DOI: 10.1002/ejoc.200900159

New Options for the Reactivity of the Burgess Reagent with Epoxides in Both Racemic and Chiral Auxiliary Modes – Structural and Mechanistic Revisions, Computational Studies, and Application to Synthesis

Hannes Leisch,[a] Bradford Sullivan,[a] Branden Fonovic,[a] Travis Dudding,[a] and Tomas Hudlicky*[a]

Keywords: Burgess reagent / Chiral auxiliaries / Enantioselectivity / Amino alcohol derivatives / Sulfamidate synthesis / Balanol / Density functional calculations / Structure revisions

The reaction of the chiral auxiliary version of the Burgess reagent with epoxides yields diastereomeric pairs of sulfamidates, which lead to *cis* and *trans* amino alcohols in each enantiomeric series. Experimental and spectral details are provided for all new sulfamidates and the products derived from them. Structure revisions have been made for several previously reported products from the reactions of the Burgess reagent with cyclic oxiranes and styrene diols. Considerable revisions are also suggested for the possible mechanisms operating in the reactions of the Burgess reagent with 1,2-diols and epoxides. Finally, a Density Functional Theory (DFT) study for the interaction of the achiral version of the Burgess reagent with oxiranes is included along with an explanation of the lack of asymmetric induction observed in reactions conducted in a catalytic mode with C_2-symmetric catalysts.

Introduction

The Burgess reagent (**1**), discovered almost four decades ago,[1,2] has experienced renewed popularity over the past few years in a number of creative synthetic ventures. Originally designed as a mild dehydrating agent for secondary and tertiary alcohols, as shown in Figure 1, it has occasionally been used in approaches to or for the total synthesis of natural products and medicinal agents, for example, cedrene,[3] narciclasine,[4] taxol,[5] efrotomycin,[6] and pravastatin.[7]

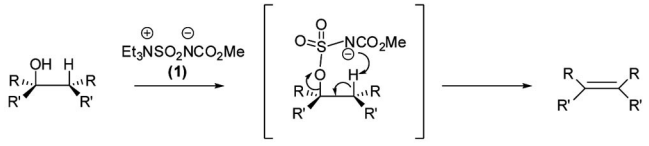


Figure 1. Dehydration of alcohols with the Burgess reagent.

It is also the reagent of choice for the synthesis of urethanes from primary alcohols[8] and dehydration of amides to nitriles.[9] Its polymer-linked version has been employed in the synthesis of oxazolines and thiazolines.[10] Recent disclosures feature the preparation of α- and β-glycosylamines from carbohydrates,[11] sulfamidates from 1,2-diols,[12] disulfides from thiols,[13] sulfamidates from 2,3-epoxy alcohols,[14] sulfamides from amino alcohols,[15] and five- and seven-membered sulfamidates from epoxides.[16]

The reactivity of epoxides with the Burgess reagent is especially noteworthy because they were believed to be inert to the action of this reagent as recently as a decade ago.[2,17] In 2003 we published the first report on the reactivity of the Burgess reagent with aliphatic and benzylic epoxides to yield five- and seven-membered sulfamidates, respectively.[16,18] The sulfamidates can serve as precursors to both *cis* and *trans* amino alcohols, which are commonly used in the pharmaceutical sector.[19]

In the course of our initial investigations we were able to propose a mechanism to account for the formation of seven-membered sulfamidates from either epoxides[16] or 1,2-diols[12] and suggested that the latter compounds yield in some cases seven-membered sulfamidates and not regioisomeric pairs of five-membered sulfamidates as had been reported.[12] The seven-membered sulfamidates constitute minute amounts in the reaction mixtures derived from aliphatic epoxides but become more prominent in the reaction of benzylic or otherwise activated oxiranes, as shown in Figure 2. In the case of 1,2-diols derived from various styrenes, the seven-membered sulfamidates are minor products, but their proportion increases with deactivation of the aromatic ring.[12] The discrepancies in the initial structural assignments are shown in Figure 2.

[a] Department of Chemistry and Centre for Biotechnology, Brock University,
500 Glenridge Ave., St. Catharines, Ontario, L2S 3A1, Canada
Fax: +1-905-984-4841
E-mail: thudlicky@brocku.ca
Supporting information for this article is available on the WWW under http://www.eurjoc.org/ or from the author.

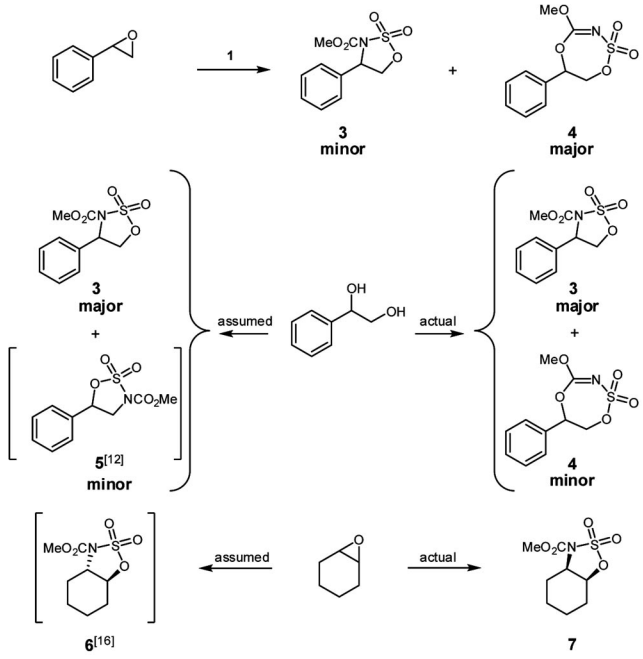


Figure 2. Sulfamidate formation from oxiranes and 1,2-diols. Assumed (reported) and actual (correctly assigned) products.

Seven-membered sulfamidates may be derived from epoxides as well as from diols. That epoxides formed in situ may be the intermediates was supported by the results of the reaction with optically active styrene oxide and with the optically pure diol derived from styrene.[16] In each case inversion of configuration occurred at the benzylic center (see below for more details).

The reaction of the Burgess reagent with oxiranes derived from cyclic compounds was of special interest to us because it could serve as a source of both *cis* and *trans* amino alcohols, as shown in Figure 3. As the reactive tendencies of sulfamidates resemble those of cyclic sulfates,[20,21] we reasoned that such a Scheme would provide the eventual access to enantiopure amino alcohols in both diastereomeric series by inverting the initially formed oxygenated center with ammonium benzoate. These considerations have led us to implement a chiral auxiliary version of the Burgess reagent (possibly also a catalytic asymmetric option) and its reactions with both cyclic and acyclic oxiranes in order to validate the idea depicted in Figure 3 in a homochiral fashion.

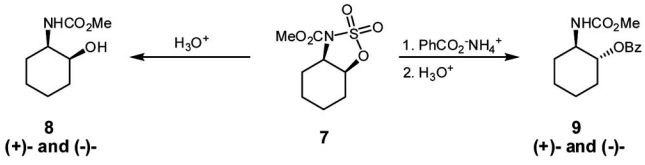


Figure 3. Synthesis of *cis*- and *trans* amino alcohols from cyclic sulfamidates.[16]

The investigations described in this paper have led to considerable revisions of some previously reported structures as well as adjustments in the current mechanism of the reaction of the Burgess reagent with epoxides and diols.[22] One of the reasons for the erroneous structural assignments may be the fact that almost all reactions performed to date on diols and epoxides were carried out on conformationally flexible substrates (exceptions being cyclohexene oxide, some of the 2,3-hydroxyoxiranes,[14] and carbohydrates[11]). The reactivity manifolds as well as identification of products and stereochemical assignments are different in cyclic oxiranes, diols, and amino alcohols. In this paper we report the details of the use of the first chiral auxiliary version of the Burgess reagent in its interactions with oxiranes and provide corrections regarding some of the previously published structures. In addition, a computational rationale Density Functional Theory (DFT) is advanced for the clarification of the mechanistic options in the reactions with oxiranes.[12,16,22]

Results and Discussion

Synthesis of Optically Pure Amino Alcohols

The original Burgess reagent, modelled after known *syn* elimination protocols (acetate and xanthate pyrolysis, Cope elimination, sulfoxide and selene oxide eliminations), was prepared only in its methyl and ethyl carbamate versions.[1] Four additional forms of the reagent, altered at the carbamate terminus, appeared in 2004 (benzyl, *o*-NO_2-benzyl, allyl, and β-trichloroethyl), and their use in milder deprotection schemes for carbamates has been suggested.[12] One report described a Burgess type reagent with quinuclidine instead of triethylamine.[23] In 2006 we published a preliminary report on the synthesis of enantiopure sulfamidates and the corresponding *trans* amino alcohols in both enantiomeric forms by employing a chiral auxiliary version of the Burgess reagent, the menthyl carbamate **10**, Figure 4. Prior to this report we also prepared several other chiral auxiliary versions such as the camphor-derived carbamate **11** and the two cyclic forms **12** and **13** prepared from the diene diol **14**;[24] however, the reactions of these reagents with oxiranes proved erratic, and we therefore focused on the investigations of reactions of the menthyl version.

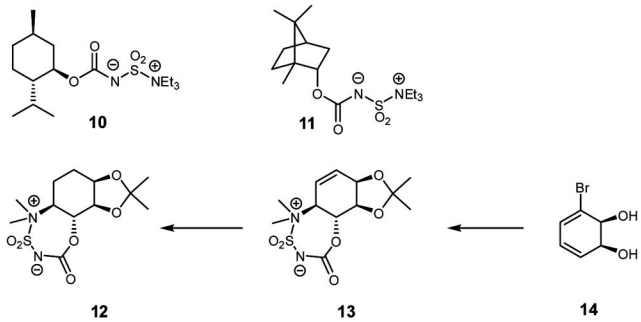
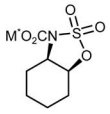
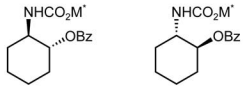
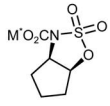
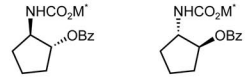
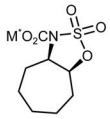
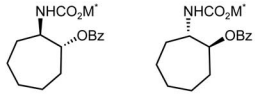
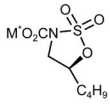
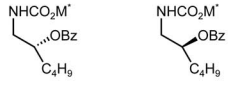
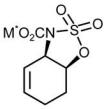
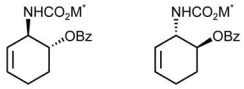


Figure 4. Chiral versions of the Burgess reagent.

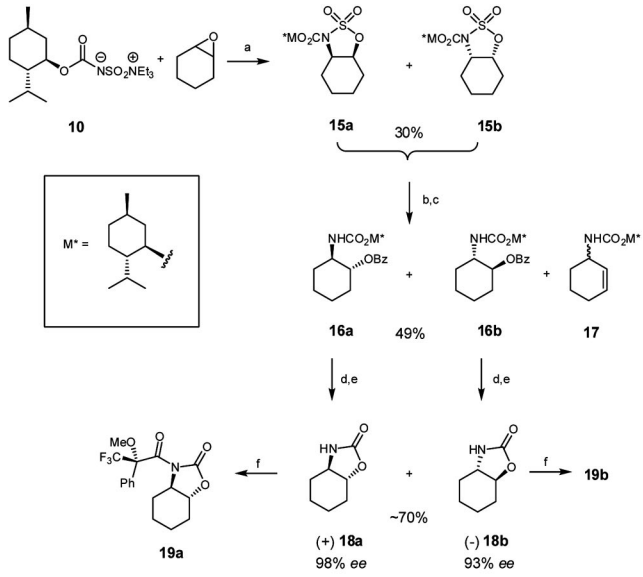
We prepared the menthyl carbamate version of the reagent **10** despite expectations that a freely rotating auxiliary group might not lead to significant levels of diastereoselection.[25] The menthol-containing reagent **10** was prepared easily by reacting menthol with chlorosulfonyl isocyanate followed by triethylamine, Scheme 1. Reaction of **10** (2.3 equiv.) with cyclohexene oxide produced a 1:1 mixture of diastereomers, identified by ^{1}H- and ^{13}C NMR, but inseparable on a silica column, in a modest yield. As optimization of reaction yields at this stage was not a priority, we decided first to evaluate the level of optical purity in the products after the removal of the auxiliary group. Sulfamidates **15a** and **15b** were treated with ammonium benzoate in DMF to yield a separable mixture of diastereomeric carbamates **16a** and **16b**, which were hydrolyzed and converted separately to oxazolidones **18a** and **18b** in excellent yields. Optical rotations of **18a** matched the literature value $[\alpha]_D^{22}$ = +7.5 (*c* = 1.0, EtOH), ref.[26] +6.0 (*c* = 1.0, EtOH) and Mosher's amide analysis of **19a** indicated >98% *ee*. Similarly, **19b** was evaluated $[\alpha]_D^{22}$ = –7.4 (*c* = 1.0, EtOH), ref.[26] –5.9 (*c* = 1.0, EtOH) and ^{19}F NMR of its Mosher amide indicated >93% *ee* (this lower value was likely due to an incomplete separation of the diastereomeric benzoates **16**). These were exciting results, especially in view of the fact that we also obtained the allylic amine **17** in reasonable yield during the ammonium benzoate reaction.[27]

It seemed prudent at this point to apply this protocol to several other epoxides in order to evaluate the generality of the process before choosing an auxiliary group that would permit full separation at the stage of sulfamidates such as **15a** and **15b**. Table 1 shows the products and their enantiomeric excess from the reactions of various oxiranes with the menthyl Burgess reagent **10**. In each case the diastereomeric pairs were separated at the stage of the protected *trans* amino benzoates. The diastereomeric excess was determined by GC/MS. The absolute stereochemistry of **27a** and **27b** were determined after hydrogenation to **16a** and **16b**.

Table 1. Reactions of oxiranes with menthyl version of the Burgess reagent.

