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Enantioselective Photochemical Synthesis of a Simple Alkene via the Solid State Ionic Chiral Auxiliary Approach

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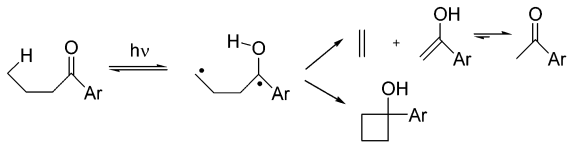
Irradiation of *cis*-bicyclo[4.3.0]non-8-ylacetophenone derivatives (**1**) in solution and the solid state yields *cis*-3a,4,5,6,7,7a-hexahydro-1*H*-indene (**2**) via a Norrish type II cleavage process. Asymmetric induction studies were conducted by providing the reactants with carboxylic acid substituents to which ionic chiral auxiliaries were attached through salt formation with optically pure amines. Irradiation of the salts (5 in total) in the crystalline state gave enantiomeric excesses of up to 44%. Single-crystal X-ray diffraction studies were performed on ketone **1a** as well as salts **1d** and **1g**, and on this basis, the structure−reactivity relationships involved are discussed.

Introduction

Owing to the wide applicability of alkenes as building blocks in organic synthesis, the development of new methods of asymmetric synthesis of chiral olefins is highly desirable. The preparation of enantiomerically pure simple (unfunctionalized) olefins is difficult because their resolution through direct Pasteur techniques is essentially impossible.[1] Several approaches have been taken to the asymmetric synthesis of simple chiral olefins: (1) asymmetric Wittig-type reactions with chiral cyclic phosphonamides,[2] (2) asymmetric elimination reactions of *N*-chiral amine oxides,[3] (3) asymmetric Hoffman elimination of *N*-chiral quaternary ammonium salts,[4] and (4) asymmetric radical fragmentation reactions of *S*-chiral sulfoxides.[5] For the most part, the thermal solution phase 1,2-elimination reactions mentioned above give low ee values. This is due mainly to the fact that the elevated temperatures used in ground-state elimination reactions facilitate equilibrium between conformational diastereomers and reduce the reaction rate differences between diastereomeric transition states. We believe that these factors can be overcome in asymmetric Norrish type II photoelimination reactions using the solid-state ionic chiral auxiliary approach.[6]

SCHEME 1



The Norrish type II photoelimination reaction is one of the most thoroughly studied and well-understood processes in organic photochemistry.[7] In its simplest form, a γ-hydrogen-containing ketone fragments to the corresponding alkene and methyl ketone (Scheme 1). In the case of aromatic ketones, the mechanism involves initial γ-hydrogen atom abstraction by the $(n,\pi^*)^3$ excited state to afford a triplet 1,4-hydroxybiradical intermediate. The 1,4-hydroxybiradical undergoes intersystem crossing and then cleaves to afford an alkene and an enol that subsequently tautomerizes to the corresponding ketone. A competing process is cyclization of the 1,4-hydroxybiradical to form a cyclobutanol (Yang photocyclization).[8] This is normally a minor reaction pathway (<10%), but it can predominate for certain ketones.[7] A third option available to the 1,4-hydroxybiradical intermediate is reverse hydrogen transfer to regenerate the starting ketone, a process responsible for lowering the quantum yield.

Consider the Norrish type II photoelimination reaction of *trans*-α-4-methylcyclohexylacetophenone (Scheme 2). The products in this case will be acetophenone and racemic 4-methylcyclohexene because the two conformers of *trans*-α-4-methylcyclohexylacetophenone are in rapid

(1) Partial kinetic resolution of unfunctionalized simple olefins has been reported. For references on kinetic resolution of axially dissymmetric cyclic alkenes by asymmetric dihydoxylation, see: Hoveyda, A. H.; Didiuk, M. T. *Curr. Org. Chem.* **1998**, *2*, 489 and references therein. For references on kinetic resolution of terminal alkenes by alkene polymerization with chiral zirconocene catalysts, see: Bercaw, J. E.; Min, E. Y.-J.; Levy, C. J.; Baar, C. R. *Polym. Mater. Sci. Eng.* **2002**, *87*, 62 and references therein.

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(7) For general reviews of the Norrish/Yang type II reaction, see: (a) Wagner, P.; Park, B.-S. In *Organic Photochemistry*; Padwa, A., Ed.; Marcel Dekker: New York, 1991; Vol. 11, Chapter 4. (b) Wagner, P. J. In *Molecular Rearrangements in Ground and Excited States*; de Mayo, P., Ed.; Academic Press: New York, 1980; Chapter 20. (c) Wagner, P. J. *Acc. Chem. Res.* **1971**, *4*, 168.

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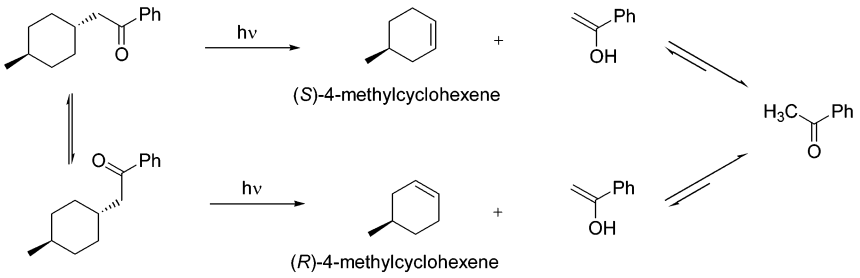
SCHEME 2



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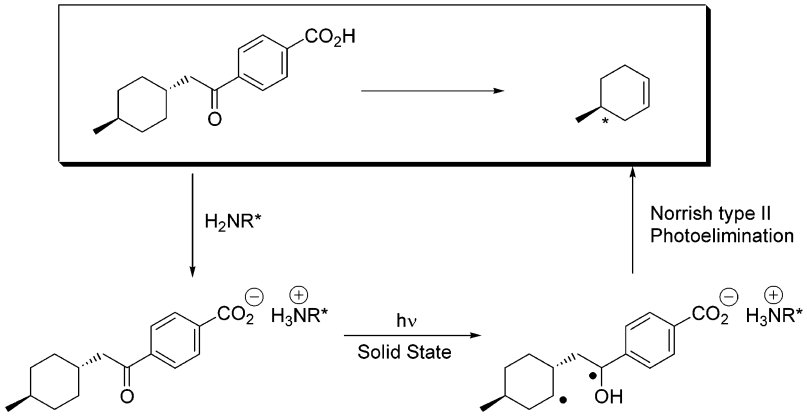

equilibrium and there is no element of asymmetry in the molecule that would favor abstraction of a γ-hydrogen from one side of the plane of symmetry over the other. Our strategy for achieving asymmetric induction in this reaction is depicted in Scheme 3 based on the formation of a crystalline salt between a prochiral, carboxylic acid-containing photoreactant and an optically pure, photoinert amine. Since the ionic auxiliary (the ammonium ion in this case) is optically pure, such salts are required to crystallize in chiral space groups, and this provides the asymmetric medium in which to carry out the photoreaction. The dense packing of the crystal prevents large conformational motions and ensures that only one conformational diastereomer of the photoreactant will be present. In other words, the molecule is pre-organized for abstraction of only one of the diastereotopic γ-hydrogen atoms. Upon photolysis, the chiral auxiliary attached to the aromatic ring of the aryl ketone is lost as part of the Norrish type II cleavage process, leaving the enantiomerically enriched olefin behind.

