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# 1,3-DIOXA-[3,3]-SIGMATROPIC OXO-REARRANGEMENT OF SUBSTITUTED ALLYLIC CARBAMATES: SCOPE AND MECHANISTIC STUDIES

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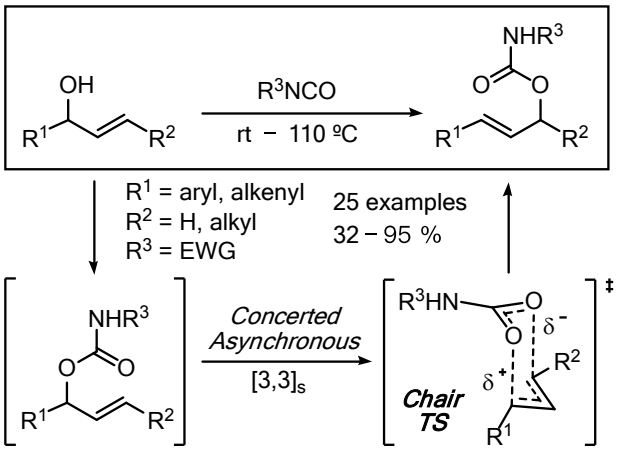



**ABSTRACT**: An unexpected 1,3-dioxa-[3,3]-sigmatropic rearrangement during the treatment of aryl- and alkenyl-substituted allylic alcohols with activated isocyanates is reported. The reorganization of bonds is highly dependent on the electron density of the aromatic ring and the nature of isocyanate used. This metal-free tandem reaction from branched allyl alcohols initiated by a carbamoylation reaction and followed by a sigmatropic rearrangement thus

offers a new access to (*E*)-cinnamyl and conjugated (*E*,*E*)-diene carbamates such as *N*-acyl and *N*-sulfonyl derivatives. A computational study was conducted in order to rationalize this phenomenon as well as a rearrangement progress kinetic analysis was performed.

## INTRODUCTION

Among the plethora of tools at the disposal of synthetic organic chemists, the [3,3]-sigmatropic rearrangements represent very useful methods for the regio and stereoselective formation of carbon-carbon or carbon-heteroatom bonds.[1] Among the C-N bond forming reactions, the sigmatropic rearrangement of allylic trichloroacetimidates, namely the Overman rearrangement,[2] occupies a place of choice as shown by the number of total synthesis involving this method.[3] The decarboxylative [3,3]-rearrangement of allylic carbamates represents also a very useful strategy for the preparation of protected allylic amines from allylic alcohols with an excellent regio-and stereoselectivity.[4,5] Initially reported by Holm et al. in 1970,[6] the allyl cyanate/isocyanate rearrangement can be now considered as an attractive alternative method to those above-mentioned, due to the fact that the transposition occurs at or below ambient temperature, under metal-free conditions and with a complete transfer of chirality.[7] The first step of this process is the formation of the transient allyl cyanate from a carbamate-type **B**, under dehydration conditions, followed by a spontaneous [3,3]-sigmatropic bond reorganization to afford the corresponding allyl isocyanate **C** (Figure 1). This domino dehydration/rearrangement sequence was successfully applied on a wide variety of carbamates coming from alkyl-substituted allylic alcohols such as **A**.[8] As a continuation of our studies on the use of this methodology for the synthesis of new reagents or original compounds,[9] we envisaged the formation of branched substituted carbamates of **B**-type in which R would be an aryl group since they have never been employed to date in this kind of rearrangement.[7b] However, as preliminary result, we observed that treatment of 1-(4-methoxyphenyl)prop-2-en-1-ol with trichloroacetyl isocyanate followed by a basic hydrolysis following a standard sequential process did not provide the expected branched compound (Figure 1). The only product formed was a primary carbamate **4a** with a well-defined stereochemistry of the double bond (*E*). In view of previous works concerning the thermal rearrangement of allylic esters,[10,11] we envisioned at this stage that the formation of **4a** could be the outcome of a rapid 1,3-dioxa-[3,3]-sigmatropic rearrangement[12] from the branched trichloroacetyl carbamate intermediate before hydrolysis.

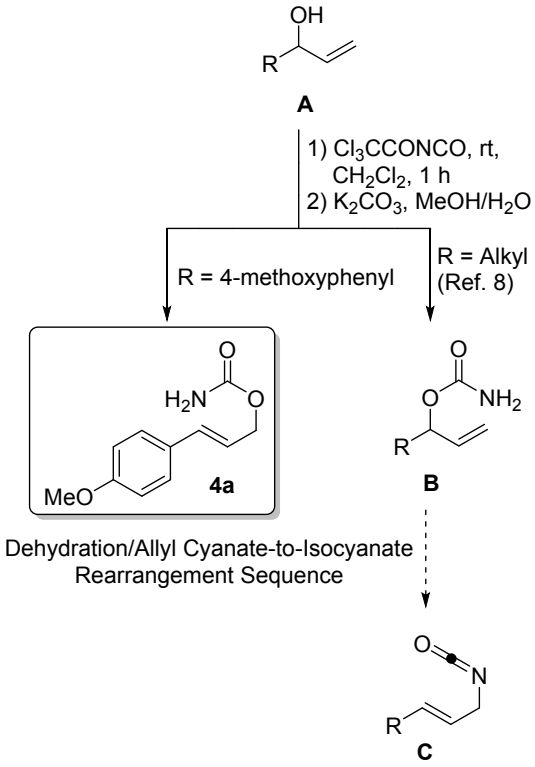



**Figure 1.** Observation of the uncatalyzed 1,3-dioxa-[3,3]-sigmatropic rearrangement.

Surprisingly, this rearrangement does not require any metal catalyst and takes place under neutral conditions.[13] Indeed, the scarce examples described in literature require catalytic methods based on palladium (II) or mercury (II) salts.[14] Taking into account the important role of molecules bearing a carbamate group as synthetic intermediates[15] as well as in modern drug discovery,[16] and that this one-pot process starting from 2-alken-1-ols (**A**, R = aryl or alkenyl) could constitute a valuable access to linear allyl carbamates (Figure 2),[17] we decided to further explore the substrate scope and limitations of this methodology in order to offer a rationalization of this phenomenon.

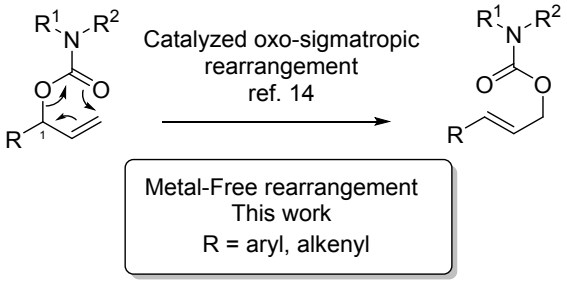


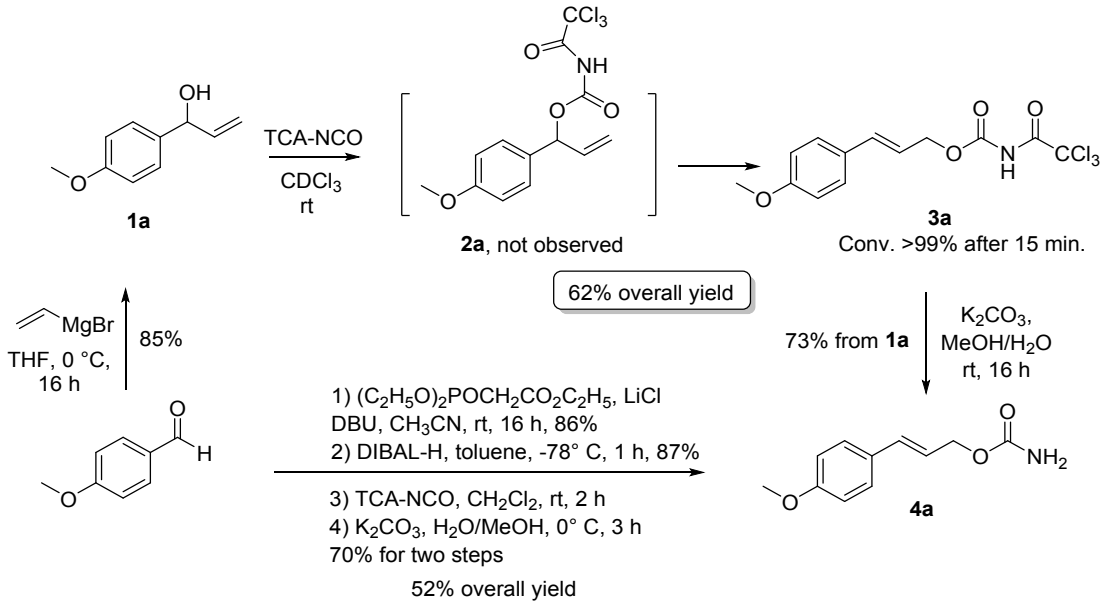

**Figure 2.** Proposed 1,3-dioxa-[3,3]-sigmatropic rearrangement of *O*-allyl carbamates.

In this paper, we report the results of our study. We show that the rate of the 1,3-dioxa-[3,3] sigmatropic rearrangement depends mainly on the electron density of the aromatic ring. These experimental observations have been confirmed by a kinetic study establishing that the rearrangement is of first kinetic order. The nature of the isocyanate used is also important for the transposition to occur. Activated reagents such as trichloroacetyl or *p*-toluenesulfonyl isocyanates were required. Other substrates, in which an aryl group at the allylic position (C1) was replaced by an alkenyl group, were also examined with success. In addition, a computational study of the mechanism has also been carried out in order to seed some light on the nature of this stereoselective thermal rearrangement.

## RESULTS AND DISCUSSION

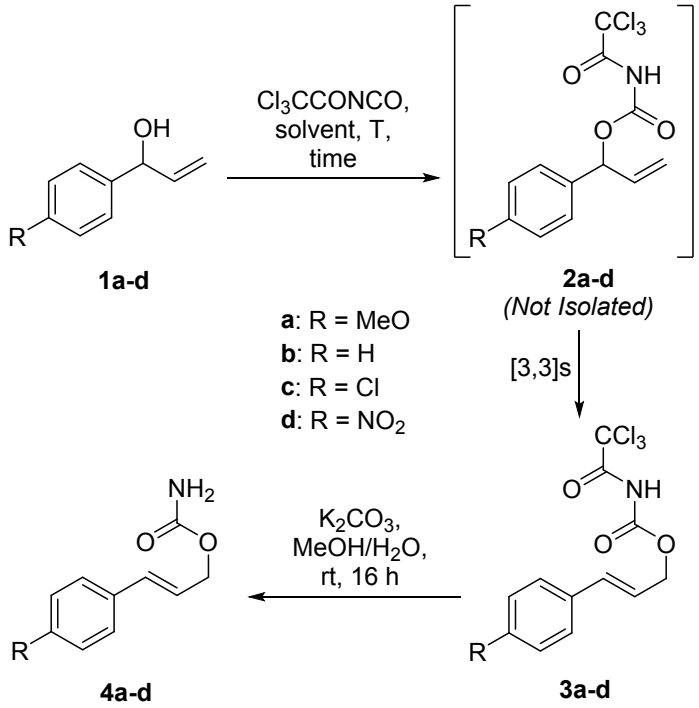
**Experimental studies.** First of all, we carefully examined the reaction of 1-(4-methoxyphenyl)prop-2-en-1-ol **1a** with trichloroacetyl isocyanate by monitoring the carbamoylation over time by $^1$H NMR (Scheme 1). At room temperature, the reaction is complete after 15 minutes in favor of the formation of **3a**, product which may result of a [3,3] sigmatropic rearrangement from intermediate **2a**. At no moment during this NMR study was the branched carbamate **2a** detected indicating the short-lived nature of this reaction intermediate even at lower temperature (-70 °C). In all cases only the linear carbamate **3a** was formed, with (*E*)-stereochemistry of the internal double bond. After evaporation of solvent,[18] **3a** could be isolated from the reaction medium by trituration techniques or used without further purification. Treatment of crude mixture under basic conditions in the presence of $K_2CO_3$ afforded the expected compound **4a** with 73% overall yield from **1a** and 62% from 4-methoxybenzaldehyde. It is noteworthy that this new compound **4a** was also prepared from the same starting material, according to a conventional longer strategy (four steps instead of three) and a poorer overall yield (52%).[19]

**Scheme 1. Synthesis of 4a Using a Rearrangement/Hydrolysis Sequence.**




In order to determine the main factors that influence this sigmatropic rearrangement, different secondary allylic alcohols bearing both electron withdrawing and electron donating groups at para position on the aromatic ring were tested in the presence of trichloroacetyl isocyanate (TCA-NCO). As summarized in Table 1, the bond reorganization is highly dependent on the nature of the substituent. Except when the mesomeric effect is positive (+M, R = OMe, entry 1), heating the reaction mixture was required for all other cases (entries 2-4). During the NMR study, the formation of intermediates **2b-d** was clearly identified as being the first step before rearrangement can occur. The results obtained confirmed that the rate of this reaction is much slower with electron-deficient aromatic rings. Indeed, conversion of **2c** into **3c** (R = Cl, -I and +M effects) was complete after 20 h at 90 °C (entry 3) while with R = $NO_2$ (-I and -M effects), the time of reaction was increased sixfold to reach only 50% conversion to **3d** (entry 4). These results suggest a significant electron-deficient character for the allyl moiety along this sigmatropic process. After evaporation of solvent and hydrolysis under basic conditions, all linear carbamates **4** were obtained as single stereoisomer (*E*) and with moderate to good yields.

**Table 1. Synthesis of Linear Carbamates 4 from Allyl Alcohols 1 Using Trichloroacetyl Iscocyanate.**



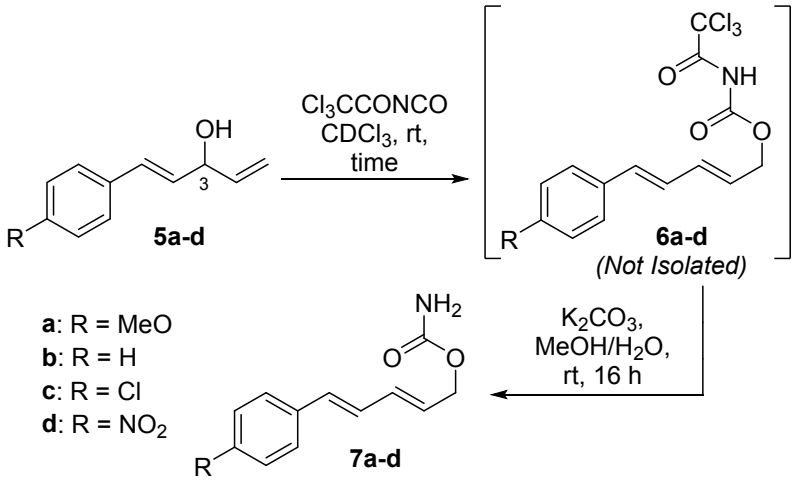

| Entry | R | Solvent | T (° C) | Time (h)[a] | Product (Yield, %)[b] |
|---|---|---|---|---|---|
| 1 | MeO | $CH_2Cl_2$ | r.t. | 0.25 | **4a**, 73 |
| 2 | H | Toluene | 90 | 16 | **4b**, 92 |
| 3 | Cl | Toluene | 90 | 20 | **4c**, 50 |
| 4 | $NO_2$ | Toluene | 90 | 120[c] | **4d**, 43 |

[a] Reaction was monitored by $^1$H-NMR until total consumption of starting material using a deuterated solvent. [b] Isolated yield of pure product. [c] 50% conversion observed.

Considering the potential importance of dienyl carbamates in the synthesis of natural products,[20] the carbamoylation/rearrangement/hydrolysis sequence was also extended to other substrates such as C3-alkenyl-substituted allylic alcohols **5**. The results indicated in Table 2 led to similar conclusions regarding the electronic effects that promote the rearrangement. More the aromatic ring was electron-rich, faster was the sigmatropic process. The difference of reaction rate between starting materials **1** and **5**, both of them possessing the same substitution pattern on the aromatic ring can be in part explained by the generation of a conjugated diene unit acting as the driving force due to the higher stability of products **6**. For instance, the rearrangement took place from **5c** in the presence of trichloroacetyl isocyanate (Table 2, entry 3) without heating, whereas a temperature of 90 ºC was required for starting alcohol **1c** (Table 1, entry 3). In the case of nitro group (entry 4, Table 2), the rearranged product **6d** was not observed by NMR analysis even after 7 days of reaction at 90 ºC, most likely due to the instability of the corresponding reaction intermediates at this temperature. In all other cases, the linear conjugated diene carbamates **7** were obtained after basic hydrolysis

in good yields, except for R = OMe (Table 2, entry 1), for which the purification on silica gel led to lose of product.

**Table 2. Carbamoylation/Rearrangement/Hydrolysis Sequence of C3-Alkenyl-Substituted Allyl Alcohols 5.**

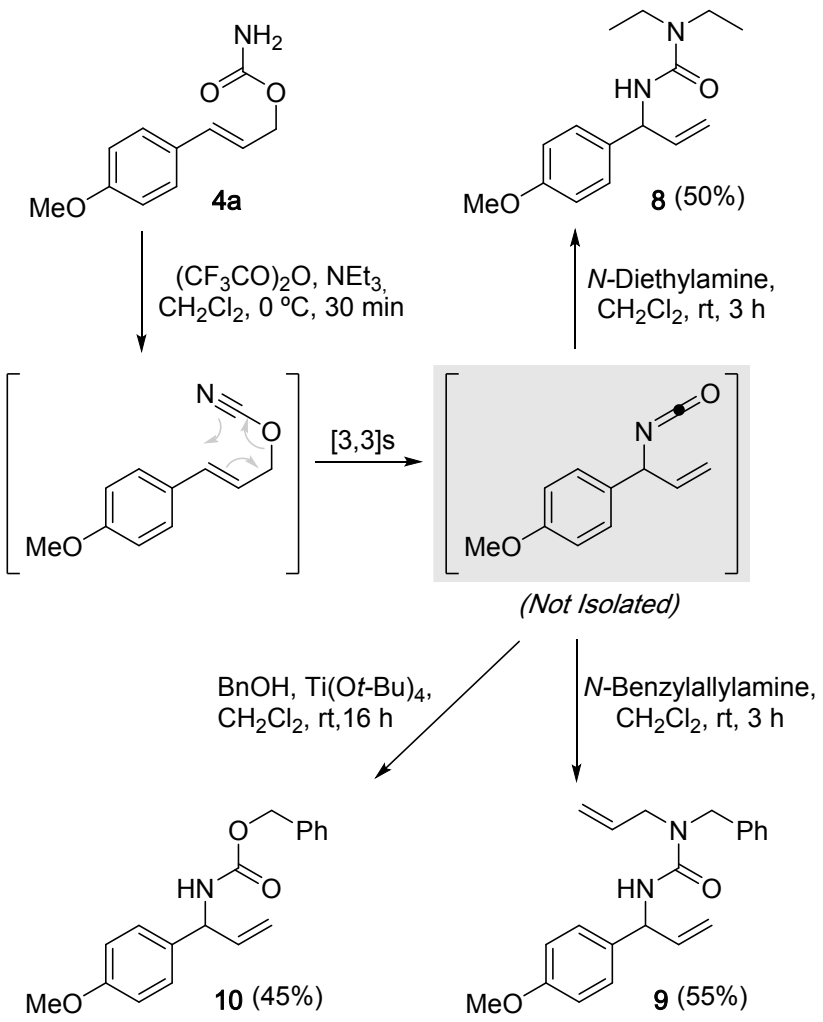



| Entry | R | Time (h)[a] | Product (Yield, %)[b] |
|---|---|---|---|
| 1 | MeO | 2 | **7a**, 24(65)[e] |
| 2 | H | 4 | **7b**, 65 |
| 3 | Cl | 4 | **7c**, 75 |
| 4[c] | $NO_2$ | 178[d] | - |

[a] Reactions were monitored by $^1$H-NMR until total consumption of starting material. [b] Isolated yield of pure product. [c] Reaction carried out in toluene-*d8* at 90 °C. [d] No formation of desired product was observed. [e] Determined by $^1$H-NMR using 1,3,5-trimethoxybenzene as internal reference.

