# An Investigation of the Yang Photocyclization Reaction in the Solid State: Asymmetric Induction Studies and Crystal Structure−Reactivity Relationships

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**Abstract:** The Norrish/Yang type II photochemistry of 16 ketones having the basic *cis*-4-*tert*-butyl-1-benzoylcyclohexane or 2-benzoyladamantane structure has been investigated in the solid state and solution. In both media, ketones bearing methyl substituents α to the benzoyl group undergo stereoselective Yang photocyclization to afford *endo*-arylcyclobutanols. Quantum yield and quenching studies in solution show that the reactions are efficient triplet-mediated processes. Asymmetric induction studies were carried out by providing the reactants with carboxylic acid substituents to which "ionic chiral auxiliaries" were attached through salt formation with optically active amines. Irradiation of the salts (17 in total) in solution gave racemic cyclobutanols, but in the crystalline state, moderate to near-quantitative enantiomeric excesses were obtained. Single crystal X-ray diffraction studies were successfully performed on 10 neutral ketones and four salts. This allowed the reactive $\gamma$-hydrogen atoms to be identified and the distance and angular parameters associated with their abstraction to be tabulated. For the 14 compounds whose crystal structures were determined, the average value of *d*, the C═O···H abstraction distance, was 2.61 ± 0.07 Å, and the values of $\omega$ (the $\gamma$-hydrogen out-of-plane angle), $\Delta$ (the C═O···$H_\gamma$ angle) and $\theta$ (the C−$H_\gamma$···O angle) were 53 ± 11, 84 ± 7, and 115 ± 2°, respectively. In a similar manner, the geometric parameters associated with the ring closure reactions of the intermediate 1,4-hydroxy biradicals were estimated from the crystallographic data. This indicates that the biradicals are 66.5 ± 9.8 and 32.7 ± 3.2° out of alignment for cleavage, but that they are well oriented for cyclization, with radical separations (*D*) of 3.08 ± 0.09 Å. For one of the salts in the adamantane series, the solid-state photoreaction was shown to be topotactic; that is, a single crystal of the reactant salt was transformed quantitatively into a single crystal of the corresponding cyclobutanol salt. Since the absolute configuration of the ionic chiral auxiliary in this case was known, this permitted the absolute steric course of the reaction to be mapped by X-ray crystallography and the abstracted $\gamma$-hydrogen to be identified unequivocally. In addition, the crystal structure of a partially reacted crystal containing 60% product and 40% reactant was successfully determined. This showed that the two compounds in the mixed crystal have nearly identical shapes and orientations, thus accounting for the single crystal nature of the process. Finally, it was found that ketones lacking methyl substituents α to the benzoyl group are either photochemically unreactive or undergo Norrish type II cleavage. Possible reasons for this difference in behavior are presented and discussed.

## Introduction

Organic photochemistry is replete with reactions that transform achiral starting materials into chiral photoproducts, and one of the challenges facing organic photochemists today is how to accomplish these reactions *enantioselectively*. While, historically, much more effort has been put into developing general methods of asymmetric synthesis for ground-state reactions compared to those occurring in the excited state, the field of photochemical asymmetric synthesis has nevertheless seen some notable advances in recent years.[1] Among the approaches that have been taken are (1) photolysis with circularly polarized light,[1,2] (2) the use of optically active solvents,[1] (3) the use of optically active photosensitizers,[1,3] (4) photolysis in the presence of optically active additives,[1,4] (5) attachment of covalently bound chiral auxiliaries,[1] (6) photolysis in the cavities of optically active host molecules[1,5] and (7) solid-state irradiation of materials that crystallize in chiral space groups.[1,6] Of these methods, the latter two most consistently lead to useful enantiomeric excesses, and it is with the second of these—photolysis of chiral crystals—that we shall be concerned in the present article.

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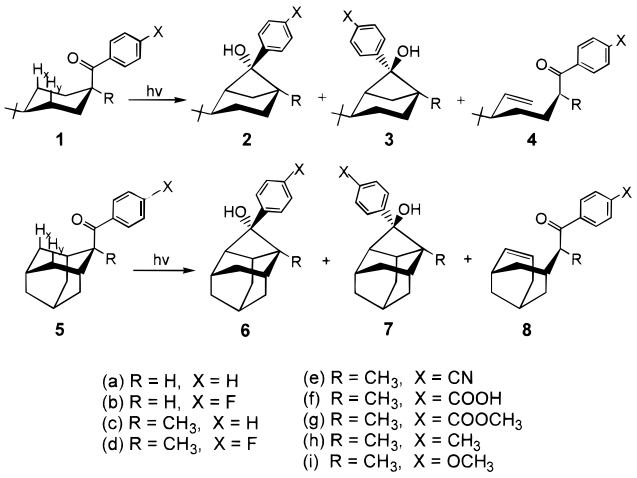
The major obstacle to be overcome in the solid-state method of asymmetric synthesis is how to ensure that the reactants adopt the requisite chiral space groups. Spontaneous crystallization of achiral compounds in chiral space groups, while well documented,[7] is rare and unpredictable and therefore unsuitable as a general method of crystal engineering asymmetric environments for photochemistry. The approach we have taken recently to solve this problem involves the use of *ionic chiral auxiliaries*.[8] In this procedure, a crystalline salt is formed between a prochiral, carboxylic acid-containing photoreactant and an optically pure, nonabsorbing amine. Since the ionic auxiliary—the cation in this case—is optically active, such salts are *required* to crystallize in chiral space groups, and this provides the asymmetric medium in which to carry out the photoreaction. Clearly, the opposite approach, in which the cationic component of the salt is the photoreactant and the anion is the chiral auxiliary, is equally valid. One of the limitations of the solid-state ionic chiral auxiliary technique is that the reactants must contain acidic or basic functional groups that allow salt formation. On the other hand, there are several advantages to working with salts, one being that their high melting points and strong lattice forces compared to purely molecular crystals permit reactions to be carried to higher conversions without crystal breakdown. A second advantage is that the photolyses can be carried out with polycrystalline samples on a gram scale if desired; there is no need to use special seeding techniques or carefully grown, enantiomorphously pure single crystals, as in the case of achiral compounds that crystallize spontaneously in chiral space groups.

In this paper, we describe the application of the solid-state ionic chiral auxiliary approach to asymmetric induction in the well-known Yang photocyclization reaction—the photochemical conversion of $\gamma$-hydrogen-containing carbonyl compounds into cyclobutanols.[9,10] As part of these studies, X-ray crystal structures were obtained for many of the starting salts as well as for some of the photoproducts. Since the absolute configurations of the ionic chiral auxiliaries are known, this allowed the absolute enantioselectivities of the photoreactions to be determined, and this in turn enabled us to identify unequivocally which $\gamma$-hydrogen was abstracted and to correlate the observed abstraction/cyclization reactions with crystallographically derived geometric data. Such correlations provide important insights into the stereoelectronic requirements for $\gamma$-hydrogen abstraction and 1,4-biradical closure.[11]

## Results

**Choice and Synthesis of Starting Materials.** In searching the photochemical literature for Yang photocyclization reactions to which the ionic chiral auxiliary approach to solid-state asymmetric synthesis could be applied, we came across a promising candidate in a paper by Lewis and co-workers.[12a] In 1974, these authors showed that solution-phase irradiation of *cis*-4-*tert*-butyl-1-methylcyclohexyl phenyl ketone (**1c**, Scheme 1) afforded excellent chemical yields of cyclobutanol **2c**. This reaction seemed nearly ideal for our purposes since (i) it converts an achiral starting material into a chiral photoproduct, (ii) only one of the two possible diastereomers of cyclobutanol **2c** is formed, thus simplifying photoproduct separation and analysis, (iii) for attachment of the ionic chiral auxiliaries, it appeared that carboxylic acid-substituted derivatives of ketone **1c** (e.g., **1f**) could be readily prepared, and (iv) it seemed likely that ketone **1c** and related compounds would crystallize in conformations favorable for $\gamma$-hydrogen atom abstraction. Organic molecules generally crystallize in their lowest energy conformations, and MM3 studies showed that ketone **1c** has a global minimum energy conformation in which the ketone oxygen is well oriented to abstract one of the enantiotopic $\gamma$-hydrogens $H_x$ or $H_y$.

**Scheme 1**




In developing crystal structure—solid-state reactivity relationships, it is desirable to have a series of closely related compounds to study, since this permits general trends to be detected. Accordingly, ketones **1a**—**i** (Scheme 1) were prepared by standard procedures that are outlined in the Experimental Section. Of these, compounds, **1a** and **1c** were previously known;[12a,13a,b] the remainder represent new compounds that are reported here for the first time. We also thought it worthwhile to extend the study to analogues of ketones **1a**—**i** and chose as our target molecules the 2-methyl-2-adamantyl phenyl ketones **5a**—**g** (Scheme 1). On the basis of the obvious similarity between ketones of general structure **1** and **5**, we anticipated that the latter would also undergo Yang photocyclization to afford cyclobutanols **6a**—**g**, and this proved to be the case. The synthesis of ketones **5a**—**g**, all of which are new, is outlined in the Experimental Section. All 16 ketones prepared for the present study were crystalline, and of these, 10 had their crystal and molecular structures determined (ketones **1a**, **1b**, **1c**, **1f**, **1h**, **1i**, **5a**, **5c**, **5d**, and **5g**); details of the crystal structure determination for ketone **1c** have been published.[13c] None of the ketones whose crystal structures were determined crystallized

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(12) (a) Lewis, F. D.; Johnson, R. W.; Johnson, D. E.; *J. Am. Chem. Soc.* **1974**, *96*, 6090. (b) MM3 calculations indicate that, in the adamantane series, *endo*-arylcyclobutanols **6** are more stable than their exo isomers **7** by ~14 kJ/mol. In the *tert*-butyl series, on the other hand, cyclobutanols **2** and **3** are approximately isoenergetic as a result of an unfavorable *endo*-phenyl/*tert*-butyl steric interaction.

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**Table 1.** Results of Photolysis of Ketones **1a**−**i** and **5a**−**g** in the Solid State and Solution

| ketone | R | X | medium | cleavage (**4** or **8**) | *endo*-arylcyclobutanol (**2** or **6**) | *exo*-arylcyclobutanol (**3** or **7**) |
|---|---|---|---|---|---|---|
| **1a** | H | H | benzene[a] | 100 | 0 | 0 |
| | | | crystal | no rxn | no rxn | no rxn |
| **1b** | H | F | benzene | 100 | 0 | 0 |
| | | | crystal | no rxn | no rxn | no rxn |
| **1c** | Me | H | benzene[a] | 0 | 100 | 0 |
| | | | crystal | 0 | 100 | 0 |
| **1d** | Me | F | benzene | 0 | 94 | 6 |
| | | | crystal | 0 | 100 | 0 |
| **1e** | Me | CN | benzene | 0 | 100 | 0 |
| | | | crystal | 0 | 100 | 0 |
| **1f** | Me | $CO_2H$ | acetone | 0 | 93[b] | 7[b] |
| | | | crystal | 0 | 100 | 0 |
| **1g** | Me | $CO_2Me$ | acetone | 0 | 93 | 7 |
| | | | crystal | 0 | 100 | 0 |
| **1h** | Me | Me | benzene | 0 | 100 | 0 |
| | | | crystal | 0 | 100 | 0 |
| **1i** | Me | OMe | benzene | 0 | 92 | 8 |
| | | | crystal | 0 | 100 | 0 |
| **5a** | H | H | benzene | no rxn | no rxn | no rxn |
| | | | crystal | no rxn | no rxn | no rxn |
| **5b** | H | F | benzene | no rxn | no rxn | no rxn |
| | | | crystal | no rxn | no rxn | no rxn |
| **5c** | Me | H | benzene | 0 | 100 | 0 |
| | | | crystal | 0 | 100 | 0 |
| **5d** | Me | F | benzene | 0 | 100 | 0 |
| | | | crystal | 0 | 100 | 0 |
| **5e** | Me | CN | benzene | 0 | 100 | 0 |
| | | | crystal | 0 | 100 | 0 |
| **5f** | Me | $CO_2H$ | benzene | 0 | 100[b] | 0 |
| | | | crystal | 0 | 100 | 0 |
| **5g** | Me | $CO_2Me$ | benzene | 0 | 100 | 0 |
| | | | crystal | 0 | 100 | 0 |

[a] Results originally reported by Lewis et al.[12a] [b] Carboxylic acid-containing photoproducts **2f** and **6f** were characterized as their methyl esters **2g** and **6g** following diazomethane workup of the photolysis mixtures.

in chiral space groups, thus precluding absolute asymmetric synthesis studies.

