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Enantioselective photoelectrocyclization of a tropolone derivative in the crystalline state†

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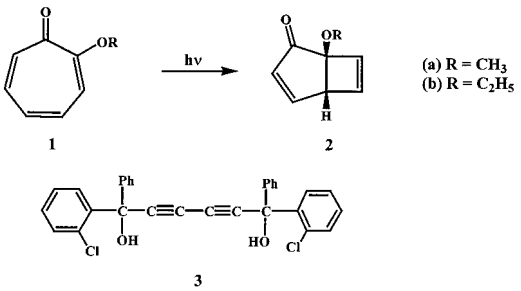
ABSTRACT: Achiral tropolone ethers are well known to undergo photochemically induced disrotatory electrocyclic ring closure in solution to form racemic bicyclo[3.2.0]hepta-3,6-dien-2-one derivatives. The present paper reports successful efforts to carry out this transformation enantioselectively through the use of the solid-state ionic chiral auxiliary method. In this method, the reactant, an achiral tropolone ether, is equipped with a carboxylic acid group to which an optically pure amine can be attached by salt formation. Salts such as these are required to crystallize in chiral space groups, which provide asymmetric reaction cavities capable of differentiating enantiomeric transition states. Irradiation of these materials in the solid state leads to enantiomerically enriched products in moderate to high enantiomeric excess depending on the amine employed. Of the amines studied, the best results were obtained with 1-phenylethylamine and 1-amino-2-indanol, which gave enantiomeric excesses in the 60–80% range depending on the extent of conversion. Because the tropolone ring is planar, it is suggested that the stereochemical outcome of the electrocyclization in the solid state is governed by environmental crystal lattice effects rather than by the initial conformation of the reactant. Copyright © 2000 John Wiley & Sons, Ltd.

KEYWORDS: enantioselective photoelectrocyclization; crystalline tropolones; electrocyclic ring closure

INTRODUCTION

Over the years, tropolone ethers such as **1a** and **1b** (Scheme 1) have served as useful probes of new methods of asymmetric synthesis in organic photochemistry. These achiral molecules undergo smooth disrotatory photocyclization to afford chiral bicyclic products of general structure **2**, the absolute stereochemistry of which depends on the direction of the electrocyclic ring closure process. In an elegant study, Toda and co-workers showed in 1986 that enantioselective photoelectrocyclization of tropolone methyl ether (**1a**) and tropolone ethyl ether (**1b**) could be achieved by forming crystalline 1:1 complexes of these compounds with optically pure (*R*)-(−)-1,6-di(*o*-chlorophenyl)-1,6-diphenylhexa-2,4-diyne-1,6-diol (**3**) and photolyzing these complexes in the solid state (Scheme 1).[1–3] While the cyclization photoproducts **2a** and **2b** were formed in low chemical yields (11 and 12%, respectively), the enantiomeric excesses (e.e.s) were high, approaching 100%.



Scheme 1

A second approach to the enantioselective photoelectrocyclization of tropolone ethers was reported recently by Joy *et al.*[4] and consists of irradiating tropolone ethers in the interior supercages of a zeolite that also contains an optically pure chiral inductor molecule such as ephedrine or norephedrine. The maximum e.e. that could be achieved using this strategy was approximately 50% in the case of tropolone methyl ether (**1a**),[4] but subsequent work by the same group on the 2-phenylethyl ether of tropolone showed that enantiomeric excesses of up to 78% could be obtained in zeolite NaY using ephedrine as the chiral inductor.[5] An even more recent paper by Joy *et al.*[6] reports that irradiation of the optically pure 2-methylbutyl ether of tropolone leads to cyclization products analogous to **2** in diastereomeric excesses of

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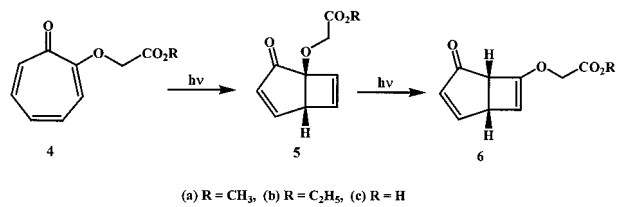
up to 92% when the reaction is conducted in the norephedrine-containing supercages of zeolite NaY.

Recent work from our laboratory has shown that an excellent method of asymmetric induction in photochemical reactions is through the use of the so-called solid-state ionic chiral auxiliary method.[7] In this approach, an achiral photoreactant is equipped with a carboxylic acid tether to which an optically pure amine can be attached by salt formation. Salts of this type are required to crystallize in chiral packing arrangements that can be thought of as providing chiral reaction cavities capable of differentiating enantiomeric transition states. As a result, irradiation of such salts in the crystalline state leads to enantiomerically enriched photoproducts following removal of the chiral auxiliary. Using this method, high e.e.s have been achieved in the Yang photocyclization reaction[8–10] and the di-π-methane photorearrangement.[11] The opposite approach, in which the photoreactant is an achiral ammonium ion and the chiral auxiliary is an optically pure carboxylate anion, is equally valid and has also been been shown to work well.[12] The purpose of this paper is to report the successful application of the solid-state ionic chiral auxiliary method to the enantioselective photoelectrocyclization reaction of tropolone ethers.

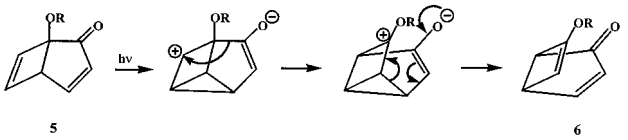


Scheme 2.