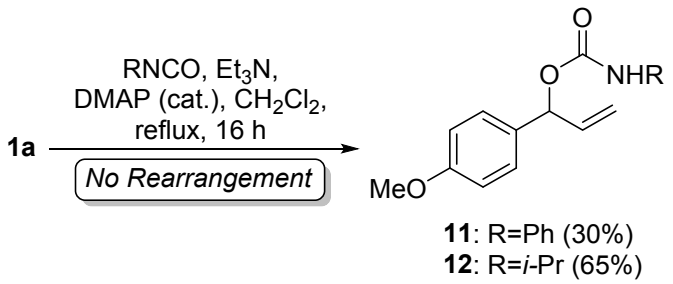
In order to bring to light the utility of this new process, the synthetic interest of linear carbamates such as **4a** was evaluated through a [3,3]-allyl cyanate rearrangement.[21] Treatment of **4a** with trifluoroacetic anhydride (TFAA, 1.5 equiv) in the presence of a large excess of $Et_3N$ at 0 °C for 30 min. led to the complete formation of isocyanate which can be quenched with various nucleophiles to afford compounds **8**, **9** and **10** in unoptimized yields (Scheme 2). When benzyl alcohol was used as nucleophile, a catalytic amount of Ti(O*t*-Bu)$_4$ was required.[22]

**Scheme 2. Selected In Situ Transformations of Rearranged Carbamate 4a.**



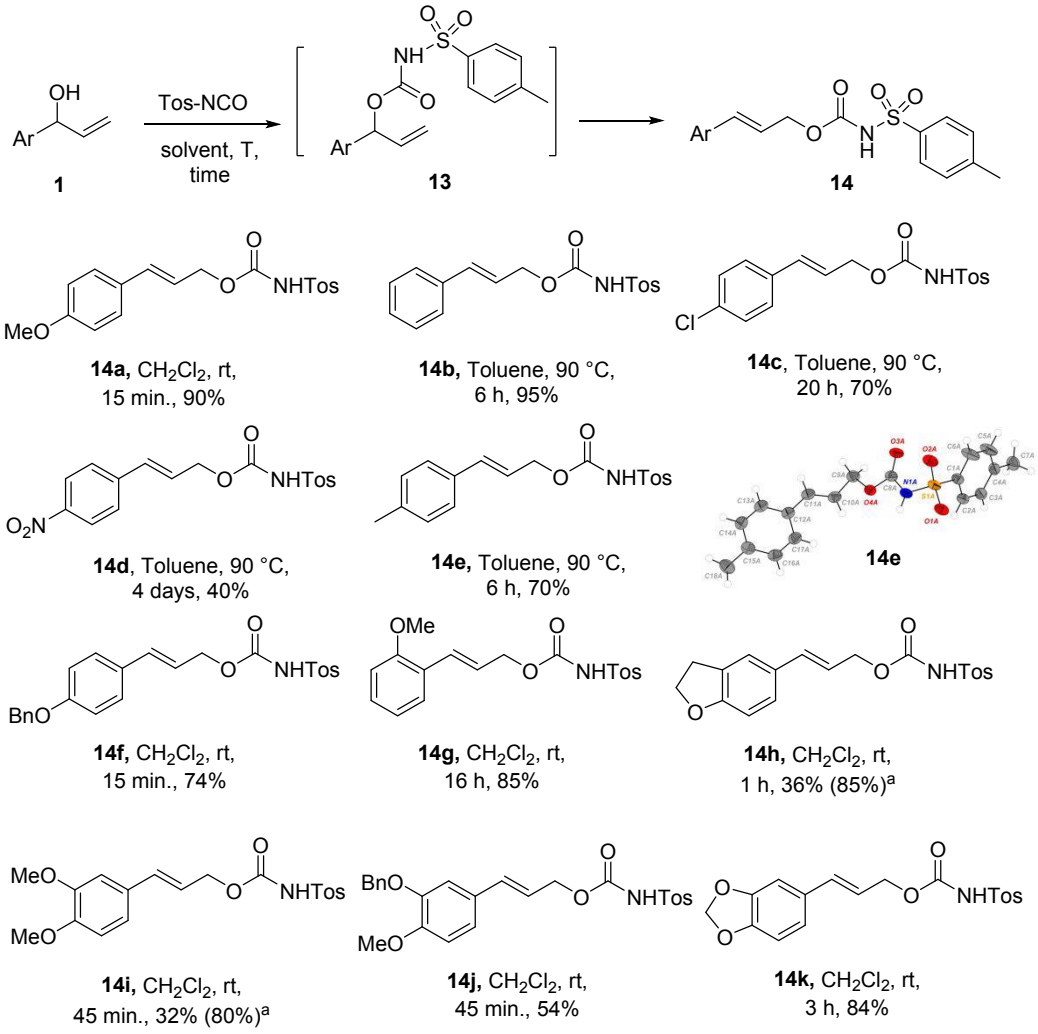

In our quest to determine the parameters influencing this 1,3-dioxa-[3,3]-sigmatropic rearrangement, the nature of the reagent was afterwards examined using deactivated isocyanates. As expected, treatment of **1a** with aliphatic or aromatic isocyanates in the presence of $Et_3N$ and a catalytic amount of DMAP gave rise to the corresponding branched carbamates **11** (R = Ph) and **12** (R = *i*-Pr) with no trace of linear rearranged carbamates, as revealed by NMR analysis of the corresponding crude reaction mixtures (Scheme 3).[23,24] When the phenyl isocyanate was used, the conversion was incomplete, which justifies the low yield obtained for the isolated compound **11** (30%). From these last results, the presence of the *N*-trichloroacetyl group in carbamates, such as **2a,** appears to be critical for the implementation of the rearrangement, likely by making the NH group less basic.

**Scheme 3. No Rearrangement Observed with Deactivated Isocyanates During The Carbamoylation Reaction**




In order to validate our hypothesis that the reorganization of branched aryl allyl carbamates could be reliant on the acidity of the carbamate NH, we tried the reaction between the allyl alcohol **1a** and *p*-toluenesulfonyl isocyanate. After 15 minutes at room temperature in $CH_2Cl_2$, the conversion into linear *N*-tosyl carbamate **14a** was complete leading exclusively the (*E*)-isomer. In these conditions, the product was obtained after purification with an excellent yield (90%) from **1a** (Table 3). The one-pot reaction was extended to other aryl allyl alcohols **1** with good to high yields of purified products **14,** except for **14h** and **14i** because of their weak stability on silica gel. For substrates with electron-poor aromatic rings (**1b**, **1c**, **1d**, **1e**), heating in toluene solution was required. In all cases, the exclusive *E*-isomer formation of the internal double bond was maintained. Structure of **14e** was determined by X-ray crystallography.

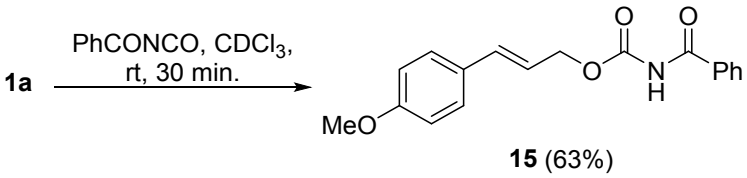
**Table 3. 1,3-dioxa-[3,3]-Sigmatropic Rearrangement Using *p*-Toluenesulfonyl Isocyanate as Reagent.**




[a] Determined by $^1$H-NMR using 1,3,5-trimethoxybenzene as internal reference.

Benzoyl isocyanate was also successfully employed to yield the rearranged product **15** from **1a** (Scheme 4). After 30 minutes in $CDCl_3$, the starting material was completely consumed and the primary carbamate **15** was obtained in 63% yield after purification.

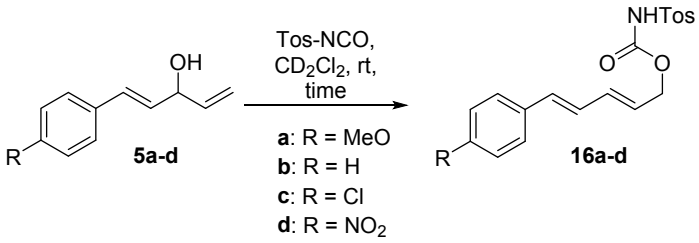
**Scheme 4. Carbamoylation/Rearrangement Sequence Using Benzoyl Isocyanate.**




In the same way, the one-pot process using tosyl isocyanate reagent was carried out successfully from C3-alkenyl-substituted allyl alcohols **5** to afford the corresponding (*E,E)*-

conjugated linear carbamates **16** (Table 4). Nevertheless, compound **16d** (R = $NO_2$, Table 4, entry 4) was obtained in moderate yield after separation of the unreacted starting material.

**Table 4. Carbamoylation/Rearrangement Sequence Using Tosyl Isocyanate From C3-Alkenyl-Substituted Allyl Alcohols 5.**

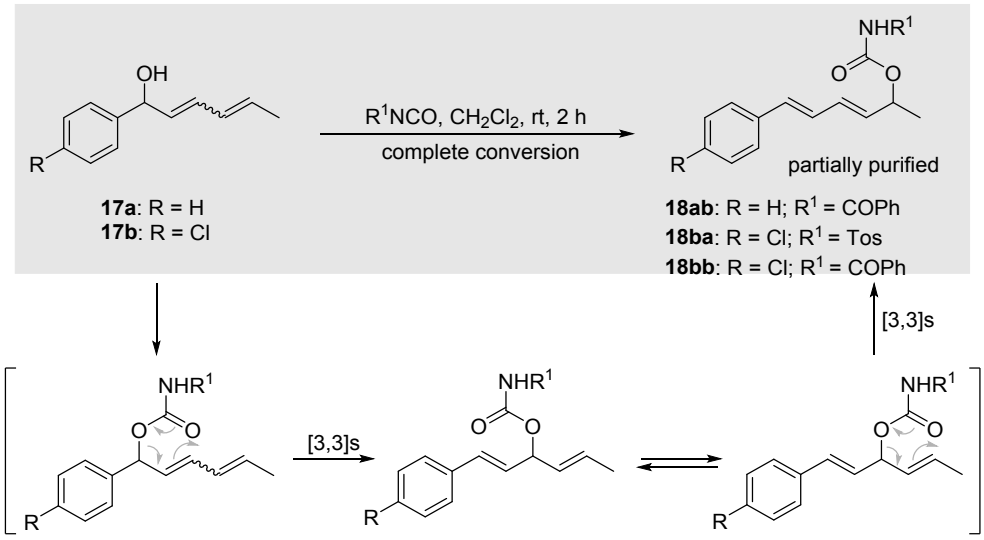



| Entry | R | Time (h)[a] | Product (Yield, %)[b] |
|---|---|---|---|
| 1 | MeO | 0.5 | **16a**, 25(85)[e] |
| 2 | H | 4 | **16b**, 75 |
| 3 | Cl | 4 | **16c**, 68 |
| 4[c] | $NO_2$ | 120[d] | **16d**, 36 |

[a] Reactions were monitored by $^1$H-NMR until total consumption of starting material. [b] Isolated yield of pure product. [c] Reaction carried out in toluene-*d8* at 90 °C. [d] 50 % conversion was observed. [e] Determined by $^1$H-NMR using 1,3,5-trimethoxybenzene as internal reference.

In order to test whether the carbamoylation reaction could be followed by a sequential double sigmatropic oxo-rearrangement in a one-pot process, 1-aryl-2,4-butadien-1-ols **17** as a mixture of stereoisomers were prepared from hexanedial according to a described procedure (Scheme 5).[25] Treatment of **17** with tosyl and benzoyl isocyanates led to the formation of the corresponding rearranged products **18ab**, **18ba** and **18bb** respectively. The reactions took place at room temperature with a complete conversion after 2 h in $CH_2Cl_2$, but unfortunately the purification of these compounds is difficult due to their instability on silica gel (see Experimental Section). It should be noted, however, that even in the presence of a deactivating group on the aromatic ring, these substrates are prone to undergo this consecutive double rearrangement under mild conditions, as demonstrated with alcohol **17b**.

**Scheme 5. Consecutive [3,3]-Sigmatropic Rearrangements from Starting Alcohols 17.**




Finally, we studied the stereoselectivity of the rearrangement in terms of the transfer of chirality when a chiral allyl alcohol is used as starting reactant. To this end, we analyzed the behavior of racemic (*E*)-1-phenylbut-2-en-1-ol **20** and its (*S*)-enantiomer (Figure 3).[26] This latter starting alcohol was separated from a racemic mixture by HPLC using a chiral stationary phase (see the Experimental Section). After this chromatographic separation, (*S*)-**20** was obtained with an enantiomeric excess of 98%. Both racemic and (*S*)-**20** were transformed into carbamates **21** (not isolated, see Figure 3) by reaction with (*R*)-[1-(4-fluoro-phenyl)ethyl]isocyanate (*R*)-**19** in the presence of triethylamine. After two days of reaction at 110 ºC in toluene the corresponding rearranged products **22** was obtained. The HPLC profile of the diastereomeric mixture of (*S*,*R*)+(*R*,*R*) carbamates **22** showed two well-defined peaks compatible, within the experimental error, with that would be expected for the reaction product stemming from racemic **20**. In the case of the product formed using (*S*)-**20** as reactant, formation of (*S*,*R*)-**22** was observed with 95% diastereomeric excess, according to the HPLC profile. These results, show that, within the experimental error, most of –if not all– the observed rearrangement takes place *via* a symmetry allowed concerted *supra-supra* mechanism, with virtually complete 1,3-transfer of the chiral information contained in the starting alcohol, together with retention of configuration of the double bond. The mechanistic aspects derived from this observation shall be discussed in the following section.

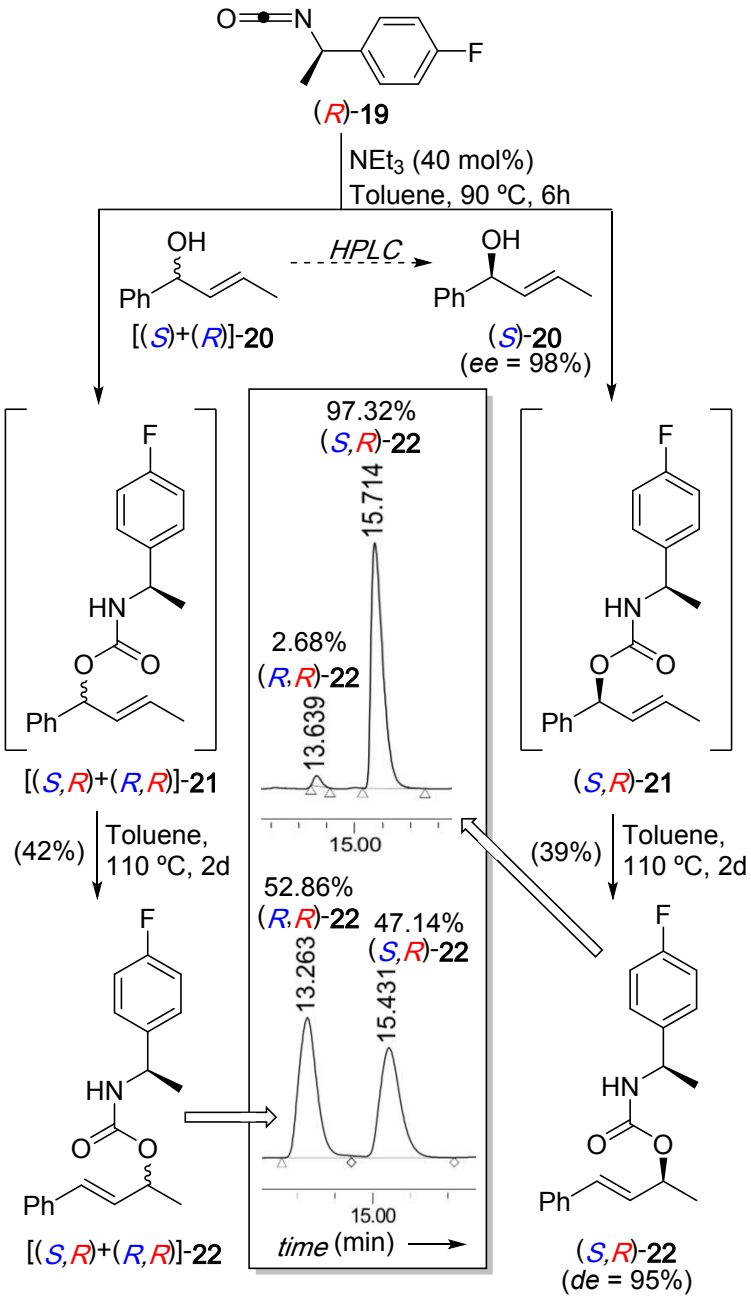



**Figure 3.** Assessment of the chirality transfer in the reaction between isocyanate (*R*)-**19** and alcohol **20**. The HPLC chromatograms are also shown.

**Mechanistic studies.** Conversion of alcohols **1b,c** (R=H, Cl, respectively) into the rearranged products **14b,c** in the presence of *p*-toluenesulfonyl isocyanate was monitored by $^{1}$H-NMR in deuterated toluene at 90 ºC. A selected ensemble of spectra recorded at different reaction times is gathered in Figure 4. These data indicate that alcohol **1c** is immediately converted into carbamate **13c**, as it can be appreciated by comparison of both spectra. This intermediate

carbamate evolves towards the rearranged product **14c** with no detectable intermediate species. Using these NMR data and applying first-order kinetics in eq 1

$$\ln[\mathbf{13c}]_t - \ln[\mathbf{13c}]_0 = -k_{obs}\mathrm{t} \quad (1)$$

we obtained $k_{obs} = 1.08(\pm 0.04)\ x\ 10^{-4}$ s$^{-1}$. A similar study for alcohol **1b** (R=H) led to a measured kinetic constant of $k_{obs} = 1.62(\pm 0.06)\ x\ 10^{-4}$ s$^{-1}$ (see the Supporting Information). These results were confirmed in a combined experiment using a 1:1 mixture of **1b** and **1c**, to which a 50 % of *p*-toluenesulfonyl isocyanate was added. After 5 min. of reaction at room temperature, the $^1$H-NMR analysis revealed that ca. 50 % of both alcohols remained unreacted, whereas carbamates **13b** and **13c** were observed in a 1.0:1.2 ratio. After 6h of reaction at 90 ºC, a complete **13b→14b** (R=H) conversion was observed, whereas for the **13c→14c** (R=Cl) rearrangement the conversion was of ca. 40 %. These results showed that the fast formation of carbamates **13** from alcohols **1** is not selective and that the subsequent dioxa-[3,3]-sigmatropic rearrangements occur through a kinetically independent process, not related to the formation of the starting carbamate. In the case of alcohol **1a** (R=OMe) the reaction was too fast to obtain a reliable first-order kinetic under the same experimental conditions used for **1b** and **1c**. However, we could measure the first-order reaction rate until 15 min of reaction at room temperature and obtained $k_{obs} = 1.63(\pm 0.05)\ x\ 10^{-3}$ s$^{-1}$, one order of magnitude faster than in the preceding cases. Similar experiments with **1d** (R=$NO_2$) were not possible because the reaction was too slow. We also examined the efficiency of the reaction in the presence of polar solvents. When alcohol **1b** and tosyl isocyanate were allowed to react in DMSO or DMF no reaction was observed, whereas in acetonitrile only 35 % conversion was observed after three days of reaction at 90 ºC. These results are in agreement with those reported in Table **3** (vide supra). We concluded from these data that electron withdrawing groups at the aryl moiety of the starting alcohols result in lower reactivity. On the contrary, electron releasing groups such as methoxy accelerate the sigmatropic rearrangement. This conclusion is compatible with an electron deficient character of the allyl moiety at the corresponding transition state, an aspect (among others) that was analyzed by DFT calculations.

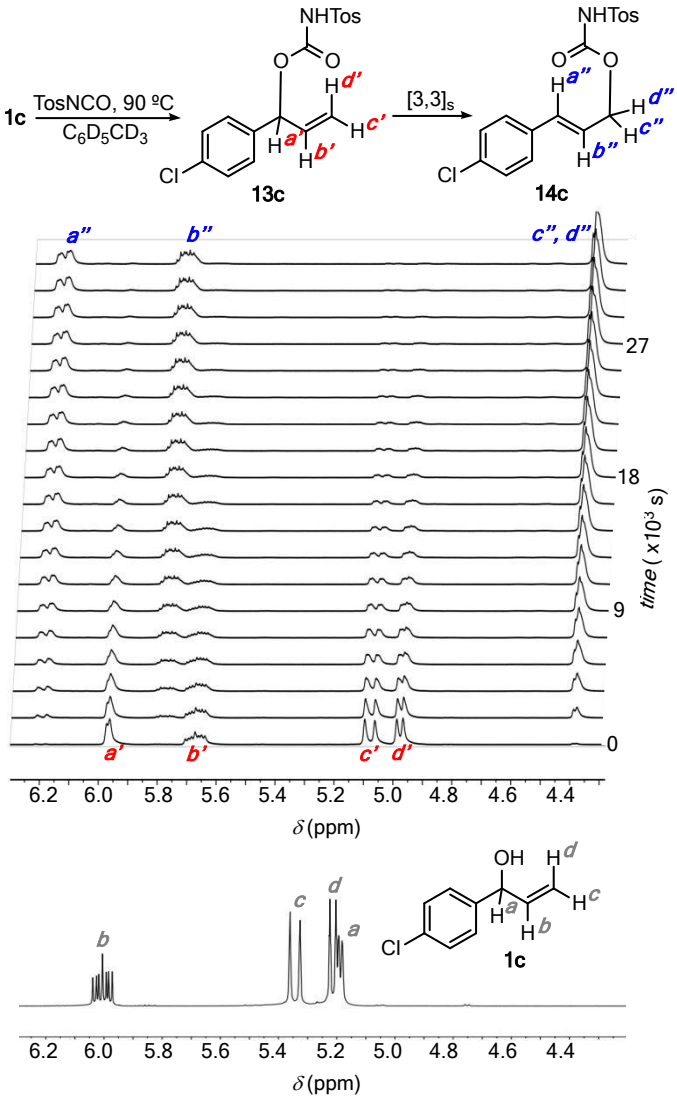


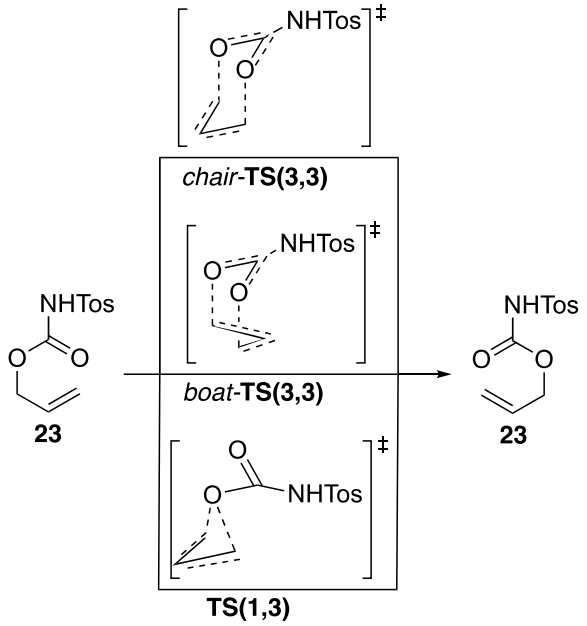

**Figure 4.** [1]H-NMR plots (500 MHz) corresponding to the reaction of 1-(4-chlorophenyl)prop-2-en-1-ol **1c** with of *N*-tosyl isocyanate at 90 ºC to yield rearranged carbamate **14c** *via* intermediate **13c**. The succesive spectra, recorded at different reaction times, show the evolution of the allylic hydrogens of both carbamates. The spectrum of the allylic region of **1c** is also shown.