**Photolysis of Ketones 1a−i and 5a−g in the Solid State and Solution; Characterization of the Photoproducts.** Table 1 summarizes the results of Pyrex-filtered irradiation of ketones **1a**−**i** and **5a**−**g** in the solid state and solution. The techniques used for the solid-state irradiations have been described previously.[14] As expected, and in agreement with the findings of Lewis et al. for ketone **1c**,[12a] *endo*-arylcyclobutanols of general structure **2** or **6** were obtained as the major photoproducts for ketones in which R = $CH_3$; small amounts (<10%) of the diastereomeric *exo*-arylcyclobutanols **3** or **7** were obtained in the solution photolyses of some of these compounds, but never in the crystalline state, even at very high conversions. The situation for ketones in which R = H, however, was quite different. Earlier work by Lewis et al.[12a] had shown that photolysis of ketone **1a** in benzene led exclusively to the type II cleavage product 1-phenyl-5-*tert*-butyl-6-hepten-1-one (**4a**), and we obtained identical results in the case of ketone **1b**. Interestingly, ketones **1a** and **1b** were found to be photoinert in the crystalline state, and in the adamantane series, ketones **5a** and **5b** were found to be completely unreactive in solution as well as in the solid state.[15,16]

Since the *endo*-phenyl stereochemical assignment by Lewis et al. in the case of photoproduct **2c** was made primarily on the basis of a 90-MHz $^1$H NMR spectrum,[12a] we thought it worthwhile to establish the stereochemical assignments on a firmer basis. To this end, we were eventually successful in growing crystals and obtaining the X-ray crystal structure of one of the *endo*-aryl photoproducts, **2i**. With this structure firmly established, it was then relatively straightforward to show by detailed comparisons of the 500-MHz $^1$H and $^{13}$C NMR spectra that photoproducts **2c**, **2d**, **2e**, **2g**, and **2h** also have the *endo*-aryl stereochemistry. A key piece of evidence relating to stereochemistry was the observation of a strong nuclear Overhauser effect between the *o*-aryl hydrogens and the methylene hydrogens on the 3-carbon bridge. This effect was absent in the *exo*-aryl photoproducts of general structure **3** and was replaced by an NOE interaction between the ortho hydrogens and the nearer methylene hydrogen on the one carbon bridge. The NMR data are given in full in the Experimental Section.

A similar procedure was followed for the *endo*-arylcyclobutanol photoproducts **6c**, **6d**, **6e**, and **6g** in the adamantane series. Here, crystals were grown of compound **6d**, its X-ray crystal structure was successfully determined, and the similarity of the 500-MHz NMR spectra of all four compounds established their common structure and stereochemistry.[12b]

Solution-phase irradiation of *cis*-4-*tert*-butyl 1-methylcyclohexyl aryl ketones **1d**, **1f**, **1g**, and **1e** gave small amounts (<10%) of a second photoproduct in each case to which the *exo*-arylcyclobutanol structure **3** was assigned. The isolation of these photoproducts in pure form was difficult owing to the small amounts of material involved and to the fact that they and their endo epimers have very similar column chromatographic retention times. Repeated chromatography ultimately

(14) Gudmundsdottir, A. D.; Lewis, T. J.; Randall, L. H.; Scheffer, J. R.; Rettig, S. J.; Trotter, J.; Wu, C.-H. *J. Am. Chem. Soc.* **1996**, *118*, 6167.

(15) Ketones **5a** and **5b** were photoinert even in *tert*-butyl alcohol, which Wagner had shown increases type II quantum yields through hydrogen bonding to the 1,4-hydroxy biradical and retardation of reverse hydrogen transfer. See: Wagner, P. J.; Kochevar, I. E.; Kemppainen, A. E. *J. Am. Chem. Soc.* **1972**, *94*, 7489.

(16) Attempted trapping of the 1,4-hydroxy biradicals from ketones **5a** and **5b** by using high concentrations of deuterated *n*-heptanethiol according to the procedure of Wagner was unsuccessful: Wagner, P. J.; Kelso, P. A.; Zepp, R. G. *J. Am. Chem. Soc.* **1972**, *94*, 7480.

**Table 2.** Quantum Yields and Kinetic Parameters for Solution-Phase Photolysis of Ketones **1a**−**i** and **5c**−**g**[a]

| ketone | conc, M | $\Phi$[b] | $\Phi_{max}$[c] | $k_q\tau$, $M^{-1}$[d] | $\tau$, $10^{-9}$ s[e] |
|---|---|---|---|---|---|
| **1a** | 0.040 | 0.0095 | 0.36 | 0.42 | 0.084 |
| **1b** | 0.032 | 0.0022 | 0.21 | 0.20 | 0.040 |
| **1c** | 0.043 | 0.074 | 0.29 | 8.1 | 1.6 |
| **1d** | 0.030 | 0.049 | 0.24 | 6.1 | 1.2 |
| **1e** | 0.030 | 0.020 | 0.17 | 13 | 2.6 |
| **1f** | 0.030 | | 0.22 | | |
| **1g** | 0.030 | 0.047 | 0.22 | 9.6 | 1.9 |
| **1h** | 0.030 | 0.067 | 0.18 | 28 | 5.6 |
| **1I** | 0.030 | 0.083 | 0.31 | 292 | 58 |
| **5c** | 0.031 | 0.15 | 0.26 | 1.6 | 0.31 |
| **5d** | 0.036 | 0.10 | 0.16 | 1.8 | 0.36 |
| **5e** | 0.023 | 0.41 | 0.69 | 4.5 | 0.90 |
| **5f** | 0.015 | | 0.24 | | |
| **5g** | 0.014 | 0.073 | 0.17 | 2.1 | 0.41 |

[a] Valerophenone (0.10 M) in benzene was used as the actinometer in parallel irradiations at 313 nm. [b] Determined in purified benzene. [c] Determined in 67% *tert*-butyl alcohol/benzene (w/w). [d] 2,5-Dimethyl-2,4-hexadiene quencher. [e] Calculated by assuming $k_q = 5 \times 10^9$ $M^{-1}$ $s^{-1}$.

gave a pure sample of *exo*-arylcyclobutanol **3d**, but the others were characterized as mixtures and the structural assignments in these cases must remain tentative, although we are quite certain they are correct. Photoproduct **3d** is an oil, and it was therefore characterized primarily by high-resolution NMR (including 500-MHz COSY, HMQC, HMBC, and NOE experiments) as well as by IR and MS. Details are provided in the Experimental Section.

**Quantum Yield and Stern−Volmer Kinetic Studies.** With the use of a merry-go-round apparatus[17] and valerophenone actinometry,[15] quantum yields of photoproduct formation were measured for ketones **1a**−**i** and **5c**−**g** in both benzene ($\Phi$) and 67% *tert*-butyl alcohol/benzene ($\Phi_{max}$) (Table 2). Determination of the quantum yields in the presence of varying amounts of the triplet quencher 2,5-dimethyl-2,4-hexadiene gave linear Stern−Volmer plots[18] with slopes equal to $k_q\tau$, and from these data, the values of $\tau$, the triplet excited-state lifetimes, could be estimated. These numbers are also compiled in Table 2.

The $k_q\tau$ values for ketones **1a** and **1c** determined by Lewis et al. in 1974 (0.74 and 7.3 $M^{-1}$, respectively)[12a] differ somewhat from our values of 0.42 and 8.1 $M^{-1}$. These differences are probably due to the different quenchers used by Lewis et al. (*trans*-1,3-pentadiene for **1a**, naphthalene for **1c**) as well as to the use of benzophenone/benzhydrol rather than valerophenone actinometry. The values of $\Phi_{max}$ measured by Lewis et al. for the same two compounds (0.098 for **1a** and 0.06 for **1c**) also differ from ours (0.36 and 0.29, respectively). Lewis numbers were determined in 8.9 M 1-propanol/benzene, whereas ours were measured in 67% *tert*-butyl alcohol/benzene (w/w), the solvent system recommended by Wagner et al. for such purposes.[19]

As an independent check of the accuracy of our steady-state kinetic data, we determined the triplet lifetime of one of our ketones by laser flash photolysis. The *p*-methoxyphenyl derivative **1i** was the only compound whose triplet was sufficiently long-lived to be measurable with the nanosecond setup available to us. By Stern−Volmer analysis using 1,3-cyclohexadiene as the triplet quencher, a lifetime of 77 ns was obtained. This is in reasonable agreement with the value of 58 ns determined in benzene via the Stern−Volmer method using 2,5-dimethyl-2,4-hexadiene as the quencher.

**Preparation of Chiral Salts of Keto Acids 1f and 5f.** To introduce the ionic chiral auxiliaries needed for solid-state asymmetric induction, keto acids **1f** and **5f** were treated with a variety of optically active amines and the resulting salts fully characterized by conventional methods. The amines were chosen more or less at random from the chiral pool, major criteria being that they should not absorb under the photolysis conditions and that they should be readily available. A total of 17 separate salts was prepared, 11 with keto acid **1f** and 6 with **5f**. Table 3 lists the amines used along with the melting points and crystal morphologies of the corresponding salts. The salts were shown to have 1:1 stoichiometry by elemental analysis. In addition, the IR and $^1$H and $^{13}$C NMR spectra were all in agreement with the proposed structures. X-ray diffraction analysis was carried out on four of the salts (**S9**, **S14**, **S15**, **S17**) to reveal additional structural features that will be discussed later in the paper.

**Photolysis of Chiral Salts in the Crystalline State: Asymmetric Induction Studies.** Each of the salts listed in Table 3 was irradiated in the crystalline state. Photolyses were generally carried out through Pyrex at room temperature, although some runs were conducted at −40 °C. No color change or melting of the crystals was observed during the reaction, and following irradiation, the mixtures were dissolved in ethyl acetate and treated with excess ethereal diazomethane to form the corresponding methyl esters **2g** and **6g** as the only detectable products. Following diazomethane treatment, the organic layer containing the esterified photoproduct and starting material was washed with water and subjected to short-path silica gel chromatography in order to remove the chiral auxiliary. The mixtures were then analyzed by GC for extent of conversion and by chiral HPLC for enantiomeric excess (ee). The salts were irradiated for varying lengths of time in order to determine the dependence of the ee values on the extent of conversion. The results are summarized in Tables 4 and 5; only those salts that gave ee's of >50% in low-conversion runs are reported. In addition to the solid-state runs, each of the salts was photolyzed in solution (acetonitrile or methanol); in every case, racemic photoproducts were obtained.