In recent years, the solid-state ionic chiral auxiliary approach has shown success in asymmetric induction in a variety of solid state-compatible photochemical reactions.[6] To demonstrate the generality of this approach, as well as to develop a new method of asymmetric synthesis of simple chiral alkenes, this paper reports the results of a study that uses this approach on the Norrish type II photoelimination reaction to synthesize the enantiomerically enriched olefin *cis*-3a,4,5,6,7,7a-hexahydro-1*H*-indene (**2**).

Results and Discussion

Choice and Synthesis of Starting Materials. In a paper published in 1988,[9] we showed that the solid-state irradiation of a series of α-cycloalkylacetophenones formed various cycloalkenes via Norrish type II photoelimination. Among them, α-cyclopentylacetophenone afforded excellent chemical yields (>90%) of cyclopentene, while α-cyclohexylacetophenone gave relatively low yields (<40%) of cyclohexene, the major product being the corresponding cyclobutanol. To study asymmetric induction in these compounds, appropriate substitution on the cycloalkane ring is required, e.g., adding substituents at the 4-position of α-cyclohexylacetophenone and at the 3- and 4-positions of α-cyclopentylacetophenone. Although preparation of photoreactants containing a 4-substituted cyclohexane ring would be easier, it seemed to us that photoreactants containing a disubstituted cyclopentane ring would be a better choice in terms of chemical yields. Bearing this in mind, we decided to synthesize compounds **1a**−**g**.

Compounds **1a**−**g** were synthesized as outlined in Scheme 4. Compound **12** was prepared as a mixture of diastereomers, and recrystallization of the mixture from EtOAc/petroleum ether gave *cis*-bicyclo[4.3.0]non-8-yl acetophenone derivative **1a**. Hydrolysis of keto-ester **1a** afforded the corresponding keto-acid **1b**, which was then reacted with a variety of optically pure amines to form chiral salts **1c**−**g** through acid−base chemistry. The amines were chosen randomly from the chiral pool, major criteria being that they should not absorb light under the photolysis conditions and that they should be readily available. The salts were shown to have 1:1 acid−base stoichiometry by elemental analysis. In addition, the IR and ^{1}H and ^{13}C NMR spectra were all in agreement with the proposed structures.

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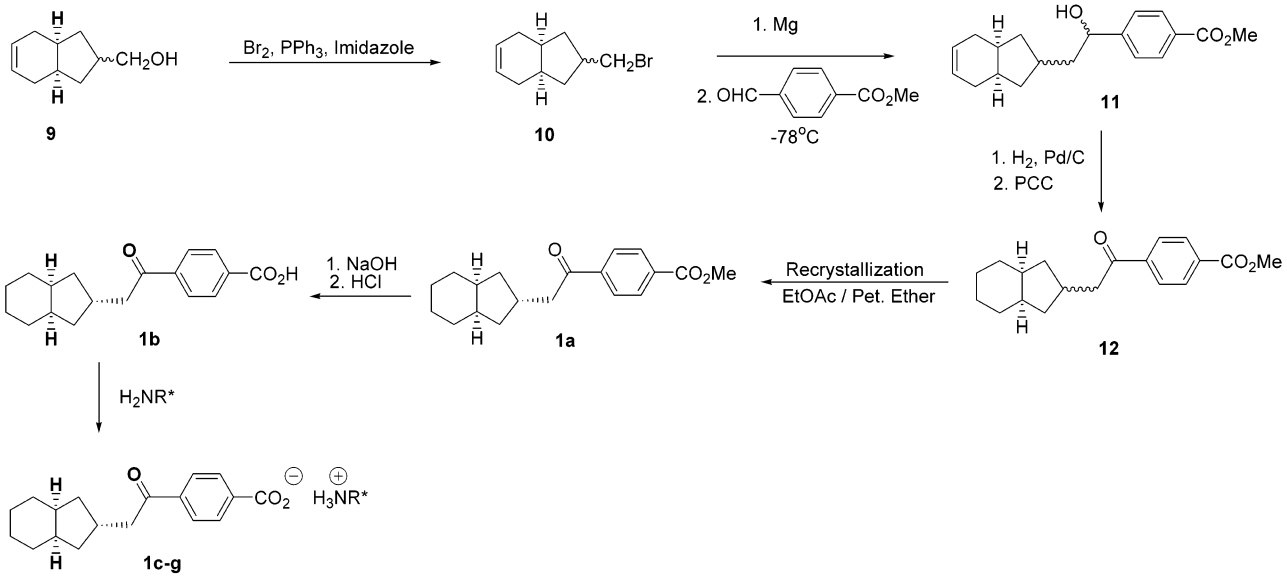
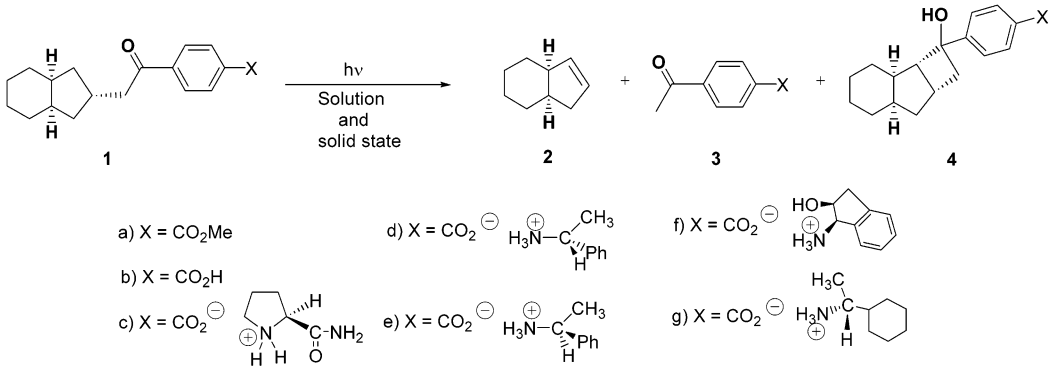
SCHEME 4



SCHEME 5



Photolysis of Ketones 1a−b in the Solid State and Solution: Establishment of a Crystal Structure−Solid-State Reactivity Correlation. All solution and solid-state photolyses were conducted by using a 450-W Hanovia medium-pressure mercury lamp fitted with a Pyrex filter (λ > 290 nm). Samples in solution were photolyzed to complete conversion and the crystalline samples were irradiated to various degrees of conversion as determined by gas chromatography (GC). Low-temperature photolyses were performed to minimize the extent of the breakdown of crystal lattice. The results of photolyzing ketones **1a** and **1b** are summarized in Table 1.