Since the [1]H-NMR showed that the formation of 1-arylallyl tosylcarbamates **13b,c** from alcohols **1b,c** was not kinetically relevant, we carried out DFT calculations on these transformations. These calculations were performed at the B3LYP-D3(PCM)/6-311G++G(d,p) level of theory. Toluene was used as solvent and the Gibbs energies were calculated at 90 ºC (363.15 K).

Previous work on the rearrangement of allyl esters[10a,b] suggested that both [3,3] and [1,3] mechanisms could occur (Scheme 6). In addition, Birney,[11,27] Duncan[28] and respective co-workers have indicated that in esters and acetimidates both pericyclic and pseudopericyclic mechanisms can compete. In order to elucidate the preference for the [1.3] or [3,3] topologies

associated with these 1,3-dioxa-sigmatropic rearrangements, we studied computationally the degenerate rearrangement of allyl tosylcarbamate **23** via [1,3] or [3,3] sigmatropic shifts. In turn, within the [3,3] reaction path, we considered chair and boat geometries for the corresponding saddle points (Scheme 6) as well as the possible occurrence of pseudopericyclic mechanisms.

**Scheme 6. Possible [3,3] and [1,3] Mechanisms for the 1,3-Dioxa Rearrangement of Allyl Tosylcarbamate 23.**




The chief geometric and energetic features of transition structures chair-TS(3,3), boat-TS(3,3) and TS(1,3) are gathered in Figure 5. Our calculations indicate that the dioxa-[3,3]-sigmatropic mechanism is clearly preferred with respect to the [1,3] rearrangement involving only one of the oxygen atoms of the carboxylate moiety. Within the [3,3] mechanism, the chair geometry of the corresponding transition state is 4.6 kcal/mol less energetic than that associated with the boat analogue. These results are in agreement with the empirical observations reported by Lewis and Hill,[10] who established that the [1,3] mechanism is substantially more energetic than the [3,3] reaction path. On the other hand, the dihedral angles calculated for the three transition structures shown in Figure 5 indicate π–π interactions between both reactants, with dihedral angles $\omega$ of 85-110 deg. Since the participation of the lone pairs (orbitally disconnected to the C=O π–orbitals) of one or two oxygen atoms should lead to $\omega$ values close to 180 deg. (vide infra), we concluded that both

[1,3] and [3,3] geometries shown in Figure 5 correspond to pericyclic and not to pseudopericyclic processes. In addition, these 1,3-dioxa-[3,3]-sigmatropic rearrangements take place via chair geometries and symmetry allowed[29] *supra-supra* topologies.

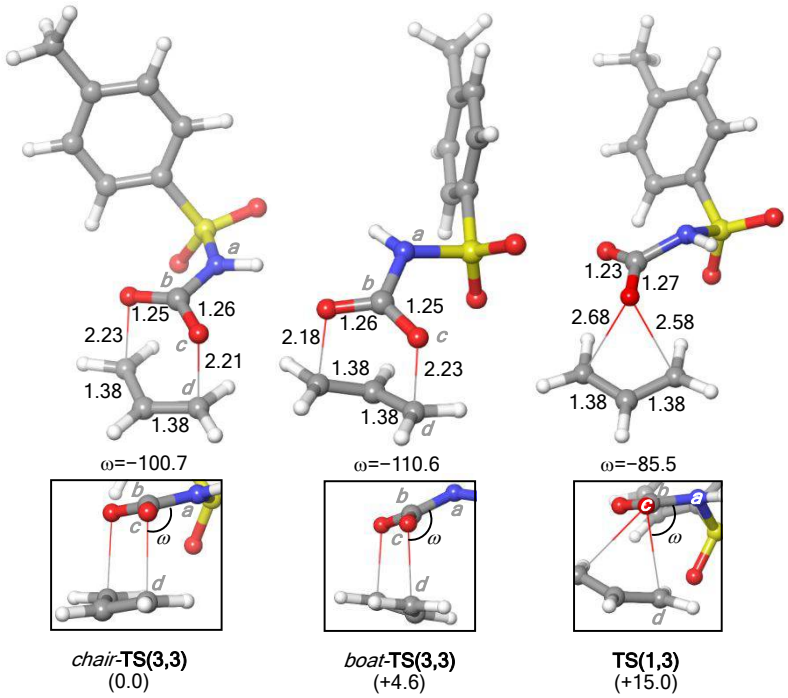



**Figure 5**. Optimized structures (B3LYP-D3(PCM=toluene)/6-311++G(d,p) level of theory) of transition structures *chair*-**TS(3,3)**, *boat*-**TS(3,3)** and **TS(1,3)** depicted in Scheme 6. Bond distances are in Å. Dihedral angle $\omega$ (in deg.) is defined by the *a-b-c-d* atoms. Numbers in parenthesis are the relative energies, in kcal/mol.

We also performed isotope labeling NMR experiments in order to verify the previously discussed computational results. These experiments were carried out by using a mixture of 11.1% $H_2{}^{17}O$, 29.7% $H_2{}^{18}O$ and 59.2% $H_2{}^{16}O$. Conversion of (trichloromethyl)benzene **24** into doubly labeled benzoic acid **25** under microwave irradiation[30] permitted two synthetic routes (Figure 6A). In the first one, we prepared diester **26** following a described procedure.[31] The $^{17}$O-NMR spectrum is shown in Figure 6B. In this spectrum two well separated signals at 340 and 136 ppm can be observed, associated with the $sp^2$ and $sp^3$-hybrydized $^{17}$O nuclei, respectively. This process permitted us to calibrate the performance of $^{17}$O-NMR to distinguish the starting and final resonances associated with the [$^{17}O_1$]**13b**→[$^{17}O_1$]**14b** transformation.

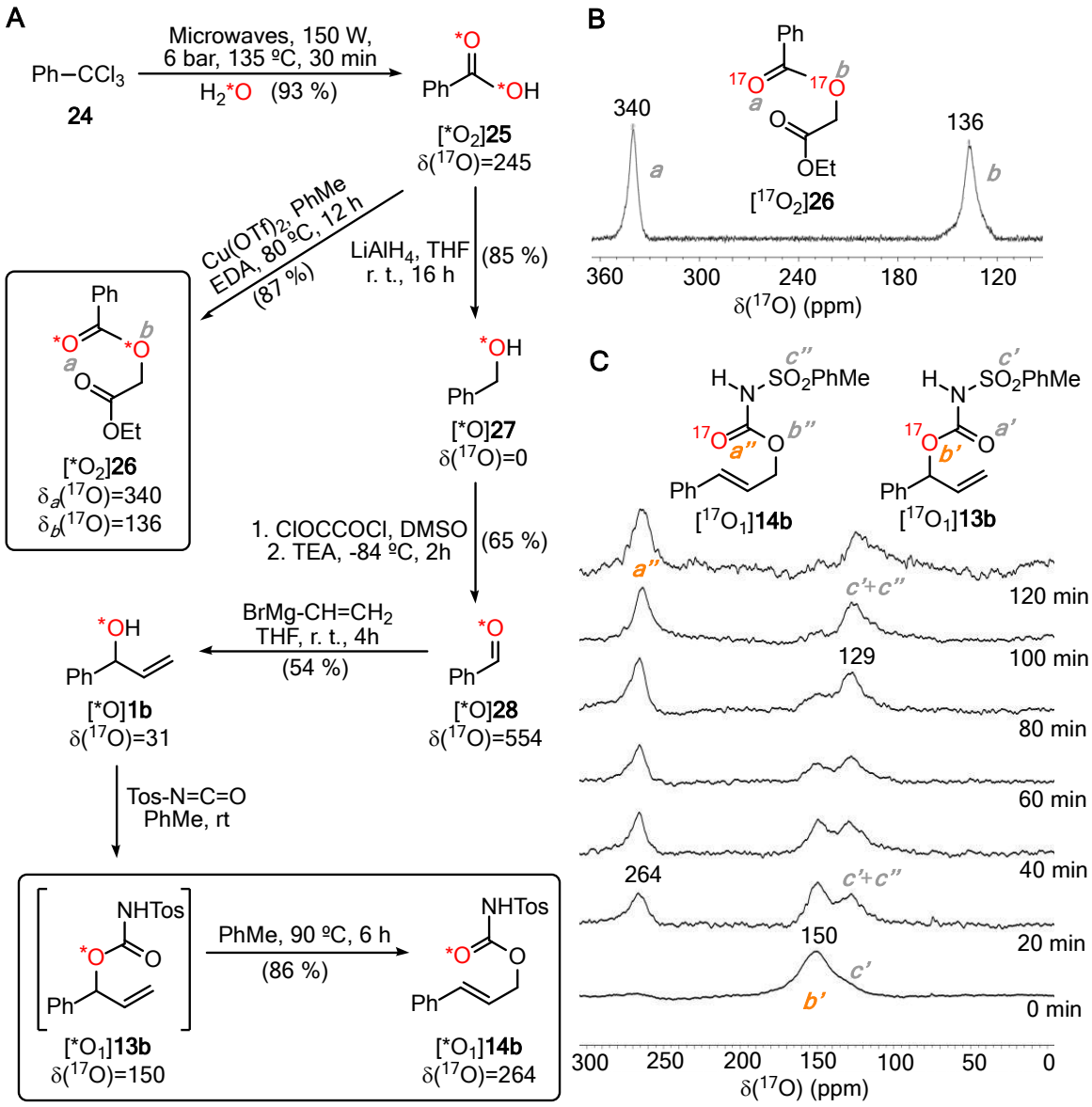



**Figure 6**. (A) Synthesis of labelled allyl tosylcarbamates [*$O_1$]**13b** and [*$O_1$]**14b**, and diester [*$O_2$]**26**. The [$^{17}$O]-labeled compounds were synthesized from a mixture of 11.1% $H_2{}^{17}O$, together with 29.7% $H_2{}^{18}O$ and 59.2% $H_2{}^{16}O$. The δ($^{17}$O) chemical shifts of the [$^{17}$O]-labelled compounds are given in ppm. (B) $^{17}$O-NMR spectrum of diester [$^{17}O_2$]**26**, in which the sp$^2$ and sp$^3$-hybridized oxygen atoms can be distinguished. (C) $^{17}$O-NMR spectra of the [$^{17}O_1$]**13b** →[$^{17}O_1$]**14b** transformation recorded in d$^8$-PhMe at different reaction times. The signals of sulfone oxygen atoms (*c'* and *c''*, natural abundances) are also given.

The second synthetic route of labeling experiments consisted of the conversion of labeled benzoic acid **25** into allyl alcohol **1b** via a sequence of reduction, oxidation and addition reactions involving O-labeled benzyl alcohol **27** and benzaldehyde **28**, whose diagnostic δ($^{17}$O) chemical shifts are gathered in Figure 6A (see the Supporting Information for further details). Reaction of labeled **1b** with tosyl isocyanate led almost immediately (vide

supra) to labeled **13b**. The $^{17}$O-NMR spectrum of labeled [$^{17}O_1$]**13b** showed a very broad signal at 150 ppm, partially superimposed to the signal associated with the sulfone moiety (natural abundance, see the Supporting Information for further details). Heating of [$^{17}O_1$]**13b** led us to observe a new signal at 264 ppm (Figure 6C), which was interpreted as associated with the sp$^2$-hybrydized $^{17}$O nucleus of [$^{17}O_1$]**14b** on the basis of the related signal of [$^{17}O_2$]**26** shown in Figure 6B. The emergent signal of [$^{17}O_1$]**14b** was coincident with the decrease of the broad signal of [$^{17}O_1$]**13b**, the broad signals of the $SO_2$ groups of both tosyl carbamates being of similar chemical shift.[32] These results, together with the above described calculations and experiments involving chiral species, led us to the conclusion that, as suggested by Lewis and Hill,[10] the conversion of carbamates **13** into their regioisomers **14** takes place via concerted pericyclic 1,3-dioxa-[3,3]-sigmatropic rearrangements.

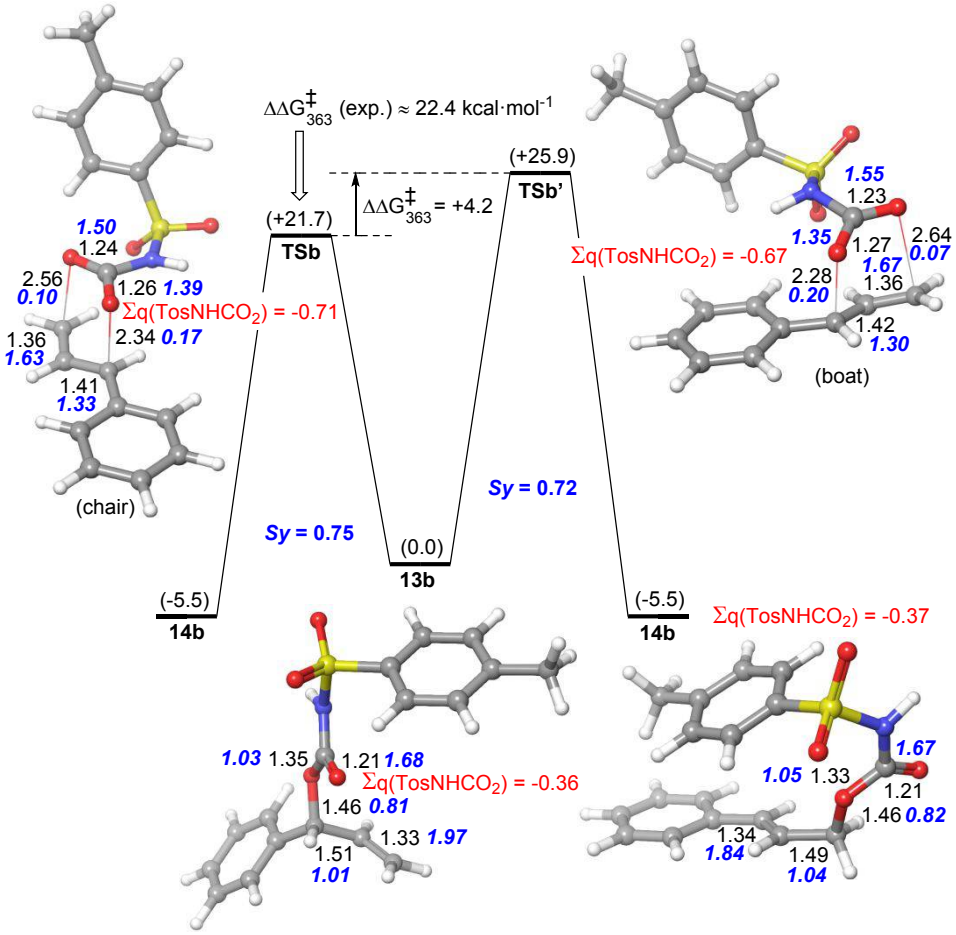



**Figure 7**. Reaction profiles of the thermal rearrangement of 1-phenylallyl tosylcarbamate **13b** to yield cinnamyl tosylcarbamate **14b**. All stationary points were calculated at the B3LYP-D3(PCM,solvent=toluene)/6-311++G(d,p) level of theory. Numbers in parentheses are the relative free energies, in kcal/mol, calculated at 363.15 K with respect to **13b**. The experimental Gibbs activation energy, estimated at the same temperature, is also provided.

Bond distances are given in Å. Σq($CO_2$) values, displayed in red, correspond to the natural charges of the carboxy moieties and are given in a. u. Numbers in blue correspond to the respective bond orders. The *Sy* parameter stands for the synchronicity of each elementary process via **TSb** and **TSb'**. For a perfectly synchronous transformation, *Sy*=1 (see text).

The reaction coordinate associated with the [3,3] sigmatropic rearrangement of 1-phenylallyl tosylcarbamate **13b** to yield cinnamyl tosylcarbamate **14b** (R=H) was analyzed first. The chief features of this reaction are gathered in Figure 7. We found two transition structures **TSb** and **TSb'** corresponding to chair and boat geometries, respectively. The former saddle point was found to be ca. 4.2 kcal/mol less energetic than its boat congener, which indicates that only the **13b**→ **TSb**→ **14b** reaction coordinate is kinetically relevant. The theoretical activation energy was calculated to be 21.7 kcal/mol. From the $^1$H-NMR data (vide supra), the experimental Gibbs activation energy at 363.15 K was estimated from the Eyring equation (eq.2) associated with $k_{obs}$:

$$k_{obs} = \kappa \frac{k_B \cdot 363.15}{h} exp\left[ -\frac{\Delta G^{\ddagger}_{363}(exp)}{R \cdot 363.15} \right] \quad (2)$$

Assuming $\kappa \approx 1$, the estimated activation energy was calculated to be 22.4 kcal/mol, in good agreement with the computational value. In addition, using the bond orders associated with the suprafacial [3,3] sigmatropic shift, we computed the earliness of the reaction path via **TSb** as the average of the degree of advancement $\delta B_{AV}$ of both saddle points, according to the following expression (eq.3):

$$\delta B_{AV} = \frac{1}{6}\sum_{i=1}^{6} \delta B_i = \frac{1}{6}\sum_{i=1}^{6} \frac{B_i^{TS} - B_i^R}{B_i^P - B_i^R} \quad (3)$$

where $B_i$ is the bond order of the *i*-th bond involved in the pericyclic reaction at the reactant (*R*) **13b**, transition state (*TS*) **TSb** and product (*P*) **14b**. For the **13b**→ **TSb**→ **14b** transformation it was found that $\delta B_{AV}$ =0.42. Since for an exactly midway transition structure $\delta B_{AV}$=0.5, this result indicates an slightly early saddle point, with $\Delta G_{rxn}$=-5.5 kcal/mol. We also calculated the synchronicity *Sy* of the reaction as

$$Sy = 1 - \frac{1}{10}\sum_{i=1}^{6} \frac{|\delta B_i - \delta B_{AV}|}{\delta B_{AV}} \quad (4)$$

According to this expression (eq.4), for a perfectly synchronous [3,3] sigmatropic reaction, $\delta B_i = \delta B_{AV}$ for any i=1,2, … ,6 and therefore $|\delta B_i - \delta B_{AV}| = 0$ and *Sy*=1. In our case, we obtained *Sy*=0.75 for the **13b**→ **14b** reaction mediated by **TSb**, which suggests a noticeable

asynchronicity. When the same reaction is mediated by **TSb'**, the reaction was computed to be slightly more asynchronous (see Figure 7). These results are in line with the geometries obtained for both saddle points, with two C···O distances associated with the bonds being broken and formed (see Figure 7). This partially asynchronous but still concerted character of the reaction mechanism agrees with the preservation of the chiral information contained in the starting enantiopure allyl alcohol (see Figure 3). Finally, the charge analysis of the carboxylate moiety along the reaction coordinate showed that this charge was ca. 0.2 e higher in the transition structures than in the reactant and product (Figure 7). This result points to relatively polar transition structures, with an associated positive charge delocalized in the allyl moiety. As a consequence, electron-withdrawing groups in the starting allyl alcohol should destabilize this partial cationic character, thus leading to higher activation energies. Likewise, electron releasing substituents should accelerate the sigmatropic rearrangement, in good agreement with our experimental results (see Tables 1-4).

We also performed the above described DFT study with tosylcarbamate **13c** (R=Cl) to yield 4-chlorocynnamyl tosylcarbamate **14c** (see the Supporting Information for further details). The computed reaction profile for this series was similar to that found for R=H case. As expected, the activation energy computed for the **13c**→ **14c** reaction via **TSc** was calculated to be 22.6 kcal/mol, a value slightly higher than that found for the parent **13b**→ **14b** reaction. The excellent agreement between this latter computational value and the corresponding experimental estimate (22.7 kcal/mol, see the Supporting Information) reflects the reliability of our calculations and reproduces correctly the lower reaction rate with respect to the parent reaction (R=H) for allyl alcohols when R=Cl.

