J|A|C|S
ARTICLES
Published on Web 02/19/2005

Asymmetric Induction during Yang Cyclization of α-Oxoamides: The Power of a Covalently Linked Chiral Auxiliary Is Enhanced in the Crystalline State

Arunkumar Natarajan,[†] Joel T. Mague, and V. Ramamurthy*,[†]

Contribution from the Department of Chemistry, Tulane University, New Orleans, Louisiana 70118

Received October 1, 2004; E-mail: murthy1@miami.edu

Abstract: γ-Hydrogen abstraction has been revealed to be the primary photoprocess in the crystalline state of α-oxoamides through photochemical and X-ray structural studies. The outstanding ability of a covalent chiral auxiliary in generating asymmetric induction in the photoproduct β-lactam has been established with 10 examples. We have shown that the crystal lattice preorganizes the reactant molecules toward a single diastereomer of the β-lactam and prevents large motions of the 1,4-diradical intermediate that would result in the loss of stereochemical memory. A rare single-crystal-to-single-crystal transformation path of one of the examples investigated establishes the direct correlation between the stereochemistries of the reactant and the product.

Introduction

Traditionally, chirality control of a photochemical reaction is a challenging task.[1] Asymmetric induction in a photochemical reaction in solution with a maximum enantiomeric excess (ee) of 2% has been achieved with circularly polarized light in a limited number of examples.[2] Following the benchmark report on geometric photoisomerization of 1,2-diphenylcyclopropane by Cole and Hammond,[3] studies on photosensitization with chiral sensitizers in solution have led to moderate success.[4] While most photoreactions with chiral sensitizers have had ee $< 15\%$, the best result of 49% ee under ambient conditions has been achieved during the sensitized photoisomerization of achiral *cis*-cyclooctene to chiral *trans*-cyclooctene.[5] Rationally designed chiral templates yield respectable chiral induction (98% ee) during photocycloaddition reactions of lactams.[6,7] This promising approach has so far been limited to a few systems. In contrast to studies in solution, those in the crystalline state have been more rewarding. For example, irradiation of a few pure chiral crystals resulting from achiral molecules leads to a quantitative ee.[8−10] The limited general applicability of this method due to a lack of understanding of the factors controlling crystallization of achiral molecules in a chiral space group has been overcome through the use of ionic chiral auxiliaries. The latter strategy of an achiral reactant ionically bonded to a chiral amine ensures crystallization of the reactant salt in a chiral space group and thus affords photoproducts in >90% diastereomeric excess (de).[11,12] Yet another successful approach relying on organic hosts containing chiral centers (e.g., deoxycholic acid, cyclodextrin, 1,6-bis(*o*-chlorophenyl)-1,6-diphenyl-2,4-diyne-1,6-diol, tartaric acid derivatives, etc.) is limited in its success to guests that can form a crystalline host−guest complex.[13,14] Identifying the correct host in a given case could lead to a rewarding chiral induction of 100% ee.[15] Recently, we have established the use of achiral zeolites as hosts in bringing about asymmetric induction in photoreactions.[16,17] Diastereomeric excesses as high as 90% and enantiomeric excesses up to 78% have been obtained with selected systems within zeolites.

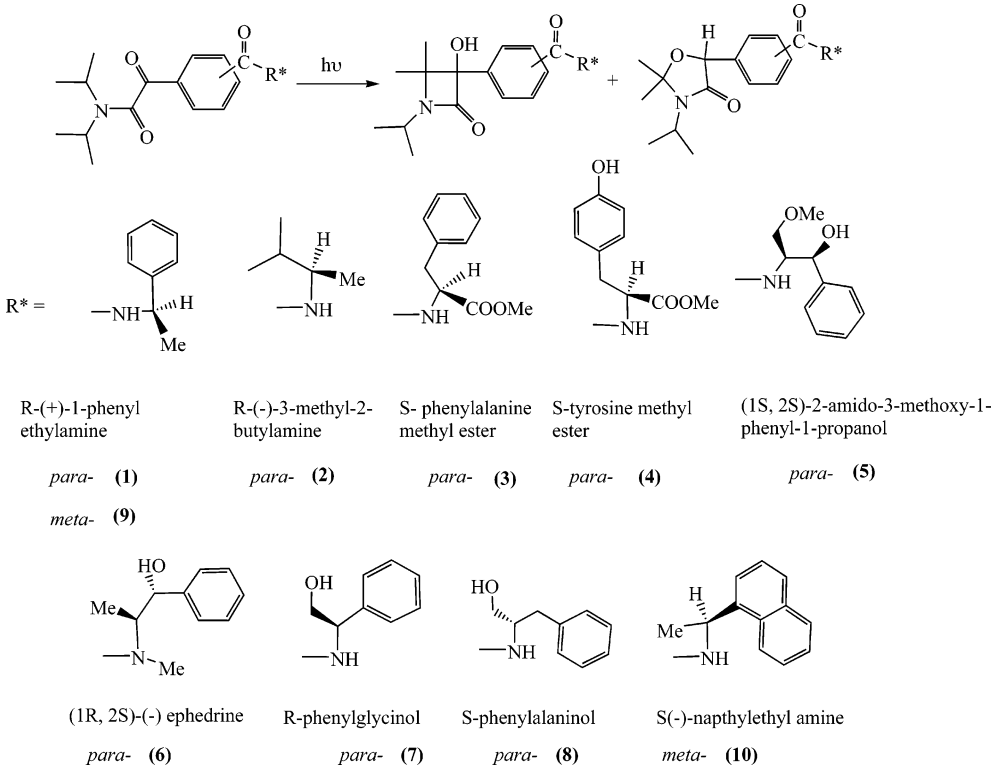
One of the best methods of asymmetric induction in solution making use of a "removable covalent chiral auxiliary" works best during cycloaddition of enones to olefins.[18,19] To our

[†] Present address: Department of Chemistry, University of Miami, Coral Gables, FL 33124.

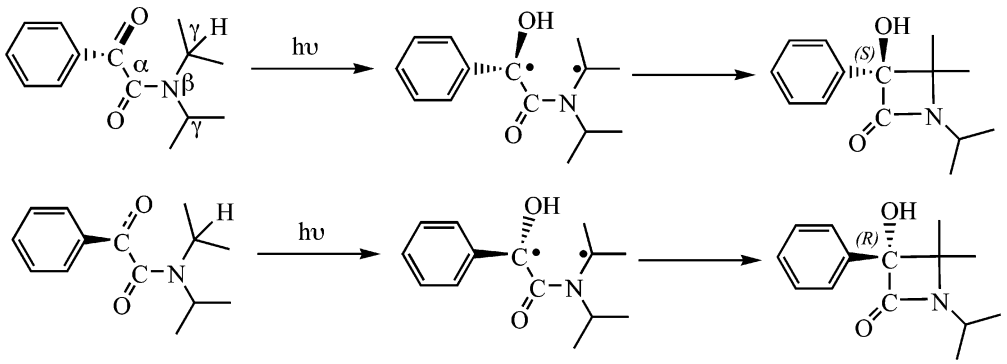
(1) *Chiral Photochemistry*; Inoue, Y., Ramamurthy, V., Eds.; Marcell Dekker: New York, 2004; Vol. 11.
(2) Rau, H. In *Chiral Photochemistry*; Ramamurthy, V., Ed.; Marcell Dekker: New York, 2004; Vol. 11, p 1.
(3) Hammond, G. S.; Cole, R. S. *J. Am. Chem. Soc.* **1965**, *87*, 3256−3257.
(4) Inoue, Y. In *Chiral Photochemistry*; Ramamurthy, V., Ed.; Marcell Dekker: New York, 2004; Vol. 11, p 129.
(5) Inoue, Y.; Wada, T.; Asaoka, S.; Sato, H.; Pete, J.-P. *Chem. Commun.* **2000**, 251.
(6) Grosch, B.; Orlebar, C. N.; Herdtweck, E.; Massa, W.; Bach, T. *Angew. Chem., Int. Ed.* **2003**, *42*, 3693.
(7) Grosch, B.; Bach, T. In *Chiral Photochemistry*; Inoue, Y., Ramamurthy, V., Eds.; Marcel Dekker: New York, 2004; Vol. 11, p 315.
(8) Elgavi, A.; Green, B. S.; Schmidt, G. M. J. *J. Am. Chem. Soc.* **1973**, *95*, 2058.
(9) Sakamoto, M. *Chem.−Eur. J.* **1997**, *3*, 684.
(10) Green, B. S.; Lahav, M.; Rabinovich, D. *Acc. Chem. Res.* **1979**, *12*, 191.
(11) Scheffer, J. R. *Can. J. Chem.* **2001**, *79*, 349.
(12) Scheffer, J. R. In *Chiral Photochemistry*; Ramamurthy, V., Ed.; Marcell Dekker: New York, 2004; Vol. 11, p 463.
(13) Toda, F.; Tanaka, K.; Miyamoto, H. In *Understanding and Manipulating Excited-State Processes*; Schanze, K. S., Ed.; Marcel Dekker: New York, 2001; Vol. 8, p 385.
(14) Toda, F. *Acc. Chem. Res.* **1995**, *28*, 480.
(15) Zimmerman, H. E.; Alabugin, I. V.; Smolenskaya, V. N. *Tetrahedron* **2000**, *56*, 6821.
(16) Sivaguru, J.; Natarajan, A.; Kaanumalle, L. S.; Shailaja, J.; Uppili, S.; Joy, A.; Ramamurthy, V. *Acc. Chem. Res.* **2003**, *36*, 509.
(17) Joy, A.; Ramamurthy, V. *Chem.−Eur. J.* **2000**, *6*, 1287.
(18) Pete, J.-P. In *Advances in Photochemistry*; Von Bunan, G., Ed.; John Wiley & Sons: New York, 1996; Vol. 21, p 135.
(19) Pete, J.-P.; Hoffmann, N. In *Chiral Photochemistry*; Ramamurthy, V., Ed.; Marcell Dekker: New York, 2004; Vol. 11, p 179.