Irradiation of ketones **1a**,**b**, either in solution or the solid state, led efficiently and exclusively to the corresponding Norrish type II cleavage products **2** and **3a**,**b** (Scheme 5). No secondary products arising from photolysis of compounds **2** and **3** were observed within the irradiation period. For convenience by GC analysis, compound **3b** was transformed quantitatively into the corresponding ester **3a** by treatment with ethereal diazomethane. Not unexpectedly, the yields of alkene **2** obtained in the solid-state irradiations (entries 2, 3, and 5) were relatively low compared to those obtained in solution (entries 1 and 4). We attribute this to the fact that alkene **2** is a volatile liquid, which evaporates partially during the crystalline-state reaction and work-up. To improve the yields, the crystalline-state irradiation of keto-acid **1b** was carried out in hexanes as a solvent in which it is insoluble (entries 6 and 7). Alkene **2** generated during the reaction dissolved in the hexanes and was retained; as a result the yields of alkene **2** were significantly improved.

TABLE 1. Results of Photolysis of Ketones 1a,b

entry	ketone	reaction medium	temp (°C)	conv (%)[a]	**2** (%)[b]	**3a** (%)[b]
1	**1a**	CH_3CN	rt[c]	100	56[d]	38[d]
2	**1a**	crystalline state	rt	51	16	33
3	**1a**	crystalline state	−20	34	12	21
4	**1b**	CH_3CN	rt	100	53[d]	44[d]
5	**1b**	crystalline state	rt	85	29	52
6	**1b**	crystalline state (hexanes suspension)	rt	100	55[d]	40[d]
7	**1b**	crystalline state (hexanes suspension)	−20	100	55[d]	38[d]

[a] Percentage of total GC integral due to the disappearance of the corresponding starting material. [b] Percentage of total GC integral due to the corresponding product. [c] rt = room temperature. [d] Compounds **2** and **3a** are not in 1:1 GC ratio. This is presumably due to different GC detector responses.

In principle, irradiation of **1** could have formed Yang cyclization product **4**, but this was not observed. To obtain a better understanding of why **1** undergoes Norrish type II photoelimination exclusively, the X-ray crystal struc-

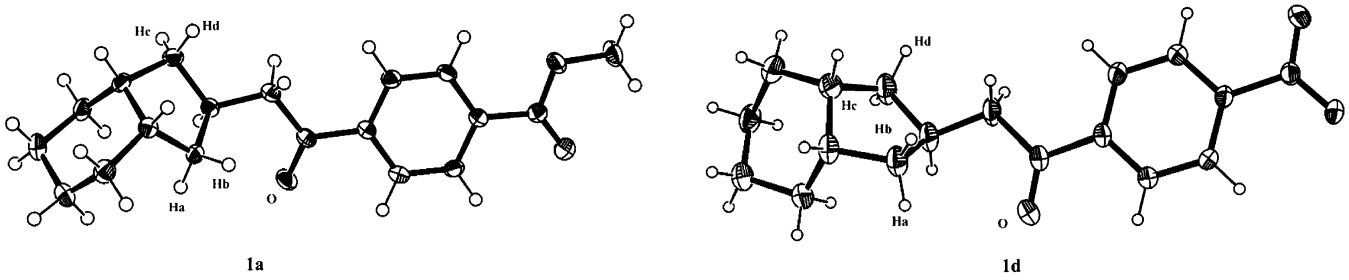


FIGURE 1. Crystal structures of keto-ester **1a** and the anion portion of salt **1d**.

SCHEME 6

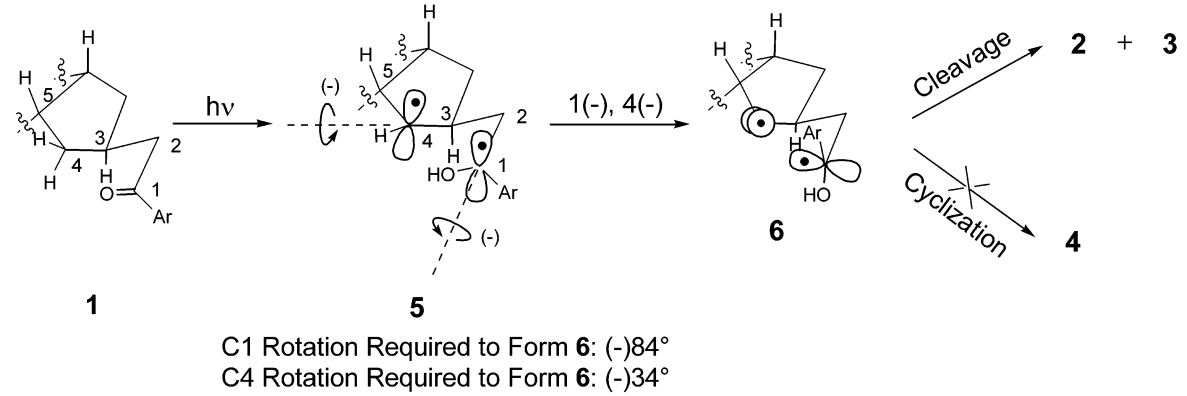


TABLE 2. Geometric Data for Compounds 1a, 1d, and 1g

compd	H	φ_1 (deg)	φ_4 (deg)	ψ (deg)	d (Å)[a]	ω (deg)[b]	Δ (deg)[c]	θ (deg)[d]
1a	a	84	34	68	3.07	29	99	85
	b	84	34	68	3.01	48	75	88
	c	84	61	172	4.65	13	65	63
	d	84	61	172	4.71	4	52	60
1d	a	82	58	68	2.82	35	97	102
	b	82	58	68	3.35	45	70	71
	c	82	35	173	4.67	2	50	65
	d	82	35	173	4.73	10	68	61
1g	a	83	31	68	2.85	37	83	95
	b	83	31	68	3.09	13	102	81
	c	83	59	174	4.78	18	60	59
	d	83	59	174	4.70	3	50	64

[a] C=O···H_γ distance. [b] Deviation of H_γ from the mean plane of the carbonyl group. [c] C=O···H_γ angle. [d] C−H_γ···O angle.

ture of keto-ester **1a** was determined (Figure 1). The geometric data derived from its X-ray structure are summarized in Table 2. Correlation of excited-state reactivity with the geometry of the ground-state ketone is considered to be valid in this case because the $(n,\pi^*)^3$ excitation is known to be highly localized on the carbonyl group such that geometric changes in the rest of the molecule are negligible.[10] Moreover, since hydrogen abstraction in the solid state is likely to occur with minimum motion of the associated heavy atoms, geometric data derived from X-ray crystallography can also be used to analyze the behavior of the 1,4-hydroxybiradical intermediate.[11] As shown in Table 2, among the four γ-hydrogens, only Ha and Hb are close enough to the carbonyl oxygen for H-abstraction to occur (d = 3.07 and 3.01 Å respectively), while Hc and Hd (d > 4.6 Å) are too far away.