In order to analyze the reasons for the preference for the chair conformation in **TSb**, we considered applying the distortion/interaction-activation strain model[33] to both saddle points. However, the intramolecular nature of the sigmatropic rearrangement hampered the analysis in terms of interacting molecules. Therefore, we decomposed the activation energy $\Delta E^{\ddagger}$ as the sum of the deformation (FDEF) and interaction (FINT) terms between two carboxylic (**C**) and allylic (**A**) fragments at transition structure **TSb**:

$$\Delta E^{\ddagger} = \Delta E^{\ddagger}_{FDEF} + \Delta E^{\ddagger}_{FINT} \quad (5)$$

The deformation of both fragments can be envisaged as the sum of the zwitterionic (ZW) and diradical (DR) contributions of both fragments:

$$\Delta E^{\ddagger}_{FDEF} = X_{ZW}\Delta E^{\ddagger}_{ZW} + (1 - X_{ZW})\Delta E^{\ddagger}_{DR} \quad (6)$$

where $X_{ZW}$ is the weight of the zwitterionic contribution, the corresponding diradical coefficient $X_{DR}$ satisfying the relation $X_{ZW} + X_{DR} = 1$. Since for the DR structures the charges of both fragments are zero, we approximated the contribution of the ZW form as $X_{ZW} = \delta$, namely the NBO charge of the allylic fragment **A** in **TSb** (Figure 8).

The $\Delta E^{\ddagger}_{ZW}$ term was computed as the sum of the single-point energies of isolated carboxylate (**C**$^-$) and allyl cation (**A**$^+$) fragments at the geometry of **TSb**, with respect to the energy $E_0$ of the reactant **13b**:

$$\Delta E^{\ddagger}_{ZW} = \left(\Delta E^{\ddagger}_{C^-} + \Delta E^{\ddagger}_{A^+}\right) - E_0 \quad (7)$$

The $\Delta E^{\ddagger}_{DR}$ term was computed in a similar way, but considering the contributions of the carboxy (**C**$^{\cdot}$) and allyl (**A**$^{\cdot}$) isolated radical fragments, also computed at the geometries of the transition state **TSb**:

$$\Delta E^{\ddagger}_{DR} = \left(\Delta E^{\ddagger}_{C^{\cdot}} + \Delta E^{\ddagger}_{A^{\cdot}}\right) - E_0 \quad (8)$$

Our results indicate that both in the chair and boat conformations of **TSb** the contributions of the ZW forms are ca. 1 kcal/mol larger than those associated with the DR forms. Thus, in *chair*-**TSb** the respective values are $\Delta E^{\ddagger}_{ZW} = 73.3$ kcal/mol and $\Delta E^{\ddagger}_{DR} = 72.3$ kcal/mol, whereas the corresponding values for *boat*-**TSb** are $\Delta E^{\ddagger}_{ZW} = 78.4$ kcal/mol and $\Delta E^{\ddagger}_{DR} = 77.6$ kcal/mol. The computed total values of $\Delta E^{\ddagger}$, $\Delta E^{\ddagger}_{FDEF}$ and $\Delta E^{\ddagger}_{FINT}$ terms of eq. (1) are shown in Figure 8. Our calculations indicate that the fragment deformation term $\Delta E^{\ddagger}_{FDEF}$ is 5.1 kcal/mol higher in *boat*-**TSb** than in *chair*-**TSb**, the difference in $\Delta E^{\ddagger}_{FINT}$ being of only 1.2 kcal/mol in favor of *boat*-**TSb**. Therefore, in the boat geometry both the deformation (destabilizing) and interaction (stabilizing) terms between the **C** and **A** fragments are higher in magnitude because of closer steric, Coulombic and electronic contacts in *boat*-**TSb** with respect to its chair congener. We conclude that $\Delta E^{\ddagger}_{FDEF}$ is responsible for the preference for the chair conformation in these pericyclic transition structures, since the more congested boat geometry induces a larger departure of the **C** and **A** fragments from their respective optimal geometries.

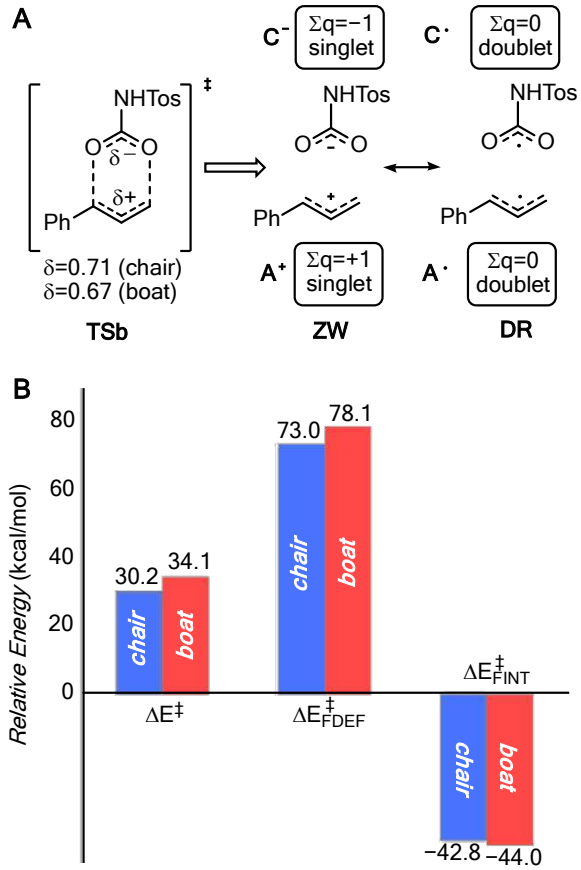



**Figure 8**. (A) Fragment deformation/interaction analysis (see text) of **TSb** in terms of resonant zwitterionic (**ZW**) and diradical (**DR**) contributions between carboxy (**C**) and allyl (**A**) fragments. Σq is the formal charge of the corresponding fragment. The expected $\langle S^2 \rangle$ values, in atomic units (a.u.) are also given. The sum of NBO charges of each fragment at chair- and boat-**TSb**, in a.u., are denoted as δ. (B) Calculated activation ($\Delta E^{\ddagger}$), deformation ($\Delta E^{\ddagger}_{FDEF}$) and interaction energies ($\Delta E^{\ddagger}_{FINT}$) for the chair and boat conformations of **TSb**, in kcal/mol.

In order to assess whether this relatively polar character of the sigmatropic shift can be extended to other para-substituted allyl alcohol derivatives, we computed at the B3LYP-D3(SCRF,solvent=toluene)/6-311++G(d,p) level the activation free energies associated with different reactants and we plotted these energies with respect to the combined Hammett parameter[34] $\langle \sigma \rangle$ of the corresponding substituents in the form

$$\langle \sigma \rangle = Z_W \cdot \sigma_p^+ + (1 - Z_W)\sigma_p \qquad (8)$$

where $\sigma_p^+$ is the Taft resonance parameter for positive charges and $\sigma_p$ is the Hammett parameter for a para-substituent (Figure 9). Our results show a moderate linear correlation between the Gibbs activation energies and the combined polar Hammett-Taft parameter $\langle \sigma \rangle$.

However, there is no linear correlation between the $\Delta G_a$ and $\Delta G_{rxn}$ values,[35] as it is shown in Figure 9B. This result does not follow the behavior observed for other pericyclic reactions such as 1,4-dihydrogenations and [4+2] cycloadditions of aromatic molecules,[36] thus suggesting that the relationship between activation and reaction energies is not reducible to Marcus-Hammond models. In our opinion, this supports our conclusion that the transition structures of these sigmatropic rearrangements follow a polar-radical carboxy/allyl model not directly connected to the reactants or products. Within this context, it is interesting to note that Houk and Ess[37] have shown a departure from the Marcus-Hammond framework in 1,3-dipolar reactions, in which the nature of the different dipoles generates different $\Delta H^{\ddagger}/\Delta H_{rxn}$ plots.

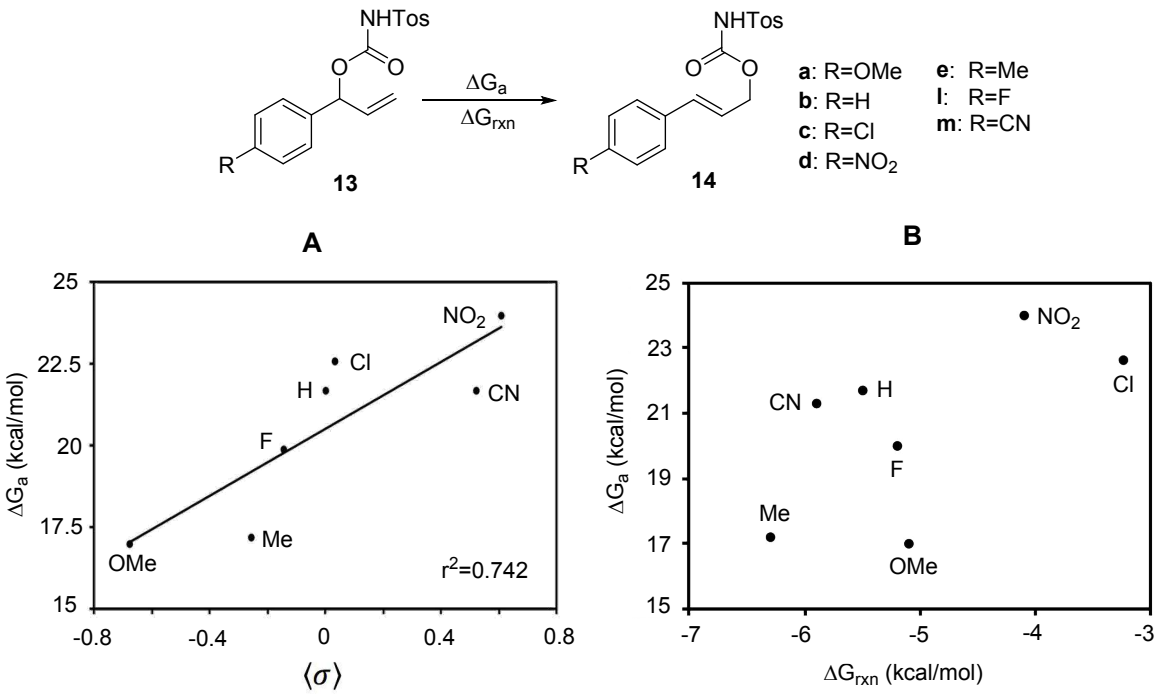



**Figure 9**. (A) Correlation between the calculated (B3LYP-D3(SCRF, solvent=toluene)/6-311++G(d,p) level of theory) activation energies ($\Delta G_a$) for different *para*-substituents of allyl alcohol derivatives and the composite Hammett parameter $\langle\sigma\rangle$ (see text). (B) Plot of the calculated activation ($\Delta G_a$) and reaction ($\Delta G_{rxn}$) free energies (computed at 363.15 K) for the substituents indicated in (A).

Finally, we explored computationally the conversion of alcohols **17a,b** into carbamates **18ab-bb** (Scheme 5). As a model case, we chose the thermal transformation of (*Z*)-buta-1,3-dien-1-yl formate **29a** into (*E*)- or (*Z*)-**31a** (Figure 10A). From the *s-trans* conformation of (*Z*)-**29a**, the 1,3-dioxa-[3,3]-sigmatropic rearrangement gives rise to

intermediate **30a** via saddle point **TS1a**. This latter intermediate has a novel terminal C=C bond and yields diene (*E*)-**31a** via **TS2a**, which in this model case is identical to **TS1a**. In turn, as we have seen in the previous cases, this model transition structure can adopt chair and boat geometries. Another possibility consists of a degenerate pseudopericyclic reaction[27,28] — not subjected to the Woodward-Hoffmann[29] rules for thermal sigmatropic rearrangements— involving the *s-cis* conformation of (*Z*)-**29a** to yield again (*Z*)-**31a** (Figure 10A). This latter process should occur via $C_s$-symmetric transition structure **TS3** by through interconversion between C-O σ–bonds, C-C π–bonds and one of the lone pairs of one oxygen of the carboxy group.

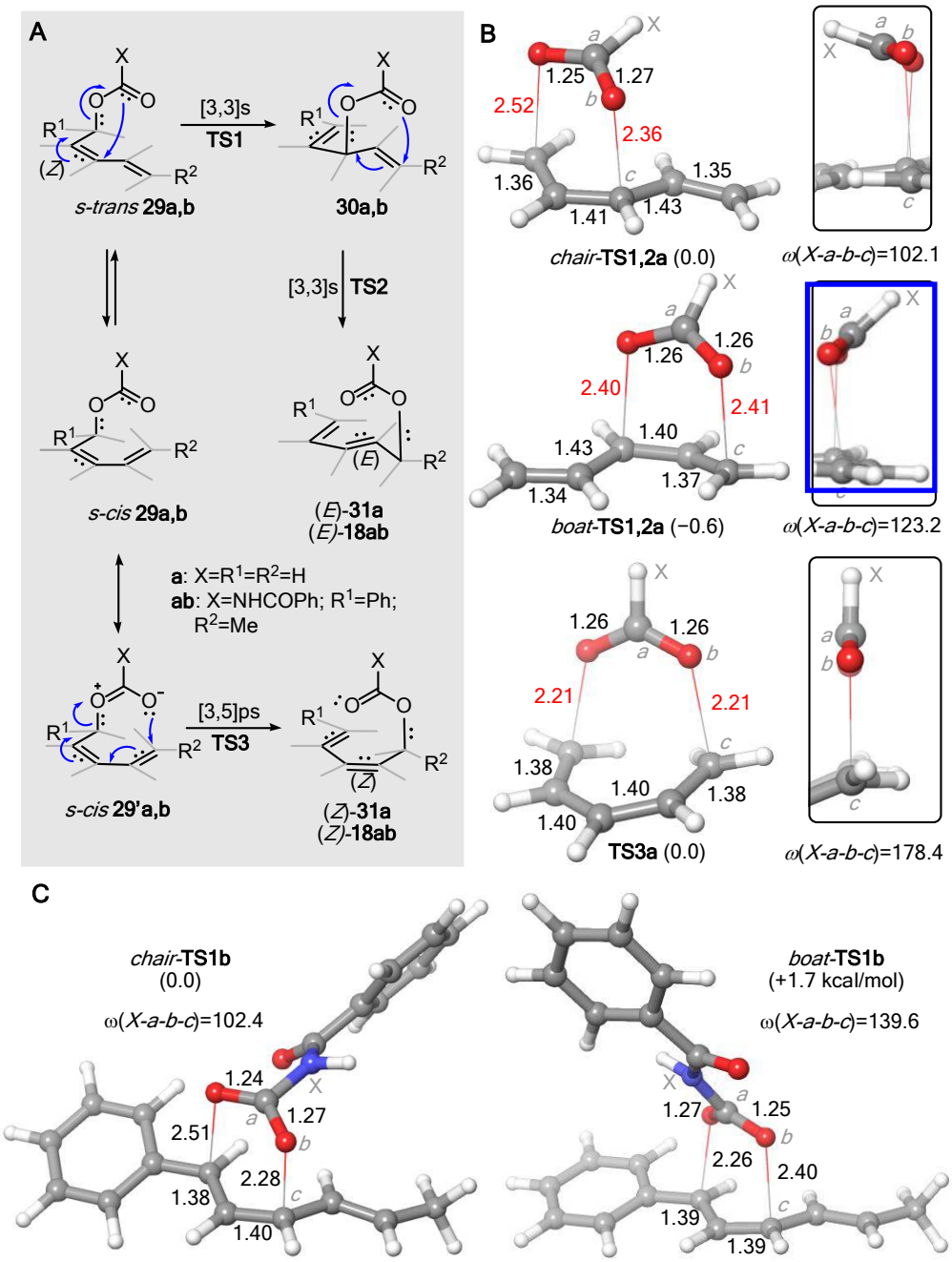



**Figure 10**. (A) Sequential vs. one-step (3,3) and (3,5) dioxa-rearrangements of model esters (*Z*)-**29a,b** to yield (*E*)- **31a,b** and (*Z*)-**31a,b**. (B) Optimized geometries (B3LYP-D3(PCM=$CHCl_3$)/6-311++G(d,p) level of theory) and relative energies of transition structures *chair*-**TS1,2a**, *boat*-**TS1,2a** and **TS3a**. (C) Chief geometric and energetic features (B3LYP-D3(PCM=$CHCl_3$)/6-311++G(d,p)/B3LYP/6-31G(d) level of theory) of transition structures *chair*-**TS1b** and *boat*-**TS1b**. Bond distances are given in Å. Numbers in parentheses are the relative energies, in kcal/mol. The dihedral angle $\omega$ (in deg.) is defined by the *X-a-b-c* atoms.

Our calculations showed that, in effect, *chair*-**TS12,a**, *boat*-**TS1,2a** and **TS3a** are practically isoenergetic. In particular, the [3,3] transition structures correspond to pericyclic

supra,supra topologies, as indicated by the corresponding dihedral angles $\omega$ (Figure 10B). On the contrary, **TS3a** eludes the geometrically demanding *supra, antara* pericyclic topology by adopting a pseudopericyclic [3,5] geometry reflected by a $\omega$ value of ca. 180 deg. Next, we computed the realistic case associated with the conversion of alcohol (*E,Z*)-**17a** into carbamate (*E*)-**18ab** (Scheme 5) through analysis of the (*Z*)-**29b**→(*E/Z*)-**18ab** transformation. In this case, the [3,5] pseudopericyclic mechanism disappeared from the potential energy hypersurface and only the pericyclic [3,3] mechanism survived. In addition, saddle point *boat*-**TS1b** was calculated to lie 1.7 kcal/mol above its congener *chair*-**TS1b** (Figure 10C). These computational permitted us to conclude that, although the pseudopericyclic [3,5] mechanism is conceivable, in this particular case the conversion of (*Z*)-**29b** into (*E*)-**18ab** via two consecutive suprafacial [3,3] processes is the only accessible mechanism. These results agree with the experimental findings summarized in Scheme 5, since a hypothetical pseudopericyclic [3,5] mechanism should preserve the Z-stereochemistry of the starting alcohol (*Z*)-**17a**.

## CONCLUSIONS

In this paper, we have described a tandem reaction from 1-arylallyl alcohols involving an initial carbamoylation reaction followed by an unexpected metal-free 1,3-dioxa-[3,3]-sigmatropic rearrangement for a non-conventional access to linear allyl carbamates. Scope and limitations of this one-pot process were carried out showing the crucial importance of the electron density from aromatic ring as well as the nature of the isocyanate used. The synthetic interest of this methodology is all greater given that this kind of sigmatropic rearrangement can occur rapidly under mild reaction conditions (room temperature) and with a complete transfer of chiral information.

The mechanism of these [3,3] sigmatropic reactions has been investigated both experimentally and computationally. $^{1}$H-NMR studies show the very fast conversion of starting alcohols **1b,c** to give rise to intermediate tosylcarbamates **13b,c** whose [3,3] sigmatropic rearrangements yielded cinnamyl tosylcarbamates **14b,c** without any noticeable reaction intermediate. The corresponding first-order reaction rates showed a relative reactivity following the order H>Cl. Computational DFT studies showed asynchronous, but concerted, suprafacial processes mediated by chair transition structures, in agreement with the observed stereoselectivities with an enantiopure substrate and NMR experiments with a $^{17}$O labeled

substrate. These latter saddle points reflect correctly the relative reaction rates and activation energies and show a polar character, in which the carboxy moiety bears a significant negative charge.

## EXPERIMENTAL SECTION

**General Information and Materials.** Tetrahydrofuran (THF) was distilled over sodium/benzophenone and dichloromethane (DCM) was distilled over $P_2O_5$. All other commercially available chemicals were used without further purification. NMR spectra were recorded at 300, 400 or 500 MHz for $^1$H and 75, 101 or 126 MHz for $^{13}$C. Chemical shifts of $^1$H were referenced to $Me_4Si$ as internal reference. Data are represented as follows: chemical shift (ppm), multiplicity (s = singlet, d = doublet, t = triplet, q = quartet, m = multiplet, br s = broad singlet), coupling constant *J* (Hz) and integration. Assignments were done with the aid of DEPT 135, COSY and HSQC experiments. High-resolution mass spectra (HRMS) were recorded on a Micro-Tof-Q II or on a Q-Tof 2 using positive ion electrospray. Purifications on silica gel were carried out on silica gel 0.006-0.200 mm, 60 Å. Infrared spectra were recorded on a FT-IR spectrometer equipped with a diamond detection and an ATR unit or a single reflection ATR module; wavenumbers are given in cm$^{-1}$. Analytical thin layer chromatography was performed on Silica gel 60 $F_{254}$ plates. Optical rotations were measured using 10-cm cell at 22 °C (sodium D-line: 589 nm), and the concentration is expressed in g/dL. Melting points were measured without correction on a digital melting point apparatus. All analytical high-performance liquid chromatography (HPLC) were performed, using Daicel Chiralpak IB column. *1-(Phenyl)prop-2-en-1-ol (***1b***)* is a commercialy available compound. The [$^{17}$O] labelled $H_2O$ (11.1% $H_2{}^{17}O$, 29.7% $H_2{}^{18}O$ and 59.2% $H_2{}^{16}O$) was purchased from Cortecnet. NMR spectra were recorded at 68 MHz for $^{17}$O.

**General procedure for the synthesis of allylic alcohols 1, 5 and 20.** To a solution of aldehyde (1.50 mmol) in THF (10 mL) was slowly added at 0° C a solution of vinyl or phenylmagnesium bromide in THF (1.80 mmol, 1 M). The reaction mixture was stirred at room temperature for 16 hours after which a saturated $NH_4Cl$ solution (5 mL) was added. The aqueous layer was extracted with $Et_2O$ (4 x 10 mL). The organic layers were dried over $MgSO_4$, filtered and concentrated *in vacuo*. The residue was purified by flash column chromatography on silica gel to afford the corresponding product.