10.1021/ja043999p CCC: $30.25

Scheme 1



Scheme 2



knowledge there are only two reports of the use of a covalent chiral auxiliary in providing asymmetric induction in the crystalline state.[20,21] In fact both reports imply that this method is less general. The less general nature of this method is clear from the good asymmetric induction of 87% during photocyclization of 2,4,6-triisopropylbenzophenones in the crystalline state with only one of the four chiral auxiliaries examined and likewise in the case of 2-benzoyladamantane-2-carboxylic acid derivative the de of 98% with one of the two chiral auxiliaries, with the other leading to the Yang cyclization product in low de (18%).[20,21] These reports prompted us to examine the general value of the covalent chiral auxiliary during solid-state photoreactions. We have investigated 10 α-oxoamides covalently linked with chiral auxiliaries to study the influence of a remote chiral auxiliary on asymmetric induction in the Yang cyclization product β-lactam.

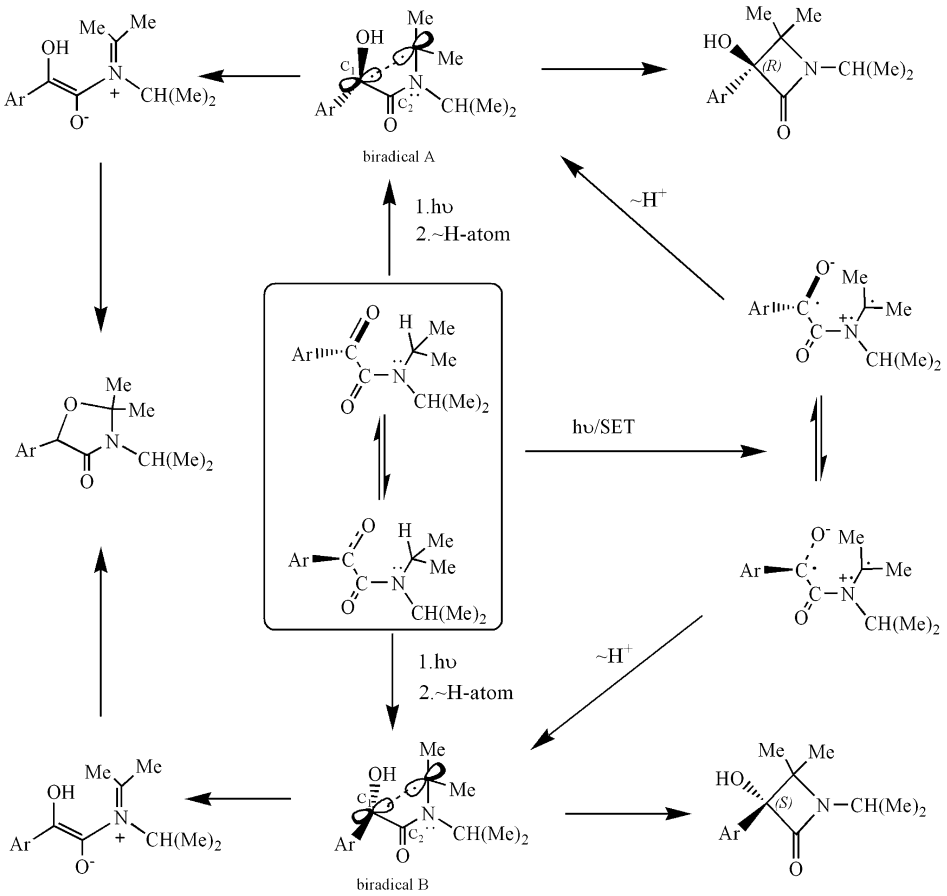
(20) Cheung, E.; Netherton, M. R.; Scheffer, J. R.; Trotter, J.; Zenova, A. *Tetrahedron Lett.* **2000**, *41*, 9673.
(21) Ito, Y.; Kano, G.; Nakamura, N. *J. Org. Chem.* **1998**, *63*, 5643.

Results and Discussion

We have undertaken photochemical and X-ray structural investigations of α-oxoamides **1**−**10** (Scheme 1) that undergo γ-hydrogen (with respect to the benzylic carbonyl) abstraction in the crystalline state. As shown in Scheme 2 abstraction of the γ-hydrogen leads to β-lactams in which a new chiral center is generated at the benzylic carbon. Earlier reports on mechanistic and asymmetric induction studies on α-oxoamide[22−26] and available literature on the use of ionic chiral auxiliaries on these systems[27] allowed us to evaluate the effectiveness of covalent chiral auxiliaries in α-oxoamides in the crystalline state. Further,

(22) Aoyama, H.; Hasegawa, M.; Watabe, M.; Shiraishi, H.; Omote, Y. *J. Org. Chem.* **1978**, *43*, 419.
(23) Aoyama, H.; Sakamoto, M.; Omote, Y. *J. Chem. Soc., Perkins Trans. 1* **1981**, 1357.
(24) Aoyama, H.; Sakamoto, M.; Kuwabara, K.; Yoshida, K.; Omote, Y. *J. Am. Chem. Soc.* **1983**, *105*, 1958.
(25) Wang, R.; Chen, C.; Duesler, E.; Mariano, P. S. *J. Org. Chem.* **2004**, *69*, 1215.
(26) Chesta, C. A.; Whitten, D. G. *J. Am. Chem. Soc.* **1992**, *114*, 2188.
(27) Natarajan, A.; Wang, K.; Ramamurthy, V.; Scheffer, J. R.; Patrick, B. *Org. Lett.* **2002**, *4*, 1443.

Scheme 3



we believed that geometrical data based on X-ray crystal structure studies would help resolve the controversy concerning the nature of the primary photoreaction (hydrogen abstraction vs electron transfer, Scheme 3) during the conversion of α-oxoamides to β-lactams.[28−37]

A mixture of β-lactam and oxazolidinone was obtained from all 10 α-oxoamides following irradiation in solution, and asymmetric induction in the β-lactam product was negligible (Table 1, Scheme 1). Remarkably, the β-lactam was the exclusive product of irradiation of **1**−**10** as crystals, and in several cases the reaction could be carried out to total conversion. Despite the slow photoreaction of **10** due to absorption by the chiral auxiliary (naphthyl unit), the asymmetric induction was excellent (de = 99%). With all 10 α-oxoamide crystals at <20% conversion β-lactams with >80% de were obtained. Our observation of decreased de in several cases with progressive conversion has been witnessed earlier in solid-state reactions and therefore is not unusual. In solid-state reactions this is believed to be due to the disruption of the reactant's long-range order in the crystalline state by accumulation of products.[38] Recently, solid-state reactions have been established to proceed in stages, and it is suggested that products from original crystals and the crystals that contain the product molecules adjacent to

Table 1. Asymmetric Induction in the β-Lactam Product Formed during Solution and Solid-State Irradiations of Oxoamides **1**−**10**

oxoamide	time of irradiation (min)	conversion (%)	% de in solid state[b]	% de in solution[a]
1	50	98	>99A	2B
2	10	22	96B	2A
	45	100	79B	
3	7	7	82A	2B
	25	37	70A	
4	10	14	>99B	3B
	30	70	87B	
5	5	15	85B	5A
	15	60	78B	
6	60	70	91B	3B
	120	100	87B	
7	10	60	93B	5B
	30	80	87B	
8	30	75	95B	10B
9	10	17	80A	0
	60	74	48A	
10	1200	4	>99B	2A

[a] Solution irradiation was done in CH_3CN for compounds **1** and **3**−**10**; that for **2** was done in benzene. [b] A refers to the first peak eluted in HPLC; B refers to the second peak eluted in HPLC.

