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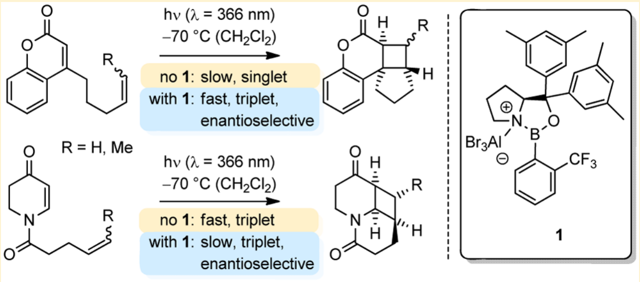
Enantioselective Lewis Acid Catalysis in Intramolecular [2 + 2] Photocycloaddition Reactions: A Mechanistic Comparison between Representative Coumarin and Enone Substrates

Richard Brimioulle, Andreas Bauer, and Thorsten Bach*

Department Chemie and Catalysis Research Center (CRC), Technische Universität München, D-85747 Garching, Germany

Ⓢ *Supporting Information*

ABSTRACT: The intramolecular [2 + 2] photocycloaddition of three 4-(alk-4-enyl)coumarins and three 1-(alk-4-enoyl)-2,3-dihydropyridones was studied in the absence and in the presence of Lewis acids (irradiation wavelength λ = 366 nm). Spectral and kinetic data were collected for the respective parent compounds with a pent-4-enyl and a pent-4-enoyl chain. For the substrates with a methyl group in *cis*- or *trans*-position of the terminal alkene carbon atom (hex-4-enyl and hex-4-enoyl substitution), the stereochemical outcome of the [2 + 2] photocycloaddition was investigated. The mechanistic course of the uncatalyzed coumarin reactions was found to be a singlet pathway, whereas Lewis acid-catalyzed reactions proceeded with higher reaction rates in the triplet manifold. Contrary to that, the dihydropyridones underwent a fast triplet reaction in the absence of the Lewis acid. In the presence of a chiral Lewis acid the reactions slowed down but, due to the high extinction coefficient of the Lewis acid/dihydropyridone complexes at λ = 366 nm, still resulted in high enantioselectivity.



INTRODUCTION

It has been known for a long time that Lewis acids can alter the course of [2 + 2] photocycloaddition reactions. More than a century ago, in 1910, Praetorius and Korn reported that dibenzylideneacetone was converted into a dimeric product when its solution in glacial acetic acid was exposed to sunlight.[1] The reaction, which was almost quantitative (4.5 g crystalline product from 5.0 g substrate), proceeded only in the presence of stoichiometric quantities of uranyl chloride as the Lewis acid. In the absence of the uranyl salt, polymeric material was observed. The reaction could also be performed in the solid state upon irradiation of the 2:1:2 complex of dibenzylideneacetone, $(UO_2)Cl_2$, and acetic acid. The product was suggested to be a cyclobutane with head-to-tail regioselectivity ("truxillic"-type dimer). Later it was shown that $SnCl_4$ shows a similar effect on the [2 + 2] photodimerization of dibenzylideneacetone[2] and the solid-state reaction was further investigated by Alcock et al., who confirmed the structure of the [2 + 2] photodimer.[3] While the influence of metal catalysts on various photochemical reactions was investigated in the 1970s and 1980s,[4] specific studies regarding the influence of Lewis acids on [2 + 2] photocycloaddition reactions of α,β-unsaturated carbonyl compounds in solution were reported by Lewis et al. in 1983.[5] It was found that the photodimerization of coumarin was catalyzed by $BF_3{\cdot}OEt_2$, and the *syn* head-to-tail dimer was obtained as a single product upon irradiation of an equimolar solution of coumarin and $BF_3{\cdot}OEt_2$ in >85% yield. The regioselectivity was different from the uncatalyzed reaction, in which the *syn* head-to-head dimer is the major reaction product.[6] The results were confirmed by Shim et al., who, like Lewis et al., noted the increase in quantum yield upon Lewis acid addition from 10^{-3} (without $BF_3{\cdot}OEt_2$) to 0.13 (with 1 equiv $BF_3{\cdot}OEt_2$).[7] In a simultaneously performed study by Ogawa et al.[8] on the photodimerization of 2-cyclopentenone it was found that the addition of $SnCl_4$ as Lewis acid changes the regioselectivity but leads to a lower reaction rate.[9] In 1989, Lewis and Barancyk observed that the Lewis acid catalysis by $BF_3{\cdot}OEt_2$, and $EtAlCl_2$ was also applicable to [2 + 2] photocycloaddition reactions of coumarin and olefins such as cyclopentene and 2-butene.[10] Based on the lack of stereospecificity in the $EtAlCl_2$-catalyzed reactions at low 2-butene concentration (5-fold excess relative to coumarin), it was concluded that the reaction proceeded under these conditions mainly by a triplet-state mechanism. At higher concentrations a stereospecific singlet pathway was suggested to operate. In a comprehensive time-resolved UV–vis spectroscopy study, Görner and Wolff compiled evidence for the fact that the BF_3-catalyzed photodimerization of coumarin is a triplet process.[11] They showed that the quantum yield for coumarin triplet formation increases from 0.03 to 0.3 upon addition of $BF_3{\cdot}OEt_2$.

