Contribution to the synthesis of chiral allenic esters

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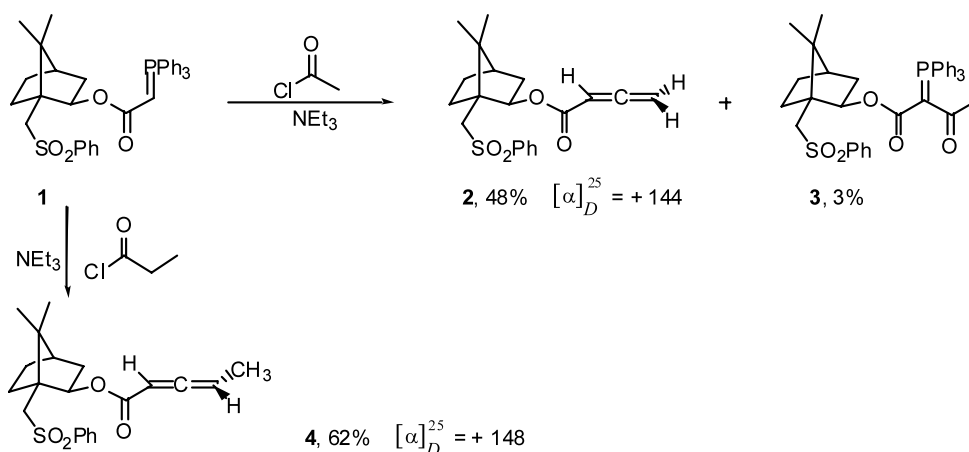
Abstract—A phosphorus ylide bearing a 10-phenylsulfonylisoborneol unit reacted with ketenes, generated in situ from acid chlorides and triethylamine, to give allenic compounds. The reaction with methylketene led to asymmetric induction with the selective synthesis of an allene with axial chirality corresponding to an *S* configuration. The structure of the chiral allene 10-phenylsulfonylisobornyl penta-2,3-dienoate was determined by X-ray crystallography. Chirooptical studies of the chiral allene derivatives were done.
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Allenes are important building blocks in organic chemistry.[1] They can be obtained by various synthetic methods but the use of the Wittig reaction[2] or the Horner–Wadsworth–Emmons reaction[3] are of particular interest since they allow regio- and stereocontrol of the carbon–carbon double bond formation.

Little attention has been given to the synthesis of chiral allenes via asymmetric Wittig type reactions.[4] However,

optical active 4,4-disubstituted allenecarboxylates have been prepared via reaction of in situ generated ketenes from phenyl acetates with chiral Horner–Wadsworth–Emmons reagents.[3c,d] On the other hand, Tömösközi and Bestmann reported the reaction of phosphorus ylides containing a chiral alcohol unit with acid chlorides leading to chiral allenes although neither the absolute configuration of the products nor the level of asymmetric induction was determined.[2f] The same
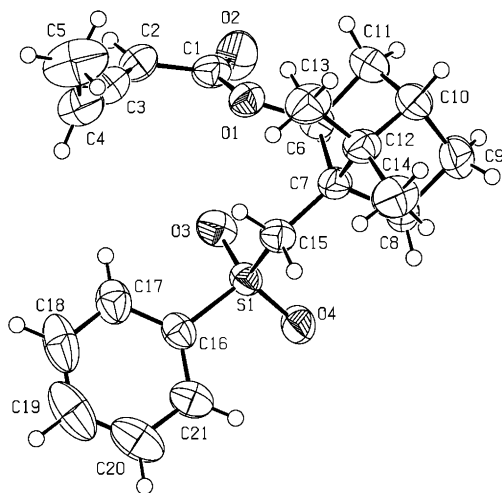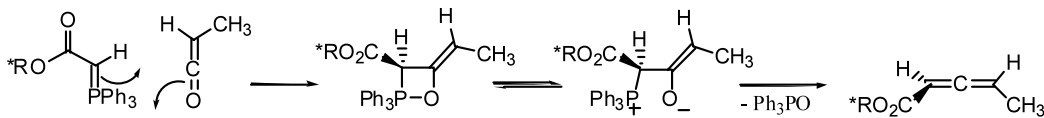

Scheme 1.