*1-(4-Methoxyphenyl)prop-2-en-1-ol (**1a**)*.[38] Prepared from 4-methoxybenzaldehyde and vinyl magnesium bromide. Purified using a hexane/ethyl acetate mixture (80/20, $R_f$ 0.25) as eluent. The product was isolated as a yellow oil (210 mg) in 85% yield. $^1$H NMR (400 MHz, $CDCl_3$) $\delta$ 7.30 (d, *J* = 8.2 Hz, 2H), 6.89 (d, *J* = 8.2 Hz, 2H), 6.05 (ddd, *J* = 17.2, 10.3, 5.9 Hz, 1H), 5.34 (dd, *J* = 17.2, 1.7 Hz, 1H), 5.22–5.12 (m, 2H), 3.81 (s, 3H), 1.89–1.86 (br s, 1H).

*1-(4-Chlorophenyl)prop-2-en-1-ol (**1c**)*.[39] Prepared from 4-chlorobenzaldehyde and vinyl magnesium bromide. Purified using a hexane/ethyl acetate mixture (85/15, $R_f$ 0.30) as eluent. The product was isolated as a pale yellow oil (187 mg) in 74% yield. $^1$H NMR (300 MHz, $CDCl_3$): $\delta$ 7.33–7.31 (m, 4H), 6.01 (ddd, *J* = 17.0, 10.1, 6.1 Hz, 1H), 5.34 (dt, *J* = 17.0, 1.2 Hz, 1H), 5.25–5.15 (m, 2H), 1.95 (d, *J* = 3.7 Hz, 1H).

*1-(4-Nitrophenyl)prop-2-en-1-ol (**1d**)*.[40] Prepared from 4-nitrobenzaldehyde and vinyl magnesium bromide. Purified using a hexane/ethyl acetate mixture (80/20, $R_f$ 0.20) as eluent. The product was isolated as an

orange oil (81 mg) in 30% yield. $^1$H NMR (400 MHz, $CDCl_3$): $\delta$ 8.15 (d, $J$ = 8.7 Hz, 2H), 7.52 (d, $J$ = 8.7 Hz, 2H), 5.96 (ddd, $J$ = 17.1, 10.2, 6.4 Hz, 1H), 5.36 (ddd, $J$ = 17.1, 1.2, 1.2 Hz, 1H), 5.28 (d, $J$ = 6.4 Hz, 1H), 5.23 (ddd, $J$ = 10.3, 1.1, 1.1 Hz, 1H), 2.67–2.65 (br s, 1H).

*1-(4-Methylphenyl)prop-2-en-1-ol* ***(1e)***.[41] Prepared from 4-methylbenzaldehyde and vinyl magnesium bromide. Purified using a hexane/ethyl acetate mixture (80/20, $R_f$ 0.32) as eluent. The product was isolated as a yellow oil (218 mg) in 98% yield. $^1$H NMR (400 MHz, $CDCl_3$): $\delta$ 7.26 (d, $J$ = 7.5 Hz, 2H), 7.18 (d, $J$ = 7.5 Hz, 2H), 6.05 (ddd, $J$ = 17.1, 10.2, 6.0 Hz, 1H), 5.35 (d, $J$ = 17.1 Hz, 1H), 5.21–5.17 (m, 2H), 2.35 (s, 3H), 1.93 (d, $J$ = 6.0 Hz, 1H).

*1-(4-Benzyloxyphenyl)prop-2-en-1-ol* ***(1f)***.[42] Prepared from 4-benzyloxybenzaldehyde and vinyl magnesium bromide. Purified using a hexane/ethyl acetate mixture (75/25, $R_f$ 0.30) as eluent. The product was isolated as a colorless oil (284 mg) in 79% yield. $^1$H NMR (400 MHz, $CDCl_3$): $\delta$ 7.48–7.35 (m, 5H), 7.35–7.22 (m, 2H), 6.97 (d, $J$ = 8.3 Hz, 2H), 6.05 (ddd, $J$ = 17.1, 10.3, 5.9 Hz, 1H), 5.34 (d, $J$ = 17.1 Hz, 1H), 5.21–5.15 (m, 2H), 5.07 (s, 2H), 1.86 (d, $J$ = 3.4 Hz, 1H).

*1-(2-Methoxyphenyl)prop-2-en-1-ol* ***(1g)***.[43] Prepared from 2-methoxybenzaldehyde and vinyl magnesium bromide. Purified using a hexane/ethyl acetate mixture (85/15, $R_f$ 0.44) as eluent. The product was isolated as a colorless oil (172 mg) in 70% yield. $^1$H NMR (400 MHz, $CDCl_3$): $\delta$ 7.32–7.25 (m, 2H), 7.01–6.94 (m, 1H), 6.90 (d, $J$ = 8.2 Hz, 1H), 6.14 (ddd, $J$ = 17.2, 10.4, 5.6 Hz, 1H), 5.41 (dd, $J$ = 5.6, 5.6 Hz, 1H), 5.31 (dd, $J$ = 17.2, 4.4 Hz, 1H), 5.17 (dd, $J$ = 10.4, 4.4 Hz, 1H), 3.87 (s, 3H), 2.77 (dd, $J$ = 4.5, 3.8 Hz, 1H).

*1-(2,3-Dihydrobenzofuran-5-yl)prop-2-en-1-ol* ***(1h)***.[44] Prepared from 2,3-dihydrobenzofuran-5-carboxaldehyde and vinyl magnesium bromide. Purified using a hexane/ethyl acetate mixture (80/20, $R_f$ 0.33) as eluent. The product was isolated as a colorless oil (259 mg) in 98% yield. $^1$H NMR (400 MHz, $CDCl_3$): $\delta$ 7.32–7.29 (m, 1H), 7.16 (d, $J$ = 8.2 Hz, 1H), 6.81 (d, $J$ = 8.2 Hz, 1H), 6.10 (ddd, $J$ = 16.7, 10.3, 5.8 Hz, 1H), 5.34 (ddd, $J$ = 17.1, 1.4, 1.4 Hz, 1H), 5.24 (ddd, $J$ = 10.4, 1.4, 1.4 Hz, 1H), 5.19 (d, $J$ = 5.8 Hz, 1H), 4.63 (t, $J$ = 8.7 Hz, 2H), 3.26 (t, $J$ = 8.7 Hz, 2H), 1.92–1.86 (br s, 1H).

*1-(3,4-Dimethoxyphenyl)prop-2-en-1-ol* ***(1i)***.[45] Prepared from 3,4-dimethoxybenzaldehyde and vinyl magnesium bromide. Purified using a hexane/ethyl acetate mixture (70/30, $R_f$ 0.27) as eluent. The product was isolated as a pale yellow oil (117 mg) in 40% yield. $^1$H NMR (400 MHz, $CDCl_3$): $\delta$ 6.94–6.89 (m, 2H), 6.85 (d, $J$ = 7.8 Hz, 1H), 6.05 (ddd, $J$ = 17.1, 10.4, 5.9 Hz, 1H), 5.36 (d, $J$ = 17.1 Hz, 1H), 5.20 (d, $J$ = 10.4 Hz, 1H), 5.17 (d, $J$ = 5.9 Hz, 1H), 3.89 (s, 3H), 3.88 (s, 3H), 1.96–1.90 (br s, 1H).

*1-(3-(Benzyloxy)-4-methoxyphenyl)prop-2-en-1-ol* ***(1j)***. Prepared from 3-benzyloxy-4-methoxybenzaldehyde and vinyl magnesium bromide. Purified using a hexane/ethyl acetate mixture (80/20, $R_f$ 0.21) as eluent. The product was isolated as a pale yellow oil (324 mg) in 80% yield. $^1$H NMR (400 MHz, $CDCl_3$): $\delta$ 7.45 (d, $J$ = 7.5 Hz, 2H), 7.36 (dd, $J$ = 7.4, 7.4 Hz, 2H), 7.31 (d, $J$ = 7.2 Hz, 1H), 6.96 (s, 1H), 6.94–6.90 (m, 1H), 6.87 (d, $J$ = 8.2 Hz, 1H), 5.99 (ddd, $J$ = 17.2, 10.3, 5.7 Hz, 1H), 5.30 (d, $J$ = 17.2 Hz, 1H), 5.19–5.16 (m, 1H), 5.14 (s, 2H), 5.12–5.10 (m, 1H), 3.87 (s, 3H), 1.87 (d, $J$ = 3.8 Hz, 1H). $^{13}$C{1H} NMR (101 MHz, $CDCl_3$): $\delta$ 149.1, 148.1, 140.3, 136.9, 135.3, 128.4, 127.7, 127.4, 119.2, 114.6, 112.3 (d, $J$ = 5.7 Hz), 111.6 (d, $J$ = 4.6 Hz), 74.6, 70.9, 55.9. IR (cm$^{-1}$) 3488, 3054, 1511, 1263, 1157, 1135, 1021, 730, 698. HRMS (ESI): *m/z* calcd. for $C_{17}H_{19}O_3$ $[M+H]^+$ 271.1334; found: 271.1335.

*1-(Benzo[d][1,3]dioxol-5-yl)prop-2-en-1-ol* ***(1k)***.[46] Prepared from piperonal and vinyl magnesium bromide. Purified using a hexane/ethyl acetate mixture (90/10, $R_f$ 0.17) as eluent. The product was isolated as a colorless oil (203 mg) in 76% yield. $^1$H NMR (400 MHz, $CDCl_3$): $\delta$ 6.88 (d, $J$ = 1.6 Hz, 1H), 6.83 (dd, $J$ = 8.0, 1.6 Hz, 1H), 6.78 (d, $J$ = 8.0 Hz, 1H), 6.02 (ddd, $J$ = 17.1, 10.3, 5.9 Hz, 1H), 5.95 (s, 2H), 5.34 (ddd, $J$ = 17.1, 1.4, 1.4 Hz, 1H), 5.19 (ddd, $J$ = 10.4, 1.4, 1.4 Hz, 1H), 5.13 (m, 1H), 1.88 (d, $J$ = 3.6 Hz, 1H).

*(E)-1-(4-Methoxyphenyl)penta-1,4-dien-3-ol* ***(5a)***. Prepared from (*E*)-3-(4-methoxyphenyl)-2-propenal and vinyl magnesium bromide. Purified using a hexane/ethyl acetate mixture (75/25, $R_f$ 0.24) as eluent. The product was isolated as a yellow oil (242 mg) in 85% yield. $^1$H NMR (400 MHz, $CDCl_3$): $\delta$ 7.33 (d, $J$ = 8.7 Hz, 2H), 6.85 (d, $J$ = 8.7 Hz, 2H), 6.56 (d, $J$ = 15.9 Hz, 1H), 6.10 (dd, $J$ = 15.9, 6.6 Hz, 1H), 5.98 (ddd, $J$ = 17.2, 10.4, 5.8 Hz, 1H), 5.33 (ddd, $J$ = 17.2, 1.4, 1.4 Hz, 1H), 5.19 (ddd, $J$ = 10.5, 1.4, 1.4 Hz, 1H), 4.80–4.78 (m, 1H), 3.81 (s, 3H), 1.77–1.73 (br s, 1H). $^{13}$C{1H} NMR (101 MHz, $CDCl_3$): $\delta$ 159.5, 139.6, 130.6, 129.5, 128.3, 127.9, 115.3, 114.1, 74.1, 55.4. IR (cm$^{-1}$) 3422, 2837, 1606, 1510, 1247, 1174, 1031, 967, 732, 702. HRMS (ESI): *m/z* calcd. for $C_{12}H_{13}O$ $[M+H-H_2O]^+$ 173.0960; found 173.0963.

*(E)-1-Phenylpenta-1,4-dien-3-ol* ***(5b)***.[47] Prepared from (*E*)-3-phenyl-2-propenal and vinyl magnesium bromide. Purified using a hexane/ethyl acetate mixture (85/15, $R_f$ 0.23) as eluent. The product was isolated as a pale yellow oil (204 mg) in 85% yield. $^1$H NMR (300 MHz, $CDCl_3$): $\delta$ 7.42–7.36 (m, 2H), 7.35–7.30 (m, 1H), 7.30–7.20 (m, 2H), 6.62 (d, $J$ = 16.1 Hz, 1H), 6.23 (dd, $J$ = 16.1, 6.4 Hz, 1H), 5.98 (ddd, $J$ = 17.2, 10.4, 5.9 Hz, 1H), 5.34 (ddd, $J$ = 17.2, 1.4, 1.4 Hz, 1H), 5.20 (ddd, $J$ = 10.4, 1.3, 1.3 Hz, 1H), 4.89–4.76 (m, 1H), 1.77–1.74 (m, 1H).

*(E)-1-(4-Chlorophenyl)penta-1,4-dien-3-ol* ***(5c)***. Prepared from (*E*)-3-(4-chlorophenyl)-2-propenal and vinyl magnesium bromide. Purified using a hexane/ethyl acetate mixture (75/25, $R_f$ 0.35) as eluent. The product was isolated as a pale yellow oil (213 mg) in 73% yield. $^1$H NMR (400 MHz, $CDCl_3$): $\delta$ 7.34–7.24 (m, 4H), 6.57 (dd, $J$ = 16.0, 1.4 Hz, 1H), 6.21 (dd, $J$ = 16.0, 6.3 Hz, 1H), 5.96 (ddd, $J$ = 17.4, 10.3, 6.0 Hz, 1H), 5.34 (ddd, $J$ = 17.4, 1.3, 1.3 Hz, 1H), 5.21 (ddd, $J$ = 10.4, 1.3, 1.3 Hz, 1H), 4.83–4.79 (m, 1H). $^{13}$C{1H} NMR (101 MHz, $CDCl_3$): $\delta$ 139.1, 135.1, 133.3, 131.1, 129.4, 128.7, 127.7, 115.5, 73.5. IR (cm$^{-1}$) 3271, 3086, 1638, 1588, 1488, 1085, 1008, 967, 924, 805. HRMS (ESI): *m/z* calcd. for $C_{11}H_{10}Cl$ $[M+H-H_2O]^+$ 177.0467; found 177.0469.

*(E)-1-(4-Nitrophenyl)penta-1,4-dien-3-ol* ***(5d)***.[48] Prepared from (*E*)-3-(4-nitrophenyl)-2-propenal and vinyl magnesium bromide. Purified using a hexane/ethyl acetate mixture (75/25, $R_f$ 0.24) as eluent. The product was isolated as an orange oil (123 mg) in 40% yield. $^1$H NMR (400 MHz, $CDCl_3$): $\delta$ 8.21–8.16 (m, 2H), 7.56–7.47 (m, 2H), 6.71 (d, $J$ = 16.9 Hz, 1H), 6.42 (dd, $J$ = 16.9, 5.8 Hz, 1H), 5.97 (ddd, $J$ = 17.1, 10.3, 6.1 Hz, 1H), 5.38 (ddd, $J$ = 17.1, 1.2, 1.2 Hz, 1H), 5.25 (ddd, $J$ = 10.3, 1.2, 1.2 Hz, 1H), 4.93–4.82 (m, 1H), 1.83 (d, $J$ = 4.2 Hz, 1H).

*Racemic (E)-1-phenylbut-2-enol* ***(20)***. Prepared from (*E*)-crotonaldehyde and phenylmagnesium bromide. Purified using a hexane/ethyl acetate mixture (80/20, $R_f$ 0.25) as eluent. The product was isolated as a yellow oil (190 mg) in 85% yield. $^1$H NMR (400 MHz, $CDCl_3$): $\delta$ 7.40–7.32 (m, 4H), 7.31–7.27 (m, 1H), 5.84–5.63 (m, 2H), 5.16 (d, $J$ = 6.4 Hz, 1H), 1.72 (d, $J$ = 5.9 Hz, 3H), 1.61 (d, $J$ = 3.4 Hz, 1H). The separation of enantiomers was carried out using a Daicel Chiralpak IB, hexane/*i*-PrOH = 99/1, flow rate = 1 mL/min, 220 nm, the (*R,E*) enantiomer **20** $t_R$=24 min (*ee* >99%, $[\alpha]_D$ = -16.9 (*c* 0.95, $CHCl_3$)), the (*S,E*) enantiomer **20** $t_R$=28 min (*ee* 98%, $[\alpha]_D$ = +24.6 (*c* 0.65, $CHCl_3$)).[49]

## General procedure for the synthesis of allylic carbamates 3, 6, 4, 7, 13, 14, 15, 16, 18, 22.

**Using trichloroacetyl isocyanate.** A solution of allylic alcohol **1 or 5** (0.3 mmol) in anhydrous toluene $CHCl_3$ or $CH_2Cl_2$ (0.2 M) under argon atmosphere was cooled to 0 °C and trichloroacetylisocyanate (0.36 mmol) was added slowly. The reaction mixture was stirred during the time and temperature indicated in Table 1 and 2. Solvent was removed *in vacuo* and in some cases, intermediates have been identified.

*(E)-3-(4-methoxyphenyl)allyl (2,2,2-trichloroacetyl)carbamate (**3a**)*. Prepared from allylic alcohol **1a** (rt, 0.25 h). The product was isolated as a colorless oil (103 mg) in 98% yield and used in the next step without further purification. $^1$H NMR (300 MHz, $CDCl_3$): $\delta$ 8.50–8.46 (br s, 1H), 7.34 (d, $J$ = 8.7 Hz, 2H), 6.86 (d, $J$ = 8.7 Hz, 2H), 6.69 (d, $J$ = 15.8 Hz, 1H), 6.17 (dt, $J$ = 15.7, 6.9 Hz, 1H), 4.88 (dd, $J$ = 6.9, 1.2 Hz, 2H), 3.81 (s, 3H). $^{13}$C{1H} NMR (75 MHz, $CDCl_3$) $\delta$ 159.9, 157.9, 149.8, 136.2, 128.1, 118.9, 114.1, 91.8, 68.3, 55.3.

*(2E,4E)-5-phenylpenta-2,4-dien-1-yl (2,2,2-trichloroacetyl)carbamate (**6b**)*. Prepared from allylic alcohol **5b** (rt, 4 h). The product was isolated as a white solid (102 mg) in 98% yield and used in the next step without further purification; mp 101–104 °C. $^1$H NMR (300 MHz, $CDCl_3$) $\delta$ 8.50–8.45 (br s, 1H), 7.42–7.36 (m, 2H), 7.35–7.28 (m, 2H), 7.27–7.21 (m, 1H), 6.76 (dd, $J$ = 15.6, 10.2 Hz, 1H), 6.62 (d, $J$ = 15.6 Hz, 1H), 6.53 (ddd, $J$ = 15.1, 1.1, 1.1 Hz, 1H), 5.88 (dt, $J$ = 15.1, 6.9 Hz, 1H), 4.83 (dd, $J$ = 6.9, 1.1 Hz, 2H). $^{13}$C{1H} NMR (75 MHz, $CDCl_3$) $\delta$ 157.8, 149.7, 136.7, 135.1, 128.7, 128.2, 127.2, 126.7, 124.7, 91.8, 67.7.

To the resulting mixture or pure compound **3 or 6**, $K_2CO_3$ (1.2 mmol) in a mixture of MeOH (1.6 mL) and water (0.4 mL) was added. The solution was stirred at room temperature overnight and then MeOH was removed *in vacuo*. The aqueous layer was extracted with $CH_2Cl_2$ (4 x 1 mL). The organic layers were dried over $MgSO_4$, filtered and concentrated *in vacuo*. The residue was purified by flash column chromatography on silica gel to afford the corresponding product.

*(E)-3-(4-Methoxyphenyl)allyl carbamate (**4a**)*. Prepared from **3a**. Purified using a hexane/ethyl acetate mixture (70/30, $R_f$ 0.31) as eluent. The product was isolated as a white solid (45 mg) in 73% yield from **1a**. mp 131–134 °C. $^1$H NMR (400 MHz, acetone-$d_6$) $\delta$ 7.35 (d, $J$ = 8.8 Hz, 2H), 6.86 (d, $J$ = 8.8 Hz, 2H), 6.57 (d, $J$ = 15.9 Hz, 1H), 6.17 (dt, $J$ = 15.9, 6.3 Hz, 1H), 5.9–05.84 (br s, 2H), 4.57 (dd, $J$ = 6.3, 1.5 Hz, 2H), 3.75 (s, 3H). $^{13}$C{1H} NMR (126 MHz, $CD_3OD$) $\delta$ 161.0, 159.8, 134.1, 130.5, 128.8, 122.7, 115.0, 66.4, 55.7. IR (cm$^{-1}$) 3423, 3329, 3263, 3203, 2954, 2834, 1682, 1603, 1509, 1244, 1028, 510. HRMS (ESI): *m/z* calcd. for $C_{11}H_{13}NO_3Na$ $[M+Na]^+$ 230.0793; found 230.0789.

*(E)-3-(phenyl)allyl carbamate (**4b**)*.[14d] Prepared from the commercially available 1-(Phenyl)prop-2-en-1-ol (90 °C, 16 h). Purified using a hexane/ethyl acetate mixture (70/30, $R_f$ 0.28) as eluent. The product was isolated as a white solid (49 mg) in 92% yield. mp 116–119 °C. $^1$H NMR (400 MHz, $CDCl_3$) $\delta$ 7.37 (d, $J$ = 7.1 Hz, 2H), 7.33–7.27 (m, 2H), 7.27–7.21 (m, 1H), 6.63 (d, $J$ = 15.9 Hz, 1H), 6.27 (dt, $J$ = 15.9, 6.3 Hz, 1H), 5.01–4.92 (br s, 2H), 4.70 (dd, $J$ = 6.3, 1.4 Hz, 2H). $^{13}$C{1H} NMR (126 MHz, $CDCl_3$) $\delta$ 156.9, 136.4, 133.9, 128.7, 128.1, 126.7, 123.7, 65.8. HRMS (ESI): *m/z* calcd. for $C_{10}H_{11}NO_2Na$ $[M+Na]^+$ 200.0687; found 200.0686.