For the purposes of discussion, we define three torsion angles with reference to Scheme 6, which is a depiction of the 1,4-hydroxybiradical intermediate (**5**) derived from ketone **1a**: ψ refers to the C1−C2−C3−C4 torsion angle; φ_1 is defined as the dihedral angle between the C2−C3 σ bond and the p-orbital lobe on C1; and φ_4 is defined as the dihedral angle between the C2−C3 σ bond and the p-orbital lobe on C4. The p-orbitals at C1 and C4 are assumed to lie perpendicular to the O1−C1−C2 and C3−C4−C5 planes, respectively. For the cleavage process to occur, overlap between the σ-bond undergoing scission (C2−C3) and both radical-containing p-orbitals (at C1 and C4) must be efficient.[12] Maximum overlap (100%) will occur when the p/σ orbitals are eclipsed, i.e., when φ_1 and φ_4 are 0° (0,0 geometry). It seems likely that cyclization, which requires through-space overlap of these same p-orbitals, will also prefer a biradical geometry close to 0,0, provided that the radical centers are gauche (or better). By using the crystal structure data for ketone **1a**, the calculated $\sigma-\pi$ orbital alignments for biradical **5** are φ_1 = 84° and φ_4 = 34° (Table 2). The results indicate that biradical **5**, while gauche (ψ = 68°), is far from the 0,0 geometry preferred for cleavage or cyclization. According to the well-known topochemical principle, which states that reactions in the crystalline state occur with a minimum of atomic and molecular motion,[13] it is reasonable to predict that biradical **5** undergoes preferential (−) rotation at both C1 and C4 to form biradical

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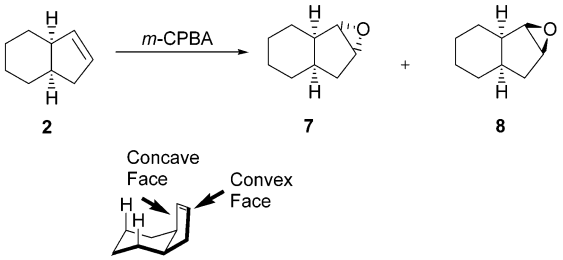
(12) Wagner, P. J.; Kelso, P. A.; Kempainen, A. E. *J. Am. Chem. Soc.* **1968**, *90*, 5896.
(13) Schmidt, G. M. J. *Pure Appl. Chem.* **1971**, *27*, 647.

SCHEME 7



conformer **6** in which the 0,0 geometry requirement is fulfilled. The directions and magnitudes of the rotations required to align the p-orbitals in the 0,0 geometry are shown in Scheme 6. Biradical **6** is a relatively unstrained species. It behaves normally in its preference for cleavage to lead to the observed products **2** and **3**.[14] The fact that Yang cyclization was not observed in this study can be explained by the fact that the *cis*-fused 5/4 ring junction-containing photoproduct **4** is quite strained ($E_{strain} = 30.5$ kcal/mol),[15] while cleavage of **1a** relieves strain (~0.4 kcal/mol) via formation of a cyclopentene ring from a cyclopentane ring.[16,17]

Asymmetric Induction. Salts **1c**−**g** formed between carboxylic acid **1b** and a number of commercially available, enantiomerically pure amines were prepared and crystallized. Each of the salts (**1c**−**g**) was irradiated as a hexane suspension. Photolyses were generally carried out through Pyrex at room temperature, although some runs were conducted at −20 °C. The salts were irradiated for varying lengths of time to determine the dependence of the ee values on the extent of conversion. Following irradiation, the mixtures were treated with excess ethereal diazomethane to form the corresponding methyl ester **3a**. After diazomethane treatment, the organic layer containing the alkene **2**, esterified photoproduct **3a**, and starting material was washed with water and subjected to short-path silica gel chromatography to remove the chiral auxiliary. The mixtures were then analyzed by GC for conversion as well as composition. Direct measurement of the ee values of alkene **2** by chiral GC met with no success (insufficient separation). Alkene **2** was thus transformed into its corresponding epoxide derivatives, compounds **7** and **8** (94:6 by GC), by treatment with *m*-CPBA (Scheme 7). The formation of epoxide **7** is favored because the convex face of alkene **2** is less sterically hindered in comparison with its concave face (Scheme 7). The stereochemistry of compound **7** was established by the NOE interactions shown in Figure 2. The optical purity of alkene **2** was thus determined by measuring the ee of epoxide **7**, using chiral GC (SUPELCO β-Dex 350 Custom Capillary Column, 120 °C at 1.37 mL/min). The results of the photochemical studies are summarized in Table 3. In addition to the solid-state runs, each of the salts was photolyzed in methanol; in every case, racemic photoproducts were obtained.

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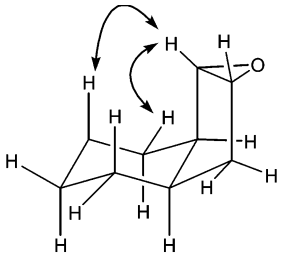

FIGURE 2. NOE interactions used in establishing the stereochemistry of compound **7**.

TABLE 3. Asymmetric Induction in the Photolyses of Chiral Salts 1c−g

salt	amine	temp (°C)	conv (%)[a]	ee (%)[b]	[α][c]
1c	L-prolinamide	rt[d]	15	30	+
		rt	59	21	+
		rt	82	17	+
		rt	>99	12	+
1d	(*R*)-(+)-1-phenylethylamine	rt	4	53	+
		rt	28	37	+
		rt	82	33	+
		rt	>99	32	+
		−20	4	67	+
		−20	>99	44	+
1e	(*S*)-(−)-1-phenylethylamine	rt	10	39	−
		rt	59	37	−
		rt	90	35	−
		rt	98	31	−
		−20	14	45	−
1f	(1*R*,2*S*)-(+)-*cis*-1-amino-2-indanol	rt	7	23	+
		rt	45	21	+
		rt	94	17	+
		−20	10	25	+
1g	(*R*)-(−)-1-cyclohexylethylamine	rt	20	15	+
		rt	77	12	+
		rt	92	11	+
		−20	21	19	+

[a] Percentage of total GC integral due to the disappearance of the corresponding starting material. [b] The enantiomeric excess of the photoproduct **2** was determined via measuring the ee values of its epoxide derivative **7**. [c] Sign of rotation of **7** at the sodium D-line. [d] rt = room temperature.