Oxirane	Sulfamidates (%)[a]		Benzoates (%)		*ee* (%)[b] or *de* (%)[c]
	 **15a** 30%	**15b**	 **16a** 49%	**16b**	(+) 98 and (–) 93[b]
	 **20a** 37%	**20b**	 **21a** 52%	**21b**	98 and 93[c]
	 **22a** 35%	**22b**	 **23a** 75%	**23b**	93 and 92[c]
	 **24a** 22%	**24b**	 **25a**[d] 36%	**25b**[d]	–[d]
	 **26a** 36%	**26b**	 **27a** 51%	**27b**	(+) 94 and (–) 84[e]

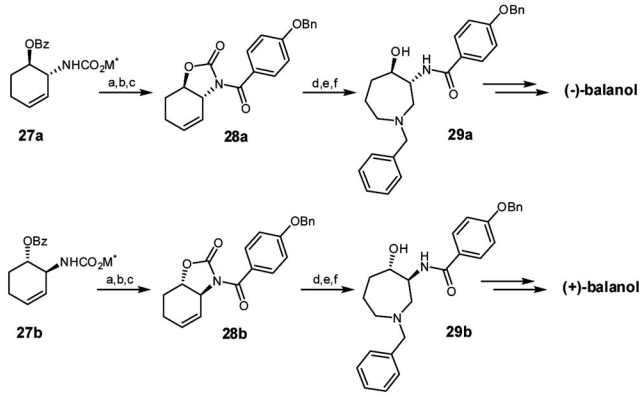
[a] Yields are isolated and unoptimized. [b] Enantiomeric excess determined by Mosher's amide formation of cyclic carbamates, derived from the corresponding benzoates by hydrolysis and cyclization. [c] Diastereomeric excess determined by GC/MS of benzoates after separation by flash column chromatography. [d] Not separable by flash column chromatography. [e] Diastereomeric excess determined by GC/MS of separated benzoates after hydrogenation.



Scheme 1. Reagents and conditions: a) **10** (2 equiv.), THF reflux, 1.5 h; b) $PhCO_2^-$ NH_4^+, DMF, 45 °C, 12 h; c) THF, H_2O, conc. H_2SO_4, room temp., 6 h; d) 1 M NaOH in MeOH, 2 h; e) NaH, THF reflux, 18 h, f) *n*BuLi, 0 °C, 30 min, (*S*)-(+)- Mosher's acid chloride, –78 °C to room temp.

Application to the Enantiodivergent Formal Synthesis of Balanol

Encouraged by the ease with which the *trans* amino alcohol derivatives were obtained, we applied this methodology to the synthesis of both (–)- and (+)-balanol. Benzoates **27a** and **27b** possess the absolute stereochemistry of (–)- and (+)-balanol, respectively, and only oxidative cleavage of the olefin followed by reductive amination is required to produce the balanol core. The conversions of **27a** to (–)-**29a** and hence to (–)-balanol and **27b** to (+)-**29b**, the intermediate for (+)-balanol, have been completed and published recently,[28] and are shown in Scheme 2.



Scheme 2. Reagents and conditions: a) 1 N NaOH, MeOH; b) NaH, THF, reflux; c) *p*-benzyloxy benzoyl chloride, NEt_3, DMAP, dichloromethane, 0 °C to room temp.; d) OsO_4, NMO, H_2O, dichloromethane, room temp.; e) i) $NaIO_4$, acetone, H_2O, room temp.; ii) $BnNH_2$, MeOH, $NaCNBH_3$, AcOH, mol. sieves (3 Å), –78 °C to room temp.; f) 0.3 N NaOH, MeOH, THF, –20 °C.

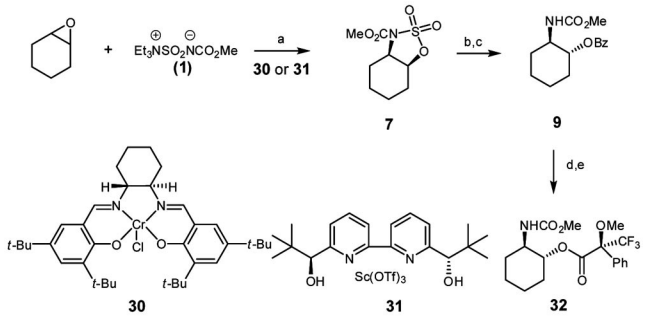
Attempted Asymmetric Catalysis in the Reaction of the Burgess Reagent with Oxiranes

In order to study the extent of asymmetric induction, we tested Jacobsen's[29] salen (**30**) catalyst as well as the scandium chelate of the C_2-symmetric bipyridine[30] **31**, reported to act as an activating Lewis acid in reactions with epoxides. The use of 0.1 equiv. of Jacobsen's catalyst (**30**) along with the Burgess reagent and cyclohexene oxide in THF or diethyl ether at either room temperature or reflux led to low yields (20%) of racemic sulfamidates with no sign of asymmetric induction. Similar results were obtained when cyclohexene oxide was treated with the Burgess reagent in the presence of 0.1 equiv. of Bolm's catalyst (**31**) in either THF or dichloromethane at room temperature. In order to determine the enantiomeric excess of the products, cyclic sulfamidate **7** was treated with ammonium benzoate in DMF, followed by acid hydrolysis to yield protected amino alcohol **9**. Basic hydrolysis of the benzoate ester followed by 3-(3-dimethylaminopropyl)-1-ethylcarbodiimide hydrochloride-mediated esterification with (*R*)-Mosher's acid gave a one-to-one mixture of diastereomers as assessed by ^{19}F NMR and GC/MS analysis. An explanation for the lack of asymmetric induction may be the propensity of the Burgess reagent acting as pseudo acid in activating the epoxide for nucleophilic attack and in doing so preventing coordination of the epoxide to the asymmetric catalyst. Some support for this view is provided by calculations (see the section on computational studies).

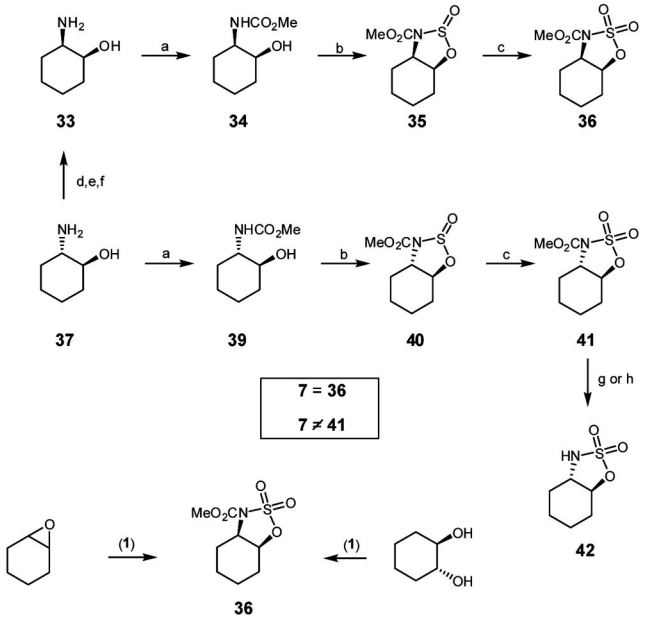
Structural and Mechanistic Revisions

During the course of this study we became concerned about discrepancies in the ^1H NMR spectra of *cis*-sulfamidates **15a** and **15b** and those of the previously reported *trans*-sulfamidates **6** (Figure 2).[16] Especially troubling was the comparison of spectral properties of the protected *cis* amino benzoate derived from the reaction of **6** with ammonium benzoate (reported in our 2003 publication as compound **9**, Scheme 3)[16] with those of the products obtained from treatment of sulfamidates **15** with ammonium benzoate (Scheme 1). Results of the repetition of the synthesis of **6** and preparation of standards confirmed our suspicions that our original assumption of the *trans*-epoxide opening followed by rapid intramolecular sulfonation was incorrect and that epoxides yield *cis* not *trans*-sulfamidates upon reaction with the Burgess reagent. The synthesis and structure revisions are shown in Scheme 4. The *cis*-sulfamidate **36** was prepared as shown from *cis* amino alcohol **33**, generated from the commercially available *trans*-isomer **37** by Jacobsen's protocol.[31] Selective protection of the amine functionality of **33** followed by treatment with thionyl chloride in CH_3CN furnished heterocycle **35** in 78% yield, which upon ruthenium-mediated oxidation gave *cis*-sulfamidate **36**. The *trans*-isomer, **41**, was generated from commercial **37** in a similar fashion. It became clear that **6** (Figure 2) is identical to **41** and not **36**; therefore, **7** (Figure 2) must be the same as **36**, a *cis*, not *trans*-isomer. This argument eliminates the possibility of direct intramolecular sulfonation, which we have studied by dilution experiments and sub-

strate-to-reagent ratios. In all cases, it is the *cis*-isomer of sulfamidate that is formed from epoxides and not the expected *trans*-isomer. Thus the mechanism operating on epoxides is similar in concept but not procedure to that operating on diols, as *trans*-cyclohexane diol yields exclusively *cis*-sulfamidate **36**. *cis*-Cyclohexane diol is unreactive because the bis sulfonated intermediate cannot undergo a S_N2 displacement.



Scheme 3. Reagents and conditions: a) THF, 48 h; b) $PhCO_2^-NH_4^+$, DMF, 45 °C, 12 h; c) THF, H_2O, conc. H_2SO_4, room temp., 6 h; d) 1 M NaOH in MeOH, 2 h; e) (*R*)-(+)-Mosher's acid, EDC, DMAP, dichloromethane, 0 °C to room temp., 18 h.



Scheme 4. Reagents and conditions: a) methyl chloroformate, $NaHCO_3$, $CHCl_3/H_2O$; b) $SOCl_2$, CH_3CN, –40 °C; c) $RuCl_3{\cdot}H_2O$, $NaIO_4$, CH_3CN/H_2O; d) Ac_2O; e) $SOCl_2$; f) 10% HCl; g) $PhCO_2^-NH_4^+$, DMF, 45 °C, 12 h; h) $MeNH_2$, THF, CH_3CN, H_2O, room temp., 18 h.

Two other observations are worth mentioning. First, the *trans*-sulfamidate yields **42** on treatment with ammonium benzoate and not the expected "inverted" *cis*-disposed benzoate. Such mild hydrolysis conditions for a methyl carbamate are interesting. Second, methylamine in acetonitrile also provides the free sulfamidate **42** under very mild conditions. Clearly, the hydrolysis (or reductive) conditions require fine tuning in order to provide protected amino alcohols in either series of diastereomeric sulfamidates.

The mechanism for the conversions of 1,2-diols to sulfamidates requires the participation of two equivalents of the Burgess reagent, only one of which remains in the product. To date the published results reported the conversions of diols on freely rotating side chains, and, with the exception of the carbohydrate-glycosylamine transformations, no rigid cyclic diols have been evaluated to determine which of the sulfonates in **44** becomes a leaving group. In the carbohydrate cases, it is almost self-evident, although not unambiguously validated. An experiment on a cyclic *trans*-diol with known absolute stereochemistry and labelled at one of the hydroxylated sites with deuterium would be required to confirm the exact course of events leading from **44** to either **7a** or its regioisomer **7b**, Figure 5. With epoxides, two equivalents are also required but, unlike in the reactions with diols, one returns unchanged into the reaction cycle. The alkoxide **45**, generated upon opening of the oxirane ring, is sulfonated by the second equivalent faster than it can undergo the intramolecular sulfonation to produce *trans*-sulfamidate **41** (path a). There is little doubt that the actual conversion to **46** (path b) is facilitated to some extent by the energetically unfavourable formation of a *trans*-fused five-membered ring as an alternative. Displacement of the second Burgess reagent from **46** then leads to *cis*-fused **7** and not to *trans*-fused **41** as was assumed originally.[16]

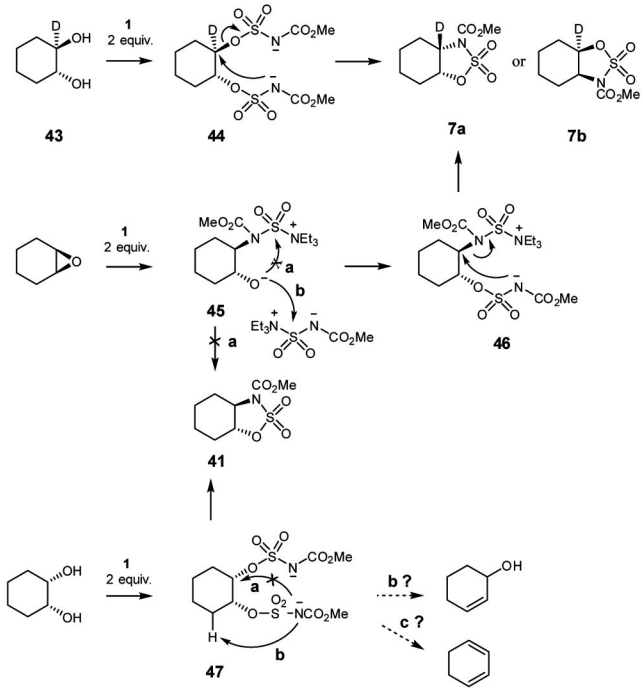


Figure 5. Mechanistic options for the reaction of the Burgess reagent with *cis* or *trans*-cyclohexadiol or cyclohexene oxide.

The lack of reactivity of *cis*-diols is clear from stereoelectronic considerations; no S_N2 displacement is possible from the doubly sulfonated compound **47**. However, it should be interesting to investigate possible single elimination pathways to allylic alcohols (path b) or double eliminations to dienes at elevated temperatures.

With activated epoxides and diols, such as those that contain a benzylic carbon–oxygen bond, the formation of both five- and seven-membered sulfamidates is possible, as demonstrated in our preliminary publication.[16] The mechanistic divergence regarding which of the two hybrids of the amide resonance participates in the reaction may depend on hard-soft matching of the polarized C–O bond with either nitrogen- or oxygen-centered anion. The more activated benzylic position, the more the seven-membered sulfamidate predominates the reaction mixtures. It is not yet clear that the seven-membered sulfamidates are formed from epoxides and not from the intermediates of type **55**. Again, this question can only be answered by performing the synthesis on diols (or epoxides) of known absolute stereochemistry and with the Burgess reagents containing two different carbamate groups. Neither parameter is sufficient to distinguish between the two pathways, A and B, shown in Figure 6.