The observation of a significant rate increase in coumarin [2 + 2] photocycloaddition chemistry invited attempts to achieve enantioselective reactions[12,13] with appropriately chosen Lewis acids. In 2010, it was found in our laboratories that Lewis acid **1**

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was suitable to enantioselectively (82% ee) catalyze the intramolecular [2 + 2] photocycloaddition of coumarin **2a** (Figure 1).[14] The reaction was later extended to other coumarins (up to 90% ee), and investigations regarding the mode of action of the Lewis acid were performed.[15]

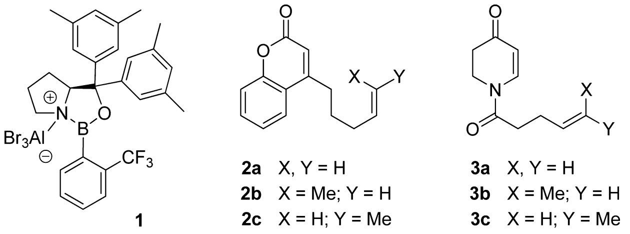

Figure 1. Structures of chiral Lewis acid **1** and of [2 + 2] photocycloaddition precursors **2** and **3**.

Given the above-mentioned observations that Lewis acids slow down the reaction rate of an enone dimerization,[8,9] it was surprising that the same Lewis acid **1** was capable to induce also a high enantioselectivity (88% ee) in the intramolecular [2 + 2] photocycloaddition of dihydropyridone **3a**. This reaction is applicable to related dihydropyridones, and it was successfully employed in the total synthesis of lupin alkaloids.[16] Recently, it was shown in our laboratories that the [2 + 2] photocycloaddition of 3-alkenyloxy-2-cycloalkenones can be performed enantioselectively with an oxazaborolidine-based Lewis acid related to **1**,[17] and it was found by the Sivaguru group that the intramolecular [2 + 2] photocycloaddition of coumarin **1a** and related coumarins can be enantioselectively catalyzed by a chiral Brønsted acid.[18,19]

The purpose of the present study was to disclose the similarities and differences of the two substrate classes **2a** and **3a** in [2 + 2] photocycloaddition reactions. Substrates **2b**/**2c** and **3b**/**3c** were used to investigate the stereochemical reaction course of the photocycloaddition reactions. Stereospecific reactions are indicative of a singlet-state mechanism, while a nonstereospecific transformation is expected for photochemical reactions which occur in the triplet manifold.[20,21] As achiral Lewis acids $BF_3 \cdot OEt_2$, BCl_3, and $EtAlCl_2$ were employed.[22] Results of previous studies are implemented where required but are clearly marked.