In the presence of chiral auxiliaries, enantiomeric excess was induced in the *cis*-3a,4,5,6,7,7a-hexahydro-1*H*-indene (**2**), although only to a moderate extent. With (*R*)-(+)-1-phenylethylamine as the chiral auxiliary, the product alkene **2** from salt **1d** was obtained in 32% ee at complete conversion, while in the presence of (*S*)-(−)-1-phenylethylamine (salt **1e**), the opposite enantiomer was obtained in 31% ee. Access to both enantiomers is thus available by simple exchange of the ionic chiral auxiliary. Table 3 also shows that an increase in conversion leads to decreasing ee values. This is not unexpected, since the salts react to give products that presumably do not "fit" into the original crystal lattice, and defect sites are generated. As shown in Table 3, low-temperature photolysis can be used to compensate this effect. For reactions conducted at reduced temperature (−20 °C), enantioselectivities were better than those obtained at room temperature. Specifically, at −20 °C, quantitative conversion to alkene **2** from salt **1d** occurred in 44% ee compared to 32% ee at room temperature. This is probably due mainly to heat removal from the photolyzed crystals, thus maintaining crystallinity.

Two salts (**1d** and **1g**) of keto-acid **1b** provided crystals that were suitable for X-ray craystallographic analysis. The geometric data summarized in Table 2 reflect their high similarity to the crystal structure of keto-ester **1a**, which accounts for their photochemcial reactivity and lack of cyclization reaction. Figure 1 shows the solid-state conformation of the anion portion of salt **1d**. Since the absolute configuration of the counterion is known, the absolute configuration of the reacting ketone can be assigned unequivocally. The X-ray crystal structure of **1d** clearly shows the carbonyl group poised to abstract only one γ-hydrogen (Ha), while the others are too far away (Hb, Hc, and Hd, $d > 3.3$ Å). The biradical formed on abstraction of Ha would have a gauche geometry (C−OH and C_γ−Hb bonds in a syn relationship), and subsequent cleavage of C2−C3 should lead to the (3a*R*,7a*R*)-enantiomer of photoproduct **2**. On the other hand, formation of the (3a*S*,7a*S*)-enantiomer would require a ∼180° rotation of the benzoylmethyl group about the C2−C3 axis prior to hydrogen abstraction, which is presumably topochemically unfavorable in the solid state. These findings clearly explain the enantioselectivity observed for salt **1d**. However, with all five salts studied in this work, only low to moderate ee values were obtained for photoproduct **2**. How can this be explained? The answer to this question lies in the nature of the Norrish type II photoelimination reaction itself. Photoelimination of ketone **1**, a process involving breaking one molecule into two, unavoidably destroys the original crystal lattice. Also, photoproduct **2** , a liquid, softens the solid-state medium. As a result, topochemical control decreases as the reaction proceeds. Nevertheless, the solid-state medium remains viscous to retard complete conversion of the original conformer to a diastereomeric mixture via rotation about the C2−C3 bond, and this accounts for moderate ee values observed in this work.

Conclusion and Outlook

In summary, we have demonstrated that the solid-state ionic chiral auxiliary approach can be used to synthesize the enantiomerically enriched simple alkene *cis*-3a,4,5,6,7,7a-hexahydro-1*H*-indene (**2**) via a Norrish type II photoelimination reaction. X-ray crystallographic studies of the starting photoreactants allowed us to explain the selectivity of the reaction. Future studies will be focused on systems that afford solid alkene products and are less subject to crystal lattice breakdown during the photolysis process.[18]

Experimental Section

Preparation of Starting Materials. (a) (3aα,7aα)-2-(Bromomethyl)-2,3,3a,4,7,7a-hexahydro-1*H*-indene (10). To a cold (0 °C), stirred solution of triphenylphosphine (5.58 g, 21.3 mmol) and imidazole (2.90 g, 42.6 mmol) in CH_3CN (50 mL) was added bromine (3.71 g, 23.2 mmol) dropwise. Stirring was continued at 0 °C for 30 min after which time (3aα,7aα)-2,3,3a,4,7,7a-hexahydro-1*H*-indene-2-methanol (**9**, a ∼1:1 mixture of two isomers)[19] (1.62 g, 10.6 mmol in 50 mL of diethyl ether) was added. After 5 h the reaction was warmed to room temperature and stirred overnight. The reaction was then quenched with 5% sodium bicarbonate. Extraction with petroleum ether was followed by successive washing of the combined organic extracts with 5% aqueous sodium bicarbonate and brine. The organic layer was dried ($MgSO_4$) and the solvent was removed in vacuo. Silica gel chromatography (100% petroleum ether) and distillation (92−94 °C, 5 mmHg) provided the title compound (2.01 g, 88%, ∼1:1 diastereomeric mixture by ^{1}H NMR) as a colorless liquid. ^{1}H NMR ($CDCl_3$, 400 MHz): δ 1.16−2.15 (m, 10H), 2.40−2.58 (m, 1H), 3.40 (m, 2H), 5.60 (m, 2H) ppm. ^{13}C NMR ($CDCl_3$, 75 MHz): δ 26.5, 27.7, 35.5, 36.0, 37.1, 37.8, 38.5, 40.3, 40.8, 40.9, 125.2, 125.7 ppm. IR (neat): 3020, 2912, 2834, 1656, 1450, 1433, 1220, 637 cm^{-1}. HRMS (EI): calcd for $C_{10}H_{15}{}^{81}Br$ 216.0337, found 216.0340; calcd for $C_{10}H_{15}{}^{79}Br$ 214.0357, found 214.0354.

