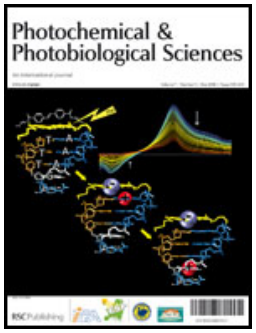

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Papers in this issue:

Vibrational deactivation of singlet oxygen: does it play a role in stereoselectivity during photooxygenation?†‡

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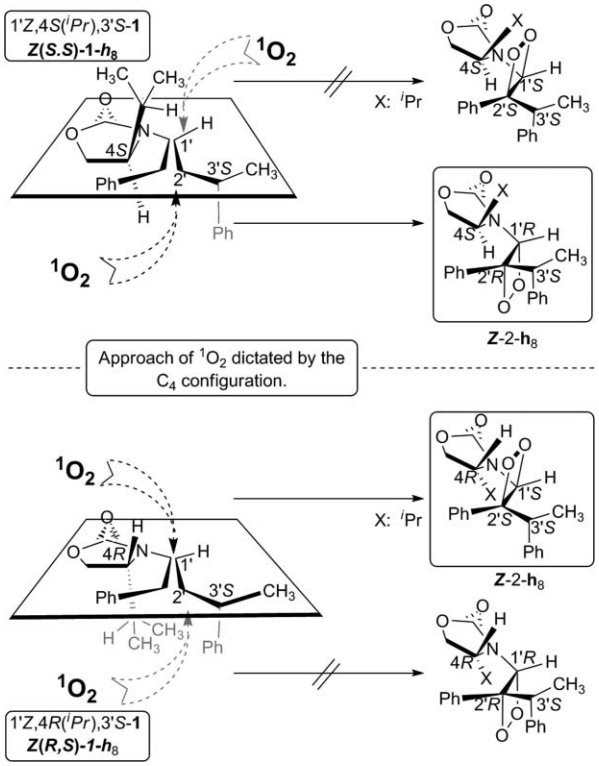
Oxazolidinone-substituted enecarbamates offer a system to explore vibrational quenching and the strategic placement of CH bonds as a method for manipulating the stereoselectivity of photoreactions.

The difficulty in manipulating the special requirements for stereoselection in photoreactions, due to the short lifetimes of the reactive species and/or intermediates, has forced photochemists to devise new methodologies.[1,2] Unlike ground-state thermal reactions, the lifetime of the reactive species dictates how much stereocontrol will be achieved in the photoproduct and hence presents photochemists with a formidable challenge.[3] Of the many elegant methods being devised and investigated, organized media like crystals,[4,5] polymer-thin films,[6,7] zeolites,[8–11] have been explored with varying degrees of success.

For the past few years, our efforts have focused on enhancing stereoselectivity in solution by employing the inherent properties of photoreactions for imprinting stereocontrol. To explore this concept, we chose singlet oxygen ($^1O_2$) as the reactive excited-state species, since its lifetime (μs to s) may be controlled by environmental parameters such as solvent and temperature.[12–15] The main reason for this distinct behavior is the physical deactivation of the $^1O_2$ excited state to its triplet ground state when it encounters CH bonds. Our studies exploited this unique property in an attempt to augment the extent of the stereoselection in photooxygenations, as well as explore whether this methodology could be extended generally for photoreactions.

Previously, we showed that the approach of $^1O_2$ onto the double bond of enecarbamates ***Z*-1-h$_8$** may proceed with complete diastereoselectivity to afford the corresponding dioxetane product ***Z*-2-h$_8$** (Scheme 1).[16–18] The selectivity was independent of the size of the alkyl group (*Me*, ^{i}Pr or ^{t}Bu) at the C_4 position of the oxazolidinone, but did depend on whether this stereogenic center was *R* or *S* configured. Moreover, the stereoselectivity



Scheme 1 Stereoselective photooxygenation of oxazolidinone functionalized enecarbamates **Z-1-h$_8$** to afford the dioxetane cycloadducts ***Z*-2-h$_8$**.

did not depend on the configuration at the $C_{3'}$ position.[16–20] For example, irrespective of the configuration at the $C_{3'}$ position, the oxazolidinone with an *S* configuration at the C_4 position favored the 1′*R*/2′*R* dioxetane ***Z*-2-h$_8$** (Scheme 1, top). Alternatively, the oxazolidinone with an *R* configuration at the C_4 position favored the 1′*S*/2′*S* dioxetane ***Z*-2-h$_8$** (Scheme 1, bottom).[16–20]

Remarkable about our findings is the fact that irrespective of the size of the substituent at the C_4 position (*Me*, ^{i}Pr and ^{t}Bu groups), essentially complete diastereocontrol is achieved in the cycloaddition of $^1O_2$, the smallest of all cyclophiles.[16–20] This speaks against traditional steric effects in controlling the approach of the $^1O_2$ onto the oxazolidinone double bond. We suspected that vibrational deactivation (physical quenching)[21,22] of the electronically excited $^1O_2$ plays a significant role in enhancing the stereoselectivity.[19,23,24]