■ RESULTS AND DISCUSSION

Spectral Data. Coumarin **2a** is in its physical properties very similar to the parent compound, which has been previously studied extensively.[23] To summarize the most relevant data, coumarin **2a** exhibits (c = 0.8 mM in CH_2Cl_2) two strong UV–vis absorptions at λ = 272 nm (ε =11100 M^{-1} cm^{-1}) and at λ = 313 nm (ε = 6400 M^{-1} cm^{-1}). The extinction coefficients at λ = 300 nm are ε = 5300 M^{-1} cm^{-1} and at λ = 366 nm $\varepsilon \leq 10$ M^{-1} cm^{-1}. At an excitation wavelength of λ = 300 nm there is essentially no fluorescence.[15] Addition of Lewis acids changes the spectra in full agreement with the work of Lewis and Baranczyk.[10] They had determined the equilibrium constant (K) for the coumarin–$EtAlCl_2$ complex in CD_2Cl_2 as 140 M^{-1} at room temperature. The complex showed different UV–vis spectra and a significant fluorescence. The UV–vis spectra for the $EtAlCl_2$-complex of coumarin **2a** at various $EtAlCl_2$ concentrations are shown in the SI in comparison to the same data for 4-methylcoumarin. The absence of defined isosbestic points in the former data set, as compared to the latter, indicates the high photochemical reactivity of the complex (vide infra). The complex **2a**·$EtAlCl_2$ exhibits a strong UV–vis absorption at λ = 313 nm (ε = 15500 M^{-1} cm^{-1}), while the intensity of the short wavelength absorption decreases. The extinction coefficient at λ = 366 nm is ε = 84 M^{-1} cm^{-1}.

Lewis acid **1** is in situ prepared from the respective oxazaborolidine and $AlBr_3$. While satisfactory NMR spectra of the oxazaborolidine were obtained, the Lewis acid itself could—in line with previous experience[24]—not be fully characterized. The solution of **1** in CH_2Cl_2 is orange-colored, and its UV–vis spectrum is depicted in the SI. Upon treatment of coumarin **2a** with Lewis acid **1**, the absorption change in the long wavelength region of the UV–vis spectrum is similar to the $EtAlCl_2$ complex. Due to a very broad band at $\lambda \cong 260$ nm (ε = 4600 M^{-1} cm^{-1}), the long wavelength region appears as a shoulder. The extinction coefficient (10 equiv **1**) at λ = 366 nm is ε = 3500 M^{-1} cm^{-1}.[25] Fluorescence of the complex is observed with an emission maximum at λ = 436 nm.[15]

The intermolecular [2 + 2] photocycloaddition of 2,3-dihydropyridin-4(1*H*)-ones has been studied by the group of Neier,[26] and there is a detailed study on the *N*-methoxycarbonyl analogue of compound **3a** as chromophor in these reactions.[27] However, Lewis acid coordination of this compound class has not been previously investigated. The UV–vis spectrum of **3a** in CH_2Cl_2 (c = 0.5 mM) reveals one strong absorption at 291 nm (ε = 17400 M^{-1} cm^{-1}) and a weak broad absorption at $\lambda \cong 360$ nm (ε = 70 M^{-1} cm^{-1}).[16] Upon addition of $EtAlCl_2$, a new strong band evolves at λ = 343 nm, and the UV–vis spectra reveal an isosbestic point at λ = 311 nm (Figure 2). In this concentration range, Lewis acid coordination occurs at the enone carbonyl oxygen atom but not at the amide carbonyl oxygen atom. Chemical shift changes in the ^{13}C NMR spectra are observed exclusively at the former but not at the latter position (Figure 2).

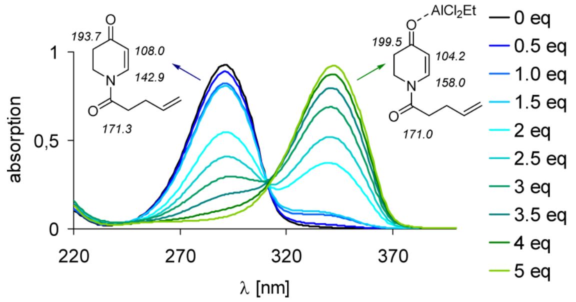

Figure 2. UV–vis spectra of compound **3a** (c = 0.5 mM in CH_2Cl_2) in the presence of variable concentration of $EtAlCl_2$ and selected ^{13}C NMR data for **3a** and its complex with $EtAlCl_2$ (2.2 equiv) in CD_2Cl_2.