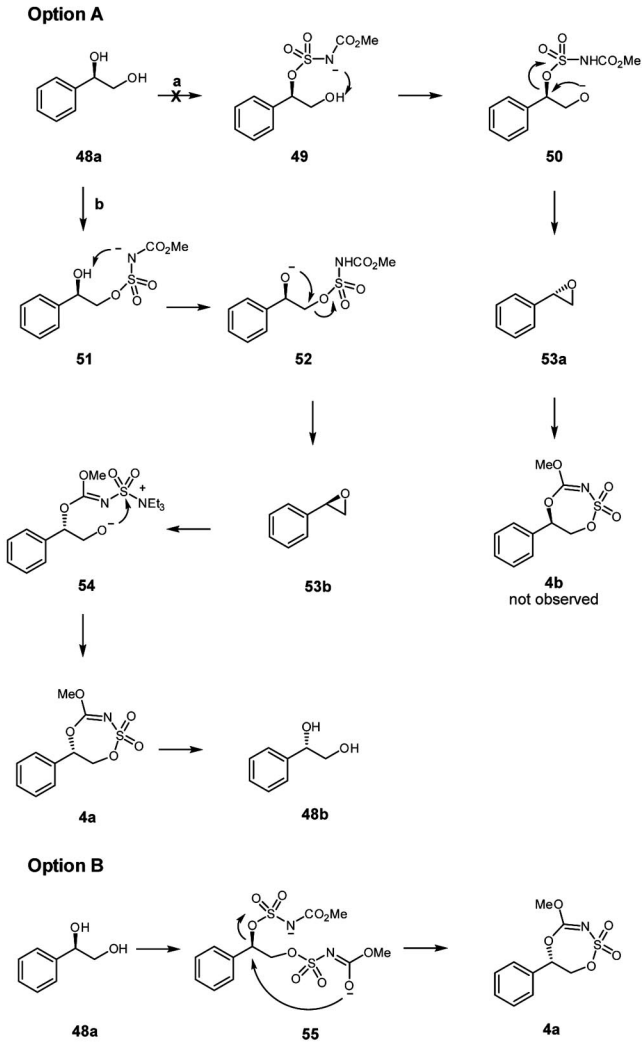
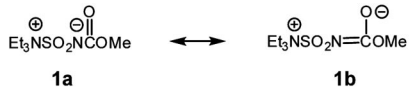


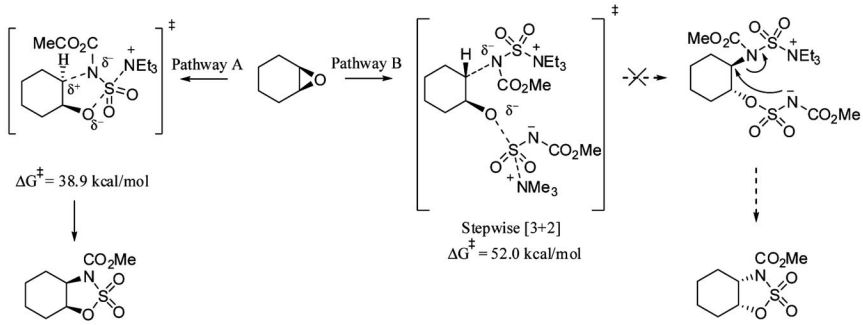
Figure 6. Mechanistic options for the reaction of the Burgess reagent with styrene oxide.

We performed the reaction on optically pure diol **48a**, which can form an epoxide by two different pathways: a and b in option A. If pathway a occurred, sulfonation to **49**, deprotonation to **50**, and displacement to **53a** should be the outcome. Path b assumes sulfonation of the primary alcohol, intramolecular deprotonation of **51** to **52**, and the final closure to **53b**. Reaction with the second equivalent of the Burgess reagent then leads to **54**, through the participation of hybrid **1b**, favored in these reactions on account of the hard–soft acid–base arguments. Ejection of triethylamine completes the formation of **4a**, in which the benzylic carbon configuration is opposite to that in **48**. We have demonstrated that indeed path b seems to be operating in this sequence and have isolated **48b** by hydrolysis of **4a** in pure enantiomeric form, indicating that path a with the formation of **53a** did not take place. These experiments support the intermediacy of epoxides in the formation of minor products, seven-membered sulfamidates, from the reactions of diols. However, the alternative, formation of **55** from **48a** and intramolecular displacement to **4a** cannot be excluded. We also performed an additional set of experiments in which 20% of racemic styrene oxide was added to a reaction of the Burgess reagent with racemic styrene diol and in another experiment 20% of racemic styrene diol was added to the reaction of racemic styrene oxide. In each case, the ratio of the sulfamidates changed in favor of the minor product: in the reaction of styrene oxide, the minor component, five-membered sulfamidate, increased from 8% to 20% and in the reaction of styrene diol, the amount of the minor component, the seven-membered sulfamidate, increased from 10% to 23%. These experiments do not unambiguously exclude option B, Figure 6, but validate that epoxides are potential intermediates in the reaction since the formation of the diol from the epoxide cannot take place under the reaction conditions. To exclude or validate the existence of **55** a set of mixed Burgess reagents must be used, with sequential sulfonation and determination whether the transformation of **55** to **4a** occurs. For the moment option A seems as the more reasonable.



Computational Studies

The apparent mechanistic complexity of the Burgess reagent's reactivity is attested to by a number of corrections having appeared within the chemical literature over the last several years.[16,25] Constitutional and stereochemical structural assignments have been corrected, and to date there has not been a single computational study addressing the Burgess reagent's reactivity.[32] With this knowledge in hand, our efforts next turned to the use of (GGA)-hybrid Kohn–Sham density functional theory (KS-DFT) at the B3LYP[33]-6-31G(d)[34] level in order to gain mechanistic insight into this reaction dynamic. First we examined the mechanistic origin of chemoselective formation of five-membered *cis*-sulfamidate (Table 1) formation from the re-



Scheme 5. Mechanistic possibilities for reaction of the Burgess reagent (**1**) with cyclohexene oxide.

actions of *meso* cyclo[*n*.1.0]alkanes (*n* = 3–6). Second, we attempted to explain why no discernible level of diastereoselection was found from reactions conducted using chiral Burgess reagent **10** and cyclohexene oxide. Finally these results were extrapolated to rationalize the lack of observed enantioinduction within ring-opening reactions of cyclohexene oxide with achiral Burgess reagent **1** catalyzed by C_2-symmetric 2,2′-bipyridine·Sc(OTf)$_3$ **31** as well as Jacobsen's [(salen)Cr^{I}Cl] complex **30**.

Our attention turned towards conducting an initial set of representative studies investigating reaction scenarios comprising Burgess reagent **1** and cyclohexene oxide (Scheme 5). In line with this reasoning, first-order saddle points corresponding to backside S_N2 addition of the Burgess reagent to cyclohexene oxide were located by way of an exhaustive scan of the potential energy surface (PES)[35] using the Gaussian 03[36] suite of programs, Pathway B, Scheme 5. However, all optimized geometries possessed activation barriers that were unrealistically large ($\Delta G^{\ddagger} > 50$ kcal/mol).[37] Accordingly a more extensive investigation of the reaction hypersurface was conducted, from which front side attack [3+2] concerted asynchronous ($\Delta G^{\ddagger} = 38.9$ kcal mol^{-1}) was located, Pathway A, Scheme 5 and Figure 7.[38] Regarding the specific metrics of five-membered-TS1, contained within are multiple bond-forming and bond-breaking events, namely one C···O bond of the epoxide fragments at a distance of 2.10 Å, while the C···N (2.62 Å) and O···S (1.84 Å) bonds are formed simultaneously. Of particular interest is the presence of multiple hydrogen bonding interactions, which contribute to an overall weak stabilization of the transition state. Specifically, there exists a S=O$^{\delta-}$···H–C hydrogen bond identified by atoms in molecules[39] (AIM) quantum theory (∇ = –0.0156) at 2.38 Å in length. using natural bond orbital[40] (NBO) analysis to quantify the interaction yields a stabilizing interaction energy of 2.56 kcal/mol. Finally, two hydrogen bond contacts generated from the ester functionality were identified: a C=O$^{\delta-}$···H–C–N^{+} hydrogen bond contact of 2.69 Å (∇ = –0.00604, NBO = 1.43 kcal/mol) as well as a C–O$^{\delta-}$···H–C–C$^{\delta+}$ contact at 2.46 Å (∇ = –0.00865, NBO = 1.52 kcal/mol).

Irrespective of the highlighted metrics and stereoelectronic attributes of 5-mem-TS1 noted above, it is of perhaps even greater significance that 5-mem-TS1 corresponds to a

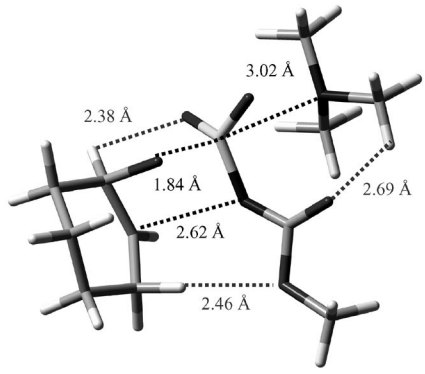


Figure 7. Five-membered-TS1 corresponding to *syn* sulfamidate formation.

[3+2] concerted asynchronous bond-forming event,[41] the direct product of which is a local minimum for *cis* five-membered sulfamidate **7**,[42] a finding which is consistent with experiment.

The absence of diastereoselection for the case of **15** may be understood as being an artefact of remote chiral induction. To support this supposition a refined frozen-core (TS)-MCMM conformational search conducted at the semi-empirical PM3 level of theory was performed by means of **10** and cyclohexene oxide. This search revealed low energy conformers wherein the heavy atoms of the chiral auxiliary resided far from the site of oxirane opening.[43]

Regarding the addition of chiral Lewis-acid reagents for stereoinduction, it is readily apparent that during asynchronous concerted five-membered-TS1 the Burgess reagent occupies a large volume of space surrounding the oxirane moiety. According to these results it is impossible for a Lewis acid to be bound to the oxirane during this transition state.[44] Last, it should also be noted that, in the presence of a Lewis acid co-catalyst such as Cr^{I} or Sc^{III}, the Burgess reagent **1** is thought to undergo rapid degradation and in doing so generates an excess of achiral species capable of competitively catalyzing these reactions.[45]

Conclusions

The reactivity of the Burgess reagent with epoxides and 1,2-diols was examined for possible mechanistic duality.

Several structural assignments previously reported in the literature were corrected and a computational study (DFT) was performed to rationalize the lack of asymmetric induction in the reactions of *meso* epoxides with the Burgess reagent in the presence of C_2-symmetric catalysts. The mechanisms by which the Burgess reagent reacts with epoxides and diols may proceed through common intermediates as the experimental evidence seems to suggest. The DFT studies revealed that the formation of *syn* sulfonamidate **15** from the reaction of cyclohexene oxide and the Burgess reagent proceeds via a concerted asynchronous [3+2] transition state. In addition, this transition state provided a structural basis for rationalizing the lack of diastereo- and enantioselectivities observed when a chiral Lewis acid, or a chiral version of the Burgess reagent was used within a reaction with cyclohexene oxide. The chiral auxiliary version of the Burgess reagent was exploited in the synthesis of *cis* and *trans* amino alcohol derivatives and in the total synthesis of balanol. Future work in this area will address design of new Burgess reagents and exploitations of catalytic asymmetric versions in the reactions with epoxides and diols.

Experimental Section

All non-aqueous reactions were carried out in under argon using standard Schlenk techniques for the exclusion of moisture and air. Dichloromethane was distilled from calcium hydride. THF and benzene were dried with potassium/benzophenone. Analytical thin-layer chromatography was performed on Silicycle 60 Å 250 μm TLC plates with F-254 indicator. Flash column chromatography was performed using Natland 200–400 mesh silica gel. Melting points were recorded with a Hoover Unimelt apparatus and are uncorrected. IR spectra were obtained with a PerkinElmer One FT-IR spectrometer. Optical rotation was measured on a Perkin–Elmer 341 polarimeter. ^{1}H-, ^{19}F- and ^{13}C-NMR spectra were recorded on a Bruker (300 MHz or 600 MHz) spectrometer. All chemical shifts are referenced to TMS or residual undeuterated solvent ($CHCl_3$, CH_2Cl_2). Combustion analyses were performed by Atlantic Microlabs, Norcross, GA. Mass spectra were recorded with Kratos/MsI Concept 1S mass spectrometer at Brock University.

General Procedure for Reactions Between Oxiranes and the Burgess Reagent: (Methoxycarbonylsulfamoyl)triethylammonium hydroxide, inner salt (2.38 g, 9.2 mmol) was added to a stirred solution of the oxirane (4.0 mmol) in THF (20 mL) at room temperature in a single portion. The resulting reaction mixture was brought to reflux immediately by submerging it into a preheated oil bath (70 °C). The reaction was stirred until complete consumption of the oxirane (TLC), then cooled to room temperature and filtered through a plug of silica to remove salts formed during the reaction. The reaction mixture was concentrated, and the resulting residue was purified by flash column chromatography using an appropriate solvent gradient to yield the sulfamidate product(s).

Methyl 4-Phenyl-1,2,3-oxathiazolidine-3-carboxylate 2,2-Dioxide (3): Colorless oil; R_f = 0.44 (hexanes/ethyl acetate, 3:1). IR (film): $\tilde{\nu}_{max}$ = 2962, 1746, 1321, 1192 cm^{-1}. ^{1}H NMR (300 MHz, $CDCl_3$): δ = 7.38–7.47 (m, 5 H), 6.15 (dd, J = 3.3, 10.5 Hz, 1 H), 4.68–4.51 (m, 2 H), 3.94 (s, 3 H) ppm. NMR (75 MHz, $CDCl_3$): δ = 158.6, 132.1, 130.4, 129.4, 126.7, 82.7, 72.8, 58.8 ppm. HRMS (EI): calcd. for $C_{10}H_{11}NO_5S$: 257.0358; found 257.0357.

4-Methoxy-6-phenyl-2,26,7-dihydro-1,5,2,3-dioxathiazepine 2,2-Dioxide (4): Colorless crystals; m.p. 100–105 °C (ethyl acetate/hexanes); R_f = 0.50 (hexanes/ethyl acetate, 3:1). IR (film): $\tilde{\nu}_{max}$ = 2959, 1603, 1305 cm^{-1}. ^{1}H NMR (300 MHz, $CDCl_3$): δ = 7.36–7.47 (m, 5 H), 6.15 (dd, J = 3.6, 10.7 Hz, 1 H), 4.62 (dd, J = 10.5, 12.6 Hz, 1 H), 4.52 (dd, J = 3.6, 12.6 Hz, 1 H), 3.93 (s, 3 H) ppm. ^{13}C NMR (75 MHz, $CDCl_3$): δ = 158.6, 132.1, 130.5, 129.6, 126.8, 82.8, 72.9, 58.9 ppm. HRMS (EI): calcd. for $C_{10}H_{11}NO_5S$: 257.0358; found 257.0352. $C_{10}H_{11}NO_5S$ (257): calcd. C 46.23, H 4.31; found C 46.23, H 4.51.

Methyl *cis*-Hexahydro-3*H*-1,2,3-benzoxathiazole-3-carboxylate 2,2-Dioxide (7): Compound **7** was prepared in 64% yield (604 mg) as colorless crystals following the general procedure for reactions of oxiranes with the Burgess reagent (**1**), using cyclohexene oxide as starting material; m.p. 97–98 °C (ethyl acetate/hexanes); R_f = 0.49 (hexanes/ethyl acetate, 1:1). IR (film): $\tilde{\nu}_{max}$ = 2943, 1743, 1385, 1183 cm^{-1}. ^{1}H NMR (300 MHz, $CDCl_3$): δ = 5.00 (br. s, 1 H), 4.22 (br. s, 1 H), 3.90 (br. s, 3 H), 2.33 (br. s, 2 H), 1.45–1.85 (m, 4 H), 1.16–1.33 (m, 2 H) ppm. ^{13}C NMR (75 MHz, $CDCl_3$): δ = 150.4, 80.0, 58.3, 54.7, 27.4, 27.2, 22.0, 19.1 ppm. HRMS (FAB) [M + H$^+$]: calcd. for $C_8H_{14}O_5NS$: 236.0593; found 236.0608. $C_8H_{13}NO_5S$ (235): calcd. C 40.84, H 5.70; found C 40.98, H 5.70.