To validate our suspicion that the enhanced diastereoselectivity may be attributed to vibrational deactivation of $^1O_2$, we deuterated the enecarbamate substrate **1** at the C_4 position of the oxazolidinone ring (Scheme 2). The deuterated *Z*-enecarbamate ***Z*-1-d$_8$** was photooxygenated and the stereoselectivity of the dioxetane

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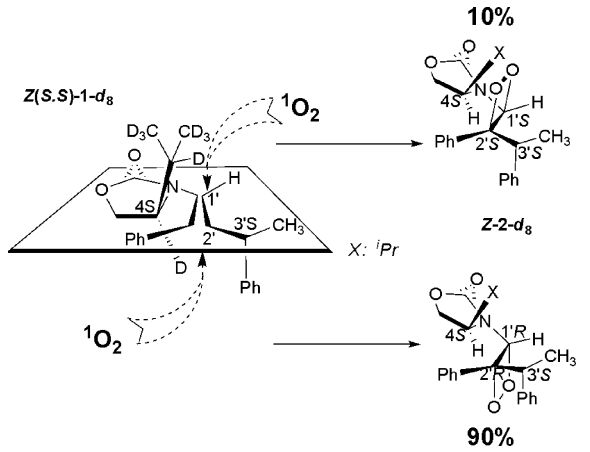
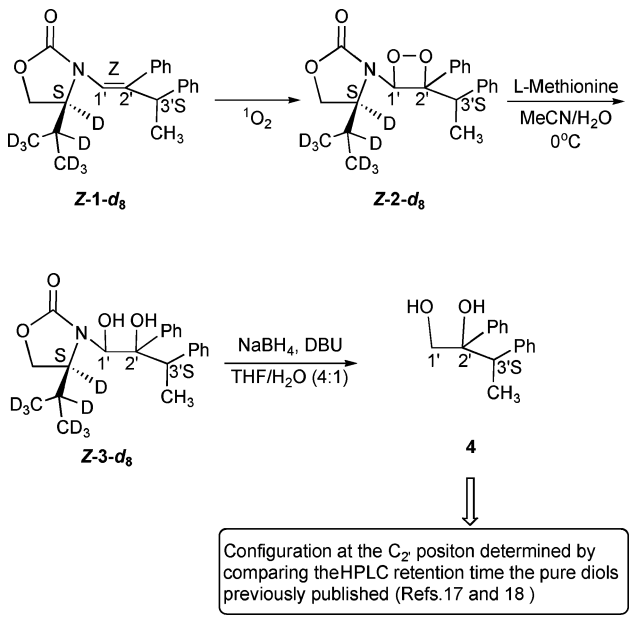
‡ Electronic supplementary information (ESI) available: Additional experimental details, ^{1}H-NMR spectra and HPLC traces. CCDC reference number 678264. For crystallographic data in CIF or other electronic format see DOI: 10.1039/b719387d



Scheme 2 Attack of $^1O_2$ on the *Z*-enecarbamate ***Z*-1-d$_8$** with ^{i}Pr-d$_8$ substituent at the C_4 position in the oxazolidinone ring.

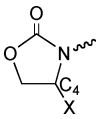
***Z*-2-d$_8$** determined[16] by NMR spectroscopy (see the electronic supplementary information (ESI) for details).‡ The dioxetane ***Z*-2-d$_8$** was isolated and converted[16] to the corresponding diol ***Z*-3-d$_8$**, then to the diol **4** (Scheme 3), and submitted to HPLC analysis, to assess the extent of stereocontrol.‡



Scheme 3 Conversion of dioxetane ***Z*-2-d$_8$**, derived upon photooxygenation of the enecarbamate ***Z*-1-d$_8$**, to the diol **4**.

Direct comparison of the stereoselectivity results of the dioxetane products ***Z*-2-h$_8$** and ***Z*-2-d$_8$**, by keeping in mind the established trends in the stereocontrol exercized by the Evans chiral auxiliary,[25] should reveal the contribution of the deuteration effect. In this way, the relative efficacy of $^1O_2$ vibrational deactivation *versus* steric interactions imposed by the C_4 substituent should be disclosed. Further chiral HPLC analysis of the diol **4** products should also offer additional corroboration of the structural details provided by NMR studies of the dioxetane products.