**Geometric Data Derived from X-ray Crystallography.** To develop crystal structure−solid-state reactivity relationships, it is necessary at this point to define some geometric parameters associated with the Norrish/Yang type II reaction and to tabulate the value of these parameters for the compounds described above.

As depicted in Figure 1a, the hydrogen abstraction geometry can be described by four parameters: $d$ (the C═O···$H_\gamma$ distance−expected to be optimal at 2.72 Å, the sum of the van der Waals radii), $\omega$ (the angle by which the $\gamma$-hydrogen deviates from the mean plane of the carbonyl group), $\Delta$ (the C═O···$H_\gamma$ angle), and $\theta$ (the C−$H_\gamma$···O angle−according to theory,[20] best at 180°). Assuming abstraction by the nonbonding orbital on oxygen,[21] the optimum values of $\omega$ and $\Delta$ are expected to be 0 and 90−120° respectively.[22] Table 6 summarizes the values

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(22) Scheffer, J. R. In *Organic Solid State Chemistry*; Desiraju, G. R., Ed.; Elsevier: Amsterdam, 1987; pp 1−45.

**Table 3.** Preparation of Optically Active Salts from Keto Acids **1f** and **3f**

| entry | keto acid | amine | recryst solvent | cryst morphol | mp (°C) |
|---|---|---|---|---|---|
| **S1** | **1f** | (*S*)-(+)-prolinol | $CH_3CN$ | powder | 167−169 |
| **S2** | **1f** | (1*S*,2*S*)-(+)$\psi$-ephedrine | $CH_3CN$ or sublimation | long, thin plates | 151−154 |
| **S3** | **1f** | (*S*)-(+)-arginine | EtOH | powder | 222−224 |
| **S4** | **1f** | (*S*)-(−)-α-methyl benzylamine | $CH_3CN$ | long, thin flat needles | 224−225 |
| **S5** | **1f** | (*R*)-(+)-α-methylbenzylamine | $CH_3CN$ | long, thin flat needles | 224−225 |
| **S6** | **1f** | (1*R*,2*S*)-(−)-ephedrine | $CH_3CN$ | long, thin plates | 179−181 |
| **S7** | **1f** | (*S*)-(−)-proline *tert*-butyl ester | $CH_3CN$ | powder | 227−229 |
| **S8** | **1f** | (1*R*,2*S*)-(−)-norephedrine | $CH_3CN$/EtOH | long, flat plates | 171−174 |
| **S9** | **1f** | (*S*)-(−)-prolinamide | $CH_3CN$ | plates[a] | 147−148 |
| **S10** | **1f** | (1*S*)-(−)-2,10-camphorsultam | $CH_3CN$/MeOH | flakes | 219−225 |
| **S11** | **1f** | (*S*)-(+)-lysine | EtOH | light yellow plates | 204−206 |
| **S12** | **5f** | (*S*)-(+)-prolinol | $CH_3CN$ | powder | 133−135 |
| **S13** | **5f** | (1*S*,2*S*)-(+)-$\psi$-ephedrine | $CH_3CN$ | long, thin plates | 158−161 |
| **S14** | **5f** | (*S*)-(−)-α-methylbenzylamine | $CH_3CN$/EtOH | long, thin flat needles[a] | 210−212 |
| **S15** | **5f** | (*R*)-(+)-α-methylbenzylamine | $CH_3CN$/EtOH | long, thinflat needles[a] | 210−212 |
| **S16** | **5f** | (1*R*,2*S*)-(−)-ephedrine | $CH_3CN$ | long, thin plates | 186−188 |
| **S17** | **5f** | (1*R*,2*S*)-(−)-norephedrine | $CH_3CN$/EtOH | long, flat plates[a] | 147−149 |

[a] X-ray crystal structure obtained.

**Table 4.** Asymmetric Induction in the Solid-State Photochemistry of Salts of Keto Acid **1f**

| salt | amine | photolysis method[a] and temp | irradn time (min) | convrsn (%) | ee (%)[b] **2g** |
|---|---|---|---|---|---|
| **S2** | (1*S*,2*S*)-(+)-$\psi$-ephedrine | slides, RT[c] | 5 | 2 | (−)-99.5 |
| | | | 20 | 18 | 97.3 |
| | | | 173 | 82 | 63.5 |
| | | tube, RT | 7.5 | 3 | (−)-99.5 |
| | | | 73 | 40 | 79.2 |
| | | | 90 | 61 | 72.7 |
| | | | 120 | 59 | 71.0 |
| | | | 480 | 87 | 63.5 |
| **S3** | (*S*)-(+)-arginine | slides, RT | 5 | 12 | (+)-90.5 |
| | | | 15 | 29 | 84.6 |
| | | | 42 | 74 | 83.0 |
| **S4** | (*S*)-(−)-α-methylbenzylamine | slides, RT | 2 | 0.7 | (+)-97.3 |
| | | | 6 | 24 | 95.8 |
| | | | 14 | 44 | 90.4 |
| | | | 52 | 92 | 84.8 |
| **S5** | (*R*)-(+)-α-methylbenzylamine | slides, RT | 5 | 7 | (−)-96.9 |
| | | | 15 | 24 | 96.5 |
| | | | 25 | 66 | 94.3 |
| | | | 45 | 85 | 92.1 |
| **S6** | (1*R*,2*S*)-(−)-ephedrine | slides, RT | 9 | 0.4 | (+)-78.5 |
| | | | 21 | 1.0 | 77.2 |
| | | | 103 | 26 | 67.3 |
| | | | 200 | 65 | 58.7 |
| | | slides, −40 °C | 69 | 3 | (+)-81.7 |
| | | | 160 | 8 | 78.6 |
| **S7** | (*S*)-(−)-proline *tert*-butyl ester | slides, RT | 0.5 | 0.6 | (−)-52.0 |
| | | | 2 | 7 | 51.0 |
| | | | 5 | 19 | 46.6 |
| | | | 15 | 53 | 25.5 |
| | | | 42 | 93 | 2.8 |
| | | slides, −40 °C | 21 | 11 | (−)-55.2 |
| | | | 69 | 32 | 50.4 |
| **S8** | (1*R*,2*S*)-(−)-norephedrine | slides, RT | 5 | 8 | (+)-96.5 |
| | | | 15 | 34 | 95.8 |
| | | | 42 | 58 | 86.4 |
| | | | 90 | 97 | 81.1 |
| **S9** | (*S*)-(−)-prolinamide | slides, RT | 6 | 7 | (+)-86.5 |
| | | | 30 | 51 | 68.2 |
| | | | 52 | 83 | 28.7 |
| | | tube, RT | 2 | 0.5 | (+)-85.2 |
| | | | 6 | 12 | 82.4 |
| | | | 52 | 78 | 33.4 |

[a] Slides means that the salt was crushed between two Pyrex microscope slides and irradiated; tube means that the salt was irradiated in an NMR tube, so that the crystal morphology remained intact. [b] The first enantiomer of photoproduct **2g** eluted from the Chiralcel OD column has a (−) rotation at the sodium D line. [c] RT, room temperature.

of these four parameters for the 14 ketones and salts whose crystal structures were determined.

Since hydrogen abstraction in the solid state is likely to occur with a minimum of motion in the carbon framework, geometric data derived from X-ray crystallography can also be used to analyze the behavior of the 1,4-hydroxy biradical intermediate. For this purpose, we define two torsion angles with reference to Figure 1b, which is a depiction of the 1,4-biradical intermedi-

**Table 5.** Asymmetric Induction in the Solid-State Photochemistry of Salts of Keto Acid **5f**

| entry | amine | photolysis method[a] and temp | irradn time (min) | convrsn (%) | ee (%)[b] **6g** |
|---|---|---|---|---|---|
| **S14** | (*S*)-(−)-α-methylbenzylamine[c] | slides, RT | 2 | 1.8 | (+)-87.5 |
| | | | 5 | 13.5 | 87.5 |
| | | | 10 | 39.5 | 86.9 |
| | | | 20 | 64.0 | 86.0 |
| | | | 47 | 89.4 | 81.0 |
| | | tube, RT | 10 | 42.6 | (+)-88.5 |
| | | | 96 | 99.9 | 79.9 |
| | | slides, −40 °C | 30 | 8.4 | (+)-89.4 |
| | | | 90 | 19.9 | 88.2 |
| **S15** | (*R*)-(+)-α-methylbenzylamine[c] | slides, RT | 2 | 3.5 | (−)-88.0 |
| | | | 4 | 17.9 | 86.9 |
| | | | 8 | 37.8 | 86.4 |
| | | | 19 | 60.5 | 86.2 |
| | | | 43 | 82.3 | 82.4 |
| | | tube, RT | 10 | 33.9 | (−)-87.8 |
| | | | 96 | 99.9 | 78.9 |
| | | slides, −40 °C | 30 | 10.5 | (−)-87.9 |
| | | | 90 | 22.6 | 87.3 |
| **S17** | (1*R*,2*S*)-(−)-norephedrine | slides, RT | 2 | 1.8 | (−)-88.0 |
| | | | 4 | 2.9 | 87.8 |
| | | | 15 | 11.6 | 81.9 |
| | | | 41 | 26.8 | 74.8 |
| | | tube, RT | 7 | 4.7 | (−)-87.8 |
| | | | 96 | 43.3 | 73.7 |
| | | | 210 | 92.4 | 69.8 |
| | | slides, −40 °C | 30 | 1.9 | (−)-88.2 |
| | | | 90 | 7.8 | 87.9 |

[a] Slides means that the salt was crushed between two Pyrex microscope slides and irradiated; tube means that the salt was irradiated in an NMR tube, so that the crystal morphology remained intact. [b] The first enantiomer of photoproduct **6g** eluted from the Chiralcel OD column has a (+) rotation at the sodium D line. [c] This salt undergoes a single crystal-to-single crystal (topotactic) reaction. See text for details. [d] RT, room temperature.

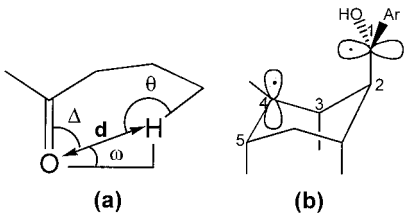



**Figure 1.** (a) Definition of geometric parameters $d$, $\omega$, $\Delta$, and $\theta$ for intramolecular $\gamma$-hydrogen atom abstraction. (b) 1,4-Hydroxy biradical intermediate derived from ketones of general structures **1** and **5**.

ate derived from ketones of general structure **1** and **5**: $\varphi_1$ is defined as the angle that the shaded lobe of the p-orbital on C1 makes with respect to the C2−C3 bond), and $\varphi_4$ is the angle that the shaded lobe of the p-orbital on C4 makes with respect to the C2−C3 bond. The p-orbitals at C1 and C4 are assumed to lie perpendicular to the O1−C1−C2 and C3−C4−C5 planes, respectively. The basis of this analysis is the generally accepted idea that cleavage of 1,4-biradicals requires good overlap between the radical-containing p-orbitals and the C2−C3 bond, i.e., $\varphi_1 = \varphi_4 \sim 0°$.[10] Failing that, and provided that C1 and C4 are within reasonable bonding distance, cyclization will predominate. The C1···C4 interatomic distance is given the symbol $D$. The crystallographically determined values of $\varphi_1$, $\varphi_4$, and $D$ are given in Table 6.