Alternatively, compound **7** was prepared by the following procedure. Ruthenium(III) chloride hydrate (catalytic amount), sodium periodate (439 mg, 2.05 mmol) and water (5 mL) were added sequentially, at 0 °C to a solution of oxathiazolidine **35** (300 mg, 1.37 mmol) in CH_3CN (5 mL). The reaction mixture was warmed to room temperature and was stirred at ambient temperature for an additional 3 h. The reaction mixture was extracted three times with Et_2O. The organic layers were combined, washed with water, then brine, and dried with anhydrous magnesium sulfate. Filtration, evaporation of the solvent, and purification by flash column chromatography (hexanes/ethyl acetate, 4:1) afforded 287 mg (82%) of compound **36** as white solid after recrystallization from hexanes/ethyl acetate. The analytical data obtained for compound **36** is identical to data of compound **7**.

***trans*-2-(Methoxcarbonylamino)cyclohexyl Benzoate (9):** Ammonium benzoate (651 mg, 4.68 mmol) was added to a solution of benzoxathiazole **7** (550 mg, 2.34 mmol) in dry DMF (10 mL). The solution was heated to 55 °C until TLC analysis indicated full conversion of the starting material (18 h). The solvent was evaporated, and the residue was dissolved in THF (6 mL), three drops of water and three drops of hydrosulfuric acid were added. The reaction mixture was stirred at room temperature for 3 h, before the pH was adjusted to 8 with saturated aqueous $NaHCO_3$ solution. The layers were separated, and the aqueous layer was extracted three times with dichloromethane. The organic layers were combined and washed with H_2O and brine. After the solvent was evaporated under reduced pressure, the residue was purified by flash column chromatography (hexanes/ethyl acetate, 9:1) affording 265 mg of colorless oil (41%). R_f = 0.55 (hexanes/ethyl acetate, 2:1). IR (film): $\tilde{\nu}_{max}$ = 3339, 3064, 2940, 2861, 1714, 1538, 1452, 1320, 1279, 1235, 1115, 713 cm^{-1}. ^{1}H NMR (300 MHz, $CDCl_3$): δ = 8.04 (d, J = 7.5 Hz, 2 H), 7.55 (m, 1 H), 7.43 (t, J = 7.5 Hz, 2 H), 4.83 (m, 2 H), 3.71–3.88 (m, 1 H), 3.53 (s, 3 H), 2.02–2.24 (m, 2 H), 1.69–2.02 (m, 2 H), 1.49–1.68 (m, 1 H), 1.18–1.48 (m, 3 H) ppm. ^{13}C NMR (75 MHz, $CDCl_3$): δ = 167.0, 156.8, 133.2, 130.3, 129.9, 128.5, 75.9, 54.5, 52.2, 32.6, 31.3, 24.6, 24.2 ppm. HRMS (FAB): calcd. for $C_{15}H_{20}NO_4$: 278.1392; found 278.1382.

***N*,*N*-Diethyl-*N*-{[({[(1*R*,2*S*,5*R*)-5-methyl-2-(1-methylethyl)cyclohexyl]-oxy}carbonyl)amino]sulfonyl}ethanaminium, Inner Salt (10):** A solution of (–)-menthol (5.00 g, 32 mmol) in benzene (15 mL) was

added dropwise to a stirred solution of chlorosulfonyl isocyanate (5.21 g, 36.8 mmol) in benzene (15 mL) over 30 min while keeping the internal temperature between 25 and 30 °C in an ice-water bath. The reaction mixture was stirred at room temperature for an additional 30 min, before ice-cold hexane (40 mL) was added while cooling the reaction mixture to 0–5 °C. The product was filtered and washed with ice-cold hexanes (2 × 20 mL) and dried under reduced pressure to yield 8.29 g (87%) of (–)-mentholsulfamoyl chloride as colorless crystals (87%); m.p. 86–88 °C (hexanes). $[a]_D^{23}$ = 64.5 (c = 0.8, $CHCl_3$). ^1H NMR (300 MHz, $CDCl_3$): δ = 8.38–8.55 (br. s, 1 H), 4.81 (td, J = 11.2, 4.6 Hz, 1 H), 2.07–2.16 (m, 1 H), 1.83–2.01 (m, 1 H), 1.61–1.77 (m, 2 H), 1.39–1.58 (m, 2 H), 1.04–1.22 (m, 2 H), 0.93 (t, J = 6.8 Hz, 6 H), 0.83 (d, J = 6.8 Hz, 3 H) ppm. (–)-Mentholsulfamoyl chloride was used without further purification for the next step.

A solution of (–)-mentholsulfamoyl chloride (7.00 g, 23.5 mmol) in benzene (40 mL) was added dropwise to a stirred solution of triethylamine (6.53 mL, 47.0 mmol) in benzene (20 mL) over 1 h, keeping the internal temperature between 10 and 15 °C in an ice-water bath. The reaction mixture was stirred at room temperature for an additional 30 min and then filtered to remove the triethylamine hydrochloride salt. The filtrate was evaporated under reduced pressure, then dissolved in THF (50 mL) at 30 °C and cooled to 0–5 °C and treated with hexanes (50 mL) to precipitate out the title compound **10** (7.24 g, 85%) as a colorless solid; m.p. 87–89 °C (THF/hexanes). $[a]_D^{23}$ = –48.7 (c = 0.48, $CHCl_3$). IR (film): $\tilde{\nu}_{max}$ = 3426, 3020, 2958, 2872, 1682, 1457, 1389, 1369, 1340, 1285, 1253, 1216, 1105, 982, 922, 891 cm^{-1}. ^1H NMR (300 MHz, $CDCl_3$): δ = 4.51 (td, J = 11.0, 4.6 Hz, 1 H), 3.45 (q, J = 7.7 Hz, 6 H), 3.14–3.26 (m, 1 H), 1.93–2.08 (m, 2 H), 1.65 (d, J = 11.9 Hz, 2 H), 1.30–1.44 (m, 11 H), 0.92–1.03 (m, 2 H), 0.87 (t, J = 7.7 Hz, 6 H), 0.76 (d, J = 6.6 Hz, 3 H) ppm. ^{13}C NMR (75 MHz, $CDCl_3$): δ = 157.7, 76.4, 50.7, 47.3, 46.7, 41.3, 34.6, 31.8, 26.4, 23.7, 21.2, 16.6, 9.8, 8.8 ppm.

General Procedure for the Synthesis of Sulfamidates from Oxiranes with the Menthyl Version of the Burgess Reagent: Compound **10** (4.60 mmol) was added to a stirred solution of oxirane (2.0 mmol) in THF (5 mL) at room temperature in a single portion. The resulting reaction mixture was brought to reflux immediately by submerging it into a preheated oil bath (70 °C). The reaction mixture was stirred until complete consumption of the oxirane (TLC), then cooled to room temperature and filtered through a plug of silica to remove salts formed during the reaction. Following concentration of the reaction mixture, the residue was purified by flash column chromatography using an appropriate solvent gradient (hexanes/ethyl aceate) to afford a 1:1 mixture of diastereomers.

5-Methyl-2-(1-Methylethyl)cyclohexyl (3a*R*,7a*S*)-*rel*-Hexahydro-1,2,3-benzoxathiazole-3(3a*H*)-carboxylate 2,2-Dioxide (15a and 15b): The general procedure for the reaction of oxiranes with compound **10** and cyclohexene oxide (196 mg, 2.00 mmol) as starting material gave 215 mg (30%) of a 1:1 mixture of diastereomers **15a** and **15b** after purification by flash column chromatography (hexanes/ethyl acetate, 15:1 to 3:1) as colorless oil. R_f = 0.65 (hexanes/ethyl acetate, 3:1). $[a]_D^{23}$ = –52.2 (c = 1.00, $CHCl_3$). IR (film): $\tilde{\nu}_{max}$ = 3401, 2958, 2873, 2254, 1728, 1457, 1383, 1314, 908, 738 cm^{-1}. ^1H NMR (300 MHz, $CDCl_3$): δ = 4.98–5.04 (br. s, 1 H), 4.73 (dt, J = 10.7, 4.5 Hz, 1 H), 4.15–4.27 (m, 1 H), 2.28–2.40 (m, 2 H), 1.97–2.17 (m, 2 H), 1.43–1.89 (m, 9 H), 1.02–1.37 (m, 4 H), 0.94 (d, J = 3.1 Hz, 3 H), 0.92 (d, J = 3.1 Hz, 3 H), 0.80 (d, J = 6.6 Hz, 3 H) ppm. ^{13}C NMR (75 MHz, $CDCl_3$): δ = 149.9, 79.7, 79.3, 58.2, 58.1, 47.2, 47.1, 41.0, 40.9, 34.3, 31.8, 27.6, 27.5, 27.4, 26.1, 23.5, 23.4, 22.30, 22.25, 21.3, 21.2, 19.3, 16.4, 16.3 ppm. HRMS (EI): calcd. for $C_{17}H_{29}NO_5S$: 359.1766; found 359,1761. $C_{17}H_{29}NO_5S$ (359): calcd. C 56.80, H 8.12; found C 57.12, H 8.30.

5-Methyl-2-(1-methylethyl)cyclohexyl (3a*R*,6a*S*)-*rel*-Tetrahydrocyclopenta[*d*][1,2,3]oxathiazole-3(3a*H*)-carboxylate 2,2-Dioxide (20a and 20b): The general procedure for the reaction of oxiranes with compound **10** and cyclopentene oxide (168 mg, 2.00 mmol) as starting material gave 305 mg (37%) of a 1:1 mixture of diastereomers after purification by flash column chromatography (hexanes/ethyl acetate, 15:1 to 3:1). Colorless oil; R_f = 0.81 (hexanes/ethyl acetate, 2:1). $[a]_D^{23}$ = –79.2 (c = 1.02, $CHCl_3$). IR (film): $\tilde{\nu}_{max}$ = 3400, 3019, 2962, 2400, 1731, 1522, 1423, 1383, 1307, 1030, 669 cm^{-1}. ^1H NMR (300 MHz, $CDCl_3$): δ = 5.21 (t, J = 5.3 Hz, 1 H), 4.74 (dt, J = 10.9, 4.4 Hz, 1 H), 4.55 –4.63 (m, 1 H), 2.08–2.15 (m, 5 H), 1.81–1.89 (m, 2 H), 1.66–1.74 (m, 2 H), 1.42–1.50 (m, 2 H), 1.10–1.18 (m, 2 H), 0.88–0.95 (m, 7 H), 0.76–0.85 (m, 3 H) ppm. ^{13}C NMR (75 MHz, $CDCl_3$): δ = 150.1, 83.8, 79.1, 78.3, 71.2, 61.4, 61.3, 46.7, 40.6, 40.5, 33.9, 32.75, 32.7, 32.3, 31.4, 31.4, 26.2, 26.0, 25.6, 23.3, 23.2, 22.9, 22.6, 21.9, 20.8, 20.8 ppm. HRMS (FAB) [M + H^+]: calcd. for $C_{16}H_{27}NO_5S$: 346.1688; found 346.1659.

5-Methyl-2-(1-Methylethyl)cyclohexyl (3a*R*,8a*S*)-*rel*-Hexahydrocyclohepta[*d*][1,2,3]oxathiazole-3(3aH)-carboxylate 2,2-Dioxide (22a and 22b): The general procedure for the reaction of oxiranes with compound **10** and cycloheptene oxide (224 mg, 2.00 mmol) as starting material gave 211 mg (35%) of a 1:1 mixture of diastereomers after purification by flash column chromatography (hexanes/ethyl acetate, 15:1 to 4:1). Colorless oil; R_f = 0.57 (hexanes/ethyl acetate, 4:1). $[a]_D^{23}$ = –60.5 (c = 0.75, $CHCl_3$). IR (film): $\tilde{\nu}_{max}$ = 2958, 2931, 1729, 1457, 1381, 1332, 1307, 1190 cm^{-1}. ^1H NMR (300 MHz, $CDCl_3$): δ = 5.00–5.17 (m, 1 H), 4.72 (dt, J = 11.0, 4.5 Hz, 1 H), 4.21–4.36 (m, 1 H), 2.20–2.37 (m, 1 H), 1.63–2.18 (m, 10 H), 1.35–1.58 (m, 4 H), 1.03–1.33 (m, 3 H), 0.85–1.00 (m, 8 H), 0.71–0.84 (m, 3 H) ppm. ^{13}C NMR (75 MHz, $CDCl_3$): δ = 149.8, 149.8, 81.6, 81.6, 79.1, 79.0, 63.1, 63.0, 46.8, 46.7, 40.6, 40.5, 33.9, 31.5, 31.4, 30.2, 30.2, 29.2, 28.6, 28.5, 26.0, 25.9, 25.6, 23.3, 22.9, 22.6, 21.9, 21.6, 20.9, 20.8, 15.8 ppm. MS (FAB): m/z (%) = 374 (52) [M + H^+]: 139, 137 (22), 97 (19), 95 (44), 83 (100), 81 (37), 79 (11), 77 (12), 69 (46), 67 (21), 57 (36), 55 (62), 53 (14). HRMS (FAB) [M + H^+] Calcd for $C_{18}H_{33}NO_5S$: 374.2001; found 374.2018.

5-Methyl-2-(1-methylethyl)cyclohexyl 5-Butyl-1,2,3-oxathiazolidine-3-carboxylate 2,2-Dioxide (24a and 24b): The general procedure for the reaction of oxiranes with **10** and 2-butyloxirane (200 mg, 2.00 mmol) as starting material gave 159 mg (22%) of a 1:1 mixture of diastereomers **24a** and **24b** after purification by flash column chromatography (hexanes/ethyl acetate, 20:1 to 5:1). Colorless oil; R_f = 0.68 (hexanes/ethyl acetate, 5:1). $[a]_D^{23}$ = –51.7 (c = 2.3, $CHCl_3$). IR (film): $\tilde{\nu}_{max}$ = 3019, 2961, 2400, 1730, 1384, 1316, 1215, 1046, 928, 724, 669 cm^{-1}. ^1H NMR (300 MHz, $CDCl_3$): δ = 4.71–4.84 (m, 1 H), 4.58–4.71 (m, 1 H), 3.90–4.09 (m, 1 H), 3.57–3.71 (m, 1 H), 2.10 (m, 3 H), 1.52–1.77 (m, 4 H), 1.25–1.53 (m, 6 H), 1.16–1.23 (s, 3 H), 0.92–1.12 (m, 2 H), 0.85–0.91 (m, 6 H), 0.70–0.74 (m, 3 H) ppm. ^{13}C NMR (75 MHz, $CDCl_3$): δ = 149.8, 79.9, 79.2, 50.6, 46.7, 40.5, 33.9, 32.1, 31.4, 29.7, 26.6, 25.8, 23.1, 22.1, 21.9, 20.8, 16.0, 13.7 ppm. MS (EI): m/z (%) = 361 (1), 176 (44), 83 (88), 42 (60), 43 (39), 54 (31), 55 (61). HRMS (EI): calcd. for $C_{17}H_{31}NO_5S$: 361.1923; found 361.1920.