*(E)-3-(4-Chlorophenyl)allyl carbamate (**4c**)*.[15c] Prepared from allylic alcohol **1c** (90 °C, 20 h). Purified using a hexane/ethyl acetate mixture (70/30, $R_f$ 0.27) as eluent. The product was isolated as a white solid (32 mg)

in 50% yield. $^1$H NMR (400 MHz, $CDCl_3$) $\delta$ 7.32–7.28 (m, 4H), 6.60 (d, $J$ = 15.9 Hz, 1H), 6.26 (dt, $J$ = 15.9, 6.3 Hz, 1H), 4.78–4.74 (br s, 2H), 4.72 (dd, $J$ = 6.3, 1.4 Hz, 2H).

*(E)-3-(4-Nitrophenyl)allyl carbamate (**4d**).*[15c] Prepared from allylic alcohol **1d** (90 °C, 120 h). Purified using a hexane/ethyl acetate mixture (70/30, $R_f$ 0.10) as eluent. The product was isolated as a yellow solid (28 mg) in 43% yield. $^1$H NMR (400 MHz, $CDCl_3$) $\delta$ 8.19 (d, $J$ = 8.5 Hz, 2H), 7.52 (d, $J$ = 8.5 Hz, 2H), 6.71 (d, $J$ = 16.0 Hz, 1H), 6.46 (dt, $J$ = 16.0, 5.8 Hz, 1H), 4.78 (dd, $J$ = 5.8, 1.5 Hz, 2H), 4.73–4.66 (br s, 2H).

*(2E,4E)-5-(4-methoxyphenyl)penta-2,4-dien-1-yl carbamate (**7a**).* Prepared from allylic alcohol **5a** (rt, 2 h). Purified using a hexane/ethyl acetate mixture (65/35, $R_f$ 0.29) as eluent. The product was isolated as a pale yellow solid (17 mg) in 24% yield. mp 150–153 °C. $^1$H NMR (400 MHz, $CDCl_3$) $\delta$ 7.33 (d, $J$ = 8.7 Hz, 2H), 6.85 (d, $J$ = 8.7 Hz, 2H), 6.65 (dd, $J$ = 15.6, 10.3 Hz, 1H), 6.53 (d, $J$ = 15.6 Hz, 1H), 6.43 (dd, $J$ = 15.2, 10.2 Hz, 1H), 5.83 (dt, $J$ = 15.1, 6.6 Hz, 1H), 4.71–4.67 (br s, 2H), 4.64 (dd, $J$ = 6.6, 1.3 Hz, 2H), 3.81 (s, 3H). $^{13}$C{1H} NMR (101 MHz, $CDCl_3$) $\delta$ 159.6, 156.8, 134.9, 133.5, 129.9, 127.9, 126.2, 125.9, 114.36, 65.7, 55.5. IR (cm$^{-1}$) 3436, 3394, 3331, 3269, 3216, 3014, 2955, 1685, 1600, 1508, 1418, 1351, 1246, 1028, 988, 820, 552, 522. HRMS (ESI): *m/z* calcd. for $C_{13}H_{15}NO_3Na$ $[M+Na]^+$ 256.0950; found 256.0953.

*(2E,4E)-5-phenylpenta-2,4-dien-1-yl carbamate (**7b**).*[20b] Prepared from **6b**. Purified using a hexane/ethyl acetate mixture (70/30, $R_f$ 0.27) as eluent. The product was isolated as a yellow solid (40 mg) in 65% yield from **5b**. $^1$H NMR (400 MHz, $CDCl_3$) $\delta$ 7.45–7.37 (m, 2H), 7.37–7.29 (m, 2H), 7.29–7.22 (m, 1H), 6.78 (dd, $J$ = 15.8, 10.4 Hz, 1H), 6.59 (d, $J$ = 15.8 Hz, 1H), 6.46 (dd, $J$ = 15.3, 10.4 Hz, 1H), 5.89 (dt, $J$ = 15.3, 6.4 Hz, 1H), 4.77–4.68 (br s, 2H), 4.66 (dd, $J$ = 6.6, 1.5 Hz, 2H).

*(2E,4E)-5-(4-Chlorophenyl)penta-2,4-dien-1-yl carbamate (**7c**).* Prepared from allylic alcohol **5c** (rt, 4 h). Purified using a hexane/ethyl acetate mixture (70/30, $R_f$ 0.27) as eluent. The product was isolated as a pale yellow solid (53 mg) in 75% yield. mp 167–170 °C. $^1$H NMR (400 MHz, $CDCl_3$) $\delta$ 7.36–7.24 (m, 4H), 6.74 (dd, $J$ = 15.8, 10.4 Hz, 1H), 6.53 (d, $J$ = 15.7 Hz, 1H), 6.44 (dd, $J$ = 15.2, 10.5 Hz, 1H), 5.90 (dt, $J$ = 15.2, 6.4 Hz, 1H), 4.66 (dd, $J$ = 6.4, 1.5 Hz, 2H), 4.63–4.58 (br s, 2H). $^{13}$C{1H} NMR (126 MHz, $CD_3OD$) $\delta$ 159.7, 137.3, 134.4, 134.2, 132.9, 130.0, 129.9, 129.8, 128.9, 65.8. IR (cm$^{-1}$) 3410, 3348, 3286, 3210, 3028, 2955, 1644, 1486, 1421, 1348, 1318, 1053, 986, 827, 508. HRMS (ESI): *m/z* calcd. for $C_{12}H_{12}ClNO_2Na$ $[M+Na]^+$ 260.0454; found 260.0457.

**Using *p*-toluenesulfonyl isocyanate.** To a solution of allylic alcohol **1, 5** or **17** (0.3 mmol) in chloroform, dichloromethane or toluene (0.2 M) under argon atmosphere, *p*-toluensulfonylisocyanate (0.36 mmol) was added dropwise and the mixture was stirred at room temperature or warmed at 90 °C during the time indicated in Table 3, Table 4 and Scheme 5. The conversion of the reaction can be followed by $^1$H NMR using deuterated solvent. The resulting mixture was concentrated in *vacuo* and the product was purified by flash column chromatography on silica gel to afford the desired product.

*1-phenylallyl tosylcarbamate (**13b**).*[5c] Prepared from **1b** (rt, 5 min) and purified using a hexane/ethyl acetate mixture (80/20, $R_f$ 0.31) as eluent. The product was isolated as a colorless oil (91 mg) in 92% yield. $^1$H NMR (400 MHz, $CDCl_3$) $\delta$ 7.88 (d, $J$ = 8.3 Hz, 2H), 7.55–7.53 (br s, 1H), 7.34–7.26 (m, 5H), 7.21 (dd, $J$ = 6.8, 3.0 Hz, 2H), 6.11 (dd, $J$ = 6.0, 1.5 Hz, 1H), 5.92 (ddd, $J$ = 16.7, 10.5, 5.9 Hz, 1H), 5.27–5.23 (m, 2H), 2.43 (s, 3H). $^{13}$C{1H} NMR (101 MHz, $CDCl_3$) $\delta$ 149.6, 145.2, 137.5, 135.1, 129.7, 128.7, 128.5, 127.3, 118.2, 79.4, 21.8; HRMS (ESI): *m/z* calcd. for $C_{17}H_{17}NO_4SK$ $[M+K]^+$: 370.0515; found: 370.0514.

*1-(4-chlorophenyl)allyl tosylcarbamate* (***13c***). Prepared from **1c** (rt, 5 min) and purified using a hexane/ethyl acetate mixture (80/20, $R_f$ 0.30) as eluent. The product was isolated as a colorless oil (93 mg) in 85% yield. $^1$H NMR (400 MHz, $CDCl_3$) $\delta$ 7.86 (d, $J$ = 8.5 Hz, 2H), 7.70–7.67 (br s, 1H), 7.33–7.23 (m, 4H), 7.14 (d, $J$ = 8.5 Hz, 2H), 6.07 (d, $J$ = 5.9 Hz, 1H), 5.87 (ddd, $J$ = 16.7, 10.8, 5.9 Hz, 1H), 5.27–5.23 (m, 2H), 2.44 (s, 3H). $^{13}$C{1H} NMR (101 MHz, $CDCl_3$) $\delta$ 149.6, 145.3, 136.1, 135.6, 134.6, 129.8, 128.9, 128.7, 128.5, 118.6, 78.5, 21.8. IR (cm$^{-1}$) 3301, 2997, 1725, 1448, 1435, 1155, 1088, 906, 728, 664, 647, 547. HRMS (ESI): *m/z* calcd. for $C_{17}H_{16}ClNO_4SNa$ $[M+Na]^+$: 388.0381; found: 388.0380.

*1-(4-nitrophenyl)allyl tosylcarbamate (**13d**).* Prepared from **1d** (rt, 5 min) and purified using a hexane/ethyl acetate mixture (60/40, $R_f$ 0.31) as eluent. The product was isolated as a yellow oil (101 mg) in 90 % yield. $^1$H NMR (400 MHz, $CDCl_3$) $\delta$ 8.14 (d, $J$ = 8.5 Hz, 2H), 7.88 (d, $J$ = 8.1 Hz, 2H), 7.37 (d, $J$ = 8.5 Hz, 2H), 7.31 (d, $J$ = 8.1 Hz, 2H), 6.16 (d, $J$ = 6.1 Hz, 1H), 5.85 (ddd, $J$ = 16.8, 10.5, 6.1 Hz, 1H), 5.33–5.24 (m, 2H), 2.44 (s, 3H). $^{13}$C{1H} NMR (126 MHz, $CDCl_3$) $\delta$ 149.5, 147.9, 145.5, 144.7, 135.5, 133.9, 129.8, 128.4, 127.8, 123.9, 119.7, 77.9, 21.8. IR (cm$^{-1}$) 3236, 3112, 2858, 1748, 1520, 1444, 1345, 1221, 1158, 1098, 853, 665, 548. HRMS (ESI) *m/z* calcd. for $C_{17}H_{20}N_3O_6S$ $[M+NH_4]^+$: 394.1073; found: 394.1070.

*(E)-3-(4-Methoxyphenyl)allyl tosylcarbamate (**14a**).* Prepared from **1a** (rt, 15 min.) and purified using a hexane/ethyl acetate mixture (70/30, $R_f$ 0.23) as eluent. The product was isolated as a colorless oil (98 mg) in 90% yield. NMR spectra of **14a** in $CDCl_3$ at 298K revealed the presence of two conformers (rotamers) in a ratio (55/45). $^1$H NMR (400 MHz, $CDCl_3$) $\delta$ 7.93 (d, $J$ = 8.5 Hz, 1.1H), 7.81 (d, $J$ = 8.6 Hz, 0.9H), 7.37–7.28 (m, 4H), 6.85 (d, $J$ = 4.7 Hz, 2H), 6.53 (d, $J$ = 15.9 Hz, 1H), 6.01 (dt, $J$ = 15.9, 6.6 Hz, 1H), 4.77–4.75 (br s, 1H), 4.69 (dd, $J$ = 6.6, 1.3 Hz, 2H), 3.81 (s, 3H), 2.43 (s, 1.65H), 2.42 (s, 1.35H). $^{13}$C{1H} NMR (126 MHz, $CDCl_3$) $\delta$ 159.9, 150.6, 145.1, 143.6, 139.2, 135.6, 135.3, 129.8, 129.7, 128.6, 128.5, 128.1, 126.5, 119.4, 114.2, 67.8, 55.4, 21.8, 21.6. IR (cm$^{-1}$) 3356, 3259, 2959, 1744, 1606, 1510, 1442, 1300, 1245, 1153, 1088, 812, 660, 545, 532. HRMS (ESI): *m/z* calcd. for $C_{18}H_{23}N_2O_5S$ $[M+NH_4]^+$ 379.1328; found 379.1324.

*(E)-3-(phenyl)allyl tosylcarbamate (**14b**).*[50] Prepared from **1b** (90 °C, 6 h) and purified using a hexane/ethyl acetate mixture (60/40, $R_f$ 0.39) as eluent. The product was isolated as a white solid (94 mg) in 95% yield. mp 73–76 °C. NMR spectra of **14b** in $CDCl_3$ at 298K revealed the presence of two conformers (rotamers) in a ratio (75/25). $^1$H NMR (400 MHz, $CDCl_3$) $\delta$ 7.97–7.90 (m, 1.5H), 7.82 (m, 0.5H), 7.37–7.25 (m, 7H), 6.58 (d, $J$ = 15.8 Hz, 1H), 6.14 (dt, $J$ = 15.9, 6.6 Hz, 1H), 4.72 (dd, $J$ = 6.6, 1.3 Hz, 2H), 2.43 (s, 0.75H), 2.42 (s, 2.25H). $^{13}$C{1H} NMR (126 MHz, $CDCl_3$): $\delta$ 150.7, 145.1, 143.5, 139.2, 135.8, 135.5, 135.2, 129.7, 129.6, 128.7, 128.4, 128.3, 126.7, 126.4, 121.7, 67.3, 21.7, 21.5. HRMS (ESI): *m/z* calcd. for $C_{17}H_{21}N_2O_4S$ $[M+NH_4]^+$ 349.1222; found 349.1222.

*(E)-3-(4-Chlorophenyl)allyl tosylcarbamate (**14c**).* Prepared from **1c** (90 °C, 20 h) and purified using a hexane/ethyl acetate mixture (65/35, $R_f$ 0.26) as eluent. The product was isolated as a white solid (77 mg) in 70% yield. mp 86–87 °C. NMR spectra of **14c** in $CDCl_3$ at 298K revealed the presence of two conformers (rotamers) in a ratio (60/40). $^1$H NMR (400 MHz, $CDCl_3$) $\delta$ 7.93 (d, $J$ = 8.1 Hz, 1.2H), 7.82 (d, $J$ = 8.1 Hz, 0.8H), 7.37–7.22 (m, 6H), 6.53 (d, $J$ = 15.9 Hz, 1H), 6.12 (dt, $J$ = 16.0, 6.6 Hz, 1H), 4.83–4.81 (br s, 1H), 4.71 (dd, $J$ = 6.6, 1.3 Hz, 2H), 2.43 (s, 1.8H), 2.42 (s, 1.2H). $^{13}$C{1H} NMR (126 MHz, $CDCl_3$): $\delta$ 150.6, 145.2, 143.7, 139.2, 134.4, 134.1, 133.9, 129.8, 129.7, 129.6, 128.9, 128.5, 128.3, 127.9, 126.5, 122.5, 67.1, 21.8. IR (cm$^{-1}$) 3355,

3259, 3086, 2849, 1737, 1304, 1285, 1160, 1080, 969, 813, 658, 583, 533. HRMS (ESI): *m/z* calcd. for $C_{17}H_{20}ClN_2O_4S$ $[M+NH_4]^+$ 383.0832; found 383.0829.

*(E)-3-(4-Nitrophenyl)allyl tosylcarbamate (**14d**)*. Prepared from **1d** (90 °C, 4 days, 70% conversion) and purified using a hexane/ethyl acetate mixture (80/20, $R_f$ 0.15) as eluent. The product was isolated as a yellow oil (45 mg) in 40% yield. NMR spectra of **14d** in $CDCl_3$ at 298K revealed the presence of two conformers (rotamers) in a ratio (99/1). $^1$H NMR (400 MHz, $CDCl_3$) $\delta$ 8.18 (d, $J$ = 8.5 Hz, 2H), 7.94 (d, $J$ = 8.1 Hz, 2H), 7.47 (d, $J$ = 8.5 Hz, 2H), 7.34 (d, $J$ = 8.1 Hz, 2H), 6.64 (d, $J$ = 16.0 Hz, 1H), 6.34 (dt, $J$ = 16.0, 6.2 Hz, 1H), 4.77 (dd, $J$ = 6.2, 1.4 Hz, 2H), 2.43 (s, 3H). $^{13}$C{1H} NMR (101 MHz, $CDCl_3$) $\delta$ 145.4, 142.3, 135.5, 132.41, 129.8, 128.6, 127.4, 126.8, 124.2, 66.6, 21.9. IR (cm$^{-1}$) 3450, 2996, 2950, 1723, 1448, 1434, 1272, 1241, 1190, 1148, 907, 727, 641. HRMS (ESI): *m/z* calcd. for $C_{17}H_{20}N_3O_6S$ $[M+NH_4]^+$: 394.1067; found: 394.1067.

*(E)-3-(4-methylphenyl)allyl tosylcarbamate (**14e**)*. Prepared from **1e** (90 °C, 6 h) and purified using a hexane/ethyl acetate mixture (70/30, $R_f$ 0.26) as eluent. The product was isolated as a white solid (72 mg) in 70% yield. mp 82–85 °C. NMR spectra of **14e** in $CDCl_3$ at 298K revealed the presence of two conformers (rotamers) in a ratio (65/35). $^1$H NMR (400 MHz, $CDCl_3$) $\delta$ 7.93 (d, $J$ = 8.1 Hz, 1.3 H), 7.82 (d, $J$ = 8.1 Hz, 0.7H), 7.32 (d, $J$ = 7.9 Hz, 2H), 7.23 (d, $J$ = 8.1 Hz, 2H), 7.13 (d, $J$ = 7.9 Hz, 2H), 6.55 (d, $J$ = 15.8 Hz, 1H), 6.09 (dt, $J$ = 15.8, 6.7 Hz, 1H), 4.73–4.69 (br s, 1H), 4.71 (dd, $J$ = 6.7, 1.2 Hz, 2H), 2.43 (s, 1.05H), 2.42 (s, 1.95H), 2.34 (s, 3H). $^{13}$C{1H} NMR (126 MHz, $CDCl_3$) $\delta$ 150.7, 145.1, 143.6, 139.2, 138.4, 135.4, 133.1, 129.8, 129.7, 129.4, 128.4, 126.7, 126.5, 120.7, 67.6, 21.7, 21.6, 21.3. IR (cm$^{-1}$) 3354, 3229, 3048, 2948, 1754, 1596, 1436, 1344, 1219, 1147, 1088, 970, 875, 665, 582, 544. HRMS (ESI): *m/z* calcd. for $C_{18}H_{23}N_2O_4S$ $[M+NH_4]^+$ 363.1379; found 363.1378.

*(E)-3-(4-(benzyloxy)phenyl)allyl tosylcarbamate (**14f**)*. Prepared from **1f** (rt, 15 min.) and purified using a hexane/ethyl acetate mixture (65/35, $R_f$ 0.38) as eluent. The product was isolated as a white solid (97 mg) in 74% yield. mp 106–109 °C. NMR spectra of **14f** in $CDCl_3$ at 298K revealed the presence of two conformers (rotamers) in a ratio (65/35). $^1$H NMR (400 MHz, $CDCl_3$) $\delta$ 7.97–7.88 (d, $J$ = 8.4 Hz, 1.3H), 7.86–7.78 (d, $J$ = 8.4 Hz, 0.7H), 7.50–7.25 (m, 9H), 6.97–6.86 (d, $J$ = 8.4 Hz , 2H), 6.53 (d, $J$ = 15.8 Hz, 1H), 6.01 (dt, $J$ = 15.8, 6.8 Hz, 1H), 5.07 (s, 2H), 4.76–4.73 (br s, 1H), 4.69 (dd, $J$ = 6.9, 1.3 Hz, 2H), 2.43 (s, 1.05H), 2.42 (s, 1.95H). $^{13}$C{1H} NMR (126 MHz, $CDCl_3$) $\delta$ 159.1, 150.6, 145.2, 143.6, 139.2, 136.8, 135.6, 135.2, 129.8, 129.7, 128.9, 128.7, 128.5, 128.2, 128.1, 127.6, 126.5, 119.6, 115.1, 70.1, 67.7, 21.76, 21.62. IR (cm$^{-1}$) 3356, 3250, 2950, 2869, 1738, 1605, 1512, 1433, 1300, 1153, 1064, 813, 660, 530. HRMS (ESI): *m/z* calcd. for $C_{24}H_{27}N_2O_5S$ $[M+NH_4]^+$ 455.1641; found 455.1643.

*(E)-3-(2-methoxyphenyl)allyl tosylcarbamate* (***14g***). Prepared from **1g** (rt, 16 h) and purified using a hexane/ethyl acetate mixture (70/30 $R_f$ 0.24) as eluent. The product was isolated as a yellow oil (92 mg) in 85% yield. NMR spectra of **14g** in $CDCl_3$ at 298K revealed the presence of two conformers (rotamers) in a ratio (65/35). $^1$H NMR (400 MHz, $CDCl_3$) $\delta$ 7.92 (d, $J$ = 8.1 Hz, 1.3H), 7.81 (d, $J$ = 8.1 Hz, 0.7H), 7.34–7.22 (m, 4H), 6.94–6.84 (m, 2H), 6.16 (dt, $J$ = 16.0, 6.6 Hz, 1H), 5.25–5.20 (br s, 1H), 4.70 (dd, $J$ = 6.6, 1.3 Hz, 2H), 3.82 (s, 3H), 2.40 (s, 1.05H), 2.39 (s, 1.95H). $^{13}$C{1H} NMR (126 MHz, $CDCl_3$) $\delta$ 157.0, 150.6, 145.1, 143.5, 139.3, 135.6, 130.6, 129.8, 129.7, 129.5, 128.5, 127.3, 126.5, 124.9, 122.3, 120.7, 111.0, 68.0, 55.5, 21.7, 21.6. IR (cm$^{-1}$) 3355, 2946, 1744, 1596, 1488, 1437, 1343, 1242, 1152, 1067, 868, 812, 751, 659, 576, 544. HRMS (ESI): *m/z* calcd. for $C_{18}H_{23}N_2O_5S$ $[M+NH_4]^+$ 379.1328; found 379.1325.