Table 1 Diastereoisomeric excess values calculated for the dioxetane intermediate formed in the photooxygenation of the proteated and deuterated enecarbamates to assess the relative contribution of vibrational deactivation *versus* steric interactions in the $^1O_2$ attack

Diastereoisomeric excess			
	Classic steric effect‡ (%)	$^1O_2$ Oxidiation of proteated enecarbamate (%)	$^1O_2$ Oxidation of C_4 deuterated analogs (%)
X = *Me*	72	>98	
X = ^{i}Pr	81	>98	80
X = ^{t}Butyl	>98	>98	

The results, summarized in Table 1, clearly expose that the stereoselectivity for the deutero substrate ***Z*-1-d$_8$** is appreciably less (by about 20%) than that of the proteo derivative ***Z*-1-h$_8$**. Evidently, the diminished stereocontrol in the deutero substrate ***Z*-1-d$_8$**, compared to the proteo ***Z*-1-h$_8$** analog, is attributed to the absence of vibrational deactivation of the electronically excited $^1O_2$ by the deuterium-substituted C_4-alkyl group. Were it for classical steric factors alone, the degree of stereocontrol would be about 80%, in accord with the numerous results reported for the steric efficiency exercized by an isopropyl group in the Evans oxazolidinone chiral auxiliary. The additional 20% enhancement derives from vibrational deactivation of $^1O_2$ by the C–H bonds in the proteo derivative ***Z*-1-h$_8$**. Thus, for the deutero substrate ***Z*-1-d$_8$**, only classical steric effects operate (*ca.* 80%), whereas in the proteo derivative ***Z*-1-h$_8$**, both steric factors and physical quenching (20%) cooperate synergistically to afford essentially perfect stereocontrol.

To assess the influence of the *E*/*Z* alkene geometry on the diastereoselectivity in the formation of the dioxetane **2** product, we synthesized the corresponding *E* diastereomer of enecarbamate substrate, namely ***E*-1-h$_8$** from the on-hand ***Z*-1-h$_8$**.‡ Photooxygenation of the enecarbamate ***E*-1-h$_8$** in a manner analogous to that presented in Scheme 3, gave only one dioxetane product ***E*-2-h$_8$**, as determined by ^{1}H-NMR spectroscopy. The dioxetane ***E*-2-h$_8$** was converted to the diol **4** as before and its diastereomeric purity determined by HPLC analysis, which revealed only the diol **4-(*R*,*S*)** product.‡ To rationalize the observed favored direction of the $^1O_2$ approach on the enecarbamate double bond, we inspected the X-ray crystal structures of the related ***E*-1-h$_4$** enecarbamate (unfortunately, a crystal structure of ***E*-1-h$_8$** is not available) with a C_4–*Me* methyl group instead of the here employed C_4–^{i}Pr substituent (Fig. 1).‡

By inference from the crystal structure of the C_4-*Me*-substituted enecarbamate ***E*-1-h$_4$** (Fig. 1) to the corresponding C_4-^{i}Pr derivative ***E*-1-h$_8$**, it is evident that the $C_{3'}$ configuration dictates the orientation of the oxazolidinone carbonyl group with respect to the enecarbamate double bond. In turn, the carbonyl group controls the direction of the $^1O_2$ approach. As revealed in Fig. 1, the C_4-alkyl group is positioned too far away from the double bond to interact with the attacking $^1O_2$. Hence, there is negligible vibrational deactivation by the proteated substituent at the C_4 position! Indeed, for the *E* diastereomer, the carbonyl group directs the $^1O_2$ approach to the face of the double bond without the C_4-alkyl group.

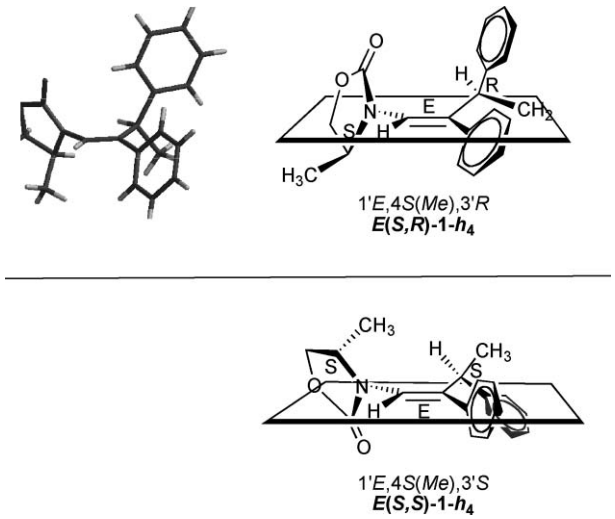


Fig. 1 X-Ray crystal structure of the $C_{3'}(R)/(S)$ epimeric pair of the C_4-*Me*-substituted ***E*-1-h$_4$** enecarbamate; both $C_{3'}$ epimers occupy the same unit cell in the crystal.

In contrast, for the corresponding *Z* isomer, the structure in Scheme 1 reveals that the carbonyl group does not play any appreciable role in directing the approaching singlet oxygen whereas the C_4-alkyl group is positioned to interact with the incoming $^1O_2$ molecule and, consequently, the vibrational deactivation by the C_4-alkyl group counts.

Our current study has convincingly demonstrated that stereoselective vibrational deactivation, a process that is unique to photoreactions, may significantly enhance the stereoselectivity in photooxygenation reactions ($^1O_2$). We anticipate that this new concept of stereocontrol may prove to be general and be of great promise to facilitate chiral selection in a variety of phototransformations.

Acknowledgements

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