(b) Methyl 4-{2-[(3aα,7aα)-2,3,3a,4,7,7a-Hexahydro-1*H*-inden-2-yl]-1-hydroxyethyl}benzoate (11). To a suspension of Mg turnings (110 mg, 4.53 mmol) in THF (5 mL) was added 1,2-dibromoethane (25 μL). The mixture was gently warmed and the bromide (**10**) (650 mg, 3.02 mmol in 5 mL of THF) was added slowly so as to maintain a gentle reflux. After being stirred for 1 h, the reaction mixture was cooled to −78 °C and methyl 4-formylbenzoate (445 mg, 2.71 mmol in 5 mL of THF) was introduced. After the solution was stirred for 1 h at −78 °C, the reaction was quenched with 5% HCl and extracted with Et_2O. The combined organic layer was washed successively with water and brine. After drying ($MgSO_4$) and removal of the solvent in vacuo, the residue was subjected to silica gel chromatography (10% EtOAc in petroleum ether). Solvent removal in vacuo provided the title compound (467 mg, 51%, ∼1:1 diastereomeric mixture by ^{1}H NMR) as a white solid. Mp: 65−68 °C (EtOAc/petroleum ether). ^{1}H NMR ($CDCl_3$, 300 MHz): δ 0.97−2.30 (m, 14H), 3.87 (s, 3H), 4.67 (m, 1H), 5.62 (m, 2H), 7.36 (d, J = 8.3 Hz, 2H), 7.95 (d, J = 8.3 Hz, 2H) ppm. ^{13}C NMR ($CDCl_3$, 75 MHz): δ 26.6, 27.9, 27.9, 31.8, 34.2, 35.3, 35.4, 35.9, 36.0, 38.1, 38.4, 38.7, 39.0, 47.4, 47.5, 52.0, 73.3, 73.5, 125.4, 125.8, 126.1, 129.0, 129.7, 150.2, 150.3, 166.9 ppm. IR (KBr): 3421, 3019, 2929, 2836, 1723, 1611, 1435, 1279, 1106, 709 cm^{-1}. HRMS (EI): calcd for $C_{19}H_{24}O_3$ 300.1725, found 300.1723.

(c) Methyl 4-[(2α,3aα,7aα)-Octahydro-1*H*-inden-2-ylacetyl]benzoate (1a). A suspension of 10% palladium on charcoal (50 mg) and methyl benzoate **11** (4.54 g, 15.1 mmol) in EtOAc (150 mL) was placed under an atmosphere of H_2. The mixture was stirred for 8 h and filtered through Celite545. Removal of the solvent in vacuo provided the corresponding alcohol (4.33 g, 95%) as a white solid. The alcohol obtained above was added to a mixture of Celite545 (9.5 g) and PCC (6.17 g, 28.6 mmol) in dichloromethane and the solution was stirred overnight at room temperature. The reaction mixture was filtered through a short column of Celite545 on Florisil and the remaining solids were triturated with anhydrous Et_2O. Solvent removal in vacuo was followed by silica gel chromatography (2% EtOAc in petroleum ether) to give a cis, trans mixture of methyl 4-octahydro-1*H*-inden-2-ylacetylbenzoate (**12**) (3.83 g, 85% from **11**, ∼1:1 diastereomeric mixture by ^{1}H NMR) as a white solid. Repeated recrystallization from EtOAc/petroleum ether yielded pure methyl 4-[(2α,3aα,7aα)-octahydro-1*H*-inden-2-ylacetyl]benzoate (**1a**) (1.19 g, 31%, 26% from **11**) as thin colorless needles. Mp: 103.5−105 °C (EtOAc/petroleum ether). UV/vis (2.40×10^{-4} M, MeOH): 250 (15244), 290 (1423), 340 (216) nm (M^{-1} cm^{-1}). ^{1}H NMR ($CDCl_3$, 400 MHz): δ 1.23−1.46 (m, 10H), 1.75−1.96 (m, 4H), 2.60 (m, 1H), 2.99 (d, J = 7.2 Hz, 2H), 3.92 (s, 3H), 7.96 (d, J = 8.2 Hz, 2H), 8.08 (d, J = 8.2 Hz, 2H) ppm. ^{13}C NMR ($CDCl_3$, 75 MHz): δ 23.0, 27.3, 31.9, 36.8, 38.8, 47.2, 52.4, 127.9, 129.8, 133.6, 140.5, 166.3, 199.9 ppm. IR (KBr): 2943, 2886, 2850, 1722, 1683, 1279, 1111, 765 cm^{-1}. HRMS (EI): calcd for $C_{19}H_{24}O_3$ 300.1725, found 300.1725. Anal. Calcd for $C_{19}H_{24}O_3$: C, 75.97; H, 8.05. Found: C, 76.15; H, 8.04.

(18) Using the solid-state ionic chiral auxiliary approach, high ee values have been obtained in the Norrish type II cleavage reaction with the alkene product being a solid: Chong, K. C. W.; Scheffer, J. R. *J. Am. Chem. Soc.* **2003**, *125*, 4040.

(19) Turecek, F.; Vystrcil, A. *Collect. Czech. Chem. Commun.* **1976**, *41*, 1571.

The structure of this compound was confirmed by X-ray crystallography.

(d) 4-[(2α,3aα,7aα)-Octahydro-1*H*-inden-2-ylacetyl]benzoic Acid (1b). To a solution of ester **1a** (600 mg, 2.00 mmol) in THF (40 mL) was added a solution of NaOH (10 g, 250 mmol) in water (90 mL). The reaction mixture was refluxed for 20 h, then cooled to room temperature. Diethyl ether was used to extract the mixture and the aqueous layer was treated with concentrated hydrochloric acid until it was strongly acidic. A large amount of white precipitate was formed. Water was added to dissolve the sodium chloride and the mixture was extracted with Et_2O. The combined organic extracts were washed with water and brine, then dried ($MgSO_4$) and concentrated in vacuo to afford acid **1b** as a white solid. Recrystallization of acid **1b** from EtOH/H_2O gave analytically pure acid **1b** (490 mg, 87%) as colorless flakes. Mp: 221−222.5 °C (EtOH/H_2O). UV/vis (2.03×10^{-4} M, MeOH): 250 (18053), 290 (1911), 340 254) nm (M^{-1} cm^{-1}). ^{1}H NMR (DMSO, 400 MHz): δ 1.19−1.48 (m, 10H), 1.68−1.96 (m, 4H), 2.58 (m, 1H), 3.08 (d, J = 7.2 Hz, 2H), 8.02 (m, 4H) ppm. Carboxylic acid proton was not observed. ^{13}C NMR (DMSO, 75 MHz): δ 22.6, 26.9, 31.4, 36.2, 38.7, 46.5, 128.0, 129.5, 134.3, 139.9, 166.6, 199.7 ppm. IR (KBr): 3300−2300 (br), 2920, 2850, 1690, 1298, 1205, 769 cm^{-1}. HRMS (EI): calcd for $C_{18}H_{22}O_3$ 286.1569, found 286.1568. Anal. Calcd for $C_{18}H_{22}O_3$: C, 75.50; H, 7.74. Found: C, 75.65; H, 7.96.

