0.161 $mm^{-1}$. The X-ray data were collected on an Bruker APEX2 single crystal diffractometer, at 293(3) K, using graphite-monochromated Mo Kα radiation (l=0.71073 Å). The structures were solved by direct methods as implemented in SHELXS97[11] and refined by full-matrix least-squares using SHELXL97.[11] 54,252 reflections measured, 6419 independent, *R*=0.0399 (4486 reflections with $I>2\sigma(I)$), $R_w$=0.1104 for all reflections, GOF=1.036, 319 parameters, non-H atoms refined anisotropically The Flack parameter[12] refined to 0.02(7).


## Acknowledgements

Thanks are due to FCT (Project: PTDC/QUI/64470/2006; Grant: SFRH/BPD/34569/2007), COMPETE, QREN and FEDER for financial support. We acknowledge the Nuclear Magnetic Resonance Laboratory of the Coimbra Chemical Centre (www.nmrccc.uc.pt), University of Coimbra for obtaining the NMR data.


## References and notes


1. (a) Trost, B. M.; Brennan, M. K. *Synthesis* **2009**, 3003–3025; (b) Bella, M.; Gasperi, T. *Synthesis* **2009**, 1583–1614; (c) Riant, O.; Hannedouche, J. *Org. Biomol. Chem.* **2007**, *5*, 873–888; (d) Cozzi, P. G.; Hilgraf, R.; Zimmermann, N. *Eur. J. Org. Chem.* **2007**, 5969–5994; (e) Christoffers, J.; Baro, A. *Adv. Synth. Catal.* **2005**, *347*, 1473–1482; (f) Denissova, I.; Barriault, L. *Tetrahedron* **2003**, *59*, 10105–10146.
2. Recent selected examples on the generation of quaternary centers: (a) Duplessis, M.; Waltz, M.-E.; Bencheqroun, M.; Cardinal-David, B.; Guindon, Y. *Org. Lett.* **2009**, *11*, 3148–3151; (b) Smith, C. R.; Lim, H. L.; Zhang, A.; RajanBabu, T. V. *Synthesis* **2009**, 2089–2100; (c) Smejkal, T.; Han, H.; Breit, B.; Krische, M. J. *J. Am. Chem. Soc.* **2009**, *131*, 10366–10367; (d) Cheng, L.; Liu, L.; Jia, H.; Wang, D.; Chen, Y.-J. *J. Org. Chem.* **2009**, *74*, 4650–4653; (e) Hashimoto, T.; Naganawa, Y.; Maruoka, K. *J. Am. Chem. Soc.* **2009**, *131*, 6614–6617; (f) Shintani, R.; Tsutsumi, Y.; Nagaosa, M.; Nishimura, T.; Hayashi, T. *J. Am. Chem. Soc.* **2009**, *131*, 13588–13589; (g) Campanyó, X.; Alba, A.-N.; Cárdenas, F.; Moyano, A.; Rios, R. *Eur. J. Org. Chem.* **2009**, 3075–3080; (h) Koester, D. C.; Werz, D. B. *Angew. Chem., Int. Ed.* **2009**, *48*, 7971–7973.
3. (a) *Modern Allene Chemistry*; Krause, N., Hashmi, A. S. K., Eds.; WILEY-VCH GmbH & KgaA: Weinheim, 2004; (b) Ma, S. *Chem. Rev.* **2005**, *105*, 2829–2871; (c) Ma, S. *Aldrichimica Acta* **2007**, *40*, 91–102; (d) Hassan, H. H. A. M. *Curr. Org. Chem.* **2007**, *4*, 413–439; (e) Lu, X.; Zhang, C.; Xu, Z. *Acc. Chem. Res.* **2001**, *34*, 535–544; (f) Ye, L.-W.; Zhou, J.; Tang, Y. *Chem. Soc. Rev.* **2008**, *37*, 1140–1152; (g) Cowen, B. J.; Miller, S. J. *Chem. Soc. Rev.* **2009**, *38*, 3102–3116; Pinho e Melo, T. M. V. D. *Curr. Org. Chem.* **2009**, *13*, 1406–1431.
4. For some examples see: (a) Lopes, S. M. M.; Matos Beja, A.; Ramos Silva, M.; de los Santos, J. M.; Pinho e Melo, T. M. V. D.; Palacios, F. *Tetrahedron* **2009**, *65*, 9116–9124; (b) Pinho e Melo, T. M. V. D.; Cardoso, A. L.; Palacios, F.; de los Santos, J. M.; Pais, A. A. C. C.; Abreu, P. E.; Paixão, J. A.; Matos Beja, A.;