The maximum absorption for the Lewis acid-induced band at λ = 343 nm was obtained with 20 equiv $EtAlCl_2$ (ε = 21400 M^{-1} cm^{-1}). With BCl_3 (20 equiv) the band was observed at λ = 348 nm (ε = 24200 M^{-1} cm^{-1}). With chiral Lewis acid **1** (20 equiv) the band appears at λ = 346 nm (ε = 19300 M^{-1} cm^{-1}). The extinction coefficient (10 equiv **1**) at λ = 366 nm is ε = 12600 M^{-1} cm^{-1}. If the concentration of $EtAlCl_2$ was further increased, the absorption maximum was shifted to a slightly shorter wavelength, and a defined isosbestic point could not be longer detected. It appears likely that coordination of a second equivalent $EtAlCl_2$ to the 1:1 complex **3a**·$EtAlCl_2$ becomes feasible at high Lewis acid concentration. UV–vis titration data corroborate this assumption and delivered an equilibrium constant (K) of 4300 M^{-1} for the complex **3a**·$EtAlCl_2$ in CH_2Cl_2 at ambient temperature (see the SI for further details). Apparently, the compound is significantly more Lewis basic than coumarin and shows a much higher affinity to Lewis acids.

Kinetic Studies. Irradiation experiments with substrates **2a** and **3a** were performed at a substrate concentration of 20 mM and at an irradiation wavelength[28] of λ = 366 nm.[29] The reaction solution in CH_2Cl_2 was precooled to −70 °C, and the temperature was kept constant by a cryostat. These conditions were found optimal in previous experiments to achieve the highest enantioselectivity in the presence of Lewis acid **1** (50 mol %). The photocycloaddition reactions proceed for both substrates with excellent diastereoselectivity, and the products are formed as single diastereoisomers. In the absence of a chiral source the racemic products *rac*-**4a** and *rac*-**5a** (Figure 3) are obtained, i.e., there is no selectivity for either enantiomer. The chiral catalyst induces a high enantioselectivity in favor of **4a** and **5a** as major enantiomers (vide infra).[14]

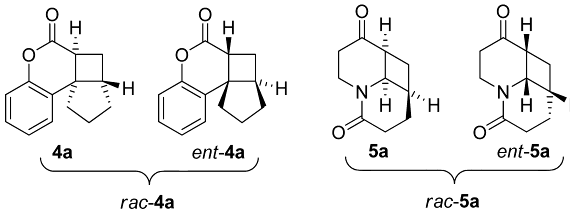

Figure 3. Structures of chiral [2 + 2] photocycloaddition products **4a** and **5a** and their respective enantiomers *ent*-**4a** and *ent*-**5a**.

Substrate **2a** showed a very slow reaction in the absence of the catalyst (Figure 4a). After an irradiation time of 5 h the product concentration was 2.2 mM (11% conversion). Side reactions were not observed, as indicated by the equally low decrease in substrate concentration. In the presence of catalyst **1**, the reaction rate significantly increased (Figure 4b). 50% conversion was achieved after 25 min, and the reaction followed a zero-order rate law in this time interval. Employing a ferrioxalate actinometer[30] to quantify the photon flux and assuming complete photon absorption by the substrate, the quantum yield for the latter reaction was determined as Φ = 0.09. In the former reaction (Figure 4a) a lower barrier for the quantum yield was estimated to be $\Phi \geq 2 \times 10^{-3}$.[31]

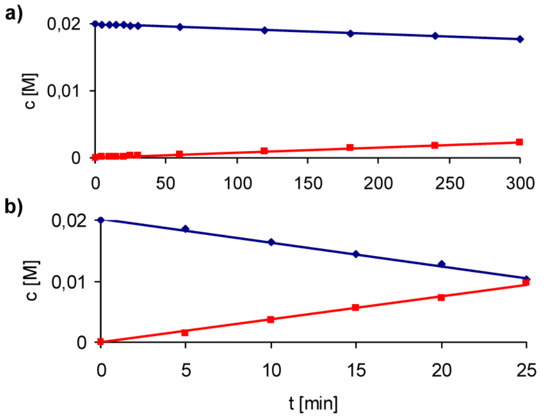

Figure 4. Rate profile for the intramolecular [2 + 2] photocycloaddition of substrate **2a** in the absence (Figure 4a) and in the presence (Figure 4b) of chiral Lewis acid **1** (50 mol %; λ = 366 nm, T = −70 °C, c = 20 mM in CH_2Cl_2).