Figure 1. ORTEPII plot of compound **4** with anisotropic displacement ellipsoids calculated at the 50% probability level. The angle between the least-squares planes C2–C1–O1–O2 and C2–C3–C4–C5 is 87.3(3)°. The absolute configuration of chiral carbons was determined by the Flack method ($\eta = -0.013(15)$) using the anomalous scattering of the sulphur atom at the Cu Kα wavelength, confirming the *S,R,S* absolute configuration of C10, C7 and C6.

authors also reported the reaction of racemic phosphorus ylides with chiral acid chlorides which gave enantionerically enriched allenes.[2g]

We have been interested in exploring the reactivity of phosphorus ylides namely their use in a non-classical Wittig reaction which offers a route to tetrasubstituted alkenes.[5] In this context we became interested in preparing chiral phosphorus ylide **1**.[6] We carried out the reaction of ylide **1** with acetyl chloride and triethylamine (Scheme 1). This gave two products, the chiral allene **2** in 48% yield and the ylide **3** in 3% yield. The synthesis of allene **2** can be rationalized as the result of the Wittig reaction between the in situ generated ketene and phosphorus ylide **1**.

A crucial aspect of this reaction to be studied would be to evaluate the possibility of having asymmetric induction. The presence of the 10-phenylsulfonylisoborneol unit in ylide **1** could allow the selective synthesis of allenes with axial chirality in the reaction with monosubstituted acetyl chloride and triethylamine. Accordingly, the reaction of ylide **1** with methylketene, generated from propionyl chloride and triethylamine, was carried out leading to chiral allene **4**[7] in 62% yield
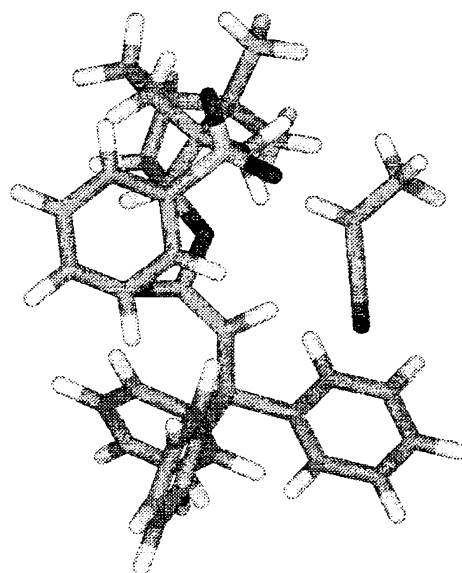

Figure 2. Lowest energy conformation of **1** and of methylketene determined by molecular mechanics calculations.[8–10]

(Scheme 1). The ^{1}H NMR spectrum of **4** showed signals for a single diastereoisomer.

The structure of 10-phenylsulfonylisobornyl (*S*)-penta-2,3-dienoate (**4**) was determined by X-ray crystallography as illustrated in Figure 1.[†] The diffraction spectrum of the powder was obtained and was identical to the simulation of the diffraction spectrum for compound **4** based on the X-ray diffraction data collected from the single crystal. This is also in agreement with the existence of only one stereomer.

The stereochemical outcome of this asymmetric Wittig type reaction can be explained considering the mechanism outlined in Scheme 2. The presence of the chiral unit in the starting phosphorus ylide could determine the geometry of approach of the ketene as shown, leading to an allene with axial chirality corresponding to an *S* configuration. In order to corroborate this interpretation the lowest energy conformation of phosphorus ylide **1** and methylketene were determined by molecular mechanics calculations and indicated that the proposed geometry of approach corresponds to a favorable stereochemical interaction[8–10] (Fig. 2).

The cleavage of the chiral auxiliary was achieved by promoting the alkaline hydrolysis[3b] of allene **4**. Penta-2,3-dienoic acid[11] was isolated and showed $[\alpha]_D^{25} = +98$.

Scheme 2.

The sign of the optical rotation values may be predicted and a rough estimation may be done. In fact, the concept of an asymmetric screw pattern of polarisability at a chiral center was applied by Lowe[12a] and Brewster[12b] to work out an empirical rule for assigning the absolute configuration of optically active allenes. Therefore, according to the Lowe–Brewster's rule the penta-2,3-dienoic acid with *S* configuration should be dextrorotatory as indeed is the case.