Ramos Silva, M. *Tetrahedron* **2008**, *64*, 8141–8148; (c) de los Santos, J. M.; López, Y.; Aparicio, D.; Palacios, F. *J. Org. Chem.* **2008**, *73*, 550–557; (d) Palacios, F.; Aparicio, D.; López, Y.; de los Santos, J. M. *Tetrahedron* **2005**, *61*, 2815–2830; (e) Palacios, F.; Ochoa de Retana, A. M.; Gil, J. I.; Ezpeleta, J. M. *J. Org. Chem.* **2000**, *65*, 3213–3217; (f) Palacios, F.; Aparicio, D.; de los Santos, J. M.; Rodríguez, E. *Tetrahedron Lett.* **1996**, *37*, 1289–1292; (g) Palacios, F.; Aparicio, D.; Garcia, J. *Tetrahedron* **1996**, *52*, 9609–9628.

5. Cristau, H.-J.; Viala, J.; Christol, H. *Bull. Soc. Chim. Fr.* **1985**, 980–988.
6. Trost, B. M.; Li, X. *J. Am. Chem. Soc.* **1994**, *116*, 3167–3168.
7. Zhang, C.; Lu, X. *Synlett* **1995**, 645–646.
8. (a) Smith, S. W.; Fu, G. C. *J. Am. Chem. Soc.* **2009**, *131*, 14231–14233; (b) Chen, Z.; Zhu, G.; Jiang, Q.; Xiao, D.; Cao, P.; Zhang, X. *J. Org. Chem.* **1998**, *63*, 5631–5635.
9. (a) Pinho e Melo, T. M. V. D.; Cardoso, A. L.; Rocha Gonsalves, A. M. d'A.; Costa Pessoa, J.; Paixão, J. A.; Matos Beja, A. *Eur. J. Org. Chem.* **2004**, 4830–4839; (b) Santos, B. S.; Matos Beja, A.; Ramos Silva, M.; Paixão, J. A.; Palacios, F.; Pinho e Melo, T. M. V. D. *Synthesis* **2009**, 2403–2407; (c) Lopes, S. M. M.; Santos, B. S.; Palacios, F.; Pinho e Melo, T. M. V. D. *ARKIVOC* **2010**, *v*, 70–81; (d) Ribeiro Laia, F. M.; Pinho e Melo, T. M. V. D. *Tetrahedron Lett.* **2009**, *50*, 6180–6182; (e) Santos, B. S.; Cardoso, A. L.; Matos Beja, A.; Ramos Silva, M.; Paixão, J. A.; Pinho e Melo, T. M. V. D.; Palacios, F. *Eur. J. Org. Chem.* **2010**, 3249–3256; (f) Lopes, S. M. M.; Nunes, C. M.; Pinho e Melo, T. M. V. D. *Tetrahedron* **2010**, *66*, 6078–6084.
10. Benzyl 2,3-butadienoate prepared via Wittig reaction of benzyl triphenylphosphoranylideneacetate with ketene following the general procedure described in Ref. 9a.
11. Sheldrick, G. M. *SHELXS97 & SHELXL97*; Univ. of Göttingen: Germany, 1997.
12. Flack, H. D. *Acta Crystallogr., Sect. A* **1983**, *A39*, 876–881.
13. Marvin was used for drawing, displaying, and characterizing chemical structures, substructures, and reactions, Marvin 5.3.2, 2010, ChemAxon (http://www.chemaxon.com).
14. Stewart, J. J. P. *J. Mol. Model.* **2007**, *13*, 1173–1213.
15. MOPAC2009 Stewart, J. J. P. *Stewart Computational Chemistry*; Colorado Springs, CO: USA, 2008; http://OpenMOPAC.net.
16. Klamt, A.; Schüümann, G. *J. Chem. Soc., Perkin Trans. 2* **1993**, 799–805.