5-Methyl-2-(1-methylethyl)cyclohexyl (3a*R*,7a*S*)-*rel*-3a,6,7,7a-Tetrahydro-2λ⁶-1,2,3-benzoxathiazole-3-carboxylate 2,2-Dioxide (26a and 26b): The general procedure for the reaction of oxiranes with compound **10** and cyclohexadiene oxide (192 mg, 2.00 mmol)

as starting material gave 257 mg (36%) of a 1:1 mixture of diastereomers **26a** and **26b** after purification by flash column chromatography (hexanes/ethyl acetate, 15:1 to 3:1). White solid; m.p. 115–118 °C (hexanes/ethyl acetate); R_f = 0.55 (hexanes/ethyl acetate, 4:1). $[\alpha]_D^{23}$ = –54.5 (*c* = 1.25, $CHCl_3$). IR (film): $\tilde{\nu}_{max}$ = 3443, 3031, 2959, 2930, 2873, 1731, 1599, 1457, 1432, 1371, 1331, 1307, 1241, 1217, 1189, 1170, 1125 cm^{-1}. ^1H NMR (300 MHz, $CDCl_3$) (two rotamers): δ = 6.02–6.28 (m, 1 H), 5.56–5.85 (m, 1 H), 5.13–5.33 (m, 1 H), 4.66–4.84 (m, 2 H), 1.82–2.44 (m, 5 H), 1.39–1.75 (m, 5 H), 1.00–1.31 (m, 3 H), 0.87–0.96 (m, 6 H), 0.74–0.85 (m, 3 H), ppm. ^{13}C NMR (75 MHz, $CDCl_3$) (two rotamers): δ = 147.9, 135.0, 129.5, 119.0, 117.9, 81.7, 81.6, 79.2, 75.5, 75.3, 75.1, 74.6, 72.9, 72.8, 53.2, 53.2, 51.5, 45.2, 44.9, 44.8, 44.7, 38.6, 37.9, 37.7, 32.0, 29.5, 29.3, 29.3, 24.2, 23.9, 23.7, 22.6, 22.1, 21.2, 20.3, 19.9, 18.9 18.8, 18.7 ppm. HRMS (EI): calcd. for $C_{17}H_{27}NO_5S$: 357.1610; found 357.1593.

General Procedure for the Synthesis of Benzoates: Ammonium benzoate (346 mg, 2.49 mmol) was added to a stirred solution of sulfamidate diastereomers (1.25 mmol) in dry DMF (5 mL). The solution was heated to 55 °C and stirred for 18 h before the solvent was evaporated, and the resulting residue was dissolved in THF (3 mL). Three drops of H_2O and three drops of concentrated H_2SO_4 were added, and the reaction mixture was stirred at room temperature for 12 h. The reaction mixture was diluted with H_2O and the pH adjusted to 9 (satd. aq. $NaHCO_3$) before the layers were separated. The aqueous layer was extracted with dichloromethane (3 × 5 mL), then the organic layers were combined and washed with brine (1 × 5 mL), dried with Na_2SO_4, and the solvents evaporated. The diastereomers were separated via flash column chromatography using the appropriate solvent system (CH_2Cl_2/MeOH).

(1*R*,2*S*,5*R*)-5-Methyl-2-(1-methylethyl)cyclohexyl [(1*R*,2*R*)-2-(Benzoyloxy)cyclohexyl]carbamate (16a) and (1*R*,2*S*,5*R*)-5-Methyl-2-(1-methylethyl)cyclohexyl[(1*S*,2*S*)-2-(benzoyloxy)cyclohexyl]carbamate (16b): The general procedure for the syntheses of benzoates using a mixture of **15a** and **15b** (449 mg, 1.25 mmol) as starting materials gave a mixture of two diastereomers (246 mg, 49%), which were separated by flash column chromatography (CH_2Cl_2/MeOH, 200:1). **Compound 16a:** M.p. 111–113 °C (ethyl acetate/hexanes); R_f = 0.50 (CH_2Cl_2/methanol, 100:1). $[\alpha]_D^{20}$ = –77.8 (*c* = 1.05, $CHCl_3$). IR (film): $\tilde{\nu}_{max}$ = 3434, 3368, 3019, 2954, 2868, 1711, 1603, 1585, 1513, 1452, 1370, 1318, 1279, 1216, 1115, 1038, 1028, 757, 712, 668 cm^{-1}. ^1H NMR (300 MHz, $CDCl_3$): δ = 8.07 (d, *J* = 7.7 Hz, 2 H), 7.55 (t, *J* = 7.2 Hz, 1 H), 7.43 (t, *J* = 7.7 Hz, 2 H), 4.83 (dt, *J* = 10.6, 4.5 Hz, 1 H), 4.59 (d, *J* = 9.3 Hz, 1 H), 4.34–4.46 (m, 1 H), 3.76–3.90 (m, 1 H), 2.07–2.19 (m, 2 H), 1.73–1.93 (m, 3 H), 1.13–1.69 (m, 10 H), 0.91–1.06 (m, 1 H), 0.86 (d, *J* = 10.0 Hz, 3 H), 0.75 (d, *J* = 6.6 Hz, 3 H), 0.46–0.68 (m, 4 H) ppm. ^{13}C NMR (75 MHz, $CDCl_3$): δ = 167.1, 156.5, 133.4, 130.6, 130.2, 128.7, 76.6, 74.7, 54.3, 47.5, 41.2, 34.6, 32.8, 31.5, 26.6, 25.0, 24.5, 23.8, 22.2, 21.1, 16.8 ppm. HRMS (EI): calcd. for $C_{24}H_{35}NO_4$: 401.2566; found 401.2579. $C_{24}H_{35}NO_4$ (401): calcd. C 71.79, H 8.79; found C 71.82, H 8.80. **Compound 16b:** M.p. 138–141 °C (ethyl acetate/hexanes); R_f = 0.45 (CH_2Cl_2/MeOH, 100:1). $[\alpha]_D^{20}$ = –15.8 (*c* = 1.05, $CHCl_3$). IR (film): $\tilde{\nu}_{max}$ = 3685, 3435, 3020, 2956, 2869, 1711, 1515, 1452, 1318, 1279, 1216, 1115, 1039, 929, 759, 714, 669 cm^{-1}. ^1H NMR (300 MHz, $CDCl_3$): δ = 8.05 (d, *J* = 7.7 Hz, 2 H), 7.55 (t, *J* = 7.1 Hz, 1 H), 7.43 (t, *J* = 7.7 Hz, 2 H), 4.86 (dt, *J* = 10.6, 4.5 Hz, 1 H), 4.69 (d, *J* = 9.3 Hz, 1 H), 4.35–4.49 (m, 1 H), 3.73–3.90 (m, 1 H), 2.12 (d, *J* = 12.5 Hz, 2 H), 1.98 (d, *J* = 11.9 Hz, 1 H), 1.73–1.88 (m, 2 H), 1.08–1.68 (m, 10 H), 0.79–0.97 (m, 5 H), 0.55 (d, *J* = 6.4 Hz, 3 H), 0.30 (d, *J* = 6.4 Hz, 3 H) ppm. ^{13}C NMR (75 MHz, $CDCl_3$): δ = 167.2, 156.3, 133.3, 130.4, 130.1, 128.7, 76.0, 74.6, 54.4, 47.6, 41.8, 34.6, 33.2, 31.7, 31.6, 26.5, 24.9, 24.5, 23.9, 22.4, 20.7, 16.3 ppm. HRMS (EI): calcd. for $C_{24}H_{35}NO_4$: 401.2566; found 401.2575. $C_{24}H_{35}NO_4$ (401): calcd. C 71.79, H 8.79; found C 71.84, H 8.76.

(1*R*,2*S*,5*R*)-5-Methyl-2-(1-methylethyl)cyclohexyl *trans*-2-(Benzoyloxy)cyclopentylcarbamate (21a and 21b): The general procedure for the syntheses of benzoates using a mixture of **20a** and **20b** (433 mg, 1.25 mmol) as starting material gave a mixture of two diastereomers (252 mg, 52%), which were separated by flash column chromatography (CH_2Cl_2/MeOH, 200:1). **Diastereomer 1:** M.p. 85–86 °C (ethyl acetate/hexanes); R_f = 0.73 (CH_2Cl_2/MeOH, 400:1). $[\alpha]_D^{23}$ = –99.6 (*c* = 1.00, $CHCl_3$). IR (film): $\tilde{\nu}_{max}$ = 3684, 3019, 2961, 2400, 1711, 1512, 1424, 1031, 929, 669, 627 cm^{-1}. ^1H NMR (300 MHz, $CDCl_3$): δ = 8.03 (d, *J* = 7.2 Hz, 2 H), 7.42–7.52 (m, 3 H), 5.16 (q, *J* = 5.8 Hz, 1 H), 4.91 (br. s, 1 H), 4.40–4.48 (m, 1 H), 4.03–4.12 (m, 1 H), 2.19–2.23 (m, 2 H), 1.73–1.85 (m, 5 H), 1.51–1.58 (m, 7 H), 1.20–1.25 (m, 2 H), 0.67–0.85 (m, 7 H) ppm. ^{13}C NMR (75 MHz, $CDCl_3$): δ = 156.0, 132.9, 130.2, 129.7, 128.3, 80.4, 75.0, 47.3, 41.3, 34.2, 31.3, 26.2, 22.0, 20.8 ppm. HRMS (FAB) [M + H^+]: calcd. for $C_{23}H_{33}NO_4$: 388.2488; found 388.2474. **Diastereomer 2:** M.p. 86–89 °C (ethyl acetate/hexanes); R_f = 0.70 (CH_2Cl_2/MeOH, 400:1). $[\alpha]_D^{23}$ = –5.59 (*c* = 1.05, $CHCl_3$). IR (film): $\tilde{\nu}_{max}$ = 3436, 3019, 2960, 2400, 1711, 1512, 1037, 929, 669 cm^{-1}. ^1H NMR (300 MHz, $CDCl_3$): δ = 8.02 (d, *J* = 6.9 Hz, 2 H), 7.50–7.57 (m, 3 H) 5.11–5.19 (m, 1 H), 4.78–4.82 (m, 1 H), 4.52–4.57 (m, 1 H), 4.11–4.14 (m, 1 H), 2.11–2.21 (m, 2 H), 1.80–1.83 (m, 1 H), 1.72–1.79 (m, 4 H), 1.46–1.58 (m, 6 H), 1.38–1.45 (m, 4 H), 0.80–1.25 (m, 6 H) ppm. ^{13}C NMR (75 MHz, $CDCl_3$): δ = 156.0, 132.9, 130.2, 129.7, 128.3, 80.1, 74.7, 47.3, 41.4, 34.2, 31.3, 29.7, 26.2, 23.5, 22.0, 20.7, 16.3 ppm. HRMS (FAB) [M + H^+]: calcd. for $C_{23}H_{33}NO_4$: 388.2488; found 388.2481.

(1*R*,2*S*,5*R*)-5-Methyl-2-(1-methylethyl)cyclohexyl *trans*-2-(Benzoyloxy)cycloheptylcarbamate (23a and 23b): The general procedure for the syntheses of benzoates with a mixture of **22a** and **22b** (468 mg, 1.25 mmol) as starting material gave a mixture of two diastereomers **23a** and **23b** 389 mg (75%), which were separated by flash column chromatography (CH_2Cl_2/MeOH, 200:1). **Diastereomer 1:** M.p. 89–91 °C (ethyl acetate/hexanes); R_f = 0.55 (CH_2Cl_2/MeOH, 100:1). $[\alpha]_D^{23}$ = –105.1 (*c* = 0.8, $CHCl_3$). IR (film): $\tilde{\nu}_{max}$ = 3363, 2930, 2867, 1714, 1602, 1585, 1526, 1452, 1370, 1316, 1279, 1239, 1179, 1117, 1070, 1028 cm^{-1}. ^1H NMR (600 MHz, $CDCl_3$): δ = 7.98 (d, *J* = 7.5 Hz, 2 H), 7.46 (t, *J* = 7.5 Hz, 1 H), 7.35 (t, *J* = 7.5 Hz, 2 H), 4.91 (dt, *J* = 9.0, 3.4 Hz, 1 H), 4.63 (d, *J* = 9.2 Hz, 1 H), 4.28–4.36 (m, 1 H), 3.83–3.93 (m, 1 H), 1.85–1.94 (m, 2 H), 1.74–1.93 (m, 2 H), 1.47–1.71 (m, 10 H), 1.36–1.44 (m, 1 H), 1.16–1.27 (m, 1 H), 0.89–1.02 (m, 1 H), 0.81–0.88 (m, 2 H), 0.77 (d, *J* = 7.0 Hz, 3 H), 0.67 (d, *J* = 6.8 Hz, 3 H), 0.56–0.61 (m, 3 H) ppm. ^{13}C NMR (150 MHz, $CDCl_3$): δ = 166.5, 155.9, 132.9, 130.3, 129.8, 128.3, 127.8, 78.4, 74.4, 56.2, 47.2, 40.9, 34.2, 32.0, 31.2, 26.2, 25.9, 23.9, 23.5, 22.4, 21.9, 20.7, 16.5 ppm. MS (EI): *m*/*z* (%) = 415 (1), 137 (13), 123 (11), 111 (20), 105 (100), 97 (11), 95 (27), 83 (44), 82 (11), 81 (20), 77 (23), 71 (25), 69 (26), 67 (10), 57 (29), 56 (26), 55 (30). HRMS (EI): calcd. for $C_{25}H_{37}NO_4$: 415.2723; found 415.2715. **Diastereomer 2:** M.p. 121–124 °C (ethyl acetate/hexanes); R_f 0.50 (CH_2Cl_2/MeOH, 100:1). $[\alpha]_D^{23}$ = –37.6 (*c* = 0.75, $CHCl_3$). IR (film): $\tilde{\nu}_{max}$ = 3369, 2928, 2866, 1714, 1524, 1452, 1369, 1315, 1279, 1180, 1116, 1070, 1028 cm^{-1}. ^1H NMR (600 MHz, $CDCl_3$): δ = 7.96 (d, *J* = 7.4 Hz, 2 H), 7.47 (t, *J* = 7.4 Hz, 1 H), 7.35 (t, *J* = 7.4 Hz, 2 H), 4.93 (dt, *J* = 8.7, 3.7 Hz, 1 H), 4.69–4.77 (m, 1 H), 4.29–4.40 (m, 1 H), 3.85–3.94 (m, 1 H), 1.77–1.93 (m, 4 H), 1.64–1.74 (m, 2 H), 1.43–1.62 (m, 8 H), 1.31–1.41 (m, 1 H), 1.04–1.11 (m, 1 H), 0.76–0.88 (m, 5 H), 0.66–0.73 (m, 1 H), 0.49 (d, *J* = 5.3 Hz, 3 H), 0.27 (d, *J* = 0.48 Hz, 3 H) ppm. ^{13}C NMR (150 MHz, $CDCl_3$): δ = 166.6, 155.8, 132.9, 130.3, 129.7, 128.3,

127.8, 78.2, 74.3, 56.5, 47.3, 41.5, 34.3, 32.2, 31.3, 27.5, 26.2, 24.0, 23.6, 22.4, 22.0, 20.4, 16.1 ppm. MS (EI): *m*/*z* (%) = 415 (1), 155 (10), 138 (18), 137 (14), 123 (16), 111 (20), 105 (100), 97 (11), 96 (12), 95 (43), 94 (10), 83 (47), 82 (16), 81 (31), 77 (23), 71 (28), 69 (34), 67 (14), 57 (32), 56 (25), 55 (37). HRMS (EI): calcd. for $C_{25}H_{37}NO_4$: 415.2723; found 415.2720.