RESULTS AND DISCUSSION

The ionic chiral auxiliary approach to asymmetric synthesis requires a reactant possessing an acidic or basic functional group that allows for salt formation. For the present study, we chose as our target molecule the tropolone ether carboxylic acid derivative **4c** (Scheme 2). The corresponding ethyl ester **4b** is readily available through the reaction of tropolone with ethyl bromoacetate in the presence of base,[13] and hydrolysis of the ester was expected to afford acid **4c**. In practice, hydrolysis of ester **4b** proved to be tricky, as conventional methods using aqueous sodium or potassium hydroxide gave only tropolone. The problem was eventually solved by using barium hydroxide octahydrate in methanol, which afforded the desired acid **4c** in approximately 60% yield.

Prior to embarking on the solid-state asymmetric induction studies, the solution-phase photochemistry of ethyl ester **4b** and methyl ester **4a** was investigated. Irradiation of these esters at wavelengths >290 nm (Pyrex) in acetonitrile solution afforded excellent chemical yields of the rearrangement products **6b** and **6a**, respectively (Scheme 2). It should be noted that these are not the expected products of simple photoelectrocyclization (**5a** and **5b**), but rather are derived from the primary photoproducts by a secondary, deep-seated photorearrangement whose mechanism was worked out (for ester **1a**) by Dauben *et al.*[14] (Scheme 3). Attempts to halt the photoreaction of esters **4a** and **4b** at an earlier stage and thereby isolate photoproducts **5a** and **5b** were not successful. Although gas chromatographic peaks consistent with the formation of compounds **5a** and **5b** could be detected in the early stages of the photoreaction, they never accumulated beyond $\sim$ 10% of the total mixture and were not isolated. The same proved to be true in the crystalline state and therefore, unexpectedly, we were forced to carry out the asymmetric induction studies on these secondary photoproducts. This actually turned out to be a bonus, since it gave us the opportunity to assess the overall enantioselectivity of two *consecutive* photochemical reactions in the solid state, something that had not been attempted previously.



Scheme 3.

For the asymmetric induction studies, tropolone carboxylic acid derivative **4c** was treated with a variety of commercially available, optically pure amines (Table 1) and the resulting crystalline salts were fully characterized by conventional methods. Seven salts were investigated. The solid-state photolyses were conducted by placing the recrystallized salts between two quartz or Pyrex plates and sealing the resulting 'sandwiches' in polyethylene bags under nitrogen. The samples were irradiated at ambient temperature in a Rayonet reactor using six RPR 3500 ($\lambda \approx 350$ nm) lamps. No melting of the samples was observed, and the color of the samples changed from white to light brown. After reaction, the samples were dissolved in methanol, treated with excess ethereal diazomethane to form the corresponding methyl esters, filtered, analyzed for extent of conversion by gas chromatography and subjected to radial chromatography using a Chromatotron. The fractions corresponding to methyl ester **6a** were then analyzed for enantiomeric excess by chiral HPLC. The data are summarized in Table 1.

The results indicate that ester **6a** can be formed in respectable optical and chemical yields through the use of the solid-state ionic chiral auxiliary method. For reasons that we do not fully understand, the amines vary in their ability to bring about asymmetric induction—a feature we have noted previously.[10] Crystallographic evidence on this point is lacking in the present instance, however,

Table 1. Asymmetric induction in the solid-state photochemistry of salts of acid **4**

Optically pure amine	Irradiation time (min)	Conversion (%)	Enantiomeric excess (%)[a]
(*R*)-(+)-1-Phenylethylamine	5	7	79A
	30	23	73
	150	55	71
	210	77	56
(*S*)-(−)-1-Phenylethylamine	5	11	77B
	30	24	76
	150	56	69
	200	81	53
(*S*)-(−)-1-(1-Naphthyl)ethylamine	5	39	57A
	30	56	45
	120	83	30
(*R*)-(+)-1-*p*-Tolylethylamine	5	15	33A
	30	54	26
	120	85	19
(−)-*cis*-Myrtanylamine	8	13	37B
	30	35	21
	120	89	17
(+)-Bornylamine	8	11	75B
	20	30	72
	90	81	63
(1*R*,2*S*)-(+)-1-Amino-2-indanol	3	45	73A
	20	81	70
	30	95	63
			60

[a] The letter A indicates that the predominant enantiomer of photoproduct **6a** corresponds to the first chiral HPLC peak, absolute stereochemistry unknown. The letter B indicates a predominance of the second HPLC peak.

as none of the salts formed crystals suitable for x-ray diffraction studies. Fortunately, it has always been possible to find two or three amines that work well. In previous studies, 1-phenylethylamine consistently outperformed other chiral amines, and the present case is no exception. One advantage of 1-phenylethylamine is that both enantiomers are commercially available, and this allows the preparation of both enantiomers of photoproduct **6a;** the observation that the e.e.s are equal and opposite indicates that the system is well behaved. The decrease in e.e. with increasing conversion is a general characteristic of asymmetric induction in the solid state and can reasonably be attributed to crystal breakdown and loss of topochemical control as product molecules accumulate within the crystal lattice of the reactant.

The e.e.s were only slightly improved by lowering the photolysis temperatures. For example, irradiation of the 1-phenylethylamine salt for 30 min at −78 °C led to a 17% conversion and an e.e. of 78% (compared with 23% conversion and 73% e.e. at ambient temperature). Similarly, photolysis of the 1-*p*-tolylethylamine salt for 30 min at −78 °C afforded ester **6a** in 29% e.e. at 33% conversion, a very modest improvement over the results observed at ambient temperature (26% e.e., 54% conversion). Finally, we note that, as in all our solid-state ionic chiral auxiliary studies, irradiation of the chiral salts in solution (methanol in the present instance) afforded only racemic products. This highlights the true solid-state nature of the asymmetric induction process.

