Highly Diastereoselective Dioxetane Formation in the Photooxygenation of Enecarbamates with an Oxazolidinone Chiral Auxiliary: Steric Control in the [2 + 2] Cycloaddition of Singlet Oxygen through Conformational Alignment

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Chiral auxiliaries have been successfully employed in controlling the diastereoselectivity of numerous reactions.1 A notoriously difficult problem is the manipulation of the stereochemical course of singlet oxygen (1O2), the smallest possible cyclophile. In the past few years, we have shown that through the appropriate choice of the chiral inductor it is possible to control the stereoselectivity of the [4 + 2] cycloaddition of 1O2.2 For this purpose, optically active 2,2-dimethyl-2,3-dihydro-1H-oxazolidin-5-ones have been equipped with an urea functionality.3 The diastereoselective [4 + 2] cycloaddition of 1O2 has been reported.4 In this paper we report the first example of a chiral-auxiliary-induced [2 + 2] cycloaddition between 1O2 and oxazolidinone-functionalized enecarbamates, which proceeds with complete diastereoselectivity as a result of steric repulsions.

Evans’ chiral auxiliary4 was introduced into the enecarbamate substrate 2 by condensing the 4-alkyl-substituted oxazolidinones with the aldehyde 1, which was prepared in three steps from methyl phenylacetate (Scheme 1). The 1-phenylethyl substituent at the C3 position of the double bond was chosen to minimize the ene reaction since the required coplanar alignment of the only allylic hydrogen atom is encumbered.5 The optically active enecarbamates 2 were photooxygenated at −35 °C with 5,10,15,20-tetrakis(pentafluorophenyl)porphine (TPFPP) as sensitizer and a 800-W sodium lamp as light source. The dioxetanes 3 (Table 1) were obtained exclusively by reduction to the diol 4 by sodium borohydride (DBU), as shown exemplarily for enecarbamate 2c (Scheme 2). From the mass balance was ≥95% at complete conversion in all cases; determined by 1H NMR spectroscopy with dimethyl sulfoxide as internal standard.6 Determined by the area under the characteristic signals in the 1H NMR spectrum directly on the photooxygenated sample (error ±5% of the stated value); in brackets are given the configurations of the dioxetane at the new stereogenic centers.7 CD3OD:CDCl3 (4.1:1).CD3OD:CDCl3 (2.4:1).

The [2 + 2] cycloaddition between the unsubstituted enecarbamate 2a and 1O2 displayed no diastereoselectivity (Table 1, entry 1), whereas the methyl derivative 2b(3S) (Table 1, entry 2) and the isopropyl derivative 2c (entries 3 and 4) afforded the diastereomerically pure dioxetanes [1S,2S]-3c(3R) and [1S,2S]-3e(3S). Within the experimental error of 5%, the other possible diastereomer could not be observed in the 600-MHz 1H NMR spectra of the photooxygenated sample. When the configuration of the oxazolidinone stereogenic center was changed from R to S, the inverse configuration at the new stereogenic centers was obtained (entries 4 and 5). Also, in the polar solvent mixtures CD3OD:CDCl3 (4.1:1) and CD3OD:CDCl3 (2.4:1), the diastereomerically pure dioxetane [1S,2S]-3c(3R) and [1S,2S]-3e(3S) was formed in the photooxygenation of enecarbamate 2c(3R).

The absolute configuration of the dioxetanes 3 was established by reduction to the diol 4 with l-methionine (Scheme 2). From the diol 4, the chiral auxiliary was removed by treatment with NaBH4/DBU to afford the diol 5, as shown exemplarily for dioxetane 3c (see Supporting Information).

The R configuration at the C3 position is known (Scheme 2) from an X-ray diffraction analysis of the (S)-configured enecar-
A stereogenic center is R establishes that 1\textsuperscript{O} 2 attacks exclusively from above (see Scheme 2). The two diastereomers of the diol were separated by silica gel chromatography and the NMR spectra of the bamate diastereomer were identical with those of the diol [the configuration was determined by X-ray analysis (Figure 1)].

Chemical Correlation for the Configurational Assignment of the Dioxetane 3c

Scheme 2. Supporting Information Available: Experimental details (PDF).

Two new stereogenic centers are introduced with complete control of diastereoselectivity; the resulting dioxetane may be derivatized synthetically useful, enantiomerically pure hydroxylated products.

Our unprecedented results for the reaction of oxazolidinone-substituted enecarbamates with 1\textsuperscript{O} 2 demonstrate that an appropriate choice of the chiral auxiliary enables complete diastereofacial control in the [2 + 2] cycloaddition even for 1\textsuperscript{O} 2, the smallest of all cyclophiles. This high diastereoselectivity is rationalized in terms of effective \(\pi\)-facial control through steric shielding by the substituent at the chirality center of the oxazolidinone auxiliary. Two new stereogenic centers are introduced with complete control of diastereoselectivity; the resulting dioxetane may be derivatized to synthetically useful, enantiomerically pure hydroxylated products.

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Supporting Information Available: Experimental details (PDF). This material is available free of charge via the Internet at http://pubs.acs.org.

References

(10) Note that in the chemical correlation (Scheme 2), the 3c(3R) dioxetane was used, whereas the NOE effects (Figure 2) were determined on the 3c(3S) enecarbamate; fortunately, the stereogenic center at the C3 position does not influence the \(\pi\)-facial attack (Scheme 3).