(1*R*,2*S*,5*R*)-5-Methyl-2-(1-methylethyl)cyclohexyl [2-(Benzoyloxy)-hexyl]carbamate (25a and 25b): The general procedure for the syntheses of benzoates with a mixture of **24a** and **24b** (451 mg, 1.25 mmol) as starting materials gave a mixture of two diastereomers (181 mg, 36%), which were inseparable by flash column chromatography. **Mixture of two Diastereomers:** Colorless solid; M.p. 121–124 °C (ethyl acetate/hexanes); R_f = 0.50 (CH_2Cl_2/MeOH, 100:1). $[\alpha]_D^{23}$ = –37.6 (*c* = 0.75, $CHCl_3$). IR (film): $\tilde{\nu}_{max}$ = 3684, 3401, 3019, 2961, 2400, 1713, 1517, 1423, 1215, 1046, 929, 641, 669, 627 cm^{-1}. ^1H NMR (300 MHz, $CDCl_3$): δ = 7.97 (d, *J* = 7.3 Hz, 2 H), 7.46–7.54 (m, 1 H), 7.33–7.43 (m, 2 H), 5.03–5.20 (m, 1 H), 4.70–4.86 (m, 1 H), 4.35–4.54 (m, 1 H), 3.33–3.49 (m, 2 H), 1.88–2.01 (m, 1 H), 1.72–1.88 (m, 2 H), 1.46–1.73 (m, 6 H), 1.23–1.44 (m, 6 H), 1.08–1.22 (m, 2 H), 0.90–1.06 (m, 2 H), 0.77–0.88 (m, 3 H), 0.64–0.75 (m, 4 H), 0.58 (d, *J* = 6.9 Hz, 1 H) ppm. ^{13}C NMR (75 MHz, $CDCl_3$): δ = 163.9, 154.0, 130.6, 127.2, 125.9, 72.2, 71.7, 44.9, 41.9, 38.9, 31.8, 29.0, 28.9, 28.8, 24.9, 23.8, 21.1, 20.1, 19.6, 18.3, 13.9, 13.9, 11.5 ppm. MS (EI): *m*/*z* (%) = 403 (1), 221 (15), 176 (13), 55 (61), 54 (31), 43 (37). HRMS (EI): calcd. for $C_{24}H_{37}NO_4$: 403.2723; found 403.2720.

(1*R*,2*S*,5*R*)-5-Methyl-2-(1-methylethyl)cyclohexyl [(1*S*,6*R*)-2-(Benzoyloxy)cyclohex-2-enyl]carbamate (27a) and (1*R*,2*S*,5*R*)-5-Methyl-2-(1-methylethyl)cyclohexyl [(1*R*,6*S*)-2-(Benzoyloxy)cyclohex-2-enyl]carbamate (27b): The general procedure for the syntheses of benzoates using a mixture of **26a** and **26b** (446 mg, 1.25 mmol) as starting materials gave a mixture of two diastereomers (254 mg, 51%), which were separated by flash column chromatography (CH_2Cl_2/MeOH, 400:1). **Compound 27a:** M.p. 103–105 °C (ethyl acetate/hexanes); R_f = 0.67 (CH_2Cl_2/MeOH, 400:1). $[\alpha]_D^{23}$ = –100.8 (*c* = 0.25, $CHCl_3$). IR (film): $\tilde{\nu}_{max}$ = 3436, 3019, 2962, 1713, 1602, 1511, 1424, 1277, 1117, 1048, 1028 cm^{-1}. ^1H NMR (300 MHz, $CDCl_3$): δ = 8.07 (d, *J* = 7.4 Hz, 2 H), 7.56 (t, *J* = 7.4 Hz, 1 H), 7.44 (t, *J* = 7.8 Hz, 2 H), 5.85 (d, *J* = 10.2 Hz, 1 H), 5.69 (dd, *J* = 9.5, 1.5 Hz, 1 H), 5.04–5.11 (m, 1 H), 4.66 (d, *J* = 9.2 Hz, 1 H), 4.52–4.62 (m, 1 H), 4.46 (dt, *J* = 10.7, 3.9 Hz, 1 H), 2.25–2.28 (m, 2 H), 2.08–2.11 (m, 1 H), 1.96–2.00 (m, 1 H), 1.88–1.93 (m, 1 H), 1.59–1.72 (m, 4 H), 1.26–1.42 (m, 2 H), 1.21–1.25 (m, 1 H), 0.98–1.04 (m, 1 H), 0.87 (d, *J* = 7.1 Hz, 3 H), 0.78 (d, *J* = 6.6 Hz, 3 H), 0.72 (d, *J* = 5.8 Hz, 3 H) ppm. ^{13}C NMR (75 MHz, $CDCl_3$): δ = 166.5, 156.2, 133.0, 130.2, 129.8, 129.5, 128.4, 128.3, 126.8, 77.2, 74.8, 73.9, 51.7, 47.2, 41.0, 34.2, 31.2, 26.4, 26.3, 24.0, 23.5, 21.9, 20.8, 16.5 ppm. HRMS (EI): calcd. for $C_{24}H_{33}NO_4$: 399.2410; found 399.2403. $C_{24}H_{33}NO_4$ (399): calcd. C 72.15, H 8.33; found C 72.42, H 8.44. **Compound 27b:** M.p. 107–109 °C (ethyl acetate/hexanes); R_f = 0.62 (CH_2Cl_2/MeOH, 400:1). $[\alpha]_D^{23}$ = +16.2 (*c* = 0.4, $CHCl_3$). IR (film): $\tilde{\nu}_{max}$ = 3369, 3033, 2954, 2928, 2869, 1714, 1523, 1277, 1241, 1116, 1027 cm^{-1}. ^1H NMR (600 MHz, $CDCl_3$): δ = 8.06 (d, *J* = 7.2 Hz, 2 H), 7.56 (t, *J* = 7.5 Hz, 1 H), 7.44 (t, *J* = 7.8 Hz, 2 H), 5.84 (d, *J* = 8.6 Hz, 1 H), 5.59 (dq, *J* = 9.8, 2.2 Hz, 1 H), 5.04–5.12 (m, 1 H), 4.70 (d, *J* = 9.5 Hz, 1 H), 4.55–4.61 (m, 1 H), 4.49 (td, *J* = 10.8, 3.7 Hz, 1 H), 2.23–2.29 (m, 2 H), 2.06–2.13 (m, 1 H), 1.91–2.03 (m, 2 H), 1.54–1.71 (m, 3 H), 1.41–1.49 (m, 1 H), 1.21 (t, *J* = 11.5 Hz, 1 H), 0.85–0.97 (m, 6 H), 0.65 (d, *J* = 6.6 Hz, 3 H), 0.42 (d, *J* = 6.6 Hz, 3 H) ppm. ^{13}C NMR (75 MHz, $CDCl_3$): δ = 166.5 156.0, 132.9, 130.1, 129.8, 129.3, 128.3, 127.0, 74.5, 73.7, 51.7, 47.3, 41.4, 34.2, 31.3, 26.6, 26.2, 24.0, 23.5, 22.0, 20.5, 16.1 ppm. HRMS (EI): calcd. for $C_{24}H_{33}NO_4$: 399.2410; found 399.2410.

(3a*R*,7a*R*)-3*H*-Hexahydrobenzoxazolidin-2-one (18a): 2-(Menthylcarbonylamino)cyclohexyl benzoate **16a** (260 mg, 0.65 mmol) was dissolved in 1 M NaOH in MeOH (30 mL), and the reaction mixture was stirred at room temperature for 10 h. The reaction mixture was diluted with water (30 mL) and extracted three times with dichloromethane. The organic layers were combined, washed with brine, dried with anhydrous magnesium sulfate, filtered and the solvent was evaporated. Flash column chromatography (hexanes/ethyl acetate, 4:1) of the residue afforded menthol [(1*R*,2*R*)-2-hydroxycyclohexyl]carbamate as colorless solid (152 mg, 79%); m.p. 130–132 °C (hexanes/ethyl acetate); R_f = 0.15 (hexanes/ethyl acetate, 1:1). $[\alpha]_D^{20}$ = –53.7 (*c* = 1.35, $CHCl_3$). IR (film): $\tilde{\nu}_{max}$ = 3685, 3620, 3020, 2870, 2401, 1693, 1510, 1477, 1451, 1423, 1215, 1046, 1024, 929 cm^{-1}. ^1H NMR (300 MHz, $CDCl_3$): δ = 4.60–4.79 (br. s, 1 H), 4.53 (dt, *J* = 11.2, 4.0 Hz, 1 H), 3.21–3.44 (m, 2 H), 3.00–3.21 (br. s, 1 H), 1.79–2.09 (m, 4 H), 1.54–1.75 (m, 2 H), 1.38–1.53 (m, 2 H), 0.66–1–38 (m, 17 H) ppm. ^{13}C NMR (75 MHz, $CDCl_3$): δ = 158.1, 75.8, 75.4, 57.2, 47.7, 41.7, 34.6, 34.5, 32.2, 31.7, 26.6, 25.0, 24.4, 23.8, 22.4, 21.2, 16.8 ppm. MS (EI): *m*/*z* (%) = 297 (1), 158 (10), 139 (27), 138 (17), 115 (19), 114 (28), 98 (100), 97 (21), 96 (19), 95 (23), 83 (90), 82 (14), 81 (43), 71 (21), 70 (10), 69 (46), 67 (13). HRMS (EI): calcd. for $C_{17}H_{31}NO_3$: 279.2304; found 297.2298. $C_{17}H_{31}NO_3$ (297.44): calcd. C 68.65, H 10.51; found C 68.65, H 10.81.

Menthyl [(1*R*,2*R*)-2-Hydroxycyclohexyl]carbamate (140 mg, 0.47 mmol) was dissolved in THF (5 mL) and sodium hydride (42 mg, 1.04 mmol) was added in one portion. The reaction mixture was heated at reflux for 12 h until TLC indicated complete conversion of starting material. The reaction mixture was quenched by the addition of an aqueous saturated solution of NH_4Cl. The aqueous layer was extracted three times with ethyl acetate. The organic layers were combined, washed with brine, dried with anhydrous magnesium sulfate, filtered, and the solvent was evaporated. Flash column chromatography (hexanes/ethyl acetate, 2:1 to 1:1) of the residue afforded (+)-**18** as colorless solid (55 mg, 83%); m.p. 133–134 °C (hexanes/ethyl actate). $[\alpha]_D^{22}$ = +7.5 (*c* = 1.0, EtOH); R_f = 0.45 (hexanes/ethyl acetate, 1:1). IR (film): $\tilde{\nu}_{max}$ = 3684, 3622, 3020, 1757, 1521, 1476, 1423, 1215, 1034, 929 cm^{-1}. ^1H NMR (300 MHz, $CDCl_3$): δ = 5.96–6.19 (br. s, 1 H), 3.81 (dt, *J* = 11.1, 4.3 Hz, 1 H), 3.16–3.33 (m, 1 H), 2.05–2.20 (m, 1 H), 1.93–2.05 (m, 1 H), 1.67–1.90 (m, 2 H), 1.49–1.65 (m, 1 H), 1.14–1.47 (m, 3 H) ppm. ^{13}C NMR (75 MHz, $CDCl_3$): δ = 161.2, 84.2, 61.3, 29.5, 28.9, 24.1, 23.9 ppm. MS (EI): *m*/*z* (%) = 141 (32), 140 (11), 99 (6), 96 (5), 69 (42), 57 (15), 56 (100), 54 (8), 43 (40). HRMS (EI): calcd. for $C_7H_{11}NO_2$: 141.0790; found 141.0788.

(3a*S*,7a*S*)-3*H*-Hexahydrobenzoxazolidin-2-one (18b): 2-(Menthylcarbonylamino)cyclohexyl Benzoate **16b** (270 mg, 0.67 mmol) was dissolved in 1 M NaOH in MeOH (30 mL), and the reaction mixture was stirred at room temperature for 10 h, then diluted with water (30 mL) and extracted three times with dichloromethane. The organic layers were combined, washed with brine, dried with anhydrous magnesium sulfate and the solvent was evaporated. Flash column chromatography (hexanes/ethyl acetate, 4:1) of the residue afforded menthol [(1*S*,2*S*)-2-hydroxycyclohexyl]carbamate as colorless solid (179 mg, 89%); m.p. 151–153 °C (hexanes/ethyl acetate); R_f = 0.15 (hexanes/ethyl acetate, 1:1). $[\alpha]_D^{20}$ = –58.2 (*c* = 1.2, $CHCl_3$). IR (film): $\tilde{\nu}_{max}$ = 3684, 3621, 3437, 3020, 2939, 2869, 2400, 1693, 1510, 1477, 1451, 1424, 1389, 1215, 1046, 1023, 929 cm^{-1}. ^1H NMR (300 MHz, $CDCl_3$): δ = 4.62–4.85 (br. s, 1 H), 4.55 (dt, *J* = 11.1, 4.2 Hz, 1 H), 3.21–3.42 (m, 2 H), 2.98–3.21 (br. s, 1 H), 1.81–2.14 (m, 4 H), 1.56–1.80 (m, 2 H), 1.39–1.55 (m, 2 H), 0.60–1.39 (m, 17 H) ppm. ^{13}C NMR (75 MHz, $CDCl_3$): δ = 158.2, 75.8, 75.5, 57.3, 47.9, 41.8, 34.6, 34.5, 32.1, 31.8, 26.6, 25.0, 24.4, 23.8, 22.4,

21.2, 16.8 ppm. MS (EI): *m*/*z* (%) = 297 (1), 160 (8), 159 (8), 158 (9), 139 (24), 138 (17), 115 (19), 114 (28), 98 (100), 97 (22), 96 (23), 95 (30), 83 (96), 82 (18), 81 (49), 71 (29), 70 (13), 69 (54), 67 (17). HRMS (EI): calcd. for $C_{17}H_{31}NO_3$: 279.2304; found 297.2303. $C_{17}H_{31}NO_3$ (297.44): calcd. C 68.65, H 10.51; found C 68.82, H 10.79.