In stark contrast to substrate **2a**, substrate **3a** underwent a fast [2 + 2] photocycloaddition upon irradiation at λ = 366 nm (Figure 5a). The reaction was complete within 1 h and followed a first-order rate law. No significant background reaction was observed. The quantum yield of the reaction was high, and it was shown to exceed $\Phi \geq 0.23$[31] by ferrioxalate actinometry. For the intermolecular reaction of related dihydropyridones quantum yields between 0.5 and 0.9 have been reported at room temperature.[27] In the presence of Lewis acid **1**, the reaction rate slowed down significantly (Figure 5b). A zero-order reaction was observed, and the conversion after 10 h was ca. 50%. The quantum yield was determined as $\Phi = 4 \times 10^{-3}$.

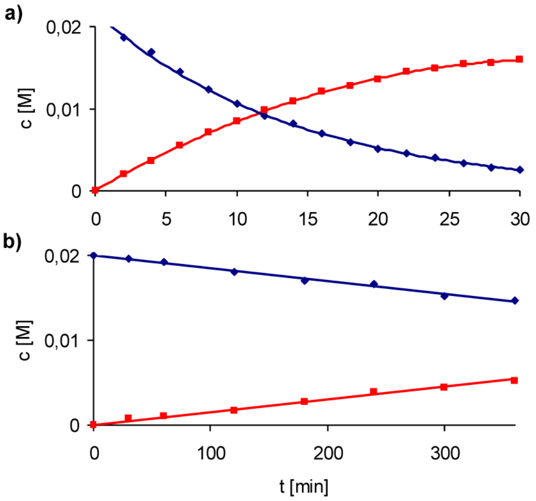

Figure 5. Rate profile for the intramolecular [2 + 2] photocycloaddition of substrate **3a** in the absence (a) and in the presence (b) of chiral Lewis acid **1** (50 mol %; λ = 366 nm, T = −70 °C, c = 20 mM in CH_2Cl_2).

Stereochemical Reaction Course. Irradiation experiments performed with the methyl-substituted substrates **2b**, **2c**, **3b**, and **3c** lead to products which bear an additional stereogenic center as compared to products **4a** and **5a** (Figure 3). While the relative configuration around the cyclobutane is determined by the rigidity of the attached rings, the methyl group at the additional stereogenic center can be positioned either *cis* to the photoanellated ring (products **4b** and **5b**) or *trans* to it (products **4c** and **5c**). In Figure 6, the relative configuration is drawn for one enantiomer of the respective products.

Upon irradiation at λ = 366 nm, substrate **2b** with a *cis*-configuration of the olefinic double bond in the alkenyl tether, reacted slowly to form racemic products *rac*-**4** (Table 1, entries 1 and 2). At −70 °C (entry 1), a conversion of 55% was reached after 22 h. The product was isolated in 53% yield and consisted mainly of *cis*-diastereoisomer *rac*-**4b** (d.r. = 92/8). The relative configuration of the recovered starting material was shown to be essentially unchanged (**2b**/**2c** = 87/13). At ambient temperature (entry 2), the reaction was interrupted after 5 h resulting in 17% yield of *rac*-**4b** (d.r. = 92/8) and in 74% of recovered starting material (**2b**/**2c** = 98/2). If the *trans*-diastereoisomer **2c** was used (entry 3) under the same conditions (λ = 366 nm, ambient temperature), diaster-

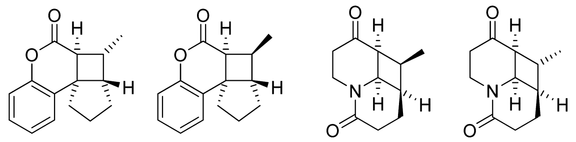
4b **4c** **5b** **5c**

Figure 6. Structures of chiral [2 + 2] photocycloaddition products **4b**, **4c**, **5b**, and **5c**.