(28) Aoyama, H.; Hasegawa, T.; Omote, Y. *J. Am. Chem. Soc.* **1979**, *101*, 5343.
(29) Asahi, T.; Nakamura, M.; Kobayashi, J.; Toda, F.; Miyamoto, H. *J. Am. Chem. Soc.* **1997**, *119*, 3665.
(30) Toda, F.; Tanaka, K.; Yagi, M. *Tetrahedron* **1987**, *43*, 1495.
(31) Hashizume, D.; Kogo, H.; Sekine, A.; Ohashi, Y.; Miyamoto, H.; Toda, F. *J. Chem. Soc., Perkin Trans. 2* **1996**, 61.
(32) Toda, F.; Miyamoto, H. *J. Chem. Soc., Perkins Trans. 1* **1993**, 1129.
(33) Sekine, A.; Hori, K.; Ohashi, Y.; Yagi, M.; Toda, F. *J. Am. Chem. Soc.* **1989**, *111*, 697.
(34) Toda, F.; Miyamoto, H.; Matsukawa, R. *J. Chem. Soc., Perkin Trans. 1* **1992**, 1461.
(35) Toda, F.; Miyamoto, H.; Kanemoto, K. *Chem. Commun.* **1995**, 1719.
(36) Toda, F.; Miyamoto, H.; Koshima, H.; Urbanczyk-Lipkowska, Z. *J. Org. Chem.* **1997**, *62*, 9261.
(37) Aoyama, H.; Miyazaki, K.-I.; Sakamoto, M.; Omote, Y. *Tetrahedron* **1987**, *43*, 1513.
(38) Keating, A. E.; Garcia-Garibay, M. A. In *Molecular and Supramolecular Photochemistry*; Schanze, K. S., Ed.; Marcel Dekker: New York, 1998; p 195.

Table 2. Crystallographically Derived γ-Hydrogen Abstraction Parameters for Oxoamides[a] **1**−**10**

oxoamide	space group	*d* (Å)	ω (deg)	Δ (deg)	θ (deg)	torsion angle (deg)
1	$P2_1$	2.814	50.89	52.90	117.87	90.36
		5.077	20.95	54.00	50.08	
2	$P2_12_12_1$	2.776	51.35	53.97	118.28	89.55
		5.066	19.94	54.57	49.99	
3	$P2_1$	2.618	56.08	60.18	128.03	−89.51
		5.130	21.31	51.75	50.44	
4	$P2_1$	2.562	53.34	59.04	122.58	−86.99
		5.091	17.88	53.00	51.32	
5	$P2_12_12_1$	2.766	50.76	53.31	116.77	81.83
		5.025	19.67	56.10	50.01	
6	$P2_1$	2.804	51.51	55.94	114.85	86.48
		5.030	20.21	54.07	49.93	
7	$P2_1$	2.662	52.71	58.57	119.44	88.12
		5.034	17.19	56.99	51.27	
9[b]	$P2_1$	2.713	53.66	61.66	113.32	−69.12
		4.850	15.92	64.63	52.30	−75.90
		2.686	55.02	61.23	117.46	
		4.956	18.45	59.74	52.01	
10	$P2_1$	2.737	52.99	55.30	127.39	−100.00
		5.214	20.66	46.75	48.20	
av **1**−**10**[b]		2.71 ± 0.08	52.9 ± 1.7	57.2 ± 3.3	119.6 ± 4.95	
av lit. value		2.64 ± 0.08	53.7 ± 9.7	81.96 ± 8.14	115.52 ± 2.8[c]	
ideal value		2.72	0	90−120	180	

[a] See Figure 1 for definitions of the parameters. [b] Two independent molecules in the asymmetric unit; average based on Scheffer's 57 examples. [c] Average based on Scheffer's 40 examples (θ not calculated for 17 examples): Leibovitch, M.; Olovsson, G.; Scheffer, J. R.; Trotter, J. *J. Am. Chem. Soc.* **1998**, *120*, 12755. Scheffer, J. R.; Scott, C. In *CRC Handbook of Photochemistry and Photobiology*, 2nd ed.; Horspool, W., Lenci, F., Eds.; CRC Press: Boca Raton, FL, 2004; Vol. 54, pp1−25. Ihmels, H.; Scheffer, J. R. *Tetrahedron* **1999**, *55*, 885.

the reactant molecules may not yield the same products.[39,40] Given this literature knowledge, the noteworthy photobehavior of *p*-(*R*)-phenylethylamide **1** was that the de in the β-lactam product remained constant (100%) even at 100% conversion. As expected the *p*-(*S*)-phenylethylamide as the chiral auxiliary gave the opposite diastereomer in 100% excess. The importance of the crystalline medium is obvious in recognizing that the same chiral auxiliaries have a negligible effect in solution (de < 5%).

To gain insight into the factors that control the photobehavior of α-oxoamides **1**−**10** in the crystalline state, X-ray crystal structures of nine of the compounds were determined. Single crystals of α-oxoamide **8** suitable for X-ray studies could not be obtained. In Table 2 the geometrical parameters[12,41−43] derived from X-ray data for hydrogen abstraction (Figure 1) in α-oxoamides are provided. Also included are the average values based on 54 ketones undergoing γ-hydrogen abstraction reported by Scheffer's group.[12,41−43] In α-oxoamides **1**−**10** one of the two abstractable γ-hydrogens is closer to the reactive carbonyl group, and we believe that the closer hydrogen is the one that is being abstracted in the crystalline state. Except for the CO---H distance, all other parameters are slightly far from ideal values.[12,41−43] Such deviations could be due to differences in structure between the ground state (X-ray data that are used to correlate the reactivity) and the excited state (from which the reaction occurs). Closeness in hydrogen abstraction parameters for α-oxoamides with numerous ketones[12,41−43] reported in the literature (Table 2) prompts us to suggest that the primary process during cyclization of α-oxoamides to β-lactams is the γ-hydrogen abstraction (Scheme 3). Mariano and co-workers have reached a similar conclusion for photoreactions of *N*,*N*-dialkyl-α-oxoamides.[25]

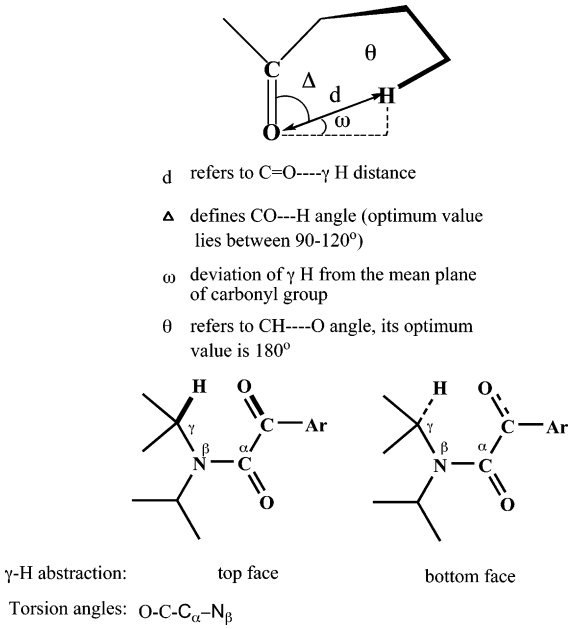


Figure 1. Definition of geometrical parameters *d*, Δ, *ω*, and *θ* for intramolecular γ-hydrogen abstraction.

In general, the chirality of the β-lactam product is decided at the stage of the ring closure of the 1,4-diradical intermediate (Scheme 3), i.e., to which face of the prochiral benzylic radical center the γ-carbon radical adds. In media where the equilibrium between the two rotomers of the diradical (diradicals A and B in Scheme 3) is not reached, the chirality would be decided at the hydrogen abstraction stage itself. Note that, as illustrated in Figure 1, the torsion angle O=C−C_α−N_β in α-oxoamide could be positive or negative, and such a possibility leads to abstraction of the isopropyl hydrogen from the top or bottom phase of the

(39) Zimmerman, H. E.; Nesterov, E. E. *Acc. Chem. Res.* **2002**, *35*, 77.
(40) Zimmerman, H. E.; Nesterov, E. E. *J. Am. Chem. Soc.* **2002**, *124*, 2818.
(41) Ihmels, H.; Scheffer, J. R. *Tetrahedron* **1999**, *55*, 885.
(42) Gudmundsdottir, A. D.; Lewis, T. J.; Randall, L. H.; Scheffer, J. R.; Rettig, S.; Trotter, J.; Wu, C.-H. *J. Am. Chem. Soc.* **1996**, *118*, 6167.
(43) Leibovitch, M.; Olovsson, G.; Scheffer, J. R.; Trotter, J. *J. Am. Chem. Soc.* **1998**, *120*, 12755.