**Table 6.** Crystallographically Derived Hydrogen Abstraction and Biradical Parameters[a]

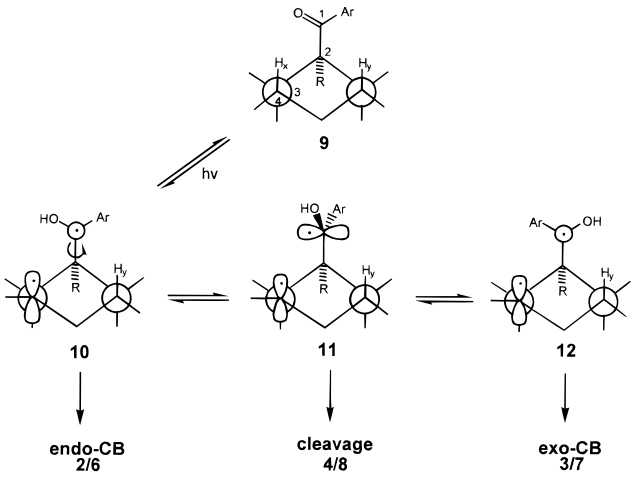
| ketone or salt | $d$ (Å)[b] | $\omega$ (deg) | $\theta$ (deg) | $\Delta$ (deg) | $\varphi_1$ (deg) | $\varphi_4$ (deg) | $D$ (Å) |
|---|---|---|---|---|---|---|---|
| **1a** | 2.61 | 32 | 116 | 95 | 85 | 36 | 3.23 |
| | 3.17 | 57 | 113 | 63 | −30 | −31 | 3.15 |
| **1b** | 2.59 | 32 | 116 | 96 | 84 | 36 | 3.23 |
| | 3.17 | 57 | 113 | 63 | −29 | −31 | 3.15 |
| **1c** | 2.70 | 57 | 114 | 81 | 64 | 33 | 3.09 |
| **1f**[c] | 2.65 | 55 | 113 | 85 | 68 | 35 | 3.11 |
| | 2.61 | 52 | 114 | 88 | 72 | 35 | 3.12 |
| | 3.44 | 48 | 108 | 49 | −47 | −31 | 3.12 |
| **1h** | 2.69 | 57 | 112 | 83 | 57 | 35 | 3.11 |
| **1i** | 2.63 | 56 | 113 | 85 | 68 | 35 | 3.10 |
| | 3.49 | 45 | 108 | 46 | −51 | −31 | 3.11 |
| **5a** | 2.47 | 29 | 117 | 98 | 82 | 31 | 3.17 |
| | 3.13 | 57 | 113 | 64 | −27 | −30 | 3.12 |
| **5c** | 2.50 | 57 | 117 | 84 | 66 | 29 | 3.02 |
| | 3.41 | 44 | 110 | 44 | −53 | −28 | 3.05 |
| **5d** | 2.54 | 61 | 116 | 80 | 61 | 29 | 2.99 |
| | 3.47 | 41 | 109 | 41 | −58 | −29 | 3.04 |
| **5g** | 2.58 | 61 | 115 | 79 | 61 | 30 | 3.00 |
| **S9** | 2.75 | 60 | 112 | 77 | −59 | −33 | 3.06 |
| **S14** | 2.62 | 62 | 114 | 75 | −55 | −38 | 2.96 |
| **S15** | 2.60 | 62 | 114 | 75 | 55 | 27 | 2.95 |
| **S17** | 2.55 | 60 | 116 | 80 | 61 | 29 | 3.00 |
| | 3.47 | 42 | 109 | 41 | −57 | −28 | 3.05 |

[a] See text for definition of parameters. [b] $\gamma$-Hydrogen atoms for which $d \geq 3.50$ Å are not included in this table. [c] Two independent molecules in the asymmetric unit.

## Discussion

The photochemical and photophysical results with ketones **1a**−**i** and **5a**−**g** (Tables 1 and 2) conform very closely to the standard picture of the Norrish/Yang type II reaction of aryl alkyl ketones, viz., hydrogen atom abstraction from a triplet excited state (presumably n,$\pi$* in nature) to produce a triplet 1,4-hydroxy biradical that partitions itself among closure, cleavage, and return to starting material.[10] Despite this general concordance with previous investigations, there are still some questions raised by the present study that need answering. These include the following: (1) for compounds that undergo Yang photocylization, why are the *endo*-arylcyclobutanols **2** and **6** invariably favored over their *exo* isomers **3** and **7**? (2) Why are ketones **1a** and **1b** photochemically reactive in solution and not in the solid state and why are they the only compounds to undergo cleavage rather than Yang photocyclization? (3) Why

**Scheme 2**




are ketones **5a** and **5b** photochemically unreactive in *both* the solid state and solution? The answers to these questions clearly have something to do with the nature of the α-substituent, R, which is a hydrogen atom for the anomalous compounds **1a**, **1b**, **5a**, and **5b** and a methyl group for the ketones that undergo Yang photocyclization.

To address these points, consider the idealized reaction pathway shown in Scheme 2. X-ray crystallography and MM3 calculations are in agreement that, regardless of the nature of the α-substituent, ketones of type **1** and **5** adopt chair conformations such as that shown by structure **9**, in which the aroyl group is axial and the mean plane of the carbonyl group is roughly orthogonal to the plane bisecting the cyclohexane ring between γ-hydrogen atoms $H_x$ and $H_y$. As a result, one of these hydrogens ($H_x$ in the case of structure **9**) is much more favorably oriented for abstraction than than the other, a fact that is apparent from the *d* values in Table 6, which range from 2.47 to 2.70 Å for the nearer hydrogens and are ≥3.13 Å for the more distant ones. As will become apparent later, we can state with virtually complete certainty that (1) it is the closer γ-hydrogen that is abstracted in the case of ketones of type **1** and **5** and (2) the failure of any of these compounds to form cyclization and/or cleavage photoproducts is not associated with an unfavorable hydrogen abstraction geometry.

With reference to Scheme 2, therefore, 1,4-hydroxy biradical **10** will be the initially formed intermediate. This species is poorly aligned for cleavage (from Table 6, $\varphi_1 = 66.5 \pm 9.8°$, $\varphi_4 = 32.7 \pm 3.2°$), but with $D = 3.08 \pm 0.09$ Å, it is well set up for closure, since this distance is less than the sum of the van der Waals radii for two carbon atoms (3.40 Å) and there is good orbital overlap. As a result, cyclization occurs with "retention of configuration" at C1 and C4 and leads directly to the experimentally observed major *endo*-aryl photoproducts **2** and **6**.[23] Cleavage, on the other hand, requires an approximately 90° rotation about the 1−2 bond of biradical **10** in order to align the orbital on C1 with the C2−C3 bond (cf. structure **11**), and this motion is slowed when R = $CH_3$ (Ar/$CH_3$ eclipsing) but less so when R = H. As a result, cleavage is seen only when R = H. Similar effects of α-substituents in promoting type II cyclization over cleavage are well documented in acyclic ketones, and this effect has been termed the "α-alkyl group effect".[24]

An additional 90° rotation about the C1−C2 bond leads to biradical **12**, closure of which forms *exo*-arylcyclobutanols **3** and **7**. It is paradoxical that small amounts of these compounds, but not cleavage products, are formed in solution when R = $CH_3$: after all, both processes involve unfavorable rotations about the C1−C2 bond. The explanation could be that the triplet biradical spends very little time near eclipsed conformation **11**, the result being that intersystem crossing to the singlet manifold and formation of cleavage products from this geometry cannot compete with rotation.[25] In addition, overlap between the radical-containing orbitals is less in biradical **11** than **10**, and this may reduce the rate of intersystem crossing (and reaction) in the former.[26] In any event, it is clear that, in the crystalline state, large-amplitude motions of the aryl and hydroxyl groups accompanying rotation about the C1−C2 bond would be topochemically forbidden and have no chance of competing with closure to *endo*-arylcyclobutanols. It is therefore perfectly reasonable that these are the only products formed in this medium.

But why do ketones lacking α-methyl groups (i.e., **1a**, **1b**, **5a**, and **5b**) fail to photocyclize in the solid state? The X-ray crystal structure data for the first three of these (crystals of **5b** were not suitable for crystallography) suggest that part of the answer may lie in the distance between the radical centers in biradical **10**. The data in Table 6 show that the average C1−C4 distance *D* for compounds **1a**, **1b**, and **5a** is 3.21 Å (for ketone **5b**, the MM3 calculated value for *D* is 3.15 Å), whereas the average distance for ketones with α-methyl groups that do photocyclize is 3.04 Å. This difference is caused by a steric interaction between the α-methyl group and the aryl group that "pushes" C1 toward C4. For example, the C1−C2−C3 angle in the nonmethylated compounds is 114−115°, whereas it is 108−109° for the methylated derivatives.

Orbital overlap is a second factor that may contribute to the failure of the nonmethylated compounds to form cyclobutanols in the crystalline state. With only a hydrogen atom in the α-position to interfere with the aryl group, these ketones adopt conformations in which the C═O group essentially eclipses the C2−C3 bond (O1−C1−C2−C3 ≈ 0°). Owing to methyl/aryl steric repulsion, the same angle in the α-methylated compounds is ∼−30°. The result, therefore, is that for the nonmethylated compounds the p-orbital on the carbonyl carbon is rotated *away* from the C4 γ-hydrogen and the ensuing p-orbital at this site. With cyclization thus slowed by increased distance and reduced orbital overlap between the radical centers, reverse hydrogen transfer—which is presumably as geometrically favorable as the

(23) Very similar structure−reactivity relationships for biradical cyclization were found in our recent study of the solid-state type II photochemistry of a series of medium-sized ring and macrocyclic diketones.[14] In this work, stereoselective cyclization with "retention of configuration" at C1 and C4 was observed in biradicals for which $\varphi_1 \sim 70°$ and $\varphi_4 \sim 25°$ and $D \sim 3.15$ Å.

(24) (a) Lewis, F. D.; Hilliard, T. A. *J. Am. Chem. Soc.* **1970**, *92*, 6672. (b) Lewis, F. D.; Ruden, R. A. *Tetrahedron Lett.* **1971**, 715. (c) Wagner, P. J.; Kelso, P. A.; Kemppainen, A. E.; McGrath, J. M.; Schott, H. N.; Zepp, R. G. *J. Am. Chem. Soc.* **1972**, *94*, 7506.

(25) For recent experimental evidence that geometry-dependent intersystem crossing in triplet biradicals occurs dynamically during reaction and determines product ratios, see: (a) Wagner, P. J.; Zand, A.; Park, B.-S. *J. Am. Chem. Soc.* **1996**, *118*, 12856. For additional contributions to this topic, see: (b) Griesbeck, A. G.; Mauder, H.; Stadtmüller, S. *Acc. Chem. Res.* **1994**, *27*, 70. (c) Scaiano, J. C. *Tetrahedron* **1982**, *38*, 819.