Preparation of Salts. (a) L-Prolinamide Salt of Keto-Acid 1b (1c). Salt **1c** was prepared by dissolving keto-acid **1b** (43 mg, 0.15 mmol) and L-prolinamide (18 mg, 0.16 mmol) in a hot mixture of acetonitrile and methanol. Upon cooling the mixture to room temperature, salt **1c** was obtained as thin colorless needles (57 mg, 95%). Mp: 145−146.5 °C (MeOH/MeCN). ^{1}H NMR (CD_3OD, 300 MHz): δ 1.11−1.95 (m, 17H), 2.28 (m, 1H), 2.57 (m, 1H), 2.94 (d, J = 7.3 Hz, 2H), 3.21 (m, 1H, partly hidden under the solvent peak), 4.12 (dd, J = 6.8 and 6.7 Hz, 1H), 7.82−7.91 (m, 4H) ppm. No NH_2 or NH_3^+ signal was observed due to proton exchange with the solvent. ^{13}C NMR (CD_3OD, 75 MHz): δ 24.2, 25.3, 28.4, 31.2, 33.4, 37.7, 40.3, 47.3, 48.0, 60.9, 128.8, 130.4, 139.8, 143.2, 172.7, 173.8, 202.5 ppm. IR (KBr): 3387, 3168, 2918, 2886, 2852, 1708, 1680, 1596, 1552, 1391, 1208, 1001, 778 cm^{-1}. HRMS (FAB, +LSIMS, matrix: glycerol): calcd for $C_{23}H_{33}N_2O_4$ 401.2440, found 401.2433 (M + H) $^+$. Anal. Calcd for $C_{23}H_{32}N_2O_4$: C, 68.97; H, 8.05; N, 6.99. Found: C, 68.69; H, 8.06; N, 6.75.

(b) (*R*)-(+)- and (*S*)-(−)-1-Phenylethylamine Salt of Keto-Acid 1b (1d and 1e). Keto-acid **1b** (43 mg, 0.15 mmol) and (*R*)-(+)-1-phenylethylamine (20 μL, 19 mg, 0.16 mmol) were dissolved in a hot mixture of acetonitrile and methanol. Upon cooling the mixture to room temperature, salt **1d** was obtained as colorless needles (55 mg, 90%). Mp: 172−173 °C (MeOH/MeCN). ^{1}H NMR (CD_3OD, 300 MHz): δ 1.15−1.45 (m, 10H), 1.52 (d, J = 6.8 Hz, 3H), 1.67−1.95 (m, 4H), 2.58 (m, 1H), 2.96 (d, J = 7.2 Hz, 2H), 4.33 (q, J = 6.8 Hz, 1H), 7.32 (m, 5H), 7.87 (m, 4H) ppm. No NH_3^+ signal was observed due to proton exchange with the solvent. ^{13}C NMR (CD_3OD, 75 MHz): δ 21.0, 24.2, 28.5, 33.4, 37.7, 40.2, 48.0, 52.3, 127.6, 128.7, 130.0, 130.3, 130.4, 139.7, 140.1, 143.2, 174.0, 202.6 ppm. IR (KBr): 2923, 2854, 1681, 1586, 1530, 1388, 1207, 778, 700 cm^{-1}. HRMS (FAB, +LSIMS, matrix: glycerol): calcd for $C_{26}H_{34}NO_3$ 408.2539, found 408.2526 (M + H) $^+$. Anal. Calcd for $C_{26}H_{33}NO_3$: C, 76.62; H, 8.16; N, 3.44. Found: C, 76.83; H, 8.23; N, 3.49.

The (*S*)-(−)-1-phenylethylamine salt **1e** was prepared analogously (87% yield) and also gave satisfactory MS and elemental analysis results.

(c) (1*R*,2*S*)-(+)-*cis*-1-Amino-2-indanol Salt of Keto-Acid 1b (1f). Salt **1f** was prepared by dissolving 43 mg (0.15 mmol) of keto-acid **1b** and 23 mg (0.15 mmol) of (1*R*,2*S*)-(+)-*cis*-1-amino-2-indanol in a hot mixture of acetonitrile and methanol. Upon cooling the solution to room temperature, salt **1f** was obtained as a white powder (60 mg, 90%). Mp: 146−148 °C (MeOH/MeCN). ^{1}H NMR (CD_3OD, 300 MHz): δ 1.15−1.45 (m, 10H), 1.64−1.93 (m, 4H), 2.57 (m, 1H), 2.85−3.14 (m, 2H), 2.92 (d, J = 7.2 Hz, 2H), 4.43 (d, J = 6.0 Hz, 1H), 4.58 (dt, J = 6.0 and 5.4 Hz, 1H), 7.20 (m, 5H), 7.85 (m, 4H) ppm. No OH or NH_3^+ signal was observed due to proton exchange with the solvent. ^{13}C NMR (CD_3OD, 75 MHz): δ 24.2, 28.4, 33.4, 37.7, 40.1, 40.1, 48.0, 58.6, 71.9, 126.2, 126.6, 128.4, 128.7, 130.4, 130.8, 138.2, 139.7, 142.8, 143.3, 174.0, 202.6 ppm. IR (KBr): 3216, 2922, 2853, 1683, 1591, 1542, 1391, 1309, 1208, 1098, 780 cm^{-1}. HRMS (FAB, +LSIMS, matrix: glycerol): calcd for $C_{27}H_{34}NO_4$ 436.2488, found 436.2484 (M + H) $^+$. Anal. Calcd for $C_{27}H_{33}NO_4$: C, 74.45; H, 7.64; N, 3.22. Found: C, 74.83; H, 7.82; N, 3.23.

(d) (*R*)-(−)-1-Cyclohexylethylamine Salt of Keto-Acid 1b (1 g). Salt **1g** was prepared by dissolving keto-acid **1b** (43 mg, 0.15 mmol) and (*R*)-(−)-1-cyclohexylethylamine (23 μL, 20 mg, 0.16 mmol) in a hot mixture of acetonitrile and methanol. Upon cooling the mixture to room temperature, salt **1g** was obtained as long colorless needles (59 mg, 94%). Mp: 169−171 °C (MeOH/MeCN). ^{1}H NMR (CD_3OD, 300 MHz): δ 0.90−1.95 (m, 28H), 2.59 (m, 1H), 2.96 (d, J = 7.2 Hz, 2H), 2.97 (m, 1H, partly overlapped with the peak at 2.96 ppm), 7.88 (m, 4H) ppm. No NH_3^+ signal was observed due to proton exchange with the solvent. ^{13}C NMR (CD_3OD, 75 MHz): δ 16.1, 24.2, 27.0, 28.5, 28.8, 30.0, 33.5, 37.7, 40.2, 42.7, 48.0, 53.4, 128.7, 130.4, 139.6, 143.3, 174.0, 202.6 ppm. IR (KBr): 2922, 2853, 1684, 1584, 1536, 1381, 1206, 986, 780 cm^{-1}. HRMS (FAB, +LSIMS, matrix: glycerol): calcd for $C_{26}H_{40}NO_3$ 414.3008, found 414.3008 (M + H) $^+$. Anal. Calcd for $C_{26}H_{39}NO_3$: C, 75.50; H, 9.50; N, 3.39. Found: C, 75.69; H, 9.61; N, 3.56.