As mentioned earlier, the photochemical conversion of tropolone ethers into products such as **6** is a two-step process—photoelectrocyclization to **5** followed by photorearrangement to **6**—and it is fair to ask which of these is the enantiodifferentiating step in the case of the crystalline salts. It is virtually certain that the first step, electrocyclic ring closure, determines the enantioselectivity. Disrotatory ring closure can form either the *R,S* or the *S,R* enantiomer of photoproduct **5**, and the subsequent transformation of **5** into **6** cannot be anything but stereospecific, since at no point in the proposed mechanism (Scheme 3) is there a chance for formation of both stereoisomers of **6** from a given stereoisomer of **5**.

Precedent for asymmetric induction in a solid-state electrocyclic reaction can be found in the work of Garcia-Garibay *et al.*,[15] who showed through crystallographically based computer simulations that the source of the enantioselectivity was *environmental*, that is, due to steric interactions between the reacting molecule and its neighbors in the crystal lattice. This stands in contrast to certain other enantioselective solid state photoreactions that are controlled *conformationally*.[10] In these reactions, asymmetric induction results when the reacting moiety crystallizes in a homochiral conformation that favors formation of only one of two possible enantiomeric photoproducts. Because tropolone ethers are essentially planar—and therefore conformationally unbiased with respect to electrocyclic ring closure—environmental

control is most likely in the solid-state photochemistry of salts of acid **4c**. Crystallographic evidence on this point is lacking, however, since, as mentioned above, attempts to grow well formed single crystals of these salts have so far been unsuccessful.

EXPERIMENTAL

General. Melting points were determined on a Fisher-Johns melting point apparatus and were not corrected. Elemental analyses were carried out by Mr Peter Borda, Department of Chemistry, University of British Columbia. Infrared spectra were recorded on a Perkin-Elmer 1710 Fourier transform spectrometer. The position of the absorption maxima (ν_{max}) are reported in cm^{-1}. Solid samples were prepared by grinding the compound with anhydrous potassium bromide in a mortar and pestle and pelleted in an evacuated die (Perkin-Elmer 186-0002) with a laboratory press (Carver, Model B) at 17 000 psi. Liquid samples were run neat as thin films between two sodium chloride plates. Low- and high-resolution electron ionization (EI) mass spectra were obtained on a Kratos MS50 instrument. Liquid secondary ion mass spectrometry (LSIMS) was performed on a Kratos Concept IIHQ hybrid mass spectrometer. Fast atom bombardment (FAB) mass spectra were obtained on an AEI MS-9 mass spectrometer with xenon bombardment of an alcohol matrix (as indicated in parentheses) of the sample. Mass to charge ratios (*m/z*) are reported with relative intensities (%) in parentheses (only for EI). Molecular ions are designed as M^+ (for EI) and $M^+ + 1$ (for FAB).

Ultraviolet spectra were recorded on a Perkin-Elmer Lambda-4B UV/Vis spectrometer. Wavelengths for each absorption maximum (λ_{max}) are reported in nanometers, and molar absorptivities (ε, $l\,mol^{-1}\,cm^{-1}$) are given in parentheses. Spectral-grade solvents available from Fisher were used without further purification. The spectrometers used to record ^1H NMR were Bruker AC-200 (200 MHz), Varian XL-300 (300 MHz), Bruker WH-400 (400 MHz) and Bruker AMX 500 (500 MHz). Signal positions are given as chemical shifts (δ) in parts per million using the following standards: residual $CHCl_3$, 7.24 ppm; Me_4Si as an external standard, 0 ppm for ^{29}Si. The chemical shifts are reported, followed by the multiplicity of the signals, number of protons, coupling constants (*J*) in Hz and the molecular assignment. The multiplicities are abbreviated as follows: s = singlet, d = doublet, dd = doublet of doublets, dt = doublet of triplets, t = triplet, q = quartet, m = multiplet, br = broad. In some cases, HMQC (heteronuclear multiple quantum coherence, ^1H–^{13}C correlation) and HMBC (heteronuclear multiple-bond connectivities, ^1H–^{13}C long range correlation) experiments were carried out on the Bruker AMX 500 spectrometer, and COSY (correlated spectroscopy) experiments on the Bruker WH-400 instrument in order to verify structures. The spectrometers used to record ^{13}C NMR spectra were Bruker AC-200 at 50 MHz, Varian XL-300 at 75 MHz, Bruker AM-400 at 100 MHz and Bruker AMX 500 at 125 MHz. All spectra were run under broadband proton decoupling. Signal positions are given as chemical shifts (δ) in parts per million using the central transition of $CDCl_3$ as the internal standard. Assignments were supported by APT (attached proton test) spectra. For APT, positive (+) signifies C or CH_2 and negative (−) signifies CH or CH_3.

Gas chromatographic analyses were run on a Hewlett-Packard 5890A gas chromatograph, using a 30 m × 0.25 mm i.d. fused-silica capillary column with a column head pressure (carrier gas: helium) of 14 psi. The injector temperature was kept at 250 °C unless specified otherwise. The signal from a flame ionization detector was integrated by a Hewlett-Packard 3392A integrator. High-performance liquid chromatography was performed on a Waters 600E system controller connected to a tunable absorbance UV detector (Waters 486). A chiral column, Chiralpak AS, 250 mm × 4.6 mm i.d. (Chiral Technologies), was used to determine enantiomeric excesses (optical purities). Thin-layer chromatography (TLC) was performed on commercial pre-coated silica gel plates (Merck, Silica gel 60, 230–400 mesh) with an aluminum backing and fluorescent indicator (F_{254}). Flash column chromatography was carried out by using 230–400 mesh size silica gel slurry packed and eluting with the appropriate solvent combination. All solvents were used as supplied by Fisher Scientific, unless specified otherwise. Deuterated solvents were obtained from Cambridge Isotope Laboratories. Unless specified otherwise, reagents were used as supplied by Aldrich.