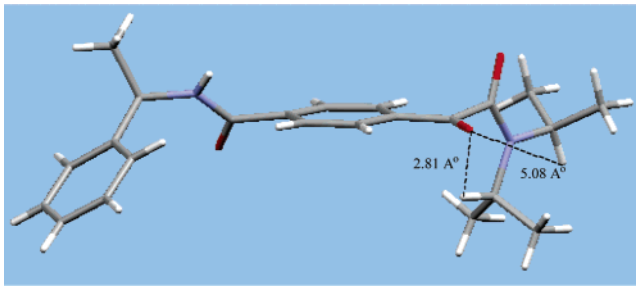


Figure 2. Oxoamide **1** showing one independent molecule in the asymmetric unit. Note the two abstractable γ-hydrogens are at different distances from the carbonyl chromophore.

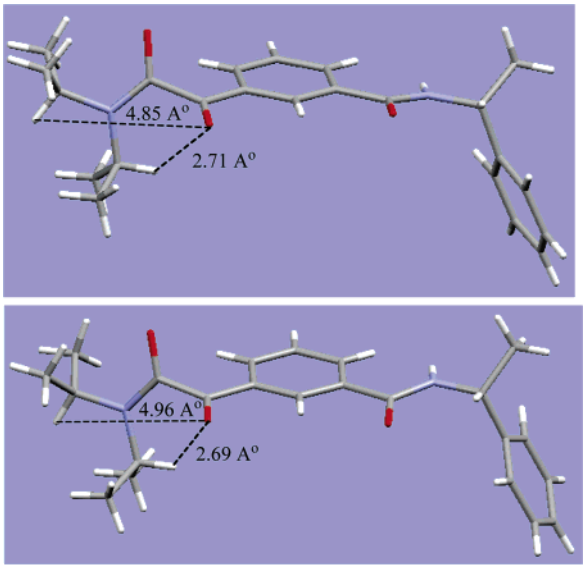


Figure 3. Oxoamide **9** showing two independent molecules in the asymmetric unit which are not related by a plane of symmetry.

carbonyl, leading to two diradical rotomers, A and B. Under ideal conditions both rotomers of the reactant α-oxoamide would be present in equal amounts, leading to the β-lactam with 0% ee (Scheme 2). Clearly, in the crystalline state this is not the case, and exclusive formation of a single diastereomer suggests that the hydrogen abstraction occurs preferentially from one rotomer of the reactant α-oxoamide. This is possible only when all molecules in the reactant crystal are frozen in a homochiral conformation; i.e., all have the same O═C−C_α−N_β torsion angle. In the crystals of eight of the systems there is a single independent molecule in the asymmetric unit, indicating that all molecules in the crystal adopt the same conformation. As a representative, the structure of *p*-(*R*)-phenylglycinol amide **7** is shown in Figure 2.[44] On the basis of the distance between the carbonyl oxygen and the two abstractable isopropyl hydrogens (see also Table 1), it is clear that only one would be preferentially abstracted. Further, every molecule in the reactant crystal has the same O═C−C_α−N_β torsion angle (Table 2), suggesting that the geometry of the reactive C═O with respect to the γ-hydrogen is fixed, prompting the photoreaction in the crystal to be diastereoselective. Despite having two independent molecules per asymmetric unit, α-oxoamide **9** gave the β-lactam product in 80% de. Careful analysis of the structure (Figure 3), especially the dihedral angles (O═C−C_α−N_β and OC−C_α−C_β−C_γ) for the two independent molecules, reveals that the reactive carbonyl is tilted toward the same abstractable isopropyl hydrogen in both molecules. Note that the above dihedral angles for molecule 1, −75.9° and −7.9°, and molecule 2, −69.1° and −15.9°, are fairly close and more importantly in the same direction. The geometrical parameters listed in Table 2 (Figure 1) for γ-hydrogen abstraction for compounds **1**−**7**, **9**, and **10** clearly bring out the preference for abstraction of one of the two hydrogens.

The covalent chiral auxiliary method reported here compares well with the established ionic chiral auxiliary approach.[11,12] Excellent de's (>85%) in the β-lactam product have been reported with five α-oxoamides linked with ionic chiral auxiliaries.[27] Four crystal structures reported by Scheffer's group are clearly suggestive of the chiral auxiliary's role in ensuring crystallization of each molecule in a chiral space group. In the current study the covalent chiral auxiliary assumes a similar role to result in asymmetric induction in all nine systems investigated. As revealed by X-ray structural data for nine crystals, the remote chiral auxiliary orients the molecules to crystallize in a chiral space group (Table 2, $P2_1$ or $P2_12_12_1$) that forces them to adopt a homochiral conformation which predisposes them to react diastereoselectively. The absence of direct interaction between the chiral auxiliary and the photoreactive carbonyl chromophore in all of the structures is indicative of the chiral auxiliary passively preorganizing the reactive α-oxoamides toward a single diasteromer of the β-lactam product.

During irradiation of the *p*-(*R*)-(+)-phenylethylamide of *N*,*N*-diisopropyl-α-oxoamide-4-carboxylic acid **1**, the crystal remained intact throughout the course of the reaction and the de obtained in the β-lactam product was 100%, suggesting that the photoreaction might belong to the rare single-crystal-to-single-crystal category.[43,45−60] To explore this possibility, the structure of the reactant crystal was determined prior to irradiation and at 20%, 50%, 80%, and 100% conversions.[61] To monitor the integrity of the crystal with respect to conversion, several single crystals were irradiated for various times and the conversion was monitored by analyzing the product by HPLC after the crystal was dissolved in a suitable solvent while yet another single crystal from this batch was chosen for X-ray structural analysis. Crystallinity was maintained at all stages of the reaction. The structures at various stages of irradiation are

(44) Bruno, I. J.; Cole, J. C.; Edgington, P. R.; Kessler, M. K.; Macrae, C. F.; McCabe, P.; Pearson, J.; Taylor, R. *Acta Crystallogr.* **2001**, *B58*, 815.
(45) Ohasi, Y.; Sakai, Y.; Sekine, A.; Arai, Y.; Ohgo, Y.; Kamiya, N.; Iwasaki, H. *Bull. Chem. Soc. Jpn.* **1995**, *68*, 2517.
(46) Leibovitch, M.; Olovsson, G.; Scheffer, J. R.; Trotter, J. *J. Am. Chem. Soc.* **1997**, *119*, 1462.
(47) Sakamoto, M.; Takahashi, M.; Kamiya, K.; Yamaguchi, K.; Fujita, T.; Watanabe, S. *J. Am. Chem. Soc.* **1996**, *118*, 10664.
(48) Hosomi, H.; Ito, Y.; Ohba, S. *Acta Crystallogr., B* **2000**, *B56*, 682.
(49) Hosomi, H.; Ohba, S.; Tanaka, K.; Toda, F. *J. Am. Chem. Soc.* **2000**, *122*, 1818.
(50) Yamamoto, S.; Matsuda, K.; Irie, M. *Angew. Chem., Int. Ed.* **2003**, *42*, 1636.
(51) Morimoto, M.; Kobatake, S.; Irie, M. *Adv. Mater.* **2002**, *14*, 1027.
(52) Kobatake, S.; Morimoto, M.; Asano, Y.; Murakami, A.; Nakamura, S.; Irie, M. *Chem. Lett.* **2002**, 1224.
(53) Kobatake, S.; Tuchida, K.; Tsuchida, E.; Irie, M. *Chem. Commun.* **2002**, 2804.
(54) Shibata, K.; Muto, K.; Kobatake, S.; Irie, M. *J. Phys. Chem. A* **2002**, *106*, 209.
(55) Irie, M.; Kobatake, S.; Horichi, M. *Science* **2001**, *291*, 1769.
(56) Irie, M.; Lifka, T.; Kobatake, S.; Kato, N. *J. Am. Chem. Soc.* **2000**, *122*, 4871.
(57) Ohba, S.; Hosomi, H.; Ito, Y. *J. Am. Chem. Soc.* **2001**, *123*, 6349.
(58) Devic, T.; Batail, P.; Avarvari, N. *Chem. Commun.* **2004**, 1538.
(59) Hosomi, H.; Ito, Y.; Ohba, S. *Acta Crystallogr.* **1998**, *B54*, 907.
(60) Harada, J.; Ueksua, H.; Ohashi, Y. *J. Am. Chem. Soc.* **1999**, *121*, 5809.
(61) Farrugia, L. J. *J. Appl. Crystallogr.* **1997**, *30*, 565.