Photochemical Procedures. All photolyses were performed using a 450-W Hanovia medium-pressure mercury lamp placed in a water-cooled, Pyrex immersion well (transmits λ > 290 nm). For solution-phase photolyses, Pyrex tubes were used and the solution was purged with nitrogen for at least 15 min prior to photolysis. For solid-state photolyses, 4−6 mg samples were crushed, using a mortar and pestle, and suspended in 3 mL of HPLC grade hexanes (mixture of isomers). The suspension was placed 10 cm from the immersion well, thoroughly degassed under nitrogen, and irradiated with stirring for the required length of time at the temperature indicated. For some compounds that required low temperature during photolysis, a Cryocool CC-100 II Immersion Cooling System (Neslab Instrument Inc.) was used with ethanol as the coolant. Temperatures were maintained within ±2 °C of the designated values. For neutral molecules, the sample was directly analyzed by gas chromatography. The reaction mixtures containing chiral organic salts were first derivatized to their corresponding methyl esters by treatment with excess ethereal diazomethane solution and then washed with water and subjected to short-path silica gel chromatography to remove the chiral auxiliary. The mixtures were then analyzed by gas chromatography for conversion as well as product composition.

Photolysis of Keto-Ester 1a. A solution of 1.01 g (3.36 mmol) of keto-ester **1a** in 50 mL of acetonitrile was photolyzed through Pyrex for 3 h. GC analysis indicated the complete consumption of starting material and the presence of two products (**2** and **3a**) in a 58:36 ratio. The reaction mixture was extracted with pentane. The pentane layer was concentrated under reduced pressure at 0 °C followed by bulb-to-bulb distillation to give alkene **2** (283 mg, 69%) as a clear oil. The acetonitrile layer was concentrated in vacuo and subjected to flash column chromatography (2% EtOAc in petroleum ether) to afford **3a** (424 mg, 71%) as a white solid. Compounds **2** and **3a** are known compounds and their spectral data are in total agreement with literature values.[20,21]

***cis*-(3aα,7aα)- 3a,4,5,6,7,7a-Hexahydro-1*H*-indene(2).** Colorless oil. ^{1}H NMR ($CDCl_3$, 300 MHz): δ 1.22−1.65 (m, 8H),

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1.98 (m, 1H), 2.10−2.28 (m, 2H), 2.50 (m, 1H), 5.67 (m, 2H) ppm. ^{13}C NMR ($CDCl_3$, 75 MHz): δ 23.1, 23.2, 27.9, 28.5, 37.6, 43.7 (br), 130.0, 136.7 ppm. IR (neat): 3055, 2928, 2853, 1656, 1446, 1355, 982, 852 cm^{-1}. HRMS (EI) calcd for C_9H_{14} 122.1096, found 122.1093.

Methyl 4-Acetylbenzoate (3a). White solid. Mp: 95−96 °C (lit.[21] mp 95.0−95.5 °C). ^{1}H NMR ($CDCl_3$, 300 MHz) δ 8.11−8.08 (d, J = 8.7 Hz, 2H), 7.99−7.96 (d, J = 8.7 Hz, 2H), 3.92 (s, 3H), 2.61 (s, 3H) ppm. ^{13}C NMR ($CDCl_3$, 75 MHz): δ 197.5, 166.2, 140.2, 133.9, 129.8, 128.2, 52.4, 26.8 ppm. IR (KBr): 2960, 1722, 1679, 1284, 1113, 770 cm^{-1}. HRMS (EI): calcd for $C_{10}H_{10}O_3$ 178.0629, found 178.0628.

(1aα,1bα,5aα,6aα)-Octahydro-1a*H*-indeno[1,2-*b*]oxirene (7). To a solution of alkene **2** (589 mg, 4.82 mmol) in CH_2Cl_2 (5 mL) was added a solution of 70% *m*-chloroperoxybenzoic acid (1.78 g, 7.23 mmol) in CH_2Cl_2 (10 mL). The resulting mixture was heated under reflux with stirring for 1 h. Upon cooling the solution, *n*-pentane was added to form a suspension. The supernatant liquid from the resulting suspension was passed through a short silica gel column. The eluent was concentrated and subjected to a second silica gel chromatography (2% Et_2O in *n*-pentane). After removal of solvent (50 °C oil bath), bulb-to-bulb distillation afforded epoxide **7** (473 mg, 71%) as a colorless oil. ^{1}H NMR ($CDCl_3$, 400 MHz): δ 0.52 (m, 1H), 0.83−0.96 (m, 2H), 1.16 (m, 1H), 1.22−1.45 (m, 5H), 1.62 (dd, J = 7.5 and 13.5 Hz, 1H), 1.84 (m, 1H), 1.95 (m, 1H), 2.97 (m, 1H), 3.08 (m, 1H) ppm. ^{13}C NMR ($CDCl_3$, 75 MHz): δ 21.9, 24.8, 25.1, 25.3, 29.1, 29.9, 37.8, 54.6, 60.0 ppm. IR (neat): 2929, 2853, 1452, 1397, 1265, 1219 cm^{-1}. HRMS (EI) calcd for $C_9H_{14}O$ 138.1045, found 138.1047.

The stereochemistry of this compound was established by the NOE interactions shown in Figure 2.

Photolysis of Keto-Acid 1b. A solution of 5 mg of keto-acid **1b** in 3 mL of acetonitrile was irradiated through Pyrex for 1 h. The mixture was treated with excess ethereal diazomethane solution. GC analysis indicated the absence of starting material and the presence of two products, whose retention times were the same as those of the products formed by photolysis of keto-ester **1a** (i.e., alkene **2** and ketone **3a**).

Photolysis of Salts 1c−g. Crystals of salts **1c**−**g** (4−6 mg) were photolyzed in 3 mL of hexanes suspension for varying lengths of time and at different temperatures (see Table 3). The reaction mixtures were treated with excess ethereal diazomethane to convert the salts to the corresponding methyl ester. After being washed with water and dried, the mixture was subjected to short-path silica gel chromatography to remove the chiral auxiliary. The eluents were then analyzed by gas chromatography to determine the percent conversion. Treatment of the eluent with a dichloromethane solution of *m*-CPBA converted alkene **2** to epoxide **7**. The enantiomeric excess of the photoproduct **2** was thus determined by measuring the ee of its epoxide derivative **7**, using chiral GC (SUPELCO β-Dex 350 Custom Capillary Column, 120 °C at 1.37 mL/min).

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Supporting Information Available: General methods and ^{1}H NMR spectra of compounds **1a**−**1g**, **7**, **10**, and **11** and crystallographic data for **1a**, **1d**, and **1g**. This material is available free of charge via the Internet at http://pubs.acs.org.

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