The CD and UV spectra were recorded for chiral allenes **2** and **4**, both having the isobornyl moiety but **4** having also axial chirality. The UV spectra of **2** and **4** are quite similar since the perturbations of molecular electronic states by alkyl groups, particularly the $-CH_3$ group, are normally small, and as mentioned by Runge et al.,[13] it was not expected that it would be very important in the allenic derivatives. However, the CD of **2** and **4** show quite distinct features, particularly in the 200–210 and 230–250 nm regions (Fig. 3). A plausible reason for the difference found in the 200–210 nm region of the CD is the contribution of the n→π* carbonyl transition of the ester group, which is expected to be in the 200–215 nm range. The application of the octant rule for compound **4** indicates that a negative CD signal is predicted for the n→π* carbonyl transition.[14,15] For **4** this is seen at 205 nm, where a negative band is recorded over two positive peaks due to benzenic and allenic transitions (at $\lambda_{max} \sim 211$ and <200 nm). Significant differences are also seen in the CD spectra of our allenes **2** and **4** in the 230–250 nm regions, where the S_7, S_8 bands are expected to appear. The origin of these bands was previously explained for the phenylallenes.[13] While in the UV spectrum there are no significant differences due to the presence of the methyl group, in the CD of **4** these bands are much more intense. Therefore, as for the phenylallenes,[13] the S_8 band appears to reflect the characteristic stereochemical features of the allenic moieties, and differences are found in the CD spectra of **2** and **4** in the 230–250 nm range.
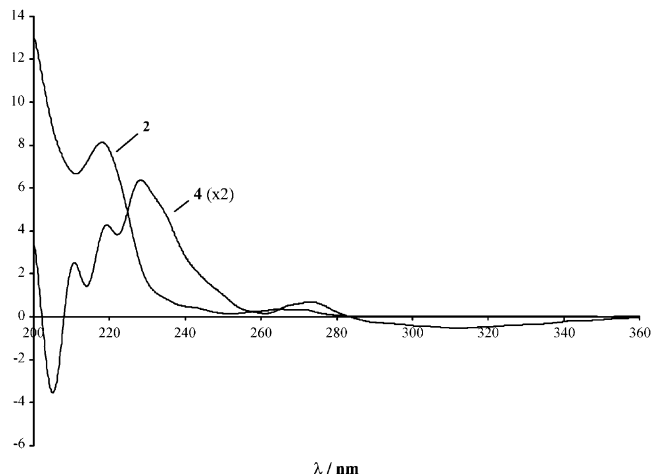
In conclusion, we report the reaction of ketenes, generated in situ from acid chlorides and triethylamine, with phosphorus ylides to give allenic compounds. The study allowed the synthesis of chiral allenic esters via an asymmetric Wittig reaction. Studies are underway in order to evaluate the scope of this synthetic methodology.

Acknowledgements

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7. *10-Phenylsulfonylisobornyl (S)-penta-2,3-dienoate* **4**: To a stirred solution of the ylide **1** (0.4 g, 0.67 mmol), and triethylamine (0.16 mL) in tetrahydrofuran a solution of propionylchloride (0.67 mmol, 0.06 mL) in tetrahydrofuran (1.0 mL) was added dropwise. The mixture was stirred under nitrogen at room temperature for 12 h, filtered and the filtrate concentrated under vacuum. The crude oil was dissolved in CH_2Cl_2, washed with water, dried ($MgSO_4$) and evaporated off. The product was purified by flash chromatography [ethyl acetate/hexane (3:1)] giving allene **4** as a white solid (0.155 g, 62%); mp 96.0–97.6°C (from ethyl ether–hexane); IR: ν_{max} 1715 and 1961 cm^{-1}; δ_H 0.85 (3H, s), 0.87 (3H, s), 1.24–1.29 (1H, m), 1.69–2.04 (9H, m), 2.99 (1H, d, $J = 14.1$ Hz), 3.60

Figure 3. CD spectra for compounds **2** and **4**.

(1H, d, $J = 14.1$ Hz), 4.69 (1H, dd, $J = 3.2$ and 8.4 Hz), 5.43–5.47 (2H, m), 7.51–7.57 (2H, m, Ar-H), 7.62–7.64 (1H, m, Ar-H), 7.89–7.91 (2H, m, Ar-H); δ_C 12.7, 19.7, 20.3, 27.1, 29.3, 39.4, 44.0, 49.4, 49.9, 55.0, 77.5, 88.1, 89.7, 127.7, 129.2, 133.5, 141.1, 164.2, 213.1; $[\alpha]_D^{25} = +148$ (*c* 1, CH_2Cl_2).

8. Molecular mechanics PCFF300 (101) force-field calculations were undertaken using the Cerius[2] (version 3.5) molecular modeling program.[10]

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14. The classic octant rule is basically applicable to the $n \rightarrow \pi^*$ transition of saturated cyclic ketones.[15] However its main basis is the division of space around the carbonyl group into eight regions (octants) and each atom (or group of atoms) of the molecule is assumed to induce a contribution to the observed CD, whose sign is determined by the octant in which the atom lies. In most theoretical approaches the CO chromophore is treated with no strict previous assumptions about the rest of the molecule (except its chirality). For the C=O group of esters, the $n \rightarrow \pi^*$ transition is shifted to higher energies, in a region where other bands are also present. The molecular structure of compound **4**, bearing a carboxylate chromophore, is known (Fig. 1) and we applied the same sector rules, considering the position of the groups in space.

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