(26) For recent updates of the original Salem−Rowland rules relating $T_1-S_0$ spin−orbit coupling in biradicals to molecular structure and conformation, see: (a) Michl, J. *J. Am. Chem. Soc.* **1996**, *118*, 3568. (b) Kita, F.; Nau, W. M.; Adam, W.; Wirz, J. *J. Am. Chem. Soc.* **1995**, *117*, 8670. (c) Zimmerman, H. E.; Kutateladze, A. G. *J. Am. Chem. Soc.* **1996**, *118*, 249. For a recent experimental study in which conformation-dependent enhanced spin−orbit coupling is suggested to control stereoselectivity in triplet 1,4-biradical reactions, see: (d) Griesbeck, A. G.; Buhr, S.; Fiege, M.; Schmickler, H.; Lex, J. *J. Org. Chem.* **1998**, *63*, 3847.

forward process—predominates for ketones **1a**, **1b**, **5a**, and **5b**, and cyclization is not observed in the solid state.

Finally, we address the question of why the adamantyl ketones **5a** and **5b** fail to to undergo type II cleavage in solution when their cyclohexyl counterparts **1a** and **1b** react efficiently in this manner. The likely answer is that the incipient C3−C4 double bond cannot easily achieve planarity in the transition state when it is part of an adamantane ring system. This apparently raises the barrier for cleavage sufficiently to make reverse hydrogen transfer the faster process.

**Hydrogen Abstraction Geometry.** It is interesting to compare the hydrogen abstraction geometries given in Table 6 with those from previous studies. Our initial work centered around compounds having the basic α-cycloalkylacetophenone structure,[22] and more recently, we have made a very thorough study of the crystal structure−solid-state reactivity relationships in the Norrish/Yang type II reactions of medium-sized ring and macrocyclic diketones.[14] For 17 examples of variously substituted α-cycloalkyacetophenones, the crystallographically determined abstraction distance $d$ was found to be 2.74 ± 0.16 Å, with $\omega = 43 \pm 9°$ and $\Delta = 84 \pm 8°$ ($\theta$ was not calculated).[22] For 11 photochemically reactive medium and large ring aliphatic diketones whose crystal structures were determined, the average value of $d$ was 2.73 ± 0.03 Å, with $\omega = 52 \pm 5°$, $\Delta = 83 \pm 4°$, and $\theta = 115 \pm 2°$.[14] For the 14 compounds studied in the present work, the corresponding values were $d = 2.61 \pm 0.07$ Å, $\omega = 53 \pm 11°$, $\Delta = 84 \pm 7°$, and $\theta = 115 \pm 2°$.

The fact that 42 compounds comprising three completely different classes of ketone react through such similar solid-state geometries argues very strongly that these data may be taken as being generally indicative of successful $\gamma$-hydrogen atom abstraction.[27] The data obviously do not provide exact information on the geometric situation in the excited state, where bond lengths and angles can differ somewhat from those in the ground state,[28] but there is every reason to believe that the structure−reactivity relationships developed above are approximately correct and can now be used in a predictive sense. Molecular mechanics programs provide rapid and reliable estimates of $d$, $\omega$, $\Delta$, and $\theta$, and this means that it should be possible to predict the outcomes of unknown type II reactions including their regioselectivity. Such work is under way in our laboratory at the present time.

**Asymmetric Induction Studies.** As summarized in Tables 4 and 5, the ionic chiral auxiliary approach to solid-state asymmetric synthesis works very well in the case of keto acids **1f** and **5f**. While not all of the optically active amines tested gave excellent results, most worked reasonably well and some were outstanding (pseudoephedrine, arginine, α-methylbenzylamine, norephedrine). Enantioselectivity increases with decreasing temperature, but significantly longer irradiation times are required. For both acids, photolysis of the (*S*)-(−)- and (*R*)-(+)-α-methylbenzylamine salts afforded equal optical yields of the enantiomers of cyclobutanols **2g** and **6g** (after diazomethane workup), indicating that the system is well-behaved. None of the salts gave any detectable asymmetric induction upon photolysis in methanol or acetonitrile solution.

Tables 4 and 5 also show that enantiomeric excess declines with increasing conversion. 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 at which the normal topochemical restrictions are relaxed. Although In some cases the decline in ee is precipitous, the pleasantly surprising feature of the results is that for many salts ee's of 80% or higher could be obtained at nearly complete conversion. This clearly indicates the considerable synthetic potential of the ionic chiral auxiliary approach to asymmetric induction. How can high ee be maintained at high conversions? Formation of the topochemically disallowed enantiomer requires a rotation of ∼180° about the C1−C2 bond (structure **9**, Scheme 2) prior to hydrogen abstraction, and evidently this process is slow in the solid state, even when the parent crystal lattice is nearly destroyed.[29] The solid-state medium therefore exerts two main effects in these reactions: (1) prior to irradiation, it orders the reactants in a single, homochiral conformation (**9**) that permits abstraction of only one of two possible enantiotopic hydrogen atoms, and (2) as the reaction proceeds and the parent crystal lattice breaks down, the medium nevertheless remains sufficiently viscous to prevent significant conversion of the original conformer **9** to its enantiomer via rotation about the C1−C2 bond; specific, anisotropic crystal lattice effects need not be invoked. An interesting question that remains unresolved, however, is why some salts give much higher ee's than others.

**Topotactic (Single Crystal-to-Single Crystal) Solid-State Photoreaction of Salts S14 and S15.** During our photochemical studies, we noticed that the salts of ketoacid **5f** with (*S*)-(−)- and (*R*)-(+)-α-methylbenzylamine (**S14** and **S15**, respectively) did not change in appearance upon irradiation, even at conversions as high as 90%. This suggested the occurrence of a single crystal-to-single crystal (topotactic) process,[30] and this possibility was therefore investigated further. Accordingly, a single crystal of salt **S15** that had been previously subjected to X-ray diffraction analysis was photolyzed for a time (2 h) sufficient to ensure complete conversion to the corresponding cyclobutanol, whereupon a second crystallographic data set was collected. Both data sets refined successfully in space group $P2_12_12_1$ to final $R$ values of 4.6 and 4.9%, thus indicating that the solid-state photorearrangement is indeed a topotactic process. Parts a and b of Figure 2 show the crystallographically determined molecular structures of the salts prior to and following irradiation, respectively. Figure 2a predicts preferential abstraction of $H_x$ (2.60 Å) over $H_y$ (3.59 Å), and in agreement with this, the molecular structure of the photoproduct salt (Figure 2b) shows that the carbon atom to which $H_x$ was attached is in fact part of the newly formed four-membered ring.

(27) Similar geometric data have been published recently for the Norrish type II reactions of phthalimidocyclohexanes. See: Griesbeck, A. G.; Henz, A.; Kramer, W.; Wamser, P. *Tetrahedron Lett.* **1998**, *39*, 1549. In this work, the success of hydrogen atom abstraction was found to depend critically on the angle Δ. For a more thorough discussion of hydrogen atom abstraction geometry, along with references to the work of others on this topic, see: Ihmels, H.; Scheffer, J. R. *Tetrahedron*, in press.

(28) For theoretical treatments that provide insights into the transition-state geometry of the type II process, see: (a) Dorigo, A. E.; McCarrick, M. A.; Loncharich, R. J.; Houk, K. N. *J. Am. Chem. Soc.* **1990**, *112*, 7508. (b) Sauers, R. R.; Edberg, L. A. *J. Org. Chem.* **1994**, *59*, 7061.

(29) It is interesting to speculate that the slightly lower ee's in the case of salts **S14**, **S15**, and **S17** (Table 5) derive from the "spherical" shape of the adamantane ring, which permits freer rotation about the C1−C2 bond in the crystalline state.

(30) Topotactic solid-state chemical reactions are rare. The following represent the majority of known examples. (a) Suzuki, T.; Fukushima, T.; Yamashita, Y.; Miyashi, T. *J. Am. Chem. Soc.* **1994**, *116*, 2793. (b) Enkelmann, V.; Wegner, G.; Novak, K.; Wagener, K. B. *J. Am. Chem. Soc.* **1993**, *115*, 10390. (c) Novak, K.; Enkelmann, V.; Wegner, G.; Wagener, K. B. *Angew. Chem., Int. Ed. Engl.* **1993**, *32*, 1614. (d) Vaida, M.; Popovitz-Biro, R.; Leiserowitz, L.; Lahav, M. In *Photochemistry in Organized and Constrained Media*; Ramamurthy, V., Ed.; Verlag Chemie: New York, 1991; Chapter 6. (e) Ohashi, Y. *Acc. Chem. Res.* **1988**, *21*, 268. (f) Wang, W.-N.; Jones, W. *Tetrahedron* **1987**, *43*, 1273. (g) Tieke, B. J. *J. Polym. Sci., Polym. Chem. Ed.* **1984**, *22*, 2895. (h) Miller, E.; Brill, T. B.; Rheingold, A. L.; Fultz, W. C. *J. Am. Chem. Soc.* **1983**, *105*, 7580. (i) Hasegawa, M. *Chem. Rev.* **1983**, *83*, 507. (j) Thomas, J. M. *Nature* **1981**, *289*, 633. (k) Thomas, J. M.; Morsi, S. E.; Desvergne, J. P. *Adv. Phys. Org. Chem.* **1977**, *15*, 63. (l) Cheng, K.; Foxman, B. *J. Am. Chem. Soc.* **1977**, *99*, 8102l (m) Wegner, G. *Pure Appl. Chem.* **1977**, *49*, 443. (n) Osaki, K.; Schmidt, G. M. J. *Isr. J. Chem.* **1972**, *10*, 189.

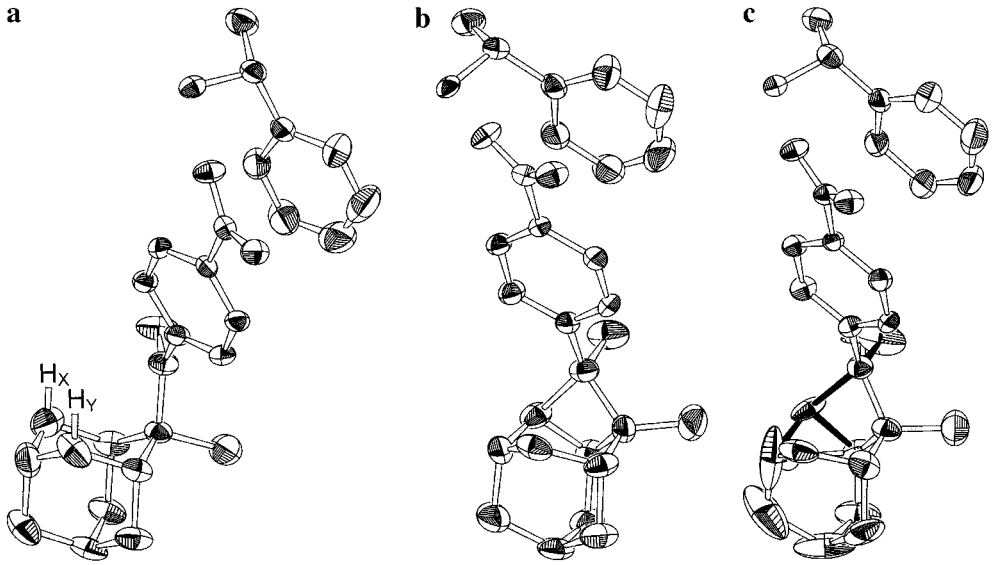



**Figure 2.** (a) Molecular structure of a crystal of salt **S15** prior to irradiation. (b) Molecular structure of the same crystal following complete conversion to the corresponding cyclobutanol salt. (c) Molecular structure of the mixed crystal composed of 40% of salt **S15** and 60% of its photoproduct. The thermal displacement ellipsoids in views (a) and (b) are drawn at the 30% probability level, 20% in view (c).