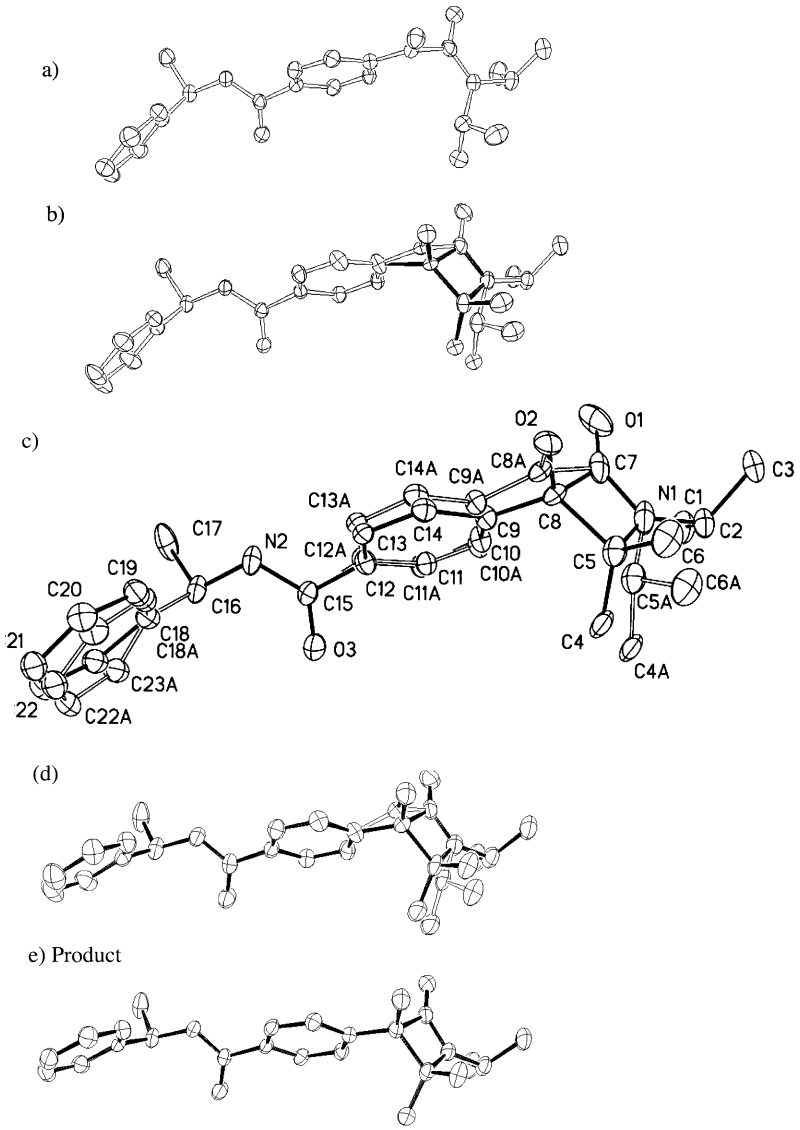


Figure 4. Molecular structure of oxoamide **1** and product β-lactam at (a) 0%, (b) 20%, (c) 50%, (d) 80%, and (e) 100% conversion. Structures are shown with thermal ellipsoids at the 50% probability level.

provided in Figure 4. The structure at 50% conversion is particularly revealing (Figure 4c). It is clear that there are modest changes in the positions of all atoms except those of C5 and C8 carbons (the ones that are involved in the reaction) and the phenyl carbons. The photoproduct seems to fit quite well in the lattice site of the reactant. The packing arrangements and the cell parameters for the reactant, the product (as formed), and the product following recrystallization are provided in Figure 5. In the crystals the reactant molecules are held by two hydrogen bonds. Upon transformation to the product the two hydrogen bonds are retained. Most importantly, the packing arrangements of the product as formed and as recrystallized are not the same. In the latter case the molecules in the crystal are held by four hydrogen bonds (indicated in Figure 5) whereas in the former they are held by two hydrogen bonds. The unit cell dimensions and packing arrangement of the product as formed in the crystal are much closer to those of the reactant than to those of the recrystallized product. The adaptability of the structure of the product within the reactant structure leads to 100% de even at complete conversion. The different packing arrangements of the product as formed on recrystallization suggest that during the photoreaction the product formed is in a metastable state. The product can accommodate itself without disrupting the lattice of the reactant molecules even though the reactant lattice may not be the most favorable for it.

The final discussion concerns the direct correlation of the structure of the reactant with that of the product. With the known absolute configuration of the chiral auxiliary the absolute configuration of the newly formed chiral center in the β-lactam can be assigned. On the basis of X-ray data the product β-lactam from *p*-(*R*)-(+)-phenylethylamide of *N*,*N*-diisopropyl-α-oxoamide-4-carboxylic acid **1** is assigned to have the *R* configuration. Formation of this isomer as the exclusive product suggesting that (a) the nearest hydrogen (2.81 vs 5.08Å) is abstracted by the excited carbonyl and (b) the intermediate 1,4-diradical collapses to the β-lactam without any large motions around any bond is easily visualized with the structure shown in Figure 4c containing reactant and product in a 1:1 ratio. In this structure following hydrogen abstraction by C(8A)═O(2), the radical center at C(5A) bonds (from the bottom face) simply by moving closer to the radical center at C(8A). Any motion that takes the radical center at C(5A) to the top face would have

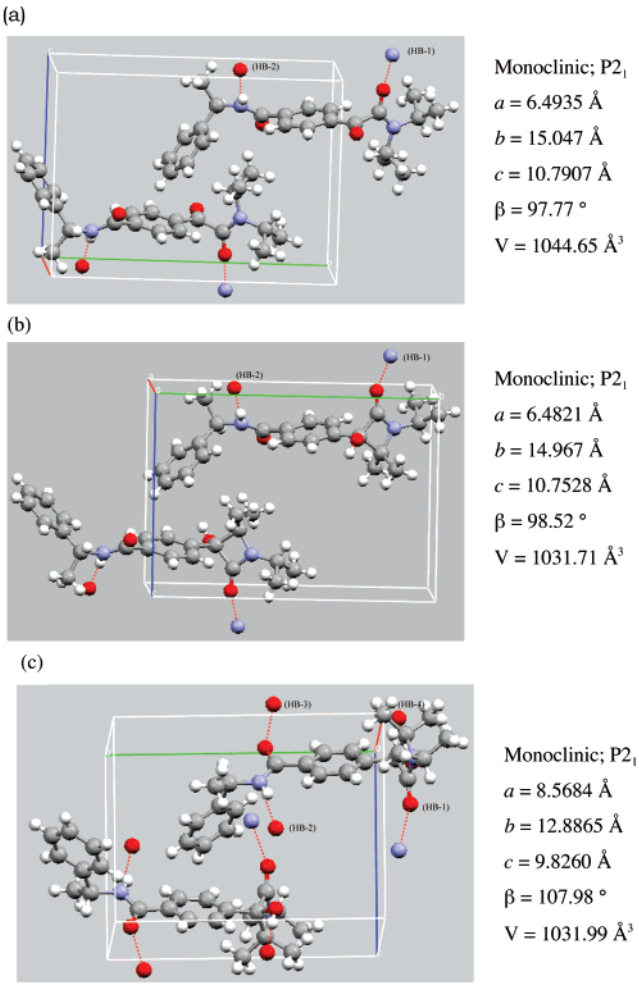


Figure 5. Packing diagram of (a) oxoamide **1** before irradiation, (b) the product β-lactam from **1** formed upon irradiation (100% conversion), and (c) the recrystallized β-lactam from **1**.

yielded the *S* isomer. Clearly the transformation from reactant to product is topochemically controlled, and any large motion is resisted by the crystal lattice.

Conclusions

We have shown in this paper that a covalent chiral auxiliary functions as effectively as an ionic chiral auxiliary during photocyclization of α-oxoamides to β-lactams. All 10 examples investigated gave excellent de's in the product β-lactam. The crystal lattice preorganizes the reactant molecules toward a single diasteromer of the β-lactam and forbids large motions of the 1,4-diradical intermediate that would lose the stereochemical memory. One of the 10 examples investigated proceeds via a rare single-crystal-to-single-crystal transformation, and X-ray structural information of the reaction at various stages of conversion has allowed us to establish a direct correlation between the sterochemistries of the reactant and the product. We are in the process of establishing the synthetic usefulness of the covalent chiral auxiliary approach in solid-state photochemistry.