Following the same procedure as for the preparation of compound (+)-**18a** using menthol [(1*S*,2*S*)-2-hydroxycyclohexyl]carbamate (160 mg, 0.54 mmol) and sodium hydride (32 mg, 1.33 mmol) as starting materials, gave 62 mg (82%) of compound (–)-**18b** as colorless crystals; m.p. 131–133 °C (hexanes/ethyl acetate). $[\alpha]_D^{22}$ = –7.4 (*c* = 1.1, EtOH). HRMS (EI): calcd. for $C_7H_{11}NO_2$: 141.0790; found 141.0785.

(3a*R*,7a*R*)-3-[(*S*)-3,3,3-Trifluoro-2-methoxy-2-phenylpropanoyl]hexahydrobenzo[*d*]oxazol-2(3*H*)-one (19a): *n*BuLi (2 M in THF, 78 μL, 0.16 mmol) was added to a solution of cyclic carbamate **18a** (20 mg, 0.14 mmol) in THF (2 mL) at 0 °C. The reaction mixture was stirred at the same temperature for 1 h then cooled to –78 °C. (*S*)-(+)-Mosher's chloride (43 mg, 0.17 mmol) was added, and the reaction mixture was warmed to room temperature over 14 h. The reaction was quenched by the addition of a saturated aqueous solution of NH_4Cl. The aqueous layer was extracted three times with ethyl acetate. The organic layers were combined, washed with brine and dried with anhydrous sodium sulfate. The organic layer was filtered and the solvent was evaporated. The crude residue was analyzed by ^{19}F NMR (282 MHz, $CDCl_3$): δ = –72.61 (not detected), –69.30 (1 F) ppm. Compound **19b** as well as a racemic standard were prepared in the same manner, using **18b** and a racemate of **18** as starting materials. **Compound 19b:** ^{19}F NMR (282 MHz, $CDCl_3$): δ = –72.61 (1 F), –69.31 (0.035 F) ppm. **Compound 19:** –72.61 (1 F), –69.30 (1 F) ppm. The results were confirmed by GC/MS analysis.

(1*R*,2*R*)-2-[(*S*)-3,3,3-Trifluoro-2-methoxy-2-phenylpropanoyloxy]cyclohexylmethylcarbamate (32): 2-(Methylcarbonylamino)cyclohexyl benzoate (**9**) (220 mg, 0.80 mmol) was dissolved in 1 M NaOH in MeOH (20 mL), and the reaction mixture was stirred at room temperature for 8 h. It was diluted with water (30 mL) and extracted three times with dichloromethane. The organic layers were combined, washed with brine, dried with anhydrous magnesium sulfate then the solvent was evaporated. Flash column chromatography (hexanes/ethyl acetate, 4:1) of the residue afforded methyl 2-hydroxycyclohexylcarbamate as colorless solid (132 mg, 95%); m.p. 109–111 °C (hexanes/ethyl acetate). IR (film): $\tilde{\nu}_{max}$ = 3436, 3156, 2942, 2863, 2253, 1708, 1517, 1452, 1517, 1452, 1384 cm^{-1}. ^1H NMR (300 MHz, $CDCl_3$): δ = 4.75–5.15 (br. s, 1 H), 3.66 (s, 3 H), 3.21–3.46 (m, 1 H), 2.98–3.18 (br. s, 1 H), 1.91–2.12 (m, 2 H), 1.60–1.79 (m, 2 H), 1.05–1.41 (m, 4 H) ppm. ^{13}C NMR (75 MHz, $CDCl_3$): δ = 158.4, 75.6, 57.5, 52.9, 34.6, 32.2, 25.1, 24.5 ppm. MS (EI): *m*/*z* (%) = 173 (1), 141 (18), 114 (75), 112 (22), 102 (12), 98 (100), 88 (42), 69 (26), 56 (51), 51 (66). HRMS (EI): calcd. for $C_8H_{15}NO_3$: 173.1052; found 173.1053. $C_8H_{15}NO_3$ (173): calcd. C 55.47, H 8.73; found C 55.16, H 8.73.

To a solution of methyl carbamate prepared as described (40 mg, 0.23 mmol) dissolved in dry dichloromethane (3 mL) were added sequentially 1-ethyl-3-[3′-(dimethylamino)propyl]carbodiimide·HCl (49 mg, 0.25 mmol), 4-(dimethylamino)pyridine (3 mg, 0.023 mmol), and Mosher's acid (54 mg, 0.23 mmol) at 0 °C. The reaction mixture was kept at 0 °C for 1 h, then stirred at room temperature for 2 d. TLC analysis indicated no further consumption of starting material. The reaction mixture was diluted with dichloromethane and washed with NH_4Cl, aq. saturated $NaHCO_3$, and brine. The organic layer was dried with $MgSO_4$, filtered, then the solvent was evaporated at reduced pressure. Flash column chromatography (hexanes/ethyl acetate, 2:1) of the residue afforded compound **32** as colorless oil 31 mg (40%). ^1H NMR (300 MHz, $CDCl_3$): δ = 7.47–7.56 (m, 2 H), 7.34–7.42 (m, 3 H), 4.53–4.97 (m, 2 H), 3.43–3.78 (m, 7 H), 1.91–2.17 (m, 2 H), 1.17–1.86 (m, 6 H) ppm. ^{13}C NMR (75 MHz, $CDCl_3$): δ = 156.6, 156.5, 132.6, 129.93, 129.90, 128.8, 127.6, 125.5, 55.7, 54.2, 52.5, 52.3, 33.0, 32.8, 31.3, 30.9, 30.1, 29.3, 24.4, 24.2, 24.1 ppm. ^{19}F NMR (282 MHz, $CDCl_3$): δ = –72.08 (1 F), –72.42 (1 F) ppm. The results were confirmed by GC/MS analysis.

Methyl *cis*-Hexahydro-3*H*-1,2,3-benzoxathiazole-3-carboxylate 2-Oxide (35): A solution of methyl carbamate **34** (0.79 g, 4.56 mmol) in CH_3CN (20 mL) was added dropwise to a solution of thionyl chloride (0.83 mL, 11.41 mmol) in CH_3CN (60 mL) at –35 °C over 10 min. The reaction mixture was stirred at –35 °C for 5 min, before pyridine (1.84 mL, 22.82 mmol) was added dropwise. The reaction mixture was warmed to room temperature over 3 h. The solvent was evaporated, and the residue was triturated with Et_2O. The suspension was filtered, and the filtrate was concentrated under reduced pressure. Purification of the residue by flash column chromatography (hexanes/ethyl acetate, 5:1) afforded 0.63 g (63%) of compound **35** as colorless oil. R_f = 0.75 (hexanes/ethyl acetate, 1:1). IR (film): $\tilde{\nu}_{max}$ = 2943, 2867, 1730, 1442, 1359, 1328, 1288, 1187, 1148 cm^{-1}. ^1H NMR (300 MHz, $CDCl_3$) (two rotamers): δ = 5.24–5.31 (br. s, 0.66 H), 4.66 (q, *J* = 4.0 Hz, 0.33 H), 3.94–4.12 (m, 1 H), 3.84 (s, 1 H), 3.82 (s, 2 H), 2.09–2.34 (m, 2 H), 1.54–2.45 (m, 4 H), 1.33–1.52 (m, 1 H), 1.08–1.31 (m, 1 H) ppm. ^{13}C NMR (75 MHz, $CDCl_3$) (two rotamers): δ = 152.9, 85.0, 80.0, 55.6, 54.1, 53.7, 53.6, 28.8, 28.4, 27.9, 26.8, 22.6, 22.2, 19.6, 19.5 ppm. MS (EI): *m*/*z* (%) = 219 (12), 171 (16), 155 (29), 154 (26), 140 (65), 127 (44), 126 (13), 124 (16), 77 (100), 75 (16), 64 (33). HRMS (EI): calcd. for $C_8H_{13}NO_4S$: 219.0565; found 219.0561.

Methyl *trans*(2-Hydroxycyclohexyl)carbamate (39): Methyl chloroformate (0.3 mL, 3.94 mmol) was added dropwise to a vigorously stirred solution of *trans*-2-aminocyclohexanol hydrochloride (0.5 g, 3.3 mmol) and $NaHCO_3$ (0.83 g, 9.9 mmol) in a 1:1 mixture of $CHCl_3$ and H_2O (30 mL). The mixture was allowed to stir at room temperature for 1 h, before the reaction mixture was neutralized with 1 M aq. HCl. The aqueous layer was extracted three times with dichloromethane. The combined organic layers were washed with brine, dried with $MgSO_4$ and evaporation of the solvent and recrystallization from hexanes/ethyl acetate furnished the title compound as colorless solid (498 mg, 87%); m.p. 109–111 °C (hexanes/ethyl acetate). IR (film): $\tilde{\nu}_{max}$ = 3436, 3156, 2942, 2863, 2253, 1708, 1517, 1452, 1517, 1452, 1384 cm^{-1}. ^1H NMR (300 MHz, $CDCl_3$): δ = 4.75–5.15 (br. s, 1 H), 3.66 (s, 3 H), 3.21–3.46 (m, 1 H), 2.98–3.18 (br. s, 1 H), 1.91–2.12 (m, 2 H), 1.60–1.79 (m, 2 H), 1.05–1.41 (m, 4 H) ppm. ^{13}C NMR (75 MHz, $CDCl_3$): δ = 158.4, 75.6, 57.5, 52.9, 34.6, 32.2, 25.1, 24.5 ppm. MS (EI): *m*/*z* (%) = 173, 141 (18), 114 (75), 112 (22), 102 (12), 98 (100), 88 (42), 69 (26), 56 (51), 51 (66). HRMS (EI): calcd. for $C_8H_{15}NO_3$: 173.1052; found, 173.1053. $C_8H_{15}NO_3$ (173): calcd. C 55.47, H 8.73; found C 55.16, H 8.73.

Methyl (3a*R*,7a*R*)-Hexahydro-3*H*-1,2,3-benzoxathiazole-3-carboxylate 2-Oxide (40): A solution of methyl [(1*R*,2*R*)-2-hydroxycyclohexyl]carbamate (0.8 g, 4.62 mmol) in CH_3CN (20 mL) was added dropwise to a solution of thionyl chloride (0.84 mL, 11.6 mmol) in CH_3CN (60 mL) at –35 °C over 10 min. The reaction mixture was stirred at the same temperature for 5 min before pyridine (1.8 mL, 23.11 mmol) was added dropwise. The reaction mixture was warmed to room temperature over 3 h. The solvent was evaporated, and the residue was triturated with Et_2O. After filtration, the mix-

ture was concentrated under reduced pressure. Flash column chromatography (hexanes/ethyl acetate, 5:1) of the residue afforded the product as colorless solid (0.79 g, 78%); m.p.51–54 °C; R_f 0.5 (hexanes/ethyl acetate, 2:1). IR (film): $\tilde{\nu}_{max}$ = 3368, 2954, 2254, 1733, 1572, 1444, 1384, 1328, 1300 cm^{-1}. ^1H NMR (300 MHz, $CDCl_3$): δ = 4.71 (dt, J = 11, 4 Hz, 1 H), 3.83 (s, 3 H), 3.13 (dt, J = 13, 3 Hz, 1 H), 2.61–2.74 (m, 1 H), 2.20–2.34 (m, 1 H), 1.79–2.02 (m, 2 H), 1.69 (dq, J = 12, 4 Hz, 1 H), 1.19–1.54 (m, 3 H) ppm. ^{13}C NMR (75 MHz, $CDCl_3$): δ = 154.7, 86.8, 63.2, 54.0, 29.8, 29.5, 24.3, 23.9 ppm. MS (EI): m/z (%) = 219 (5), 140 (10), 114 (100), 81 (12), 59 (24), 44 (17). HRMS (EI): calcd. for $C_8H_{13}NO_4S$: 219.0565; found , 219.0565. $C_8H_{13}NO_4S$ (219): calcd. C 43.82, H 5.98; found C 44.12, H 6.05.

Methyl *trans*-2,2-Hexahydro-3*H*-1,2,3-benzoxathiazole-3-carboxylate 2,2-Dioxide (41): Ruthenium(III) chloride hydrate (catalytic amount), sodium periodate (205 mg, 0.96 mmol), and H_2O (3 mL) were added at 0 °C to a solution of oxathiazolidine **40** (140 mg, 0.64 mmol) in CH_3CN (3 mL). The reaction mixture was warmed to room temperature and was stirred for 3 h. The reaction mixture was extracted three times with Et_2O. The organic layers were combined and washed with H_2O and brine, then dried with anhydrous $MgSO_4$. Filtration, evaporation of the solvent and purification by flash column chromatography (hexanes/ethyl aceate) afforded 130 mg (87%) of colorless oil. R_f = 0.55 (2:1, hexanes/ethyl aceate). IR (film): $\tilde{\nu}_{max}$ = 3367, 2958, 2870, 2255, 1746, 1444, 1384, 1329, 1299, 1193 cm^{-1}. ^1H NMR (300 MHz, $CDCl_3$): δ = 4.39 (dt, J = 11, 4 Hz, 1 H), 3.88 (s, 3 H), 3.73–3.84 (m, 1 H), 2.59–2.73 (m, 1 H), 2.19–2.31 (m, 1 H), 1.81–2.05 (m, 2 H), 2.05 (dq, J = 12, 4 Hz, 1 H), 1.30–1.58 (m, 3 H) ppm. ^{13}C NMR (75 MHz, $CDCl_3$): δ = 151.6, 84.6, 64.7, 54.9, 29.0, 28.3, 23.7, 23.5 ppm. MS (EI): m/z (%) = 235, 155 (37), 150 (100), 140 (12), 124 (13), 114 (19), 101 (52), 98 (26), 95 (22), 81 (24), 69 (44), 59 (53). HRMS (EI): calcd. for $C_8H_{13}NO_5S$: 235.0514; found , 235.0519. $C_8H_{13}NO_5S$ (235): calcd. C 40.84, H 5.57; found C 41.18, H 5.84.