*Preparation of ethyl ester **4b**.* Tropolone ester **4b** was synthesized according to the procedure reported by Bass and Gordon.[13] Modifications were made to improve the yield. In a dried 250 mL round-bottomed flask were placed tropolone (6.12 g, 50 mmol), potassium carbonate (20.75 g, 150 mmol), and 150 ml of anhydrous acetonitrile (CH_3CN). The mixture was vigorously stirred for 30 min at 40 °C until a fine yellow precipitate formed. Then ethyl bromoacetate (27.7 ml, 250 mmol) was carefully added to the reaction mixture. After stirring for 45 h at room temperature, the reaction solution turned reddish brown. A clear solution was obtained after suction filtration. The solvent was removed by rotatory evaporation. The residue was dissolved in methylene chloride and washed three times with 15 ml of 0.2 M sodium hydrogencarbonate, the organic layer was dried with anhydrous magnesium sulfate and the solvent was removed *in vacuo*. The residue was a viscous, dark-brown oil, which was purified by flash chromatography (hexane–EtOAc, 3:1). Upon removal of solvent, a clear, reddish brown oil was obtained (8.42 g, 81%).

Anal.: calculated for $C_{11}H_{12}O_4$: C, 63.44; H, 5.81; O, 31.75. Found C, 63.67; H, 5.65%. LRMS *m/z* (relative

intensity): 208 (M^+, 7), 179 (6), 163 (7), 135 (100), 105 (43), 77 (31). HRMS: calculated for $C_{11}H_{12}O_4$: 208.0733. Found: 208.0733. IR (KBr) ν_{max}: 1752 (C=O), 1596 (seven-membered ring C=O), 1181 (C—O) cm^{-1}. UV (methanol) λ_{max}: 320 (7959), 230 (15 507), 227 (15 528), 226 (15 483), 222 (15 078) nm. ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.15–7.14 (m, 2H, aromatic H), 6.95 (t, 1H, J = 9.8 Hz, aromatic H), 6.86-6.81 (m, 1H, aromatic), 6.72 (d, 2H, J = 9.7 Hz, H_6), 4.76 (S, 2H, OCH_2CO_2Et), 4.17 (q, 2H, J = 7.1 Hz, OCH_2CH_3), 1.20 (t, 3H, J = 7.1 Hz, OCH_2CH_3). ^{13}C NMR (75 MHz, $CDCl_3$): δ 180.3 (+), 167.6 (+), 163.4 (+), 137.9 (−), 136.4 (−), 132.1 (−), 129.3 (−), 116.3 (−), 65.7 (+), 61.4 (+), 13.9 (−).

Preparation of acid ***4c***. In a 100 ml flask were placed barium hydroxide octahydrate (1.10 g) and ethyl ester **4b** (6.00 g, 28.8 mmol) in methanol (40 ml). The reaction mixture became a cloudy, viscous slurry after stirring for 3 min at room temperature. Stirring was continued for 2 h. Then HCl (2 M) was added to neutralize the base and the reaction mixture turned clear. The reaction solution was concentrated by rotary evaporation to remove most of the solvent (5 ml of viscous liquid were left), and 20 ml of methylene chloride were added to the residue. A white solid was formed. The solid was filtered and washed with three 5 ml portions of diethyl ether. The product was dried under vacuum for 24 h. A grayish white solid was obtained (3.23 g, yield 59.3%). The solid was purified by recrystallization from methanol and acetonitrile. An off-white solid (2.96 g) was obtained after recrystallization.

M.p.: 144–147 °C. Anal.: Calculated for $C_9H_8O_4$: C, 60.00; H, 4.48; O, 35.52. Found C, 59.75; H, 4.50%. LRMS *m/z* (relative intensity): 181 (M + 1, 5), 180 (M^+, 36), 136 (10), 135 (100), 123 (26.), 106 (13), 105 (44), 77 (14). HRMS: calculated for $C_9H_8O_4$: 180.0423. Found: 180.0422. IR (KBr) ν_{max}: 3187 (O—H), 1735 (acid C=O), 1595 (seven-membered ring C=O), 1474 (C=C), 1269 (C—O), 1207 (C—O) cm^{-1}. UV (methanol) λ_{max}: 320 (9056), 236 (14 372), 234 (14 607), 229 (14 981), 226 (15 084) nm. ^{1}H NMR (400 MHz, CD_3OD): δ 7.38–7.33 (m, 1H, C*H*), 7.18-6.99 (m, 4H, C*H*), 4.86 (s, 2H, O—CH_2—C=O). ^{13}C NMR (75 MHz, CD_3OD): δ 179.3 (+), 171.1 (+), 165.2 (+), 140.0 (−), 138.0 (−), 135.3 (−), 131.1 (−), 117.9 (−), 66.3 (+).

Preparation of methyl ester 4a. Acid **4c** (91 mg, 0.48 mmol) was dissolved in 3 ml of methanol. Diazomethane (diethyl ether solution) was slowly added until there were no bubbles coming from the reaction mixture. The reaction mixture was stirred for 2 h, then diazomethane solution was added (1 ml) and stirring was continued for another 2 h. The solvent was removed by rotary evaporation. The residual oil was purified by radial chromatography (hexane–EtOAc, 1:1), affording 89 mg of **4a** (dark-yellow oil, yield 96%).