Table 1. Yields and Product Configuration for the [2 + 2] Photocycloaddition Reactions of Substrates 2b, 2c, 3b, and 3c in the Presence and Absence of Chiral Lewis Acid 1

entry	substrate[a]	**1** (mol %)	t (h)	yield (%)	d.r.[b]	ee[c] (%)
1	**2b**	—	22	53[d]	92/8	—[e]
2	**2b**	—	5[f]	17[g]	92/8	—[e]
3	**2c**	—	10[f]	22[h]	14/86	—[e]
4	**2b**	50	10	89	38/62	72
5	**2c**	50	10	85	23/77	78
6	**3b**	—	1.5	70[I]	<5/95	—[e]
7	**3c**	—	1.5	75	<5/95	—[e]
8	**3b**	50	20	76	<5/95	87
9	**3c**	50	20	70[j]	<5/95	53

[a] Unless noted otherwise, the reactions were performed under anhydrous and oxygen-free conditions at an irradiation wavelength of λ = 366 nm and at a substrate concentration of 20 mM in CH_2Cl_2 as the solvent at −70 °C. Entries 4 and 5 have been recorded in a previous study.[15] [b] The diastereomeric ratio (d.r. = **4b**/**4c** for entries 1−5, **5b**/**5c** for entries 6−9) was determined by ^1H NMR spectroscopy; the values were confirmed by chiral GC (**4b**/**4c**) and after derivatization by chiral HPLC (**5b**/**5c**). [c] The ee was calculated from the enantiomeric ratio, which in turn was determined for the respective major diastereoisomer (**4c** for entries 4 and 5; **5c** for entries 8 and 9) after derivatization by chiral HPLC. [d] 45% of the starting material (**2b**/**2c** = 87/13) was recovered. [e] Racemic products were obtained. [f] The reaction was performed at ambient temperature. [g] 74% of the starting material (**2b**/**2c** = 98/2) was recovered. [h] 74% of the starting material (**2b**/**2c** = 1/99) was recovered. [I] 27% of the starting material (**3b**/**3c** = >95/5) was recovered. [j] 16% of the starting material (**3b**/**3c** = <5/95) was recovered.

eoisomer *rac*-**4c** was shown to be the major product (d.r. = 14/86), and the starting material was recovered unchanged (**2b**/**2c** = 1/99). The reaction proceeded very slowly as already observed for the uncatalyzed photocycloadditions of coumarins **2a** and **2b**. Addition of chiral Lewis acid changed the situation, and the reactions of substrates **2b** and **2c** were complete after 10 h (entries 4 and 5).[15] Enantiomerically enriched products **4** were obtained. In contrast to the uncatalyzed reactions, both substrates delivered mainly the same product diastereoisomer, i.e., *trans*-product **4c**, in 72% and 78% ee, respectively. Although the diastereomeric ratio for products **4b**/**4c** varied slightly (38/62 vs 23/77), the stereoconvergent reaction course is clearly evident.

Perfect stereoconvergence was observed in all photocycloaddition reactions, in which dihydropyridones **3b** and **3c** were involved (entries 6−9). Irrespective of the substrate configuration, only a single diastereoisomeric product **5c** was observed. In the absence of Lewis acid **1**, the reaction was fast. The conversion after 90 min was 73% for substrate **3b** (entry 6) and quantitative for substrate **3c** (entry 7). Recovered starting material in the former case was shown to be exclusively *cis*-configured (**3b**/**3c** = >95/5). The racemic product *rac*-**5c** was in both cases exclusively *trans*-configured (d.r. = <5/95). In the presence of chiral Lewis acid **1**, the reaction was notably retarded. Substrate **3b** reacted slightly faster (entry 8) than substrate **3c** (entry 9) and was completely converted to *trans*-product **5c** (d.r. = <5/95, 87% ee) after an irradiation time of 20 h. Substrate **3c** (**3b**/**3c** d.r. = <5/95) was partially recovered after 20 h (entry 9) and delivered the product with lower enantioselectivity (53% ee) but also exclusively as the *trans*-product **5c**.