***trans*-Hexahydro-3*H*-1,2,3-benzoxathiazole 2,2-Dioxide (42):** Ammonium benzoate (757 mg, 5.44 mmol) was added to a solution of benzoxathiazole **41** (640 mg, 2.72 mmol) in dry DMF (5 mL) in one portion. The reaction mixture was heated at 75 °C until full conversion of starting material was indicated by TLC (24 h). The solvent was evaporated and the residue was dissolved in THF (3 mL). Three drops of water and concentrated H_2SO_4 were added, and the reaction mixture was allowed to stir at 60 °C. After 3 h the mixture was cooled to room temperature, and its pH was adjusted to pH 9 (saturated aq. $NaHCO_3$). The reaction mixture was extracted 3 times with dichloromethane. The organic layer was washed with brine and dried with anhydrous $MgSO_4$. The solvent was evaporated under reduced pressure and the residue was purified by flash column chromatography (hexanes/ethyl acetate, 4:1) affording 440 mg (91%) of the title compound **42**; m.p. 94–97 °C (hexanes/ethyl acetate); R_f = 0.6 (hexanes/ethyl acetate, 1:1). IR (film): $\tilde{\nu}_{max}$ = 3256, 2953, 2869, 1794, 1642, 1458, 1448, 1406, 1364, 1342, 1331, 1278, 1231, 1192, 1138, 1101, 1074, 1052, 1001, 950, 868, 865, 786, 650 cm^{-1}. ^1H NMR (300 MHz, $CDCl_3$): δ = 4.91 (d, J = 9.0 Hz, 1 H), 4.30 (dq, J = 10.0, 5.2 Hz, 1 H), 3.45 (m, 1 H), 2.24 (m, 1 H), 2.14 (m, 1 H), 1.91 (m, 2 H), 1.70 (dq, J = 12.0, 4.0 Hz, 1 H), 1.41 (m, 3 H) ppm. ^{13}C NMR (75 MHz, $CDCl_3$): δ = 90.1, 63.2, 28.5, 27.7, 23.8, 23.4. HRMS: calcd. for $C_6H_{11}NO_3S$: 177.0456; found 177.0454.

Supporting Information (see also the footnote on the first page of this article): Details of the computational studies as well as copies of ^1H and ^{13}C NMR spectra.

Acknowledgments

For financial support of this work, the authors are indebted to the Natural Sciences and Engineering Research Council of Canada, Canadian Foundation for Innovation, Ontario Innovation Trust, Petroleum Research Fund administered by the American Chemical Society, Research corporation, and Brock University. TDC Research, Inc. and TDC Research Foundation are acknowledged for fellowships for B. S.

[1] a) G. M. Atkins, E. M. Burgess, *J. Am. Chem. Soc.* **1968**, *90*, 4744–4745; b) E. M. Burgess, H. R. Penton, E. A. Taylor, *J. Am. Chem. Soc.* **1970**, *92*, 5224–5226; c) G. M. Atkins, E. M. Burgess, *J. Am. Chem. Soc.* **1972**, *94*, 6135–6141; d) E. M. Burgess, H. R. Penton, E. A. Taylor, *J. Org. Chem.* **1973**, *38*, 26–31.

[2] For reviews of applications of the Burgess Reagent in synthesis see: a) S. Burckhardt, *Synlett* **2000**, 559; b) C. Lamberth, *J. Prakt. Chem./Chem.-Ztg.* **2000**, *342*, 518–522; c) P. Taibe, S. Mobashery, in *Encyclopedia of Reagents in Organic Synthesis* (Ed.: L. A. Paquette), vol. 5, Wiley, Chichester, **1995**, p. 3345.

[3] J. H. Rigby, M. Kirova-Snover, *Tetrahedron Lett.* **1997**, *38*, 8153–8156.

[4] J. H. Rigby, M. E. Mateo, *J. Am. Chem. Soc.* **1997**, *119*, 12655–12656.

[5] R. A. Holton, H. B. Kim, C. Sonoza, F. Liang, R. J. Biediger, P. D. Boatman, M. Shindo, C. C. Smith, S. Kim, H. Nadizadeh, Y. Suzuki, C. Tao, P. Vu, S. Tang, P. Zhang, K. K. Murthi, L. N. Gentile, J. H. Liu, *J. Am. Chem. Soc.* **1994**, *116*, 1599–1600.

[6] R. E. Dolle, K. C. Nicolaou, *J. Am. Chem. Soc.* **1985**, *107*, 1691–1694.

[7] A. R. Daniewski, P. M. Wovkulich, M. R. Uskokovic, *J. Org. Chem.* **1992**, *57*, 7133–7139.

[8] E. M. Burgess, H. R. Penton, E. A. Taylor, W. M. Williams, *Org. Synth.* **1977**, *56*, 40–44.

[9] a) D. A. Claremon, B. T. Phillips, *Tetrahedron Lett.* **1988**, *29*, 2155–2158; b) H. Nemoto, Y. Kubota, Y. Yamamoto, *J. Org. Chem.* **1990**, *55*, 4515–4516.

[10] a) P. Wipf, S. Venkatraman, *Tetrahedron Lett.* **1996**, *37*, 4659–4662; b) P. Wipf, S. Venkatraman, *Synlett* **1997**, 1–10.

[11] K. C. Nicolaou, S. A. Snyder, A. Z. Nalbandian, D. A. Longbottom, *J. Am. Chem. Soc.* **2004**, *126*, 6234–6235.

[12] K. C. Nicolaou, X. Huang, S. A. Snyder, P. B. Rao, M. Bella, M. V. Reddy, *Angew. Chem. Int. Ed.* **2002**, *41*, 834–838.

[13] S. C. Banfield, A. T. Omori, H. Leisch, T. Hudlicky, *J. Org. Chem.* **2007**, *72*, 4989–4992.

[14] K. C. Nicolaou, S. A. Snyder, D. A. Longbottom, A. Z. Nalbandian, X. Huang, *Chem. Eur. J.* **2004**, *10*, 5581–5606.

[15] K. C. Nicolaou, D. A. Longbottom, S. A. Snyder, A. Z. Nalbandian, X. Huang, *Angew. Chem. Int. Ed.* **2002**, *41*, 3866–3870.

[16] U. Rinner, D. R. Adams, M. L. dos Santos, K. A. Abboud, T. Hudlicky, *Synlett* **2003**, 1247–1252.

[17] The following statement appeared in a review (ref.[2b]) published in 2000: "The compatibility of the Burgess reagent with many functionalities, e.g. halogens, epoxides, alkenes, alkynes, aldehydes, ketones, acetals, esters, secondary amides, makes it an attractive technique for the introduction of C–C double bonds into highly functionalized molecules."

[18] Cyclic epoxides proximal to alcohols react with the Burgess reagent to form sulfamidates (ref. 14). Distally located epoxides appear inert provided excess reagent is not used. See A. A. Nagel, J. DiBrino, L. A. Vincent, J. A. Retsema, *J. Med. Chem.* **1982**, *25*, 881–884. It was likely this report that led to the belief in inertness of epoxides.

[19] For reviews on the synthesis and utility of 1,2-amino alcohols see: a) G. Shaw, in *Comprhensive Heterocyclic Chemistry II* (Eds.: A. R. Katritzky, C. W. Rees, E. F. V. Scriven), Pergamon,

New York, **1996**, pp. 397; b) S. Wallbaum, J. Martens, *Tetrahedron: Asymmetry* **1992**, *3*, 1475–1504; c) R. Noyori, M. Kitamura, *Angew. Chem. Int. Ed. Engl.* **1991**, *193*, 34–48; d) V. K. Singh, *Synthesis* **1992**, 605–617.

[20] For reviews on synthesis and reaction of cyclic sulfates see: a) B. B. Lohray, *Synthesis* **1992**, 1035–1052; b) B. B. Lohray, V. Bhushan, *Adv. Heterocycl. Chem.* **1997**, *68*, 89–180; c) H.-S. Byun, L. He, R. Bittman, *Tetrahedron* **2000**, *56*, 7051–7091.

[21] G. R. Pettit, N. Melody, D. L. Herald, *J. Org. Chem.* **2001**, *66*, 2583–2587.

[22] The structures reported as minor products in ref.[12] (Table 1) assigned as regioisomeric sulfamidates **5** are all the corresponding seven-membered sulfamidates, as proven by comparison of reaction mixtures obtained from both diols and the corresponding epoxides (ref.[16]), and as was subsequently also reported in a later publication (ref.[14]).

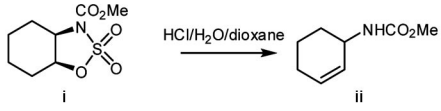
[23] U. Jaeger, W. Sundermeyer, H. Pritzkow, *Chem. Ber.* **1987**, *120*, 1191–1195.

[24] K. Finn, T. Hudlicky, unpublished observations.

[25] H. Leisch, R. Saxon, B. Sullivan, T. Hudlicky, *Synlett* **2006**, *3*, 445–449.

[26] C. A. de Parrodi, E. Juaristi, L. Quintero, A. Clara-Sosa, *Tetrahedron: Asymmetry* **1997**, *8*, 1075–1082.

[27] Similar reaction was observed in the racemic series. Sulfamidate **i** was hydrolyzed to **ii** in 95% yield using conditions described in the literature for mild hydrolysis of sulfamidates (ref.[14]).



i ii

[28] a) B. Sullivan, J. Gilmet, H. Leisch, T. Hudlicky, *J. Nat. Prod.* **2008**, *71*, 346–350; b) J. Gilmet, B. Sullivan, T. Hudlicky, *Tetrahedron* **2009**, *65*, 212–220.

[29] L. E. Martinez, J. L. Leighton, D. H. Carsten, E. N. Jacobsen, *J. Am. Chem. Soc.* **1995**, *117*, 5897–5898.

[30] C. Bolm, M. Ewald, M. Felder, G. Schlingloff, *Chem. Ber.* **1992**, *125*, 1169–1190.

[31] S. E. Schaus, J. F. Larrow, E. N. Jacobsen, *J. Org. Chem.* **1997**, *62*, 4197–4199.

[32] To the best of our knowledge, as of this report, there have been no previous computational studies addressing the Burgess reagent's reactivity.

[33] a) A. D. Becke, *J. Chem. Phys.* **1993**, *98*, 5648–5652; b) C. Lee, W. Yang, R. G. Parr, *Phys. Rev. B* **1988**, *37*, 785–789.

[34] a) W. J. Hehre, R. Ditchfield, J. A. Pople, *J. Chem. Phys.* **1972**, *56*, 2257–2261; b) P. C. Hariharan, J. A. Pople, *Theor. Chim. Acta* **1973**, *28*, 213–222; c) P. C. Hariharan, J. A. Pople, *Mol. Phys.* **1974**, *27*, 209–214; d) M. M. Francl, W. J. Pietro, W. J. Hehre, J. S. Binkley, M. S. Gordon, D. J. DeFrees, J. A. Pople, *J. Chem. Phys.* **1982**, *77*, 3654–3665; e) V. A. Rassolov, J. A. Pople, M. A. Ratner, T. L. Windus, *J. Chem. Phys.* **1998**, *109*, 1223–1229.

[35] For additional details regarding the procedural details associated with these PES scans, see SI.

[36] M. J. Frisch, G. W. Trucks, H. B. Schlegel, G. E. Scuseria, M. A. Robb, J. R. Cheeseman, J. A. Montgomery Jr., T. Vreven, K. N. Kudin, J. C. Burant, J. M. Millam, S. S. Iyengar, J. Tomasi, V. Barone, B. Mennucci, M. Cossi, G. Scalmani, N. Rega, G. A. Petersson, H. Nakatsuji, M. Hada, M. Ehara, K. Toyota, R. Fukuda, J. Hasegawa, M. Ishida, T. Nakajima, Y. Honda, O. Kitao, H. Nakai, M. Klene, X. Li, J. E. Knox, H. P. Hratchian, J. B. Cross, C. Adamo, J. Jaramillo, R. Gomperts, R. E. Stratmann, O. Yazyev, A. J. Austin, R. Cammi, C. Pomelli, J. W. Ochterski, P. Y. Ayala, K. Morokuma, G. A. Voth, P. Salvador, J. J. Dannenberg, V. G. Zakrzewski, S. Dapprich, A. D. Daniels, M. C. Strain, O. Farkas, D. K. Malick, A. D. Rabuck, K. Raghavachari, J. B. Foresman, J. V. Ortiz, Q. Cui, A. G. Baboul, S. Clifford, J. Cioslowski, B. B. Stefanov, G. Liu, A. Liashenko, P. Piskorz, I. Komaromi, R. L. Martin, D. J. Fox, T. Keith, M. A. Al-Laham, C. Y. Peng, A. Nanayakkara, M. Challacombe, P. M. W. Gill, B. Johnson, W. Chen, M. W. Wong, C. Gonzalez, J. A. Pople, *Gaussian 03*, revision C.02, Gaussian, Inc., Wallingford CT, **2004**.

[37] See Supporting Information for calculated transition states. Owing to their higher activation barrier subsequent steps along this pathway were not considered.

[38] Although even this reaction barrier is slightly too high, it was by far the lowest out of all the mechanistic possibilities considered.

[39] *Atoms in Molecules: A Quantum Theory* (Ed.: R. F. W. Bader), Oxford Press, **1990**. As implemented within the AIM program, **2000**.

[40] E. D. Glendening, A. E. Reed, J. E. Carpenter, F. Weinhold, *NBO*, version 3.1.

[41] a) K. B. Wiberg, *Tetrahedron* **1968**, *24*, 1083–1096; b) Wiberg bond indices for pertinent bond forming/breaking distances during 5-mem-TS1: C···N: 0.1588, C···O: 0.3007, and O···S: 0.4358.

[42] An Intrinsic Reaction Coordinate (IRC) calculation confirmed that *cis*-5-mem sulfamidate was the immediate product of 5-mem-TS1.

[43] See Supporting Information for details regarding these searches.

[44] Multiple attempts were made to locate 5-mem-TS1 in the presence of an epoxide bound Lewis acid, none of these attempts were successful in locating energetically feasible transition states.

[45] For example a reaction dynamic involving Brønsted acidic trimethylammonium (a likely degradation product of Burgess reagent) was computed and shown to have a reduced barrier to cyclohexene oxide ring opening as compared with that of the uncatalyzed processes (i.e. 5-mem-TS1).

Received: February 14, 2009
Published Online: April 27, 2009