It was of interest to determine the structure of a *partially reacted* crystal, and to this end, a single crystal of salt **S15** was photolyzed for 15 min and then subjected to X-ray diffraction analysis. Once again the data set refined successfully in space group $P2_12_12_1$, but this time the final $R$ value was significantly higher (6.8%). GC analysis of the reaction mixture following diazomethane workup indicated a conversion of ~60%, and this was supported by refinement of the atom occupancy factors in the X-ray study.

Figure 2c shows an ORTEP diagram of the superposition of salt **S15** and its photoproduct in the mixed crystal. Although the slightly larger values of the anisotropic displacement parameters in the adamantane ring indicate a less than perfect match in location of reactant and product, there is still a very close atom-for-atom correspondence between the two, and this is undoubtedly the source of the topotactic behavior: the photoproduct fits nearly perfectly into the lattice site of the reactant. The major difference between the two structures is an upward movement of the $\gamma$-carbon atom to accommodate the four-membered ring and a slight change in orientation of the carbon−oxygen bond. These differences are indicated by the shaded bonds in Figure 2c. Interestingly, the unit cell volume is slightly greater for the mixed crystal (2319 Å$^3$) than for either the pure starting material (2301 Å$^3$) or the pure photoproduct (2310 Å$^3$). Similar behavior has been seen in other topotactic solid-state reactions.[30b,k] Recrystallization of the "as-formed" photoproduct salt failed to give crystals suitable for X-ray diffraction analysis. There were, however, slight differences in the solid-state IR spectra and DSC traces before and after recrystallization.

## Conclusions

In contrast to solid-state chemical reactions of nonionic (molecular) crystals, which generally have to be carried out at low temperatures and/or to low conversions owing to the problem of crystal melting, the present work indicates that the analogous processes of ionic crystals can be carried to much higher conversions without significant loss of topochemical control. Such reactions thus offer genuine prospects for synthetic utility. In the case of the single crystal-to-single crystal photoreaction of salt **S15**, quantitative conversions were possible without loss of crystal quality, which raises the intriguing possibility that salts in general will prove to be more topotactically inclined than their nonionic counterparts. Further studies with salts are required before this point can be settled. In the meantime, the solid-state photochemistry of salts in which one of the ions is a chiral auxiliary promises to become a viable and general method of asymmetric synthesis. The present paper contributes to the growing list of successful applications of this method in organic photochemistry,[8] and there is every reason to believe that a similar approach will work for ground-state asymmetric syntheses as well.[31] Strategic planning along these lines is underway in our laboratory at the present time.

In addition to the points raised above, the present work provides further penetrating insight into the details of the Norrish/Yang type II reaction. A general and consistent picture is beginning to emerge as to the geometric requirements for both stages of the reaction—hydrogen atom abstraction as well as the partitioning of the 1,4-hydroxy biradical intermediate. Through molecular modeling, this now makes it possible to predict the feasibility and outcome of hypothetical Norrish/Yang type II reactions.

## Experimental Section

**General Information.** Commercial spectral-grade solvents were used for photochemical experiments unless otherwise noted. Infrared spectra were recorded on a Perkin-Elmer 1710 Fourier transform spectrometer. Solid samples were ground in KBr (1−5%) and pelleted in an evacuated die (Perkin-Elmer 186-0002) at 17 000 psi. Liquid samples were run neat as thin films between two salt plates. Melting points were determined on a Fisher-Johns hot-stage apparatus and are uncorrected. Nuclear magnetic resonance spectra were recorded in deuterated solvents from Aldrich on 200-, 400-, and 500-MHz (Brüker) and 300-MHz (Varian) instruments. $^{13}$C spectra were run under broadband $^{13}C\{^1H\}$ decoupling and assignments, where given, were supported by the attached proton test. For APT, (+) signifies C or $CH_2$ and (−) signifies CH or $CH_3$. Low- and high-resolution mass spectra were obtained from a Kratos MS 50 instrument at 70 eV. FAB mass spectra were recorded on an AEI MS-9 spectrometer with xenon bombardment

(31) The use of optically active quaternary ammonium salts to bring about the enantioselective alkylation of achiral carbonyl compounds under basic phase transfer catalysis conditions has been reported. See: Corey, E. J.; Xu, F.; Noe, M. C. *J. Am. Chem. Soc.* **1997**, *119*, 12414 and references therein.

of an alcohol matrix as noted. Ultraviolet spectra were recorded on a Perkin-Elmer Lambda-4B spectrometer in the solvents indicated. Elemental analyses were performed by the departmental microanalyst, Mr. P. Borda. Gas chromatographic analyses were performed on a Hewlett-Packard 5890 instrument fitted with a flame ionization detector and a Hewlett-Packard 3392 A integrator. The following 15 m × 0.25 mm fused-silica capillary columns from J & W Scientific, Inc. were used: DB-1, DB-5, DB-17, and HP-5. A 20 m × 0.21 mm Carbowax 20M capillary column from Hewlett-Packard was also used on occasion. Analytical thin-layer chromatography was carried out on commercial precoated silica gel plates (E. Merck, type 5554). Column chromatography was performed by using 230−400-mesh silica gel (Merck 9385) slurry packed with the eluting solvent. High-pressure liquid chromatography was performed on a Waters 600E system controller connected to a tunable UV detector (Waters 486) or programmable photodiode array detector (Waters 994). For the determination of enantiomeric excesses, a Chiralcel OD column (250 mm × 4.6 mm) from Chiral Technologies, Inc. was used.

**Preparation of Starting Materials.** Ketone **1a** was prepared as described by Padwa and Eastman,[13b] and ketone **1c** was prepared according to the procedure of Lewis et al.[12a] As far as we are aware, the remainder of the starting materials described below are new.

***cis*-4-*tert*-Butylcyclohexyl *p*-fluorophenyl ketone (1b)** was prepared as described for ketone **1a**,[13b] except that fluorobenzene was used instead of benzene in the Friedel−Crafts reaction. Recrystallization of the crude product from methanol afforded colorless plates: mp 82−84 °C, in a yield of ∼57%; $^1$H NMR ($CDCl_3$) $\delta$ 7.99−7.82 (2H, m, ArH), 7.18−7.02 (3H, m, ArH), 3.52−3.41 (1H, m, α-CH) 2.22−2.09 (2H, m), 1.72−1.50 (4H, m), 1.36−1.11 (3H, m), 0.80 (9H, s, $C(CH_3)_3$); $^{13}$C NMR ($CDCl_3$) $\delta$ 23.34 (+), 27.46 (−), 28.27 (+), 32.52 (+), 40.32 (−), 48.06 (−), 115.28 and 115.70 ($^2J_{C-F}$ = 21 Hz, −ve), 130.66 and 130.84 ($^3J_{C-F}$ = 9 Hz, −ve), 133.11 and 133.17 ($^4J_{C-F}$ = +ve), 162.71 and 167.74 ($^1J_{C-F}$ = 253 Hz, +ve), 202.60 (+); IR (KBr) 2923, 2856, 1675 (C═O), 1599, 1508, 1467, 1453, 1407, 1393, 1365, 1345, 1302, 1217, 1171, 1158, 1142, 974, 908, 856, 828, 791, 661, 607, 559, 522, 484 cm$^{-1}$; UV (hexane) 242 (15 500), 269 (3320), 325 (110) nm; MS (EI) *m*/*z* 263, 262 ($M^+$), 247, 205, 165, 151, 138, 124, 123 (100), 112, 109, 95, 83, 75, 69, 57, 55, 41, 32; HRMS (EI) *m*/*z* 262.1734 (calcd for $C_{17}H_{23}OF$, 262.1733). Anal. Calcd for $C_{17}H_{23}OF$: C, 77.82; H, 8.84. Found: C, 78.05; H, 9.10.

***cis*-4-*tert*-Butyl-1-methylcyclohexyl *p*-Fluorophenyl Ketone (1d).** A solution of 7.4 g (34.5 mmol) of an approximately 85:15 cis/trans mixture of methyl 4-*tert*-butyl-1-methylcyclohexanecarboxylate[32] was dissolved in 100 mL of anhydrous THF and refluxed for 1 h with 4.0 g (105 mmol) of lithium aluminum hydride. After cooling to room temperature, the solution was quenched with 1 N sulfuric acid and extracted with ether, and the ether layers were washed and dried. Removal of the ether in vacuo afforded a quantitative yield (6.3 g) of a mixture of *cis*- and *trans*-4-*tert*-butyl-1-methylcyclohexylmethanol. Separation of the isomers at this stage was readily accomplished via silica gel column chromatography using 7% ethyl acetate in hexanes as the eluent. The *cis*-alcohol so obtained (5.3 g) was converted directly into the corresponding aldehyde (5.1 g, 97%, light yellow oil) by standard pyridinium chlorochromate oxidation,[33] and to a portion of this material (3.0 g, 16.5 mmol) in 75 mL of dry THF was added 50 mL of a 1.6 M hexane solution of *p*-fluorophenylmagnesium bromide in hexane (Aldrich) over 5 min at 0 °C. The solution was stirred at room temperature for 5 h and then treated with saturated ammonium chloride solution. Standard workup (extraction with ether, washing, drying, and removal of solvent in vacuo) afforded 4.1 g (89%) of the secondary alcohol as a yellow liquid. Without further purification, this material was subjected to Jones oxidation (10.0 g of chromium trioxide, 5.0 mL of water, and 2.0 mL of concentrated sulfuric acid in 50 mL of acetone), and standard workup afforded ketone **1d** as a light yellow solid (3.9 g, 96%). Recrystallization from methanol gave colorless flakes: mp 76−78 °C; $^1$H NMR ($CDCl_3$) $\delta$ 7.60−7.50 (2H, m, ArH), 6.80−6.60 (2H, m, ArH), 2.48−2.42 (2H, m), 1.48−1.42 (2H, m), 1.16 (3H, s, $CH_3$), 1.11−0.90 (5H, m), 0.78 (9H, s, $C(CH_3)_3$); $^{13}$C NMR ($CDCl_3$) $\delta$ 24.48 (+), 27.39 (−), 28.45 (−), 32.28 (+), 37.49(+), 47.57 (−), 48.45 (+), 114.83 and 115.27 ($^2J_{C-F}$ = 22 Hz, −ve), 130.01 and 130.18 ($^3J_{C-F}$ = 8 Hz, −ve), 135.39 and 135.45 ($^4J_{C-F}$ = 3 Hz, +ve), 161.60 and 166.63 ($^1J_{C-F}$ = 252 Hz, +ve), 207.69 (+); IR (KBr) 2952, 2864, 1667 (C═O), 1599, 1504, 1451, 1364, 1293, 1230, 1195, 1157, 1101, 965, 846, 767 cm$^{-1}$; UV (hexane) 241 (8500), 311 (sh 200) nm; MS (EI) *m*/*z* 277, 276 ($M^+$), 262, 247, 219, 205, 187, 165, 152, 138, 123 (100), 109, 97, 83, 81, 71, 69, 57, 55, 43, 41; HRMS 276.1897 (calcd for $C_{18}H_{25}OF$, 276.1889). Anal. Calcd for $C_{18}H_{25}OF$: C, 78.22; H, 9.12. Found: C, 78.45; H, 9.18.