*(E)-3-(2,3-dihydrobenzofuran-5-yl)allyl tosylcarbamate (**14h**).* Prepared from **1h** (rt, 1 h) and purified using a hexane/ethyl acetate mixture (60/40 $R_f$ 0.30) as eluent. The product was isolated as a colorless oil (40 mg) in 36% yield. NMR spectra of **14h** in $CDCl_3$ at 298K revealed the presence of two conformers (rotamers) in a ratio (99/1). $^1$H NMR (400 MHz, $CDCl_3$) $\delta$ 7.97–7.88 (m, 2H), 7.31 (m, 2H), 7.22–7.19 (m, 1H), 7.07 (dd, $J$ = 8.2, 1.9 Hz, 1H), 6.72 (d, $J$ = 8.2 Hz, 1H), 6.52 (d, $J$ = 15.7 Hz, 1H), 5.98 (dt, $J$ = 15.7, 6.8 Hz, 1H), 4.68 (dd, $J$ = 6.8, 1.2 Hz, 2H), 4.58 (t, $J$ = 8.7 Hz, 2H), 3.19 (t, $J$ = 8.7 Hz, 2H), 2.42 (s, 3H). $^{13}$C{1H} NMR (101 MHz, $CDCl_3$) $\delta$ 160.6, 150.5, 145.2, 135.9, 135.6, 129.7, 128.6, 127.5, 123.2, 118.7, 109.5, 71.7, 67.9, 29.6, 21.8. IR (cm$^{-1}$) 3374, 3280, 3054, 1746, 1599, 1491, 1264, 1161, 731, 702, 546. HRMS (ESI): *m/z* calcd. for $C_{19}H_{19}NO_5SNa$ $[M+Na]^+$ 396.0882; found 396.0881.

*(E)-3-(3,4-dimethoxyphenyl)allyl tosylcarbamate (**14i**).* Prepared from **1i** (rt, 45 min.) and purified using a hexane/ethyl acetate mixture (60/40 $R_f$ 0.20) as eluent. The product was isolated as a colorless oil (38 mg) in 32% yield. NMR spectra of **14i** in $CDCl_3$ at 298K revealed the presence of two conformers (rotamers) in a ratio (99/1). $^1$H NMR (400 MHz, $CDCl_3$) $\delta$ 7.96–7.89 (m, 2H), 7.29 (d, $J$ = 8.0 Hz, 2H), 6.90–6.84 (m, 2H), 6.79 (d, $J$ = 8.1 Hz, 1H), 6.51 (d, $J$ = 15.8 Hz, 1H), 6.02 (dt, $J$ = 15.8, 6.7 Hz, 1H), 4.69 (dd, $J$ = 6.7, 0.9 Hz, 2H), 3.86 (s, 6H), 2.39 (s, 3H). $^{13}$C{1H} NMR (126 MHz, $CDCl_3$) $\delta$ 150.6, 149.5, 149.1, 145.1, 135.6, 135.5, 129.7, 128.9, 128.57, 120.3, 119.7, 111.1, 108.9, 67.6, 56.0, 55.9, 21.7. IR (cm$^{-1}$) 3254, 3057, 2957, 2936, 1746, 1597, 1513, 1451, 1343, 1263, 1158, 1089, 1024, 732, 510. HRMS (ESI): *m/z* calcd. for $C_{19}H_{25}N_2O_6S$ $[M+NH_4]^+$ 409.1433; found 409.1431.

*(E)-3(3-(benzyloxy)-4-methoxyphenyl)allyl tosylcarbamate (**14j**).* Prepared from **1j** (rt, 45 min.) and purified using a hexane/ethyl acetate mixture (60/40 $R_f$ 0.33) as eluent. The product was isolated as a yellow oil (76 mg) in 54% yield. NMR spectra of **14j** in $CDCl_3$ at 298K revealed the presence of two conformers (rotamers) in a ratio (90/10). $^1$H NMR (400 MHz, $CDCl_3$) $\delta$ 7.95–7.89 (d, $J$ = 8.3 Hz, 1.8H), 7.80 (d, $J$ = 8.3 Hz, 0.2H), 7.44 (d, $J$ = 7.1 Hz, 2H), 7.40–7.30 (m, 5H), 6.95–6.83 (m, 3H), 6.47 (d, $J$ = 15.7 Hz, 1H), 5.95 (dt, $J$ = 15.7, 6.7 Hz, 1H), 5.13 (s, 2H), 4.67 (dd, $J$ = 6.7, 1.3 Hz, 2H), 3.88 (s, 3H), 2.42 (s, 0.3H), 2.40 (s, 2.7H). $^{13}$C{1H} NMR (101 MHz, $CDCl_3$) $\delta$ 150.4, 150.3, 148.4, 145.2, 137.1, 135.6, 129.73, 128.90, 128.71, 128.6, 128.1, 127.5, 120.8, 119.6, 112.2, 111.8, 71.3, 67.7, 56.2, 21.8. IR (cm$^{-1}$) 3258, 2958, 2930, 1744, 1596, 1510, 1440, 1257, 1155, 1135, 1016, 660, 545. HRMS (ESI): *m/z* calcd. for $C_{25}H_{29}N_2O_6S$ $[M+NH_4]^+$ 485.1746; found 485.1745.

*(E)-3-(benzo[d][1,3]dioxol-5-yl)allyl tosylcarbamate (**14k**).* Prepared from **1k** (rt, 3 h) and purified using a hexane/ethyl acetate mixture (65/35 $R_f$ 0.27) as eluent. The product was isolated as a white solid (95 mg) in 84% yield. mp 89–91 °C. NMR spectra of **14j** in $CDCl_3$ at 298K revealed the presence of two conformers (rotamers) in a ratio (90/10). $^1$H NMR (400 MHz, $CDCl_3$) $\delta$ 7.92 (d, $J$ = 8.1 Hz, 1.6H), 7.81 (d, $J$ = 8.1 Hz, 0.4H), 7.33–7.29 (m, 2H), 6.84 (s, 1H), 6.75 (d, $J$ = 2.2 Hz, 2H), 6.47 (d, $J$ = 15.8 Hz, 1H), 6.04–5.88 (m, 3H), 5.05–5.00 (br s, 1H), 4.68 (dd, $J$ = 6.9, 1.3 Hz, 2H), 2.41 (s, 3H). $^{13}$C{1H} NMR (101 MHz, $CDCl_3$) $\delta$ 150.6, 148.2, 147.9, 145.2, 135.6, 135.3, 130.3, 129.7, 128.5, 126.5, 121.8, 119.9, 108.4, 105.9, 101.3, 67.5, 21.7, 21.6. IR (cm$^{-1}$) 3355, 3258, 1737, 1492, 1431, 1250, 1156, 1086, 1036, 852, 810, 662, 576, 549. HRMS (ESI): *m/z* calcd. for $C_{18}H_{17}NO_6SNa$ $[M+Na]^+$ 398.0670; found 398.0672.

*(2E,4E)-5-(4-methoxyphenyl)penta-2,4-dien-1-yl tosylcarbamate (**16a**).* Prepared from **5a** (rt, 30 min.) and purified using a hexane/ethyl acetate mixture (65/35 $R_f$ 0.24) as eluent. The product was isolated as a yellow oil (29 mg) in 25% yield. NMR spectra of **16a** in $CDCl_3$ at 298K revealed the presence of two conformers

(rotamers) in a ratio (75/25). $^{1}$H NMR (400 MHz, $CDCl_3$) $\delta$ 7.93 (d, $J$ = 8.2 Hz, 1.5H), 7.82 (d, $J$ = 8.2 Hz, 0.5H), 7.36–7.30 (m, 4H), 6.86 (d, $J$ = 8.7 Hz, 2H), 6.63–6.52 (m, 2H), 6.36 (dd, $J$ = 15.1, 9.8 Hz, 1H), 5.70 (dt, $J$ = 14.5, 6.9 Hz, 1H), 4.75–4.74 (br s, 1H), 4.63 (d, $J$ = 6.9 Hz, 2H), 3.81 (s, 3H), 2.44 (s, 2.25H), 2.41 (s, 0.75H). $^{13}$C{1H} NMR (101 MHz, $CDCl_3$) $\delta$ 159.8, 150.4, 145.2, 136.4, 134.4, 129.8, 128.6, 127.9, 126.6, 124.0,114.3, 67.4, 55.5, 21.8, 21.7. IR (cm$^{-1}$) 3268, 2957, 2925, 1735, 1601, 1510, 1458, 1341, 1249, 1160, 814, 664, 547. HRMS (ESI): *m/z* calcd. for $C_{20}H_{21}NO_5SNa$ [M+Na]$^+$ 410.1038; found 410.1036.

*(2E,4E)-5-phenylpenta-2,4-dien-1-yl tosylcarbamate (**16b**)*. Prepared from **5b** (rt, 4 h) and purified using a hexane/ethyl acetate mixture (70/30 $R_f$ 0.29) as eluent. The product was isolated as a yellow oil (80 mg) in 75% yield. NMR spectra of **16b** in $CDCl_3$ at 298K revealed the presence of two conformers (rotamers) in a ratio (63/37). $^{1}$H NMR (400 MHz, $CDCl_3$) $\delta$ 7.95–7.91 (m, 1.3H), 7.84–7.80 (m, 0.7H), 7.41–7.36 (m, 2H), 7.36–7.29 (m, 4H), 7.27–7.24 (m, 1H), 6.71 (dd, $J$ = 15.7, 10.3 Hz, 1H), 6.56 (d, $J$ = 15.7 Hz, 1H), 6.37 (dd, $J$ = 15.2, 10.4 Hz, 1H), 5.75 (dt, $J$ = 14.1, 6.7 Hz, 1H), 5.02–4.93 (br s, 1H), 4.64 (d, $J$ = 6.7 Hz, 2H), 2.43 (s, 1. 9H), 2.42 (s, 1.1H). $^{13}$C{1H} NMR (126 MHz, $CDCl_3$) $\delta$ 150.6, 145.2, 143.6, 139.2, 136.8, 135.6, 134.5, 129.8, 128.7, 128.4, 128.1, 127.4, 126.6, 126.5, 125.4, 67.1, 21.7, 21.6. IR (cm$^{-1}$) 3355, 3259, 1745, 1441, 1302, 1152, 660, 544. HRMS (ESI): *m/z* calcd. for $C_{19}H_{19}NO_4SNa$ [M+Na]$^+$ 380.0932; found 380.0929.

*(2E,4E)-5-(4-chlorophenyl)penta-2,4-dien-1-yl tosylcarbamate* (***16c***). Prepared from **5c** (rt, 4 h) and purified using a hexane/ethyl acetate mixture (70/30 $R_f$ 0.22) as eluent. The product was isolated as pale yellow oil (80 mg) in 68% yield. NMR spectra of **16c** in $CDCl_3$ at 298K revealed the presence of two conformers (rotamers) in a ratio (75/25). $^{1}$H NMR (400 MHz, $CDCl_3$) $\delta$ 7.96–7.88 (m, 1.5H), 7.85–7.76 (m, 0.5H), 7.31 (d, $J$ = 8.1 Hz, 2H), 7.29–7.22 (m, 4H), 6.64 (dd, $J$ = 15.7, 10.5 Hz, 1H), 6.46 (d, $J$ = 15.7 Hz, 1H), 6.33 (dd, $J$ = 15.2, 10.4 Hz, 1H), 5.75 (dt, $J$ = 15.2, 6.5 Hz, 1H), 4.62 (d, $J$ = 6.5 Hz, 2H), 2.40 (s, 2.25H), 2.39 (s, 0.75H). $^{13}$C{1H} NMR (126 MHz, $CDCl_3$) $\delta$ 150.5, 145.2, 143.7, 139.2, 135.5, 135.2, 133.7, 133.1, 129.8, 129.7, 128.9, 128.5, 127.9, 127.8, 126.5, 125.9, 67.0, 21.8, 21.6. IR (cm$^{-1}$) 3272, 3055, 1749, 1595, 1344, 1264, 1159, 1089, 732, 510. HRMS (ESI): *m/z* calcd. for $C_{19}H_{18}ClNO_4SNa$ [M+Na]$^+$ 414.0543; found 414.0542.

*(2E,4E)-5-(4-nitrophenyl)penta-2,4-dien-1-yl tosylcarbamate* (***16d***). Prepared from **5d** (90 °C, 5 days) and purified using a hexane/ethyl acetate mixture (60/40 $R_f$ 0.26) as eluent. The product was isolated as an orange oil (44 mg) in 36% yield. NMR spectra of **16d** in $CDCl_3$ at 298K revealed the presence of two conformers (rotamers) in a ratio (99/1). $^{1}$H NMR (400 MHz, $CDCl_3$) $\delta$ 8.18 (d, $J$ = 8.5 Hz, 2H), 7.93 (d, $J$ = 8.1 Hz, 2H), 7.50 (d, $J$ = 8.5 Hz, 2H), 7.35 (d, $J$ = 8.1 Hz, 2H), 6.85 (dd, $J$ = 15.7, 10.5 Hz, 1H), 6.60 (d, $J$ = 15.7 Hz, 1H), 6.41 (dd, $J$ = 15.3, 10.6 Hz, 1H), 5.90 (dt, $J$ = 15.3, 5.9 Hz, 1H), 4.67 (d, $J$ = 5.9 Hz, 2H), 2.44 (s, 3H). $^{13}$C{1H} NMR (101 MHz, $CDCl_3$) $\delta$ 150.3, 147.1, 145.4, 143.3, 135.5, 134.3, 131.9, 129.8, 128.7, 128.5, 127.1, 124.2, 66.6, 21.8. IR (cm$^{-1}$) 3237, 2957, 2927, 1749, 1594, 1514, 1450, 1340, 1158, 1089, 860, 662, 577, 547. HRMS (ESI): *m/z* calcd. for $C_{19}H_{18}N_2O_6SNa$ [M+Na]$^+$ 425.0783; found 425.0785.

*(3E,5E)-6-(4-Chlorophenyl)hexa-3,5-dien-2-yl tosylcarbamate (**18ba**)*. Prepared from **17b** (rt, 2 h). The compound is unstable on silica gel but a pure sample can be obtained by flash chromatography using a cyclohexane/ethyl acetate mixture (70/30 $R_f$ 0.28) as eluent. The product was isolated as a yellow oil. $^{1}$H NMR (300 MHz, $CD_2Cl_2$) $\delta$ 7.90 (d, $J$ = 8.4 Hz, 2H), 7.80-7.77 (br s, 1H), 7.38–7.34 (m, 2H), 7.36–7.25 (m, 4H), 6.75–6.63 (m, 1H), 6.51 (d, $J$ = 15.7 Hz, 1H), 6.32 (ddd, $J$ = 15.2, 10.3, 1.1 Hz, 1H), 5.71 (dd, $J$ = 15.2, 6.8 Hz, 1H), 5.36–5.24 (m, 1H), 2.43 (s, 3H), 1.32 (d, $J$ = 6.5 Hz, 3H). $^{13}$C{1H} NMR (75 MHz, $CD_2Cl_2$) $\delta$ 149.8, 145.3, 135.6, 135.5, 133.2, 132.5, 132.2, 131.9, 129.6, 128.7, 128.3, 128.2, 127.6, 126.3, 74.1, 21.4, 19.9. IR (cm$^{-1}$)

3227, 1740, 1596, 1490, 1436, 1344, 1222, 1157, 1088, 986, 813, 767, 660. HRMS (ESI): *m/z* calcd. for $C_{20}H_{19}ClNO_4S$ $[M-H]^-$ 404.0729; found 404.0729.

**Using phenyl and isopropyl isocyanate.** To a solution of allylic alcohol **1a** (0.7 mmol) in dry dichloromethane (0.35M) were added the desired isocyanate (1.05 mmol, 1.5 eq), $Et_3N$ (1.05 mmol, 1.5 eq) and DMAP (0.04 mmol, 5 mol%). The reaction was stirred at reflux for 16 hours. Dichloromethane was evaporated and the crude product was purified by silica gel chromatography to afford the branched carbamate.

*1-(4-Methoxyphenyl)allyl phenylcarbamate* (***11***). Prepared from phenyl isocyanate and purified using a cyclohexane/ethyl acetate mixture (80/20, $R_f$ 0.28) as eluent. The product was isolated as a colorless oil (53 mg) in 30% yield. $^1$H NMR (300 MHz, $CDCl_3$) $\delta$ 7.43–7.26 (m, 6H), 7.11–7.05 (m, 1H), 6.93 (d, $J$ = 8.7 Hz, 2H), 6.87–6.83 (br s, 1H), 6.28 (d, $J$ = 5.7 Hz, 1H), 6.10 (ddd, $J$ = 17.2, 10.4, 5.6 Hz, 1H), 5.42–5.26 (m, 2H), 3.83 (s, 3H). $^{13}$C{1H} NMR (101 MHz, Acetone-$d_6$) $\delta$ 160.5, 153.5, 140.1, 138.1, 132.4, 129.6, 129.4, 123.4, 119.1, 116.2, 114.6, 76.7, 55.5. IR (cm$^{-1}$) 3325, 2934, 2482, 1704, 1601, 1501, 1402, 1242, 1174, 1027, 827, 750, 691. HRMS (ESI) *m/z* calcd. for $C_{17}H_{17}NO_3Na$ $[M+Na]^+$ 306.1101; found 306.1099.

*1-(4-Methoxyphenyl)allyl isopropylcarbamate* (***12***). Prepared from isopropyl isocyanate and purified using a cyclohexane/ethyl acetate mixture (90/10, $R_f$ 0.18) as eluent. The product was isolated as a yellow solid (62 mg) in 65% yield. m.p. 120–123 °C. $^1$H NMR (300 MHz, $CDCl_3$) $\delta$ 7.28 (d, $J$ = 8.7 Hz, 2H), 6.88 (d, $J$ = 8.7 Hz, 2H), 6.13 (d, $J$ = 5.7 Hz, 1H), 6.01 (ddd, $J$ = 17.1, 10.4, 5.6 Hz, 1H), 5.34–5.11 (m, 2H), 4.60–4.55 (br s, 1H), 3.88–3.80 (m, 1H), 3.80 (s, 3H), 1.14 (dd, $J$ = 8.7, 6.4 Hz, 6H). $^{13}$C{1H} NMR (75 MHz, $CDCl_3$) $\delta$ 159.5, 154.9, 137.1, 131.7, 128.7, 116.1, 114.0, 113.6, 76.0, 55.3, 23.1. IR (cm$^{-1}$) 3329, 2972, 1685, 1612, 1523, 1512, 1242, 1175, 1070, 1031, 926, 828, 816, 778. HRMS (ESI) *m/z* calcd. for $C_{14}H_{19}NO_3Na$ $[M+Na]^+$ 272.1257; found 272.1254.

**Using benzoyl isocyanate.** To a solution of allylic alcohol **1a** or **17** (0.7 mmol) in dry $CH_2Cl_2$ or $CDCl_3$ (0.70M) was added the desired isocyanate (0.84 mmol, 1.2 eq). The reaction was stirred at room temperature for desired time (Scheme 4 and Scheme 5). Solvent was evaporated and the crude product was purified by silica gel chromatography to afford the desired compound.

*(E)-3-(4-Methoxyphenyl)allyl benzoylcarbamate (**15**)*. Prepared from **1a** in 30 min. and purified using a cyclohexane/ethyl acetate mixture (70/30, $R_f$ 0.31) as eluent. The product was isolated as a colorless oil (137 mg) in 63% yield. $^1$H NMR (400 MHz, $CDCl_3$) $\delta$ 8.57–8.53 (br s, 1H), 7.81 (d, $J$ = 7.2 Hz, 2H), 7.53–7.47 (m, 1H), 7.39 (dd, $J$ = 8.3, 7.1 Hz, 2H), 7.23 (d, $J$ = 8.8 Hz, 2H), 6.79 (d, $J$ = 8.8 Hz, 2H), 6.56 (d, $J$ = 15.8 Hz, 1H), 6.09 (dt, $J$ = 15.9, 6.8 Hz, 1H), 4.75 (dd, $J$ = 6.8, 1.2 Hz, 2H), 3.74 (s, 3H). $^{13}$C{1H} NMR (101 MHz, $CDCl_3$) $\delta$ 165.2, 159.8, 151.2, 135.2, 133.0, 132.9, 130.6, 128.8, 128.7, 128.0, 127.8, 119.9, 114.1, 67.7, 67.0, 55.3. IR (cm$^{-1}$) 3241, 3189, 3035, 3008, 2835, 1747, 1683, 1606, 1507, 1488, 1192, 1173, 1054, 1033, 1025, 969, 834, 778, 701. HRMS (ESI) *m/z* calcd. for $C_{18}H_{17}NO_4Na$ $[M+Na]^+$ 334.1050; found 334.1050.