Anal.: calculated for $C_{10}H_{10}O_4$: C, 61.84; H, 5.19. Found C, 61.73; H, 5.23%. LRMS *m/z* (relative intensity): 195 (M + 1, 3), 194 (M^+, 24), 179 (6), 163 (10), 136 (6), 135 (100), 107 (6), 106 (17), 105 (36), 79 (4), 78 (10), 77 (23), 65 (5), 51 (6). HRMS: calculated for $C_{10}H_{10}O_4$: 194.0579. Found: 194.0577. IR (KBr) ν_{max}: 2953 (C— H), 1757 (C=O), 1627 (C=O), 1596, 1496, 1473, 1438 (C=C), 1176 (C—O), 1094, 1033 cm^{-1}. UV (methanol) λ_{max}: 319 (7914), 229 (1514), 227 (15 501), 226 (15 124), 222 (14 821) nm. ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.24–7.14 (m, 2H, seven-membered ring C*H*), 6.97 (t, 1H, J = 9.8 Hz, seven-membered ring C*H*), 6.86 (m, 1H, seven-membered ring C*H*), 6.75 (d, 1H, J = 9.8 Hz, seven-membered ring C*H*), 4.80 (s, 2H, O—CH_2), 3.73 (s, 3H, OCH_3). ^{13}C NMR (75 MHz, $CDCl_3$): δ 180.4 (+), 168.2 (+), 163.4 (+), 138.1 (−), 136.5 (−), 132.2 (−), 129.5 (−), 116.7 (−), 65.7 (+), 52.3 (−).

Solution-phase photolysis of methyl ester 4a: characterization of photoproduct 6a. In a dried flask were placed **4a** (126 mg, 0.65 mmol) and 80 ml of acetonitrile. The reaction mixture was degassed under N_2 for 30 min. Then the mixture was irradiated for 30 h (Pyrex, λ >290 nm) by using a Hanovia 450 W medium-pressure mercury lamp. The color of the solution changed from pale orange to pale reddish brown. The solvent was removed by rotary evaporation, leaving an oily residue. The crude reaction mixture was purified by radial chromatography (hexane–diethyl ether 3:1), affording 82 mg of **6a** (oil, yield 65%).

Anal.: calculated for $C_{10}H_{10}O_4$: C, 61.84; H, 5.19. Found C, 62.11; H, 5.10%. LRMS *m/z* (relative intensity): 194 (M^+, 4), 179 (3), 166 (2), 135 (100), 121 (23), 107 (15), 106 (24), 105 (36), 93(23), 78(14), 77 (36). HRMS: calculated for $C_{10}H_{10}O_4$: 194.0580. Found: 194.0579. IR (thin film) ν_{max}: 1762 (ester C=O), 1698 (five-membered ring C=O), 1631, 1220 (C—O) cm^{-1}. UV (methanol) λ_{max}: 302 (2123), 223 (10 253) nm. ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.64 (dd, 1H, J = 5.9 and 2.3 Hz, H_3), 5.98 (dd, 1H, J = 5.9 and 0.7 Hz, H_2), 5.05 (d, 1H, J = 1.0 Hz, H_5), 4.41 (dd, 2H, J = 8.0 and 6.0 Hz, H_8), 3.74 (s, 3H, OCH_3), 3.66 (d, 1H, J = 2.3, H_7), 3.58 (m, 1H, H_4). ^{13}C NMR (75 MHz, $CDCl_3$): δ 204.2 (C_1), 168.4 (C_9), 164.4 (C_3), 153.5 (C_6), 133.4 (C_2), 103.3 (C_5), 65.8 (C_8), 54.2(C_7), 52.3 (C_{10}), 40.7 (C_4).

Solution-phase photolysis of ethyl ester 4b. In a dried flask were placed **4b** (135 mg, 0.65 mmol) and 80 ml of acetonitrile. The reaction mixture was degassed under N_2 for 30 min and then irradiated for 2.5 h (Pyrex, λ >290 nm) by using a Hanovia 450 W medium-pressure mercury lamp. The color of the solution changed from light orange to reddish brown. The solvent was removed by rotary evaporation, leaving an oily residue. The crude reaction mixture was purified by flash column chromatography (hexane–diethyl ether, 7:3), affording 93 mg of photoproduct **6b** as an oil (yield 69%).

Anal.: calculated for $C_{11}H_{12}O_4$: C, 63.44; H, 5.81; O,

31.75. Found C, 63.71; H, 5.61%. LRMS *m/z* (relative intensity): 208 (M^+, 3), 179 (3), 135 (100), 121 (25), 107 (14), 106 (24), 105 (35), 93 (20), 78 (12), 77 (31), 73 (8), 45 (6). HRMS: calculated for $C_{11}H_{12}O_4$: 208.0733. Found: 208.0732. IR (thin film) ν_{max}: 1759 (ester C=O), 1698 (five-membered ring C=O), 1631 (C=C), 1212 (C—O) cm^{-1}. UV (methanol) λ_{max}: 302 (2156), 223 (10151) nm. ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.64 (dd, 1H, J = 5.8 and 2.4 Hz, H_3), 5.96 (dd, 1H, J = 5.7 and 0.6 Hz, H_2), 5.03 (d, 1H, J = 0.9 Hz, H_5), 4.38 (dd, 2H, J = 8.0 and 4.9 Hz, H_8), 4.19 (qd, 2H, J = 7.1 and 1.7 Hz, OCH_2CH_3), 3.64 (dd, 1H, J = 2.6 and 0.6 Hz, H_7), 3.57–3.56 (td, 1H, J = 2.6 and 0.9 Hz, H_4), 1.24 (t, 3H, J = 7.1 Hz, OCH_2CH_3). ^{13}C NMR (75 MHz, $CDCl_3$): δ 204.2 (+), 167.9 (+), 164.4 (−), 153.5 (+), 133.3 (−), 103.1 (−), 65.9 (+), 61.3 (+), 54.2 (−), 40.6 (−), 14.0 (−).