Experimental Section

General Information. Commercial spectral grade solvents were used for photochemical reactions. Melting points were determined using a Mel-Temp apparatus and are uncorrected. Nuclear magnetic resonance spectra were recorded using deuterated samples ordered from Aldrich on a 400 MHz (Varian Inova) instrument. Irradiations were performed using a 450 W medium-pressure mercury arc lamp in a water-cooled immersion well. Light emitted from a Hanovia lamp was filtered through Pyrex (transmits $\lambda \geq 290$ nm). Gas chromatographic analyses were performed on a Hewlett-Packard 5890 fitted with a flame ionization detector, capillary column RTX5, 15 m × 0.25 mm. High-pressure liquid chromatography was performed on a Rainin instrument with an HPXL solvent delivery system and connected to a tunable Dynamax absorbance detector. For determinations of diastereomeric excesses, chiral columns (chiralcel-OD, OC, OJ; chiralpak-AD, ADRH), 250 mm × 4.6 mm, from Chiral Technologies, Inc. were used.

Synthesis of Oxoamides 1−10. *p*-(*R*)-(+)-Phenylethylamide of *N,N*-Diisopropylglyoxylamides (1). The carboxylic acid containing *N,N*-diisopropylglyoxylamide (*N,N*-bis(1-methylethyl)-α-oxobenzeneacetamide-4-carboxylic acid) synthesized following the procedure adopted by Scheffer et al.[62] (~150 mg) was dissolved in 25 mL of dichloromethane taken in a 100 mL round-bottom flask. 1-[3-(Dimethylamino)propyl]-3-ethylcarbodiimide hydrochloride (EDC; 1.1 equiv) was added with stirring followed by the addition of 1.1 equiv of the (*R*)-(+)-phenylethylamine. The mixture was stirred for 3−4 h. The amide product **1** was purified using column chromatography (silica gel) using hexane/ethyl acetate as eluent in the ratio 8:2. After rotovapping and drying amide **1** was obtained as a white powder (150 mg, 70%). The same procedure was adopted for the synthesis of compounds **2**, **9**, and **10** using (*R*)-(−)3-methyl-2-butylamine for **2** and (*R*)-(+)-phenylethylamine and (*S*)-naphthylethylamine for coupling with the *m*-carboxylic acid of *N,N*-diisopropylglyoxylamide to obtain **9** and **10**, respectively.

For the synthesis of the amino acid derivative *p*-(S)-phenylalanine methyl ester amide of *N,N*-diisopropylglyoxylamides (**3**), 1.1 equiv of the ester of the amino acid ((*S*)-phenylalanine methyl ester) was dissolved in dichloromethane in a 100 mL round-bottom flask cooled to 0 °C. Triethylamine (1.1 equiv) was added, and the solution was stirred for 5 min. The free amino acid obtained was added to the solution of the carboxylic acid containing *N,N*-diisopropylglyoxylamide (~150 mg) and 1.1 equiv of EDC dissolved in dichloromethane. The amino acid coupled product **3** was purified using hexane/ethyl acetate as eluent in the ratio 8:2. After rotovapping and drying amino acid derivative **3** was obtained as a white powder (180 mg, 75%). The same procedure was adopted for the synthesis of compound **4** using **(***S***)**-tyrosine methyl ester as the amino acid derivative.

Three independent steps are required for coupling of amino alcohols to the carboxylic acid unit of substituted *N,N*-diisopropylglyoxylamides.

a. Preparation of Silyl Derivatives of the Amino Alcohols. The chiral amino alcohol (1*S*,2*S*)-2-amido-3-methoxy-1-phenyl-1-propanol (0.275 mg, 1.0 equiv) was taken in a 100 mL round-bottom flask, 25 mL of dichloromethane was added to it, and the flask was flushed with nitrogen. The mixture was then cooled in an ice bath, and 2,6-lutidine (1.2 equiv) was added while the solution was stirred. TBDMS triflate (1.2 equiv) was then added to the solution. After 1 h, the reaction was quenched by addition of water, extracted with dichloromethane, and dried over $MgSO_4$. The silyl derivative was then purified using column chromatography with hexane and ethyl acetate in the ratio 8:2. The silylated product was obtained as a yellow gel (350 mg, 80%). Similarly, silylation of other amino alcohols, (−)-ephedrine, (*R*)-phenylglycinol, and (*S*)-phenylalaninol, was done.

b. Coupling of Silyl Derivatives of Amino Alcohols as Amides to the *p*-Carboxylic Acid Unit of *N,N*-Diisopropylglyoxylamides. The carboxylic acid containing *N,N*-diisopropylglyoxylamide (~150 mg, 1 equiv) was dissolved in 25 mL of dichloromethane in a 100 mL round-bottom flask. A 1.1 equiv sample of EDC (3-(dimethylamino)-propyl]-3-ethylcarbodiimide hydrochloride) was added to it, and the solution was allowed to stir for 10 min followed by the addition of 1

(62) Scheffer, J. R.; Wang, K. *Synthesis* **2001**, 1253.

equiv of chiral amino alcohol. After the reaction mixture was stirred at room temperature for 2 h, the reaction was quenched by adding water, and the organic layer was separated and dried over $MgSO_4$. Later the silyl-protected amino alcohol coupled α-oxoamide was purifed using column chromatography with hexane and ethyl acetate as the eluent in the ratio 8:2. The purified product was obtained in 75% yield, 115 mg.

c. Conversion of Silyl Derivatives to Free Amino Alcohols. The purified silyl derivative (100 mg) was dissolved in dry THF in a flame-dried round-bottom flask and was kept under a N_2 atmosphere. To this solution was added 1.2 equiv of tetrabutylammonium fluoride solution (1 M solution in THF), and the reaction mixture was allowed to stir for 30 min. Purification of the product was done using column chromatography with hexane and ethyl acetate as the eluent in the ratio 7:3. After rotovapping and drying amide **5** was obtained as a white powder (65 mg, 82%). Similar synthetic procedures (a−c) were adopted for the synthesis of compounds **6**−**8**.

Spectral Data for Compounds 1−**10. 4-(Aminoformyl-*N*,*N*-diisopropylformyl)-*N*-((*R*)-1-phenylethyl)benzamide (1).** ^{1}H NMR ($CDCl_3$, 400 MHz, δ, ppm): 1.15 (d, 6H, J = 6.8 Hz), 1.56 (d, 6H, J = 6.8 Hz), 1.62(d, 3H), 3.6 (m, 2H), 5.3 (q, 1H), 6.45 (d, 1H), 7.25−7.4 (m, 5H), 7.87 (d, 2H), 7.93 (d, 2H). ^{13}C NMR ($CDCl_3$, 100 MHz, δ, ppm): 20.4, 20.5, 21, 46.2, 50.0, 51.0, 52, 66.2, 126.5, 127.8, 127.9, 129.1, 129.95, 132, 134.2, 134.6, 135.5, 138, 143, 166, 167, 190.1. GC−MS (EI): *m*/*e* 380 (M^+), 252 (20), 225 (3), 148 (3), 128 (81), 105 (19), 86 (100), 43 (56).

4-(Aminoformyl-*N*,*N*-diisopropylformyl)-*N*-((*R*)-3-methylbutan-2-yl)benzamide (2). ^{1}H NMR ($CDCl_3$, 400 MHz, δ, ppm): 0.945−0.973 (dd, 6H, J = 6.8, 4.4 Hz), 1.146−1.167 (dd, 6H, J = 6.8, 2 Hz), 1.18−1.152 (d, 3H, J = 6.8 Hz), 1.56 (d, 6H, J = 6.8 Hz), 1.9 (m, 1H), 3.56−3.68 (m, 2H), 4.04−4.12 (m, 1H), 6.02 (d, 1H), 7.84 (d, 2H), 7.96 (d, 2H). ^{13}C NMR ($CDCl_3$, 100 MHz, δ, ppm): 17.79, 18.74, 18.89, 20.48, 20.5, 20.78, 21.78, 33.3, 46.39, 50.46, 51.03, 127.68, 129.94, 135.4, 140.5, 166, 166.6, 190.32. Mass spectral data: *m*/*e* (relative intensity) 346 (M^+, 1), 303 (1), 260 (4), 218 (11), 191 (3), 148 (2), 128 (60), 104 (33), 86 (100), 43 (97).

2-(4-Diisopropylaminooxalylbenzoylamino)-(*S*)-3-phenylpropionic Acid Methyl Ester (3). ^{1}H NMR ($CDCl_3$, 400 MHz, δ, ppm): 1.14−1.18 (dd, 6H, J = 6.8, 2.0 Hz), 1.55 (d, 6H), 3.2−3.34 (m, 2H), 3.56−3.68 (2H, m), 3.78 (3H, s), 5.08 (m, 1H), 6.67 (d, 1H), 7.0−7.3 (m, 5H), 7.8 (d, 2H), 7.9 (d, 2H).