Discussion. A clear mechanistic difference between the coumarin and dihydropyridone substrates in the uncatalyzed [2 + 2] photocycloaddition reaction is the fact that the former substrate class reacts via its singlet state, while the latter substrate class reacts via its triplet state. As a result, stereospecific photocycloaddition products *rac*-**4b** and *rac*-**4c** were obtained from coumarins **2b** and **2c** (Table 1, entries 1−3). The dihydropyridones **3b** and **3c** produced stereoconvergently a single diastereoisomer *rac*-**5c** (Table 1, entries 6 and 7). Both substrate classes absorb weakly at λ = 366 nm, but the dihydropyridones still react efficiently (Figure 5a) because rapid intersystem crossing (ISC) enables them to access the typical reaction manifold of enones. The coumarins decay rapidly to the ground state by internal conversion avoiding an ISC.[23] Lewis acid coordination changes the nature of the respective excited states. The coumarin photocycloaddition becomes rapid (Figure 4b) and occurs with relatively high quantum yield at the triplet hypersurface (Table 1, entries 3 and 4). As pointed out earlier by others,[10,11] the Lewis acid seems to stabilize the S_1 state against internal conversion and facilitates ISC. In the presence of a Lewis acid, the dihydropyridone photocycloaddition remains at the triplet hypersurface (Table 1, entries 8 and 9), but the reaction rate drops significantly (Figure 5b). A possible explanation for the latter effect could be a decreased ISC rate. Lewis acid coordination occurs at the nonbonding oxygen orbitals and lowers their energy. Thus, the triplet energy of the $n\pi^*$ triplet state, which is in typical enones close to the triplet state of the $\pi\pi^*$ triplet state,[21a] is significantly increased. As a consequence, ISC from the S_1 state, which has $\pi\pi^*$ character in the complex (vide infra) is not feasible since the energetically feasible ISC from S_1 ($\pi\pi^*$) to T_1 ($\pi\pi^*$) is symmetry forbidden according to El Sayed's rule.[32]

Regarding the bathochromic spectral shift upon Lewis acid coordination, it is evident that only the respective $\pi\pi^*$ transitions are concerned, while any $n\pi^*$ transition will be shifted hypsochromically or will disappear. Simplistically, the effect is based mainly on a decrease of the energy of the π^* orbitals upon Lewis acid coordination.[33] Indeed, the extent of the bathochromic shift on coumarins and dihydropyridones is comparable for the $\pi\pi^*$ transition. For coumarin **2a**, the absorption at λ = 272 nm (ε = 11100 M^{-1} cm^{-1}) is shifted upon $EtAlCl_2$ coordination to λ = 313 nm (ε = 15500 M^{-1} cm^{-1}). For dihydropyridone **3a**, the absorption at λ = 291 nm (ε = 17400 M^{-1} cm^{-1}) is shifted upon $EtAlCl_2$ coordination to λ = 343 nm (ε = 21400 M^{-1} cm^{-1}). The wavelength difference is thus $\Delta\lambda$ = 43 nm in the former and $\Delta\lambda$ = 52 nm in the latter case. In the former case, however, the shift leads to an overlap with the relatively intense $n\pi^*$ absorption of the uncomplexed substrate at λ = 313 nm (ε = 6400 M^{-1} cm^{-1}), and in essence the bathochromic shift at longer wavelength is detectable but minor. At λ = 366 nm, the absorption of the Lewis acid complex remains low. In stark contrast, the Lewis acid coordination of the dihydropyridone causes a high cross-section $\pi\pi^*$ transition at λ = 366 nm, which is eventually

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responsible for the enantioselective reaction course in the latter reaction. The otherwise rapid reaction of uncomplexed substrate (Figure 4a) is completely suppressed because excitation becomes impossible given its low extinction coefficient. Due to the high association constant of the complex **3a**·$EtAlCl_2$ (vide supra), the percentage of complexed vs uncomplexed substrate in the typical concentration range of the reaction is close to 50%, even at room temperature. Upon initiation of the reaction at λ = 366 nm (Figure 7), the absorption of **3a**·$EtAlCl_2$ is thus 180 times higher than the absorption of uncomplexed substrate **3a**.[34]

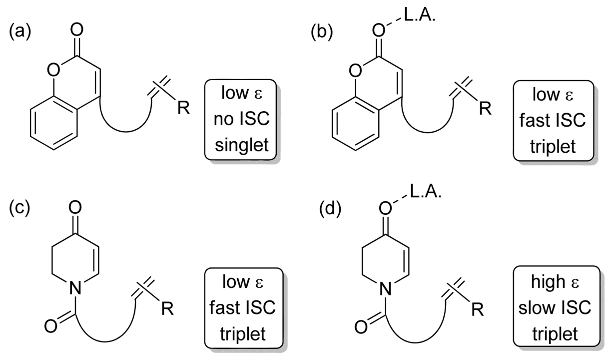

Figure 7. Excited-state properties and reaction pathways for coumarins (a,b) and dihydropyridones (c,d) in the absence and presence of a Lewis acid (L.A.) at λ = 366 nm.