***cis*-4-*tert*-Butyl-1-methylcyclohexyl *p*-Cyanophenyl Ketone (1e).** In a flame-dried 100-mL flask equipped with a stirrer and condenser, 2.90 g (10.5 mmol) of ketone **1d** and 1.4 g (21.6 mmol) of potassium cyanide were dissolved in 70 mL of anhydrous dimethyl sulfoxide. The mixture was refluxed until no starting material remained as indicated by TLC (2% ether/hexanes). The dark orange solution was poured into 100 mL of water and extracted with ether (3 × 50 mL). Standard workup afforded a yellow solid which was recrystallized from 5% ether/petroleum ether to give ketone **1e** (2.9 g, 98%) as a faintly yellow powder: mp 115−117 °C; $^1$H NMR ($CDCl_3$) $\delta$ 7.78−7.65 (4H, m, ArH), 2.52−2.30 (2H, m), 1.63−1.50 (2H, m), 1.34 (3H, s, $CH_3$), 1.25−1.10 (2H, m), 1.05−0.80 (3H, m), 0.76 (9H, s, $C(CH_3)_3$); $^{13}$C ($CDCl_3$) $\delta$ 25.54 (+), 27.38 (−), 28.29 (−), 32.31 (+), 36.91 (+), 47.44 (−), 48.85 (+), 114.16 (+), 118.07 (+), 127.73 (−), 131.97 (−), 143.58 (+), 208.74 (+); IR (KBr) 2963, 2942, 2857, 2232 (CN), 1674 (C═O), 1602, 1453, 1393, 1364, 1291, 1274, 1242, 1219, 1196, 1167, 1142, 983, 958, 931, 861, 844, 771, 563 cm$^{-1}$; UV (methanol) 241 (17 100), 280 (1500), 328 (sh 240) nm; MS (EI) *m*/*z* 284, 283 ($M^+$), 268, 255, 226, 172, 153, 131, 130, 102, 97, 95, 83, 69, 57 (100), 55, 41; HRMS (EI) *m*/*z* 283.1942 (calcd for $C_{19}H_{25}NO$, 283.1936). Anal. Calcd for $C_{19}H_{25}NO$: C, 80.52; H, 8.89; N, 4.94. Found: C, 80.67; H, 8.85; N, 4.84.

***cis*-4-*tert*-Butyl-1-methylcyclohexyl *p*-Carboxyphenyl Ketone (1f).** To a 100-mL flask equipped with a condenser was added 2.0 g (7.1 mmol) of ketone **1e**, 50 g of potassium hydroxide, 75 mL of water, and 15 mL of ethanol. The mixture was refluxed for 72 h, cooled to room temperature, and washed with ether. The aqueous layer was acidified with concentrated HCl and the resulting white precipitate collected by vacuum fitration and recrystallized from ethanol/water to afford 2.1 g (98%) of keto acid **1f** as long white needles: mp 232−233 °C; $^1$H NMR ($CDCl_3$) $\delta$ 8.26−8.00 (2H, d, $J$ = 8 Hz, ArH), 7.81−7.53 (2H, d, $J$ = 8 Hz, ArH), 2.56−2.31 (2H, m), 1.75−1.45 (2H, m), 1.38 (3H, s, $CH_3$), 1.42−1.12 (2H, m), 1.12−0.83 (3H, m), 0.78 (9H, s, $C(CH_3)_3$), no COOH resonance observed; $^{13}$C NMR ($CDCl_3$) $\delta$ 24.55 (+), 27.40 (−), 28.37 (−), 32.32 (+), 36.97 (+), 47.49 (−), 48.83 (+), 127.17 (−), 130.01 (−), 130.68 (+), 144.74 (+), 170.10 (+), 209.88 (+); IR (KBr) 3433 (OH), 2952, 2905, 2869, 2667, 2544, 2349, 2303, 1956, 1690 (C═O), 1672 (C═O), 1568, 1504, 1452, 1423, 1405, 1364, 1317, 1287, 1220, 1194, 1126, 961, 948, 931, 867, 735, 556, 534 cm$^{-1}$; UV (methanol) 244 (12 700), 284 (sh 1800), 322 (200) nm; MS (EI) *m*/*z* 303, 302 ($M^+$), 287, 278, 269, 257, 245, 227, 206, 191, 165, 153, 152, 150, 149, 136, 121, 109, 97, 95, 94, 83, 81, 71, 69, 65, 57 (100), 55, 41; HRMS (EI) *m*/*z* 302.1887 (calcd for $C_{19}H_{26}O_3$, 302.1882). Anal.Calcd for $C_{19}H_{26}O_3$: C, 75.46; H, 8.67. Found: C, 75.20; H, 8.84.

***cis*-4-*tert*-Butyl-1-methylcyclohexyl *p*-Carbomethoxyphenyl Ketone (1g).** A solution of 0.7 g (2.3 mmol) of keto acid **1f** and 0.5 g of *p*-toluenesulfonic acid in 35 mL of methanol was refluxed for 24 h. The reaction mixture was cooled, poured into 30 mL of ice/water, and extracted with five 30-mL portions of ether. Standard workup afforded a light yellow solid, and recrystallization from petroleum ether gave 0.7 g (96%) of keto ester **1g** as a white powder: mp 140−141 °C; $^1$H NMR ($CDCl_3$) $\delta$ 8.12−7.99 (2H, d, $J$ = 8 Hz, ArH), 7.71−7.55 (2H, d, $J$ = 8 Hz, ArH), 3.94 (3H, s, $COOCH_3$), 2.54−2.33 (2H, m), 1.66−1.48 (2H, m), 1.37 (3H, s, $CH_3$), 1.36−1.12 (2H, m), 1.09−0.81 (3H, m), 0.67 (9H, s, $C(CH_3)_3$); $^{13}$C NMR ($CDCl_3$) $\delta$ 24.53 (+), 27.40 (−), 28.38 (−), 32.31 (+), 37.02 (+), 47.49 (−), 52.33 (−), 127.07 (−), 129.32 (−), 131.68 (+), 143.85 (+), 166.37 (+), 209.85 (+); IR (KBr) 2963, 2948, 2865, 1722 (C═O), 1670 (C═O), 1471, 1463, 1449, 1404, 1365, 1311, 1282, 1223, 1195, 1110, 1019, 961, 865, 754, 737, 716 cm$^{-1}$; UV (methanol) 244 (17 000), 281 (1200), 327 (180) nm; MS

(32) Krapcho, A. P.; Dundulis, E. A. *J. Org. Chem.* **1980**, *45*, 3236.
(33) Corey, E. J.; Suggs, J. W. *Tetrahedron Lett.* **1975**, 2647.

(EI) *m*/*z* 317, 316 ($M^+$), 301, 285, 257, 245, 218, 192, 179, 165, 164 (100), 163, 153, 152, 136, 135, 120, 104, 97, 95, 94, 83, 81, 69, 57, 55, 41; HRMS (EI) *m*/*z* 316.2036 (calcd for $C_{20}H_{28}O_3$, 316.2039). Anal. Calcd for $C_{20}H_{28}O_3$: C, 75.91; H, 8.92. Found: C, 75.84; H, 8.91.

***cis*-4-*tert*-Butyl-1-methylcyclohexyl *p*-tolyl ketone (1h)** was prepared as described for **1d**, except that *p*-tolylmagnesium bromide was used in the Grignard step instead of (*p*-fluorophenyl)magnesium bromide. Recrystallization of the crude solid from petroleum ether afforded colorless plates of ketone **1h**: mp 96−98 °C; $^1$H NMR ($CDCl_3$) $\delta$ 7.64−7.58 (2H, d, $J$ = 8 Hz, ArH), 7.20−7.10 (2H, d, $J$ = 8 Hz, ArH), 2.60−2.42 (2H, m), 2.38 (3H, s, $ArCH_3$), 1.60−1.48 (2H, m), 1.38 (3H, s, $CH_3$), 1.30−1.10 (2H, m), 1.08−0.82 (3H, m), 0.78 (9H, s, $C(CH_3)_3$); $^{13}$C NMR ($CDCl_3$) $\delta$ 21.42 (−), 24.53 (+), 27.42 (−), 28.54 (−), 32.32 (+), 37.54 (+), 47.65 (−), 48.43 (+), 127.76 (−), 128.65 (−), 136.67 (+), 141.14 (+), 209.00 (+); IR (KBr) 2965, 2938, 2860, 2837, 1666 (C═O), 1608, 1450, 1433, 1364, 1293, 1273, 1228, 1184, 965, 829, 760, 747 cm$^{-1}$; UV (methanol) 245 (10 800), 270 (sh 860), 324 (120) nm; MS (EI) *m*/*z* 273, 272 ($M^+$), 257, 239, 215, 161, 152, 135, 121, 120, 119 (100), 97, 95, 91, 83, 67, 65, 57, 55, 41; HRMS (EI) *m*/*z* 272.2138 (calcd for $C_{19}H_{28}O$, 272.2140). Anal. Calcd for $C_{19}H_{28}O$: C, 83.77; H, 10.36. Found: C, 83.53; H, 10.22.

***cis*-4-*tert*-Butyl-1-methylcyclohexyl *p*-methoxyphenyl ketone (1i)** was prepared as described for **1d**, except that (*p*-methoxyphenyl)-magnesium bromide was used in the Grignard step instead of (*p*-fluorophenyl)magnesium bromide. Recrystallization of the crude solid from 95:5 (v/v) petroleum ether/ethanol afforded ketone **1i** as white needles: mp 106−107 °C; $^1$H NMR ($CDCl_3$) $\delta$ 7.80−7.70 (2H, m, ArH), 6.93−6.82 (2H, m, ArH), 3.83 (3H, s, $ArOCH_3$), 2.60−2.42 (2H, m), 1.60−1.50 (2H, m), 1.38 (3H, s, $CH_3$), 1.30−1.10 (2H, m), 1.05−0.80 (3H, m), 0.75 (9H, s, $C(CH_3)_3$); $^{13}$C NMR ($CDCl_3$) $\delta$ 24.52 (+), 27.42 (−), 28.59 (−), 32.31 (+), 37.85 (+), 47.71 (−), 48.24 (+), 55.32 (−), 113.18 (−), 130.19 (−), 131.50 (+), 161.73 (+), 208.84 (+); IR (KBr) 2962, 2937, 2867, 2841, 1661(C═O), 1604, 1575, 1507, 1455, 1444, 1413, 1366, 1309, 1253, 1230, 1176, 1143, 1033, 964, 836, 767, 648 cm$^{-1}$; UV (methanol) 268 (18 700), 319 (sh 700) nm; MS (EI) *m*/*z* 289, 288 ($M^+$), 273, 257, 231, 206, 163, 150, 137, 135 (100), 107, 97, 92, 77, 64, 57, 41; HRMS (EI) *m*/*z* 288.2089 (calcd for $C_{19}H_{28}O_2$, 288.2089). Anal. Calcd for $C_{19}H_{28}O_2$: C, 79.12; H, 9.78. Found: C, 79.24; H, 9.78.