*(3E,5E)-6-Phenylhexa-3,5-dien-2-yl benzoylcarbamate (**18ab**)*. Prepared from **17a** (rt, 2 h). The compound is unstable on silica gel but a pure sample can be obtained by flash chromatography using a cyclohexane/ethyl acetate mixture (70/30, $R_f$ 0.24) as eluent. The product was isolated as a slight yellow oil. $^1$H NMR (300 MHz, $CDCl_3$) $\delta$ 8.02–7.59 (br s, 1H), 7.87–7.77 (m, 2H), 7.62–7.54 (m, 1H), 7.52–7.45 (m, 3H), 7.45–7.33 (m, 2H), 7.35–7.28 (m, 2H), 6.74 (dd, $J$ = 15.6, 10.2 Hz, 1H), 6.61 (d, $J$ = 15.7 Hz, 1H), 6.50 (dd, $J$ = 15.1, 9.8 Hz, 1H), 5.82 (dd, $J$ = 15.1, 7.0 Hz, 1H), 5.54 (m, 1H), 1.47 (d, $J$ = 6.5 Hz, 3H). $^{13}$C{1H} NMR (75 MHz, $CDCl_3$) $\delta$ 165.3, 151.4, 150.6, 134.2, 133.2, 133.0, 132.9, 132.0, 128.8, 128.6, 128.5, 128.3, 127.9, 127.7,

127.5, 126.5, 73.3, 20.3. IR ($cm^{-1}$) 3285, 3028, 2984, 1754, 1665, 1510, 1488, 1192, 1035, 989, 690. HRMS (ESI) *m/z* calcd. for $C_{20}H_{19}NO_3Na$ $[M+Na]^+$ 344.1257; found 344.1257.

*(3E,5E)-6-(4-Chlorophenyl)hexa-3,5-dien-2-yl benzoylcarbamate (**18bb**)*. Prepared from **17b** (rt, 2 h). The compound is unstable on silica gel but a pure sample can be obtained by flash chromatography using a cyclohexane/ethyl acetate mixture (70/30, $R_f$ 0.34) as eluent. The product was isolated as a yellow oil. $^1$H NMR (300 MHz, $CD_2Cl_2$) $\delta$ 8.32–8.30 (br s, 1H), 7.86–7.80 (m, 2H), 7.64–7.55 (m, 1H), 7.53–7.45 (m, 2H), 7.39–7.25 (m, 4H), 6.75 (dd, $J$ = 15.4, 10.6 Hz, 1H), 6.56 (d, $J$ = 15.7 Hz, 1H), 6.48 (ddd, $J$ = 15.2, 10.4, 1.1 Hz, 1H), 5.86 (dd, $J$ = 15.2, 6.8 Hz, 1H), 5.49 (m, 1H), 1.44 (d, $J$ = 6.5 Hz, 3H). $^{13}$C{1H} NMR (75 MHz, $CD_2Cl_2$) $\delta$ 164.8, 150.1, 135.6, 133.3, 133.2, 132.9, 132.5, 132.4, 132.2, 128.8, 128.7, 128.5, 128.4, 127.7, 127.5, 127.3, 72.9, 20.0. IR ($cm^{-1}$) 3252, 2982, 2930, 1742, 1683, 1519, 1488, 1288, 1202, 1121, 1088, 992, 830, 776, 703. HRMS (ESI) *m/z* calcd. for $C_{20}H_{18}ClNO_3$ $[M-H]^-$ 354.0902; found 354.0902.

**Using (*R*)-(+)-(4-fluorophenyl)ethyl isocyanate.**

*(S,E)-4-phenylbut-3-en-2-yl ((R)-1-(4-fluorophenyl)ethyl)carbamate (**22**)*. To a solution of (+)-(*S,E*)-1-phenylbut-2-enol **20** (*ee* 98%, 0.15 mmol) in toluene (0.2 M) under argon atmosphere, (*R*)-(+)-(4-fluorophenyl)ethyl isocyanate **19** (0.17 mmol) and triethylamine (0.05 mmol) were added and the mixture was stirred at 90 °C for 6 h. The initial mixture was concentrated in *vacuo*, diluted with $Et_2O$ (2 mL) and washed with saturated NaCl (3x 2mL). The resulting crude mixture was diluted in toluene (0.2 M) and stirred at 110 °C for 48 h. The final mixture was purified by flash column chromatography on neutral aluminium oxide using a hexane/ethyl acetate mixture (83/17, $R_f$ 0.64) as eluent. The product was isolated as a colorless oil (19 mg) in 39% yield. $^1$H NMR (400 MHz, $CDCl_3$) $\delta$ 7.39–7.26 (m, 7H), 7.00 (dd, $J$ = 8.6, 8.6 Hz, 2H), 6.56 (d, $J$ = 16.0 Hz, 1H), 6.17 (dd, $J$ = 16.0, 6.5 Hz, 1H), 5.41 (dd, $J$ = 6.5, 6.5 Hz, 1H), 4.92–4.90 (br s, 1H), 4.86–4.78 (m, 1H), 1.50–1.45 (m, 3H), 1.43–1.36 (m, 3H). $^{13}$C{1H} NMR (101 MHz, $CDCl_3$) $\delta$ 162.08 (d, $^1J_{CF}$ = 244.9 Hz), 155.21, 136.56, 131.24, 129.38, 128.68, 127.97, 127.68 (d, $^3J_{CF}$ = 8.3 Hz), 126.68, 115.53 (d, $^2J_{CF}$ = 21.1 Hz), 71.66, 50.15, 22.68, 20.75; $^{19}$F NMR (376 MHz, $CDCl_3$) $\delta$ -115.58. IR ($cm^{-1}$) 3343, 2979, 2931, 1680, 1529, 1508, 1221, 1058, 548. HRMS (ESI) *m/z* calcd. for $C_{19}H_{20}FNO_2Na$ $[M+Na]^+$ 336.1376; found 336.1371. HPLC (ChiralPak IB, hexane/iPrOH = 97:3, flow rate 1 mL/min, λ 210 nm), $t_R$ (minor) 13.64 min, $t_R$ (major) 15.71 min; 95% *de*. $[\alpha]^{22}_D$ = -15.91 ( *c* 0.35, $CHCl_3$).

## General procedure for the synthesis of allylamine derivatives 8, 9 and 10 via an allyl cyanate/isocyanate rearrangement from 4a.

To a solution of carbamate **4a** (0.25 mmol) in dry dichloromethane (0.13M) cooled at 0 °C under argon atmosphere was added TFAA (0.75 mmol) and triethylamine (1.13 mmol). The reaction mixture was stirred at 0°C for 1 hour and then the desired nucleophile (0.38 mmol), and Ti(O*t*-Bu)$_4$ (0.025 mmol) if necessary, were added at 0 °C. The reaction mixture was stirred at room temperature during the required time (Scheme 2). Water was added and the aqueous layer was extracted three times with $CH_2Cl_2$. The collected organic layers were dried over $MgSO_4$, filtered and concentrated under *vacuo*. The crude product was purified by silica gel chromatography.

*1,1-Diethyl-3-(1-(4-methoxyphenyl)allyl)urea* (***8***). Prepared using $HNEt_2$ as nucleophile and purified using a cyclohexane/ethyl acetate mixture (70/30, $R_f$ 0.51) as eluent. The product was isolated as a colorless oil (33 mg) in 50% yield. $^1$H NMR (400 MHz, $CDCl_3$) $\delta$ 7.24 (d, $J$ = 8.6 Hz, 2H), 6.87 (d, $J$ = 8.6 Hz, 2H), 6.04

(ddd, $J$ = 16.8, 10.6, 5.2 Hz, 1H), 5.50 (dddd, $J$ = 7.2, 5.2, 1.7, 1.7 Hz, 1H), 5.24–5.14 (m, 2H), 4.52 (d, $J$ = 7.6 Hz, 1H), 3.79 (s, 3H), 3.27 (q, $J$ = 7.4 Hz, 4H), 1.14 (t, $J$ = 7.4 Hz, 6H). $^{13}$C{1H} NMR (101 MHz, $CDCl_3$) $\delta$ 159.0, 156.5, 139.1, 134.2, 128.5, 115.0, 114.1, 55.8, 55.4, 41.4, 14.1. IR (cm$^{-1}$) 3348, 2977, 2931, 1618, 1510, 1249, 1177, 1031, 908, 828, 810, 762. HRMS (ESI) *m/z* calcd. for $C_{15}H_{22}N_2O_2Na$ [M+Na]$^+$ 285.1574; found 285.1574.

*1-Allyl-1-benzyl-3-(1-(4-methoxyphenyl)allyl)urea* (***9***). Prepared using *N*-benzyl allylamine as nucleophile and purified using a cyclohexane/ethyl acetate mixture (70/30, $R_f$ 0.54) as eluent. The product was isolated as a colorless oil (46 mg) in 55% yield. $^1$H NMR (400 MHz, $CDCl_3$) $\delta$ 7.36–7.27 (m, 2H), 7.28–7.23 (m, 3H), 7.12 (d, $J$ = 8.6 Hz, 2H), 6.83 (d, $J$ = 8.6 Hz, 2H), 5.95 (ddd, $J$ = 17.2, 10.4, 5.2 Hz, 1H), 5.78 (ddt, $J$ = 17.5, 9.9, 5.5 Hz, 1H), 5.52–5.45 (m, 1H), 5.20–5.15 (m, 2H), 5.13–5.04 (m, 2H), 4.73 (d, $J$ = 7.8 Hz, 1H), 4.57–4.40 (m, 2H), 3.88 (dd, $J$ = 5.5, 1.6 Hz, 2H), 3.78 (s, 3H). $^{13}$C{1H} NMR (101 MHz, $CDCl_3$,) $\delta$ 158.9, 157.5, 138.9, 138.1, 134.1, 133.9, 128.8, 128.3, 127.5, 117.1, 114.8, 114.0, 56.0, 55.4, 50.5, 49.9. IR (cm$^{-1}$) 3316, 2960, 2917, 2849, 1613, 1531, 1511, 1240, 1176, 1028, 927, 803, 702. HRMS (ESI) *m/z* calcd. for $C_{21}H_{24}N_2O_2Na$ [M+Na]$^+$ 359.1730; found 359.1729.

*Benzyl (1-(4-methoxyphenyl)allyl)carbamate* (***10***).[51] Prepared using benzyl alcohol as nucleophile and purified using a cyclohexane/ethyl acetate mixture (80/20, $R_f$ 0.50) as eluent. The product was isolated as a colorless oil (33 mg) in 45% yield. $^1$H NMR (300 MHz, $CDCl_3$) $\delta$ 7.37–7.32 (m, 5H), 7.21 (d, $J$ = 8.3 Hz, 2H), 6.83 (d, $J$ = 8.3 Hz, 2H), 6.00 (ddd, $J$ = 17.4, 10.1, 5.2 Hz, 1H), 5.34–5.07 (m, 6H), 3.80 (s, 3H). $^{13}$C{1H} NMR (75 MHz, $CDCl_3$) $\delta$ 159.2, 155.6, 137.9, 136.5, 132.9, 128.6, 128.4, 128.2, 115.6, 114.2, 67.0, 55.4.

## Preparation of [$^{17}$O] labelled compounds.

*[$^{17}O_2$]benzoic acid (**[$^{17}O_2$]25**).*[30] (Trichloromethyl)benzene (1.75 mmol) and 0.59 mL of $H_2{}^{17}O$ were placed in a microwave vessel and sealed. The resulting mixture was irradiated with microwaves at 150 W, 130 °C and 6 bar for 30 minutes. Once the mixture was cooled down to room temperature, the solid formed was filtered and washed with hexane. The desired pure compound was obtained as a white solid (200 mg) in 93% yield. $^1$H NMR (400 MHz, Acetone-$d_6$): $\delta$ 8.07 – 8.02 (m, 2H), 7.66 – 7.60 (m, 1H), 7.51 (dd, $J$ = 8.4, 7.1 Hz, 2H). $^{17}$O NMR (68 MHz, Acetone-$d_6$): $\delta$ 245.

*[$^{17}O_2$]2-ethoxy-2-oxoethyl benzoate (**[$^{17}O_2$]26**).*[31] To a solution of **[$^{17}O_2$]25** (1.62 mmol) and $Cu(OTf)_2$ (5.9 mg) in toluene (10 mL) ethyl diazoacetate was added dropwise (3.24 mmol) and the resulting mixture was warmed up to 80 ºC and stirred for 12h. After completion, the reaction mixture was filtered and toluene was evaporated in vacuo. The final product was used without further purification. $^1$H NMR (500 MHz, Acetone-$d_6$): $\delta$ 8.09 (d, $J$ = 7.7 Hz, 2H), 7.68 (t, $J$ = 7.5 Hz, 1H), 7.56 (q, $J$ = 8.0 Hz, 2H), 4.91 (s, 2H), 4.23 (q, $J$ = 7.1 Hz, 2H), 1.27 (tq, $J$ = 7.2, 3.6, 2.6 Hz, 3H). $^{17}$O NMR (68 MHz, Acetone-$d_6$): $\delta$ 340, 136.

*[$^{17}$O]Benzyl alcohol **[$^{17}$O]27***. Compound **[$^{17}O_2$]25** (1.60 mmol) was dissolved in THF (20 mL). A solution of $LiAlH_4$ in THF (1.48 mL, 2.5 M) was slowly added to the resulting mixture at 0 °C and the reaction was allowed to stir at room temperature until total consumption of starting material. After completion, a solution of NaOH 1N (10 mL) was used to quench the reaction and the aqueous layer was extracted with $CH_2Cl_2$ (3 x 10 mL). The organic layers were dried over $MgSO_4$, filtered and concentrated *in vacuo*. The final product was purified by flash column chromatography on silica gel using a hexane/ethyl acetate mixture (60/40, $R_f$ 0.59) as

eluent, and isolated as a pale yellow oil (149 mg) in 85% yield. $^1$H NMR (500 MHz, $CDCl_3$): $\delta$ 7.37 (d, $J$ = 4.5 Hz, 4H), 7.32 – 7.28 (m, 1H), 4.70 (d, $J$ = 2.3 Hz, 2H), 1.67 (s, 1H). $^{17}$O NMR (68 MHz, Acetone-$d_6$): $\delta$ 0.

*[$^{17}$O]Benzaldehyde (**[$^{17}$O]28**).*[52] A solution of oxalyl chloride (2.33 mmol) in $CH_2Cl_2$ (3 mL) was cooled to -84 °C and dimethyl sulfoxide (4.65 mmol) was added slowly. The resulting mixture was stirred for additional 15 minutes. **[$^{17}$O$_1$]27** (1.37 mmol) was added to the reaction and the mixture was allowed to stir for 15 minutes. Triethylamine (6.85 mmol) was slowly added and the resulting white suspension was stirred at the indicated temperature for 2h. After completion, the reaction was warmed up to 0 °C, quenched with HCl 3 mL) and extracted with $CH_2Cl_2$ (3x 5 mL). The organic layer was washed with $NaHCO_3$ sat. (2 x 5 mL) and the combined organic layers were dried over $MgSO_4$, filtered and concentrated *in vacuo* at 0 ºC. The desired compound was isolated as a colorless oil (95 mg) in 65% yield and used in the next step without further purification. $^1$H NMR (400 MHz, $CDCl_3$): $\delta$ 10.06 (s, 1H), 7.95 – 7.88 (m, 2H), 7.72 – 7.63 (m, 1H), 7.57 (dd, $J$ = 8.2, 6.9 Hz, 2H). $^{17}$O NMR (68 MHz, $CDCl_3$): $\delta$ 554.

*[$^{17}$O]1-Phenylprop-2-en-1-ol (**[$^{17}$O]1b**).*[53] To a solution of **[$^{17}$O$_1$]28** (0.89 mmol) in THF (6 mL) was slowly added at 0° C a solution of vinylmagnesium bromide in THF (1.07 mmol, 1 M). The reaction mixture was stirred at room temperature for 4 hours after which a saturated $NH_4Cl$ solution (3 mL) was added. The aqueous layer was extracted with $Et_2O$ (4 x 6 mL). The organic layers were dried over $MgSO_4$, filtered and concentrated *in vacuo*. The residue was purified by flash column chromatography on silica gel using a hexane/ethyl acetate mixture (70:30, $R_f$ 0.60) to afford the desired product as a yellow oil (64 mg) in 54% yield. $^1$H NMR (400 MHz, $CDCl_3$): $\delta$ 7.42 – 7.34 (m, 4H), 7.29 (td, $J$ = 5.7, 2.5 Hz, 1H), 6.06 (ddd, $J$ = 16.7, 10.3, 6.0 Hz, 1H), 5.35 (dd, $J$ = 16.7, 1.6 Hz, 1H), 5.24 – 5.18 (m, 2H). $^{17}$O NMR (68 MHz, $CDCl_3$): $\delta$ 31.

*[$^{17}$O$_1$]1-phenylallyl tosylcarbamate (**[$^{17}$O$_1$]13b**).*[5c] To a solution of 1-phenylprop-2-en-1-ol **[$^{17}$O$_1$]1b** (0.073 mmol) in toluene (0.2 M) under argon atmosphere, *p*-toluenesulfonylisocyanate (0.088 mmol) was added dropwise and the mixture was stirred at room temperature for 5 minutes. The resulting mixture was concentrated *in vacuo* and purified using a hexane/ethyl acetate mixture (80/20, $R_f$ 0.31) as eluent. The product was isolated as a colorless oil (21 mg) in 90% yield. $^1$H NMR (400 MHz, $CDCl_3$) $\delta$ 7.88 (d, $J$ = 8.3 Hz, 2H), 7.55–7.53 (br s, 1H), 7.34–7.26 (m, 5H), 7.21 (dd, $J$ = 6.8, 3.0 Hz, 2H), 6.11 (dd, $J$ = 6.0, 1.5 Hz, 1H), 5.92 (ddd, $J$ = 16.7, 10.5, 5.9 Hz, 1H), 5.27–5.23 (m, 2H), 2.43 (s, 3H). $^{17}$O NMR (68 MHz, $CDCl_3$): $\delta$ 150, 129.

*[$^{17}$O$_1$](E)-3-(phenyl)allyl tosylcarbamate (**[$^{17}$O$_1$]14b**).*[50] Prepared from **[$^{17}$O$_1$]1b** (90 °C, 4 h) and purified using a hexane/ethyl acetate mixture (60/40, $R_f$ 0.39) as eluent. The product was isolated as a white solid (21 mg) in 86% yield. $^1$H NMR (400 MHz, $CDCl_3$) $\delta$ 7.97–7.90 (m, 1.5H), 7.82 (m, 0.5H), 7.37–7.25 (m, 7H), 6.58 (d, $J$ = 15.8 Hz, 1H), 6.14 (dt, $J$ = 15.9, 6.6 Hz, 1H), 4.72 (dd, $J$ = 6.6, 1.3 Hz, 2H), 2.43 (s, 0.75H), 2.42 (s, 2.25H). $^{17}$O NMR (68 MHz, Chloroform-*d*) δ 264, 125. HRMS (ESI): *m/z* calcd. for ***[$^{17}$O$_1$]14b***: calculated for $C_{17}H_{17}NO_4SNa$ $[M+Na]^+$ 354.0763; found: 354.0763 (59%); calculated for $C_{17}H_{17}NO_3{}^{17}OSNa$ $[(M+1)+Na]^+$ 355.0805; found: 355.0799 (11%); calculated for $C_{17}H_{17}NO_3{}^{18}OSNa$ $[(M+2)+Na]^+$ 356.0806; found: 356.0799 (30%).

## Procedure for NMR monitoring of the [$^{17}$O$_1$]13b → [$^{17}$O$_1$]14b transformation

To a solution of 1-phenylprop-2-en-1-ol **[$^{17}$O$_1$]1b** (0.373 mmol) in toluene (0.2 M) under argon atmosphere, *p*-toluenesulfonylisocyanate (0.447 mmol) was added dropwise. The reaction was heated to 90 °C,

and 200 μL were taken from the reaction medium every 20 minutes. The solvent was removed and the resulting colorless oil was dissolved in $CDCl_3$ to perform $^{17}O$ NMR experiments at room temperature.

**Computational Methods**. All of the calculations reported in this work were carried out with the GAUSSIAN 09 suite of programs[54] and using the hybrid DFT functional B3LYP[55] with the D3 dispersion empirical correction[56] and the 6-311++G(d,p) basis set.[57] The most stable conformations of reactants and products were previously determined by MM Monte Carlo simulations using the OPLS force field[58] as implemented in the MacroModel program Implemented in the Shrödinger Maestro suite)[59] and then subjected to DFT optimizations. All the stationary points were characterized by harmonic analysis. Reactants and products showed positive definite Hessians. Transition structures (TSs) showed one and only one imaginary frequency associated with nuclear motion along the chemical transformation under study. Free energies at 363.15 K were calculated by including the corresponding thermal corrections to Gibbs free energies (TCGE). Solvent effects were considered by means of the PCM method.[60] The solvent introduced in the calculations was toluene. Natural bonding analysis calculations were performed using the NBO program[61] as implemented in Gaussian 09.

## ASSOCIATED CONTENT

**Supporting Information.** This material is available free of charge via the Internet at http://pubs.acs.org.

- Copies of $^{1}H$, $^{13}C$ NMR spectra and chiral HPLC chromatography of all new compounds. Copies of $^{17}O$ NMR of **25**, **26**, **27**, **28**, **1b**, **13b**, **14b**. First order linear plot obtained for compounds **14a-c**. Cartesian coordinates, number of imaginary frequencies (NIMAG), and energy data of stationary points gathered in Figure 5, 7, 8, 9 and 10.
- Crystal data, CCDC 1824810 for **14e** (CIF)

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### Notes

The authors declare no competing financial interest.

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