2-(4-Diisopropylaminooxalylbenzoylamino)-3-((*S*)-4-hydroxyphenyl)propionic Acid Methyl Ester (4). ^{1}H NMR ($CDCl_3$, 400 MHz, δ, ppm): 1.16−1.2 (dd, 6H, J = 6.8, 2.0 Hz), 1.56 (d, 6H, J = 6.8 Hz), 3.085−3.223 (m, 2H), 3.577−3.653 (2H, m), 3.76 (3H, s), 4.98−5.2 (m, 1H), 6.75 (d, 1H), 6.86 (d, 2H), 7.8 (d, 2H), 7.94 (d, 2H).

4-Diisopropylaminooxalyl-*N*-((1*S*,2*S*)-2-hydroxy-1-methoxymethyl-2-phenylethyl)benzamide (5). ^{1}H NMR ($CDCl_3$, 400 MHz, δ, ppm): 1.07−1.12 (dd, 6H, J = 6.8, 2.0 Hz), 1.48−1.52 (d, 6H, J = 6.8), 3.48−3.65 (m, 4H), 3.9 (s, 3H), 4.32−4.38 (m, 1H), 5.04 (d, 1H, J = 3.6 Hz), 6.85(d, 1H), 7.16−7.36 (m, 5H), 7.72 (d, 2H), 7.88 (d, 2H).

4-(Aminoformyl-*N*,*N*-diisopropylformyl)-*N*-((1*R*,2*S*)-1-hydroxy-1-phenylpropan-2-yl)-*N*-methylbenzamide (6). ^{1}H NMR ($CDCl_3$, 400 MHz, δ, ppm): 1.1 (d, 6H, J = 6.8 Hz), 1.34 (d, 3H, J = 6.8 Hz), 1.52 (d, 6H, J = 6.8 Hz), 2.58−2.98 (two s, 3H), 3.48−3.8 (3H, m), 4.6−4.92 (two m, 1H), 6.86−7.0 (two d, 1H), 7.25−7.42 (m, 6H), 7.76−7.88 (two d, 2H). Mass spectral data: *m*/*e* (relative intensity) 424 (M^+, 1), 317 (42), 296 (5), 260 (100), 251 (3), 233 (5), 190 (3), 161 (5), 132 (17), 128 (25), 104 (33), 86 (55).

2-(4-(1-(2-Hydroxy-1-phenylethylamino)vinylphenyl)-*N*,*N*-diisopropyl-2-oxoacetamide (7). ^{1}H NMR ($CDCl_3$, 400 MHz, δ, ppm): 1.15 (dd, 6H, J = 6.8, 2.0 Hz), 1.57 (d, 6H, J = 6.8 Hz), 3.54−3.64 (m, 2H), 3.88−3.96 (m, 2H), 5.2−5.25 (m, 1H), 7.25−7.4 (m, 5H), 7.42 (d, 1H), 7.808−7.88 (m, 4H). ^{13}C NMR ($CDCl_3$, 100 MHz, δ, ppm): 20.5, 20.6, 20.7, 46.2, 50.6, 56.5, 66.2, 127, 128.1, 129.1, 129.8, 135.2, 139.1, 139.9, 167, 190.1.

4-(Aminoformyl-*N*,*N*-diisopropylformyl)-*N*-(1-hydroxy-3-phenylpropan-2-ylbenzamide (8). ^{1}H NMR ($CDCl_3$, 400 MHz, δ, ppm): 1.1−1.18 (m, 6H), 1.56−1.6 (d, 6H, J = 6.8 Hz), 2.96−3.02 (d, 2H, J = 2.4 Hz), 3.54−3.64 (m, 2H), 3.64−3.84 (m, 2H), 4.3−4.4 (m, 1H), 5.2−5.25 (m, 1H), 7.25−7.4 (m, 5H), 7.42 (d, 1H), 7.808−7.88 (m, 4H). ^{13}C NMR ($CDCl_3$, 100 MHz, δ, ppm): 20.4, 20.5, 20.6, 20.8, 46.2, 50.6, 56.5, 66.2, 127, 128.1, 128.3, 129.1, 129.8, 135.2, 139.1, 139.9, 167, 190.1.

3-(Aminoformyl-*N*,*N*-diisopropylformyl)-*N*-((*R*)-1-phenylethyl)-benzamide (9). ^{1}H NMR ($CDCl_3$, 400 MHz, δ, ppm): 1.0 (d, 6H, J = 6.8 Hz), 1.2 (d, 3H), 1.4 (d, 6H, J = 6.8 Hz), 3.3−3.5 (2H, m), 5.06 (m, 1H), 6.3 (d, 1H), 7.25−7.36 (m, 5H), 7.4 (m, 1H), 7.82 (m, 1H), 7.9 (m, 1H), 8.1 (m, 1H). ^{13}C NMR ($CDCl_3$, 100 MHz, δ, ppm): 20.5, 20.6, 21, 46.2, 50.0, 51.0, 52, 66.2, 127, 128.1, 129.1, 129.8, 132, 134, 135.5, 138, 143, 166, 167, 190.1. GC−MS (EI): *m*/*e* 380 (M^+), 252 (20), 225 (3), 148 (3), 128 (81), 105 (19), 86 (100), 43 (56).

3-(Aminoformyl-*N*,*N*-diisopropylformyl)-*N*-((*S*)-1-naphthalen-1-ylethyl)benzamide (10). ^{1}H NMR ($CDCl_3$, 400 MHz, δ, ppm): 1.06 (d, 3H, J = 8.0), 1.12 (d, 3H, J = 8.0 Hz), 1.4 (d, 3H, J = 8.0 Hz), 1.51 (d, 3H, J = 8.0 Hz), 1.77 (d, 3H, J = 8.0 Hz), 3.46−3.62 (m, 2H), 6.12 (m, 1H), 6.54 (d, 1H), 7.4−7.6 (m, 5H), 7.8−8.1 (m, 6H). ^{13}C NMR ($CDCl_3$, 100 MHz, δ, ppm): 20.3, 20.4, 20.6, 45, 46, 50, 123, 123.5, 126, 126.2, 127, 127.3, 129, 129.3, 130, 132, 133, 134, 134.5, 135, 138, 165, 166.5, 190. GC−MS (EI): *m*/*e* 430 (M^+), 302 (7), 275 (3), 260 (3), 231 (2), 155 (30), 128 (100), 104 (9), 86 (94), 76 (8).

Irradiation Procedures. a. Solution. Reaction solutions (with <4 mg of ketone) were purged by bubbling nitrogen through the solution for at least 15 min prior to irradiation. During the irradiations the reaction vessel was sealed. Photoproducts were monitored using GC, GC−MS, and TLC. The percent conversion was kept within 50−60% to avoid the formation of secondary products. For HPLC analysis the solution-irradiated sample was dissolved in appropriate solvents (^{i}PrOH) and used for analyses.

b. Solid State. The ketones (∼2−3 mg), either as ground single crystals or in polycrystalline form (powder), were sandwiched between two Pyrex plates and spread out to cover a surface area of 2−3 cm^2. The plates were sealed with Parafilm on all sides before the irradiation process. After irradiation the solid was dissolved in appropriate solvents, and the products were analyzed using GC, GC−MS, and TLC. For HPLC analysis the solution-irradiated sample was dissolved in appropriate solvents (^{i}PrOH) and used for analyses. For studies on the single-crystal−single-crystal reaction after the X-ray crystal structure of the reactant crystal was obtained, the mounted crystal was placed between Pyrex plates, the corners were completely sealed with Parafilm, and the crystal was irradiated in the UV chamber. The same crystal was irradiated for different intervals of time and the X-ray crystal structure determined after each interval.

Reaction Conversion Determinations. Conversions were determined on the basis of the results of GC analysis. The difference in the GC detector response for starting material and its reaction products was found to be negligible (all are structural isomers in most cases). Thus, no correction was made to the integration data.