Preparation of salts of acid 4a with optically pure amines. The following procedure involving (*R*)-(+)-α-methylbenzylamine is typical for all the salts reported in Table 1. In a 25 ml flask were placed acid **4a** (0.11 g, 0.58 mmol) and 15 ml of THF, then (*R*)-(+)-α-methylbenzylamine (75 mg, 0.62 mmol) in THF (3 ml) was added dropwise. A white solid formed after stirring at room temperature for 3.5 h. The solid was filtered and washed twice with 5 ml portions of diethyl ether. After standing under vacuum overnight, the salt was collected as a white powder (0.14 g, 80%). The salt was recrystallized from acetonitrile prior to photolysis.

M.p.: 109.8–112.0 °C. Anal.: calculated for $C_{17}H_{19}O_4N_1$: C, 67.74; H, 6.36; N, 4.65. Found C, 67.13; H, 6.21; N, 4.62%. LRMS + LSIMS (matrix: thioglycerol): 302 (M + 1, 54), 181 (98), 122 (82), 105 (100), 91 (32). HRMS: calculated for $C_{17}H_{19}O_4N_1$: 302.1392. Found: 302.1394. IR (KBr) ν_{max}: 2974 (C—H), 1620 (C=O), 1553 (C=O), 1474, 1407 (C=C), 1283 (C—O), 1198 (C— O), 774, 705 cm^{-1}. UV (methanol) λ_{max}: 402 (496), 320 (10 401), 229 (22386), 214 (19 703), 210 (20181) nm.

^{1}H NMR (400 MHz, CD_3OD): δ 7.49–7.24 (m, 7H, C*H*), 7.09–7.00 (m, 3H, seven-membered ring C*H*), 4.82 (broad, 3H, NH_3), 4.51 (s, 2H, O—CH_2—C=O), 4.43 (t,1H, J = 6.9 Hz, C*H*— NH_3), 1.62(d, 3 H, J = 6.9 Hz, CH_3). ^{13}C NMR (75 MHz, CD_3OD): δ 182.4 (+), 173.9 (+), 165.7 (+), 140.1 (+), 139.7 (−), 137.5 (−), 135.5 (−), 130.5 (−), 130.1 (−), 129.8 (−), 127.8 (−), 117.4 (−), 69.2 (−), 52.0 (−), 20.8 (−).

(S)-(−)-1-Phenylethylamine salt of acid 4a. M.p: 109.0–112.5 °C (acetonitrile). Anal.: calculated for $C_{17}H_{19}O_4N_1$: C, 67.74; H, 6.36; N, 4.65. Found C, 67.91; H, 6.34; N, 4.62%. LRMS + LSIMS (matrix: thioglycerol): 302 (M + 1, 75), 181 (100), 122 (80), 105 (76), 91 (28). HRMS: exact mass calculated for $C_{17}H_{19}O_4N_1$: 302.1392. Found: 302.1391. IR (KBr) ν_{max}: 2948, 1622 (C=O), 1552 (C=O), 1475, 1406 (C=C), 1283 (C— O), 1196 (C—O), 773, 703 cm^{-1}. UV (methanol) λ_{max}: 402 (491), 320 (10398), 229 (22301), 214 (19689), 210 (20175) nm. ^{1}H NMR (400 MHz, CD_3OD): δ 7.49–7.24 (m, 7H, aromatic C*H*), 7.10–7.00 (m, 3H, seven-membered ring C*H*), 4.84 (broad, 3H, NH_3), 4.50 (s, 2H, O—CH_2—C=O), 4.43 (t, 1H, J = 6.8 Hz, C*H*—NH_3), 1.62 (d, 3 H, J = 6.8 Hz, CH_3). ^{13}C NMR (75 MHz, CD_3OD): δ 182.4 (+), 173.9 (+), 165.7 (+), 140.0 (+), 139.7 (−), 137.4 (−), 135.5 (−), 130.5 (−), 130.1 (−), 129.9 (−), 127.8 (−), 117.3 (−), 69.2 (+), 52.1 (−), 20.8 (−).

(S)-(−)-1-(1-Naphthyl)ethylamine salt of acid 4a. M.p: 105.0–106.2 °C (acetonitrile). Anal.: calculated for $C_{21}H_{21}O_4N_1$: C, 71.76; H, 6.03; N, 3.99; O, 18.22. Found C, 71.84; H, 5.89; N, 4.14%. LRMS + LSIMS (matrix: thioglycerol): 352 (4), 203 (2), 181 (26), 172 (16), 156 (19), 155 (100), 153 (4), 149 (3), 141 (3), 135 (3), 129 (3), 128 (3), 127 (2), 123 (2), 121 (1), 115 (2), 107 (3), 91 (6). HRMS: exact mass calculated for $C_{21}H_{21}O_4N_1$: 352.1549. Found: 352.1547. IR (KBr) ν_{max}: 2907, 1610 (C=O), 1558 (C=O), 1475, 1408 (C=C), 1190 (C—O) cm^{-1}. UV (methanol) λ_{max}: 403 (283), 319 (7869), 292 (8011), 281 (8276), 270 (6750), 223 (29527) nm. ^{1}H NMR (400 MHz, CD_3OD): δ 8.08 (d, 1H, J = 8.4 Hz, naphthyl ring C*H*), 7.86 (dd, 1H, J = 8.3 and 6.4 Hz, naphthyl ring C*H*), 7.70 (d, 1H, J = 6.6 Hz, naphthyl ring C*H*), 7.57–7.46 (m, 4H, naphthyl ring C*H*), 7.40 (dd, 1H, J = 8.5 and 1.2 Hz, seven-membered ring C*H*), 7.25–7.14 (m, 2H, seven-membered ring C*H*), 7.03 (dd, 1H, J = 8.5 and 10.6 Hz, seven-membered ring C*H*), 6.92 (d, 1H J = 10.1 Hz, seven-membered ring C*H*), 5.36 (t, 1H, J = 6.7 Hz, C*H*—NH_3), 4.85 (broad, 3H, N*H*$_3$), 4.38 (s, 2H, O—CH_2—C=O), 1.75 (d, 3 H, J = 6.8 Hz, C*H*$_3$). ^{13}C NMR (75 MHz, CD_3OD): δ 182.3 (+), 174.0 (+), 165.5 (+), 139.6 (−), 137.4 (−), 136.0 (+), 135.5 (−), 135.3 (+), 131.5 (+), 130.5 (−), 130.3 (−), 130.1 (−), 128.0 (−), 127.2 (−), 126.5 (−), 124.0 (−), 123.3 (−), 117.3 (−), 69.1 (+), 47.1 (−), 21.0 (−).