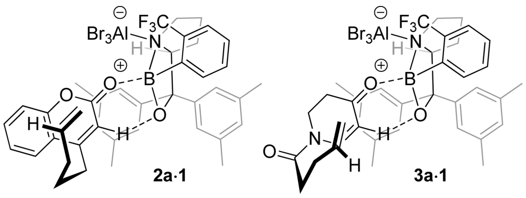

Figure 8. Suggested conformation of the substrates **2a** and **3a** in the complex with Lewis acid **1** prior to the first step of the [2 + 2] photocycloaddition.

The absolute product configuration of enantioselective [2 + 2] photocycloaddition reactions has been elucidated in previous work.[14−16] From these results, the conformations shown in Figure 8 are postulated to be responsible for enantioface differentiation. The additional hydrogen bond between the respective α-CH bond of the carbonyl compound and the oxazaborolidine oxygen atom has been suggested in thermal Lewis acid-catalyzed processes to account for the fixation of the substrate.[35] C−C bond formation is likely to occur first between the internal β-carbon atom of the α,β-unsaturated carbonyl chromophor and the internal carbon atom of the alkene.[36] The absolute configuration is determined in this step. A major difference between **2a·1** and **3a·1** is the fact that the tether which connects the alkene with the chromophor is positioned *exo* to the existing ring in the former case but *endo* in the latter case. The opposite arrangements may be possible but will be unproductive, because the resulting cyclobutane rings would be too strained. According to molecular models a substituent at the terminal carbon atom of the alkene interferes with the *ortho*-trifluoromethylphenyl group at the boron atom if positioned *cis* in the coumarin case or *trans* in the dihydropyridone case. Indeed, the enantioselectivity drops for substrates of this type as seen for the reaction of coumarin **2b** (Table 1, entry 4) and dihydropyridone **3c** (Table 1, entry 9).

Given the importance of enone [2 + 2] photocycloaddition reaction chemistry[37] for organic synthesis,[38] the observation that chiral Lewis acids can render these reactions enantioselectively is undoubtedly more important than the relatively limited enantioselective Lewis acid catalysis of coumarin photocycloaddition reactions. In search for ways to improve the catalytic performance of chiral Lewis acids, it is clear from the present study that it would be desirable to identify enone substrates, which show a relatively slow [2 + 2] photocycloaddition in a wavelength region, which can be accessed by Lewis acid coordination and by a bathochromic shift of the $\pi\pi^*$ transition. More importantly, based on the assumption that the rate decrease caused by the Lewis acid is linked to a slow ISC, the ISC rate to the enone triplet needs to be enhanced. These considerations should be useful for the development of new chiral Lewis acids.

■ CONCLUSION

In summary, this investigation has revealed new information regarding the interaction of Lewis acids and [2 + 2] photocycloaddition substrates. Most notably, the hypothesis that the complexation of Lewis acids to typical enone substrates has other photochemical consequences than the complexation to coumarins was further corroborated. In the former case, the [2 + 2] photocycloaddition proceeds in the absence and in the presence of Lewis acids on the triplet hypersurface. In the latter case, the Lewis acid induces a change of the reaction mode (singlet/triplet), and it induces a rate increase. As already discussed in previous work,[15] we assign the rate increase by the Lewis acid to several factors, i.e., a stabilization of the singlet state, a higher ISC rate, and an enhanced absorption at the irradiation wavelength (λ = 366 nm). For dihydropyridone **3a** as a typical enone substrate, the mode of action of the chiral Lewis acid rests exclusively on the fact that the strong $\pi\pi^*$ transition of the complex overlays with the weak $n\pi^*$ transition of the uncomplexed substrate. This overlay channels the reaction in an enantioselective manifold with a highly selective C−C bond formation occurring in the Lewis acid complex. The enantioselective reaction occurs at the expense of a lower reaction rate, which is proposed to be due to a decreased ISC rate.

■ ASSOCIATED CONTENT

Ⓢ Supporting Information

Detailed experimental procedures, characterization data for new compounds, rate profiles, and UV−vis data. This material is available free of charge via the Internet at http://pubs.acs.org.

■ AUTHOR INFORMATION

Corresponding Author

*thorsten.bach@ch.tum.de

Notes

The authors declare no competing financial interest.

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