Analysis Conditions. HPLC and GC conditions for β-lactam photoproducts of substrates are given below. All the samples were monitored at 254 nm. The solvent composition of the eluent and the retention times for individual diastereomers are as follows: (oxoamide **1**) HPLC-chiralcel-OD, mobile phase 90:10 hexane to 2-propanol; flow rate 0.7 mL/min; retention time of diastereomers, 48.5 and 55.4 min; (oxoamide **2**) HPLC-chiralcel-OJ, mobile phase 95:5 hexane to 2-propanol; flow rate 0.7 mL/min; retention time of diastereomers, 28.3 and 37 min; (oxoamide **3**) HPLC-chiralcel-OD, mobile phase 80:20 hexane to 2-propanol; flow rate 0.5 mL/min; retention time of diastereomers, 24.3 and 30.0 min; (oxoamide **4**) HPLC-chiralpak-AD, mobile phase 80:20 hexane to 2-propanol; flow rate 0.6 mL/min; retention time of diastereomers, 34.0 and 56.0 min; (oxoamide **5**)

HPLC-chiralpak-ADRH, mobile phase 78:22 hexane to 2-propanol; flow rate 0.3 mL/min; retention time of diastereomers, 20.7 and 24.7 min; (oxoamide **6**) HPLC-chiralpak-AD, mobile phase 90:10 hexane to 2-propanol; flow rate 0.5 mL/min; retention time of diastereomers, 95.0 and 110.0 min; (oxoamide **7**) HPLC-chiralcel-OJ, mobile phase 90:10 hexane to 2-propanol; flow rate 0.7 mL/min; retention time of diastereomers, 18.0 and 24.0 min; (oxoamide **8**) HPLC-chiralcel-OJ, mobile phase 96:4 hexane to 2-propanol; flow rate 0.9 mL/min; retention time of diastereomers, 100.0 and 115.0 min; (oxoamide **10**) HPLC-chiralpak-AD, mobile phase 85:15 hexane to 2-propanol; flow rate 0.6 mL/min; retention time of diastereomers, 25.0 and 29.8 min; (oxoamide **9**) GC-SE-30; initial temperature 100 °C; initial time 1.0; rate 20 deg/min; final temperature 240 °C; final time 60 min; retention time of diastereomers, 51.5 and 52.5 min.

Characterization of *β*-Lactam Products. *β*-Lactam Photoproduct from Oxoamide 1. ^{1}H NMR ($CDCl_3$, 400 MHz, δ, ppm): 0.7 (s, 3H), 1.3 (dd, 6H, J = 6.8 Hz, 4.8 Hz), 1.47 (s, 3H), 1.66 (d, 3H, 7.2 Hz), 3.58 (m, 1H), 5.30−5.38 (m, 1H), 7.1 (d, 1H), 7.20−7.32 (m, 5H), 7.35−7.42 (m, 2H), 7.52 (d, 2H). GC−MS (EI): *m*/*e* 380 (M^+), 360 (2), 295 (60), 280 (11), 252 (13), 191 (15), 175 (100), 148 (5), 147(5), 105 (29), 77 (10).

***β*-Lactam Photoproduct from Oxoamide 2.** ^{1}H NMR ($CDCl_3$, 400 MHz, δ, ppm): 0.81 (s, 3H), 0.945−0.973 (dd, 6H, J = 6.8 Hz), 1.18 (d, 3H, J = 6.8 Hz), 1.335−1.359 (dd, 6H, J = 6.8 Hz, 4H), 1.49 (s, 3H), 1.82 (m, 1H), 3.56−3.58 (m, 1H), 4.0−4.12 (m, 1H), 6.2 (s, 1H), 7.34 (d, 2H), 7.64 (d, 2H). GC−MS (EI): *m*/*e* 346 (M^+), 303 (7), 261 (60), 219 (11), 218 (42), 192 (21), 191 (22), 175 (100), 147(6), 105 (7), 100 (32), 43 (73).

***β*-Lactam Photoproduct from Oxoamide 3.** ^{1}H NMR ($CDCl_3$, 400 MHz, δ, ppm): 0.8 (s, 3H), 1.3 (d, 6H, J = 6.8 Hz), 1.47 (s, 3H), 3.2−3.34 (m, 2H), 3.58 (m, 1H), 3.78 (s, 3H), 5.10 (m, 1H), 6.67 (d, 1H), 7.1−7.3 (m, 5H), 7.42 (d, 2H), 7.64 (d, 2H). GC−MS (EI): *m*/*e* 438 (M^+), 381(2), 312 (4), 260 (100), 202 (5), 191 (38), 162 (48), 133 (62), 119(38), 91(78), 77 (20).

***β*-Lactam Photoproduct from Oxoamide 4.** ^{1}H NMR ($CDCl_3$, 400 MHz, δ, ppm): 0.8 (s, 3H), 1.3−1.36 (d, 6H), 1.45 (s, 3H), 3.2−3.34 (m, 2H), 3.52−3.54 (m, 1H), 3.7 (s, 3H), 4.9−5.0 (m, 1H), 6.52−6.8 (m, 4H), 7.5−7.8 (m, 4H).

***β*-Lactam Photoproduct from Oxoamide 5.** ^{1}H NMR ($CDCl_3$, 400 MHz, δ, ppm): 0.8 (s, 3H), 1.34−1.39 (dd, 6H, J = 6.8 Hz), 1.5 (s, 3H), 3.55−3.72 (m, 3H), 3.92 (s, 3H), 4.36−4.45 (s, 1H), 5.10 (m, 1H), 6.68 (d, 1H), 7.28−7.42 (m, 5H), 7.6 (d, 2H), 7.8 (d, 2H).

***β*-Lactam Photoproduct from Oxoamide 6.** ^{1}H NMR ($CDCl_3$, 400 MHz, δ, ppm): 0.854 (s, 3H), 1.23−1.25 (m, 3H), 1.34−1.39 (dd, 6H, J = 6.8 Hz), 1.49 (s, 3H), 2.62−3.0 (two s, 3H), 3.62−3.89 (m, 2H), 4.58−4.95 (two m, 1H), 7.0−7.5 (m, 9H).

***β*-Lactam Photoproduct from Oxoamide 7.** ^{1}H NMR ($CDCl_3$, 400 MHz, δ, ppm): 0.76 (s, 3H), 1.3−1.35 (dd, 6H, J = 6.8 Hz), 1.54 (s, 3H), 3.4−3.48 (m, 1H), 3.92−4.04 (m, 2H), 5.2−5.3 (m, 1H), 6.8 (s, 1H), 7.25−7.42 (m, 5H), 7.6 (d, 2H), 7.8 (d, 2H).

***β*-Lactam Photoproduct from Oxoamide 8.** ^{1}H NMR ($CDCl_3$, 400 MHz, δ, ppm): 0.75 (s, 3H), 1.32−1.34 (dd, 6H, J = 6.8 Hz), 1.48 (s, 3H), 3.01 (d, 2H, J = 7.2 Hz), 3.4−3.48 (m, 1H), 3.6−3.82 (m, 2H), 4.3−4.4 (m, 1H), 6.75 (s, 1H), 7.29−7.40 (m, 5H), 7.5−7.53 (m, 4H).

***β*-Lactam Photoproduct from Oxoamide 9.** GC−MS (EI): *m*/*e* 380 (M^+, 50), 345 (5), 295 (39), 260 (34), 233 (22), 191 (30), 175 (49), 133 (77), 119 (54), 105 (100), 77 (48).

Crystal Structure Determination. Crystals of **1**−**7** and **10** were mounted in Cryoloops with Paratone oil and placed in the cold nitrogen stream of the Kryoflex attachment of the Bruker APEX CCD diffractometer. Full spheres of data were collected using 606 scans in ω (0.3° per scan) at φ = 0°, 120°, and 240°. The raw data were reduced to F^2 values using the SAINT+ software,[63] and global refinements of unit cell parameters employing approximately 2000−5000 reflections chosen from the full data sets were performed. Multiple measurements of equivalent reflections provided the basis for empirical absorption corrections as well as corrections for any crystal deterioration during the data collection (SADABS[64]). The structures were solved by direct methods and completed by successive cycles of full-matrix, least-squares refinement followed by the calculation of difference maps. Most hydrogen atoms could be located in these maps, and those attached to nitrogen or oxygen were placed in these locations. All hydrogen atoms attached to carbon were placed in calculated positions with isotropic displacement parameters 20% larger than those of the attached atoms and allowed to ride. In the case of **2**, the isopropyl group in the chiral auxiliary is disordered over two alternate sites. These two locations were refined with restraints making corresponding distances in the two equal. All computations associated with structure solution, refinement, and presentation were performed with the SHELXTL[65] package.

Acknowledgment. V.R. thanks the NSF for financial support (Grants CHE-9904187 and CHE-0212042), J. R. Scheffer for insightful discussions, and J. R. Scheffer, Keyan Wang, and Brian Patrick for providing crystallographic help at the early stages of the project. J.T.M. thanks the Louisiana Board of Regents through the Louisiana Educational Quality Support Fund (Grant LEQSF (2003-2003)-ENH-TR-67) for the purchase of the Bruker APEX diffractometer.

Supporting Information Available: Crystallographic reports and tables of positional and thermal parameters and bond lengths and angles provided as 15 CIF files. The material is available free of charge via the Internet at http:// pubs.acs.org.

JA043999P

(63) SAINT+, Version 6.22, Bruker-AXS, Madison, WI, 2001.
(64) SADABS, Version 2.05, Bruker-AXS, Madison, WI, 2000.
(65) SHELXTL, Version 6.10, Bruker-AXS, Madison, WI, 2000.