(R)-(+)-1-p-Tolylethylamine salt of acid 4a. M.p.: 128.0–130.2 °C (acetonitrile). Anal.: calculated for $C_{18}H_{21}N_1O_4$: C, 68.54; H, 6.72; N, 4.44; O, 20.30. Found C, 68.74; H, 6.65; N, 4.64%. LRMS + LSIMS (matrix: thioglycerol): 317 (M + 2, 12), 316 (M + 1, 51), 271 (3), 182 (6), 181 (55), 137 (6), 136 (47), 135 (6), 120 (15), 119 (100), 118 (5), 105 (4), 91 (9), 77 (3), 73 (3). HRMS: exact mass calculated for $C_{18}H_{21}N_1O_4$: 316.1549. Found: 316.1545. IR (KBr) ν_{max}: 3369, 2930 (C— H), 1630 (C=O), 1597 (C=O), 1560, 1493 (C=C), 1475 (C=C), 1266, 1195 (C—O), 1089 (C—O) cm^{-1}. UV (methanol) λ_{max}: 320 (9278), 236 (15477), 235 (15347), 229 (18754), 227 (17489) nm. ^{1}H NMR (400 MHz, CD_3OD): δ 7.46 (dd, 1H, J = 8.9 and 11.3 Hz, seven-membered ring C*H*), 7.32–7.23 (m, 3H, seven-membered ring C*H*), 7.17 (d, 2H, J = 7.5, benzene

C*H*), 7.07 (t, 1H, *J* = 9.3 Hz, seven-membered ring C*H*), 7.00 (d, 2H, *J* = 10.1, benzene C*H*), 4.84 (broad, 3H, N*H*$_3$), 4.47 (s, 2H, O—C*H*$_2$—C=O), 4.38 (q, 1H, *J* = 6.8 Hz, C*H*—NH$_3$), 2.29 (s, 3H, Ph— CH$_3$), 1.60 (d, 3H, *J* = 6.8 Hz, H$_3$N—CH—C*H*$_3$). ^{13}C NMR (75 MHz, CD$_3$OD): δ 182.4 (+), 173.9 (+), 165.7 (+), 139.9 (−), 139.7 (−), 137.5 (+), 137.0 (−), 135.5 (+), 130.59 (+), 130.55 (−), 130.51 (−), 130.47 (−), 127.8 (−), 117.3 (−), 69.2 (+), 51.8 (−), 21.1 (−), 20.7 (−).

(−)-cis-Myrtanylamine salt of acid 4a. M.p.: 165.0–168.7 °C (acetonitrile). Anal.: calculated for $C_{19}H_{27}O_4N_1$: C, 68.44; H, 8.16; N, 4.20; O, 19.19. Found C, 68.42; H, 8.25; N, 4.15%. LRMS + LSIMS (matrix: thioglycerol): 335 (12), 334 (50), 181 (69), 155 (12), 154 (100), 137(4), 135 (7), 95 (11), 93 (6), 91 (5), 81 (35). HRMS: exact mass calculated for $C_{19}H_{27}O_4N_1$: 334.2018. Found: 334.2015. IR (KBr) ν_{max}: 3445, 1623 (C=O), 1588 (C=O), 1490 (C=C), 1411 (C=C), 1187 (C—O), 1081 (C—O) cm^{-1}. UV (methanol) λ_{max}: 319 (8745), 235 (14142), 234 (14025), 228 (14793), 226 (14854) nm. ^{1}H NMR (400 MHz, CD$_3$OD): δ 7.47 (dd, 1H, *J* = 8.1 and 0.9 Hz, seven-membered ring C*H*), 7.33–7.25 (m, 2H, seven-membered ring C*H*), 7.10–7.05 (m, 2H, seven-membered ring C*H*), 4.85 (broad, 3H, N*H*$_3$), 4.57 (s, 2H, O—C*H*$_2$—C=O), 2.93 (dd, 2H, *J* = 7.8 and 3.1 Hz, C*H*$_2$—NH$_3$), 2.44–2.35 (m, 2H, C*H*$_2$), 2.08–1.98 (m, 2H,C*H*$_2$), 1.95–1.90 (m, 2H, C*H*$_2$), 1.88–1.50 (m, 1H, C*H*), 1.60–1.50 (m, 1H, C*H*), 1.21 (s, 3H, C*H*$_3$), 1.01 (s, 3H, C*H*$_3$), 0.96 (d, 1H, *J* = 9.8 Hz, C*H*). ^{13}C NMR (75 MHz, CD$_3$OD): δ 182.5 (+), 173.9 (+), 165.9 (+), 139.6 (−), 137.4 (−), 135.5 (−), 130.4 (−), 117.3 (−), 69.3 (+), 46.1 (+), 44.6 (−), 42.4 (−), 40.9 (−), 39.6 (+), 33.7 (+), 28.1 (−), 26.7 (+), 23.4 (−), 20.5 (+).

(+)-Bornylamine salt of acid 4a. M.p.: 159.5–161.0 °C (acetonitrile). Anal.: calculated for $C_{19}H_{27}N_1O_4$:C, 68.44; H, 8.16; N, 4.20. Found C, 68.35; H, 8.11; N, 4.16%. LRMS + LSIMS (matrix: thioglycerol): 335 (M + 2, 12), 334 (M + 1, 53), 182 (5), 181 (43), 155 (12), 154 (100), 152 (4), 137 (32), 122 (3), 107 (3), 95 (8), 93 (7), 91 (4), 82 (5), 81 (39), 79 (3), 77 (4). HRMS: calculated for $C_{19}H_{27}N_1O_4$(M + 1): 334.2018. Found: 334.2020. IR (KBr) ν_{max}:3013(=C-H), 1607 (C=O), 1539(C=O), 1475, 1414(C=C), 1274, 1237, 1192, 1086, 1004 (C—O) cm^{-1}. UV (methanol) λ_{max}:319 (11031), 235 (15321), 234 (14895), 228 (15231), 226 (16145) nm. ^{1}H NMR (400 MHz, CD$_3$OD): δ 7.48 (dd, 1H, *J* = 8.7 and 1.3 Hz, seven-membered ring C*H*=C), 7.33–7.26 (m, 2H, seven-membered ring C*H*), 7.11–7.06 (m, 2H, seven-membered ring C*H*), 4.84 (broad, 3H, N*H*$_3$), 4.57 (s, 2H, O—C*H*$_2$—C=O), 3.71 (t, 1H, *J* = 6.6 Hz, C*H*—NH$_3$,), 2.35–2.26 (m, 1H, bridge C*H*), 1.87–1.76 (m, 2H, C*H*$_2$), 1.72–1.59 (m, 2H, C*H*$_2$), 1.50 (t, 1H, *J* = 13.1 Hz, C*H*$_2$—CH—NH$_3$), 1.35 (t, 1H, *J* = 10.5 Hz, C*H*$_2$—CH—N*H*$_3$), 1.21 (s, 3H, C*H*$_3$), 0.93 (s, 3H, C*H*$_3$), 0.92 (s, 3H, C*H*$_3$). ^{13}C NMR (75 MHz, CD$_3$OD): δ 182.4 (+), 173.9 (+), 165.7 (+), 139.8 (−), 137.5 (−), 135.5 (−), 130.5 (−), 117.4 (−), 69.3 (+), 57.7 (−), 50.1 (+), 45.9 (−), 35.4 (+) 28.5 (+), 28.1 (+), 26.5 (+), 19.9 (−), 18.8 (−), 13.5 (−).

(1R,2S)-(+)-1-Amino-2-indanol salt of acid 4a. M.p.: 178.4–180.0 °C (methanol). Anal.: calculated for $C_{18}H_{19}O_5N$: C, 65.64; H, 5.81; N, 4.25. Found C, 65.49; H, 5.71, 4.18%. LRMS + LSIMS (matrix: thioglycerol): 330 (M + 1, 8), 299 (4), 214 (4), 182 (7), 181(59), 151 (12), 150(100), 147 (5), 135 (8), 134 (9), 133 (81), 105 (8), 107 (7), 91(18), 73 (16). HRMS: calculated for $C_{18}H_{20}O_5N$ (M + 1): 330.1342. Found: 330.1337. IR (KBr) ν_{max}:3094 (=C—H), 1601, 1564 (C=O), 1482, 1443, 1413 (C=C), 1289, 1202, 1092, 1010 (C—O) cm^{-1}. UV (methanol) λ_{max}:403 (512), 321 (11447), 230 (24125), 215 (21450), 210 (21501) nm. ^{1}H NMR (400 MHz, CD$_3$OD): δ 7.46 (d, 1H, *J* = 7.1 Hz, seven-membered ring C*H*), 7.26 (m, 4H, benzene ring C*H*), 7.13 (t, 1H, *J* = 10.1 Hz, seven-membered ring C*H*), 7.03 (d, 1H, *J* = 12.0 Hz, seven-membered ring C*H*), 6.89 (dd, 1H, *J* = 10.6 and 8.3 Hz, seven-membered ring C*H*), 6.77 (d, 1H, *J* = 10.1 Hz, seven-membered ring C*H*), 4.55 (m,1H, C*H*—OH), 4.43 (d, 1H, *J* = 5.6 Hz, C*H*—NH$_3$), 4.41 (s, 2H, O—CH$_2$—C=O), 3.08 (dd, 1H, *J* = 16.2 and 6.0 Hz, five-membered ring C*H*$_2$), 2.89 (dd, 1H, *J* = 16.2 and 3.6 Hz, five-membered ring C*H*$_2$). ^{13}C NMR (75 MHz, DMSO): δ 179.5 (+), 170.1 (+), 164.6 (+), 141.4, (+), 138.5 (+), 136.7 (−), 136.1 (−), 133.5 (−), 128.6 (−), 127.4 (−), 126.6 (−), 125.2 (−), 125.0 (−), 114.1 (−), 70.5 (−), 67.8 (+), 56.6 (−), 41.3 (+).

Photolysis of salts in the crystalline state. See text for experimental procedure.

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