**2-Benzoyladamantane (5a).** A mixture of 5.0 g (27 mmol) of 2-adamantane carboxylic acid[34] and 10.0 g (84 mmol) of thionyl chloride was placed in a flame-dried 50-mL flask equipped with a condenser and stirred for 30 min under nitrogen and then for 2 h at reflux. Excess thionyl chloride was removed by distillation, and the remaining acid chloride was used in the next step without purification. A solution of 3.0 g (14.8 mmol) of acid chloride in 25 mL of anhydrous benzene was added over 30 min to a suspension of 7.0 g (52.5 mmol) of aluminum chloride in 150 mL of anhydrous benzene. After stirring for 5 h at room temperature, 100 mL of water was cautiously added and the resulting mixture was extracted with 2 × 75 mL of ether. Standard workup afforded an oil that crystallized upon standing overnight under vacuum. Recrystallization from methanol yielded 1.2 g (33%) of colorless plates: mp 91−93 °C; $^1$H NMR ($CDCl_3$) $\delta$ 7.90−7.80 (2H, m, ArH), 7.60−7.40 (3H, m, ArH), 3.50−3.40 (1H, m, α-CH), 2.30 (2H, m), 2.10−1.40 (12 H, m); $^{13}$C NMR ($CDCl_3$) $\delta$ 27.52 (−), 27.96 (−), 30.31 (−), 32.77 (+), 37.44 (+), 38.82 (+), 52.14 (−), 128.04 (−), 128.41 (−), 132.12 (−), 137.23 (+), 204.08 (+); IR (KBr) 2950, 1676 (C═O), 1447, 1364, 1221, 973, 766, 698 cm$^{-1}$; UV (methanol) 238 (17,800), 278 (sh 1500), 339 (80) nm; MS (EI) *m*/*z* 241, 240 ($M^+$), 239, 222, 197, 179, 145, 135, 120, 105, 93, 91, 79, 77, 67, 51, 41; HRMS (EI) *m*/*z* 240.1509 (calcd for $C_{17}H_{20}O$, 240.1514). Anal. Calcd for $C_{17}H_{20}O$: C, 84.96; H, 8.39. Found: C, 85.12; H, 8.43.

**2-(*p*-Fluorobenzoyl)adamantane (5b).** A solution of 3.0 g (16.5 mmol) of 2-adamantanecarboxaldehyde[34] in 75 mL of anhydrous THF was cooled in an ice bath, and to this was added (*p*-fluorophenyl)-magnesium bromide (Aldrich, 1.6 M in hexane solution, 50 mL, 80 mmol) via syringe over a period of 5 min under nitrogen. The solution was stirred at room temperature for 5 h and then carefully decomposed using saturated aqueous ammonium chloride. Extraction with ether and standard workup afforded the secondary alcohol, which was subjected directly to Jones oxidation (10 g of chromium trioxide, 5 mL of water, and 2.0 mL of concentrated sulfuric acid in 50 mL of acetone). Standard workup afforded a light yellow solid, which was recrystallized from methanol to yield 3.9 g (86%) of colorless plates: mp 93−94 °C; $^1$H NMR ($CDCl_3$) $\delta$ 7.92−7.80 (2H, m, ArH), 7.18−7.02 (2H, m, ArH), 3.40 (1H, m, α-CH), 2.25 (2H, m), 2.16−1.46 (12H, m); $^{13}$C NMR ($CDCl_3$) $\delta$ 27.47 (−), 27.92 (−), 30.40 (−), 32.70 (+), 37.38 (+), 38.80 (+), 52.05 (−), 115.24 and 115.67 ($^2J_{C-F}$ = 22 Hz, −ve), 130.52 and 130.70 ($^3J_{C-F}$ = 9 Hz, −ve), 133.36 and 133.42 ($^4J_{C-F}$ = 3 Hz, +ve), 162.61 and 167.64 ($^1J_{C-F}$ = 253 Hz, +ve), 202.32 (+); IR (KBr) 2902, 2851, 1678 (C═O), 1593, 1504, 1451, 1407, 1344, 1336, 1297, 1268, 1237, 1206, 1157, 1101, 1010, 948, 861, 846, 829, 813, 795, 619, 505 cm$^{-1}$; UV (methanol) 241 (10 700), 274 (sh 300), 342 (60) nm; MS (EI) *m*/*z* 259, 258 ($M^+$), 257, 240, 215, 197, 177, 163, 151, 138, 136, 135, 124, 123 (100), 107, 95, 93, 91, 81, 79, 67, 55, 41; HRMS (EI) *m*/*z* 258.1413 (calcd for $C_{17}H_{19}OF$, 258.1420). Anal. Calcd for $C_{17}H_{19}OF$: C, 79.04; H, 7.41. Found: 79.09; H, 7.57.

**2-Benzoyl-2-methyladamantane (5c).** Into a 100-mL flame-dried flask fitted with a condenser was placed a suspension of 2.0 g (8.2 mmol) of **5a** and 1.0 g (41.7 mmol) of powdered sodium hydride in 50 mL of anhydrous 1,2-dimethoxyethane. The mixture was refluxed for 4 h and cooled in an ice/water bath, and 2.3 g (16.2 mmol) of methyl iodide was added by syringe. After stirring for 30 min, 0.5 g more of sodium hydride was added and the mixture was then refluxed for 90 min. After cooling, the reaction mixture was treated with 30 mL of water and extracted with pentane, and the organic layer was washed, dried, and concentrated in vacuo to afford a solid residue, which was chromatographed over silica gel using 5% ether/hexanes as the eluent. The second compound to elute from the column was collected and recrystallized from hexanes to afford 1.1 g (52%) of colorless plates: mp 56−57 °C; $^1$H NMR ($CDCl_3$) $\delta$ 7.78−7.64 (2H, m, ArH), 7.50−7.30 (3H, m, ArH), 2.38 (2H), 2.18−2.07 (2H, m), 1.90−1.62 (10H, m), 1.60 (3H, s, $CH_3$); $^{13}$C NMR ($CDCl_3$) $\delta$ 23.80 (−), 27.04 (−), 27.24 (−), 32.54 (+), 34.11 (−), 35.04 (+), 38.10 (+), 53.10 (+), 127.85 (−), 127.92 (−), 130.79 (−), 139.20 (+), 210.80 (+); IR (KBr) 2950, 2913, 2862, 1666 (C═O), 1596, 1462, 1446, 1256, 1214, 1163, 1138, 1104, 1081, 1002, 968, 953, 942, 928, 888, 795, 726, 697 cm$^{-1}$; UV (methanol) 239 (9500), 270 (sh 795), 322 (143) nm; MS (EI) *m*/*z* 254 ($M^+$), 150, 149 (100), 148, 121, 107, 105, 93, 91, 81, 79, 77, 67, 55, 41; HRMS (EI) *m*/*z* 254.1668 (calcd for $C_{18}H_{22}O$, 254.1671). Anal. Calcd for $C_{18}H_{22}O$: C, 84.99; H, 8.72. Found: C, 84.78; H, 8.75.

**2-(*p*-Fluorobenzoyl)-2-methyladamantane (5d).** Methylation of 2-(*p*-fluorobenzoyl)adamantane was carried out as described above to afford a 52% yield of ketone **5d** as colorless plates (hexane): mp 86−87 °C; $^1$H NMR ($CDCl_3$) $\delta$ 7.84−7.70 (2H, m, ArH), 7.14−6.99 (2H, m, ArH), 2.34 (2H, m), 2.19−2.05 (2H, m), 1.90−1.72 (3H, m), 1.72−1.55 (7H, m), 1.50 (3H, s, $CH_3$); $^{13}$C NMR ($CDCl_3$) $\delta$ 23.67 (−), 26.97 (−), 27.19 (−), 32.50 (+), 34.21 (−), 34.96 (+), 38.01 (+), 53.00 (+), 114.74 and 115.17 ($^2J_{C-F}$ = 21 Hz, −ve), 130.30 and 130.47 ($^3J_{C-F}$ = 8 Hz, −ve), 135.01 and 135.08 ($^4J_{C-F}$ = 3 Hz, +ve), 161.64 and 166.65 ($^1J_{C-F}$ = 232 Hz, +ve), 208.47 (+); IR (KBr) 2921, 2858, 1668 (C═O), 1598, 1504, 1454, 1354, 1259, 1226, 1160, 1142, 1103, 1084, 970, 954, 940, 851, 821, 769, 759, 608, 543, 492 cm$^{-1}$; UV (methanol) 241 (8,900), 333 (70) nm; EI (MS) *m*/*z* 273, 272 ($M^+$), 189, 181, 169, 150, 149 (100), 148, 133, 123, 121, 107, 95, 93, 81, 79, 67, 55, 41; HRMS (EI) *m*/*z* 272.1571 (calcd for $C_{18}H_{21}OF$, 272.1577). Anal. Calcd for $C_{18}H_{21}OF$: C, 79.38; H, 7.77. Found: C, 79.31; H, 7.86.

**2-(*p*-Cyanobenzoyl)-2-methyladamantane (5e).** This compound was synthesized from **5d** in 98% yield by a procedure identical to that used to convert ketone **1d** to **1e**. Recrystallization of the crude product from 95:5 (v/v) petroleum ether/ether gave pale yellow plates: mp 134−135 °C; $^1$H NMR ($CDCl_3$) $\delta$ 7.81−7.65 (4H, m, ArH), 2.28 (2H, m), 2.18−2.05 (2H, m), 1.90−1.72 (2H, m), 1.72−1.55 (8H, m), 1.50 (3H, s, $CH_3$); $^{13}$C NMR ($CDCl_3$) $\delta$ 23.75 (−), 26.87 (−), 27.11 (−), 32.34 (+), 33.92 (−), 35.03 (+), 37.89 (+), 53.42 (+), 114.31 (+), 118.10 (+), 128.33 (−), 131.85 (−), 142.86 (+), 209.09 (+); IR (KBr) 2904,

(34) Alberts, A. H.; Wynberg, H.; Strating, J. *Synth. Commun.* **1972**, *2*, 79.

2855, 2230, 1669 (C═O), 1460, 1450, 1401, 1354, 1286, 1251, 1221, 1140, 1105, 1083, 973, 954, 941, 845, 768, 707, 594, 545, 528, 512 $cm^{-1}$; UV (methanol) 243 (15 600), 323 (200) nm; MS (EI) *m*/*z* 280, 279 ($M^+$), 181, 169, 150, 149 (100), 131, 130, 121, 107, 102, 95, 93, 91, 81, 79, 77, 69, 67, 55, 41; HRMS (EI) *m*/*z* 279.1621 (calcd for $C_{19}H_{21}NO$, 279.1623). Anal. Calcd for $C_{19}H_{21}NO$: C, 81.68; H, 7.58; N, 5.01. Found: C, 81.66; H, 7.67; N, 4.97.

**2-(*p*-Carboxybenzoyl)-2-methyladamantane (5f).** This compound was synthesized from **5e** in 98% yield by a procedure identical to that used to convert ketone **1e** to **1f**. Recrystallization of the crude product from aqueous ethanol gave long white needles: mp 216−218 °C; $^1$H NMR ($CDCl_3$) $\delta$ 8.20−8.10 (2H, d, $J$ = 8 Hz, ArH), 7.85−7.75 (2H, d, $J$ = 8 Hz, ArH), 2.32 (2H, m), 2.20−2.08 (2H, m), 1.92−1.74 (2H, m), 1.73−1.59 (8H, m), 1.53 (3H, s, $CH_3$), no COOH signal was detectable; $^{13}$C NMR ($CDCl_3$) $\delta$ 23.79 (−), 26.96 (−), 27.17 (−), 32.43 (+), 33.94 (−), 35.07 (+), 37.99 (+), 53.40 (+), 127.81 (−), 129.89 (−), 130.92 (+), 143.97 (+), 170.99 (+), 210.17 (+); IR (KBr) 3420 (OH), 2910, 2882, 2855, 1694 (C═O), 1681(C═O), 1506, 1456, 1435, 1404, 1322, 1298, 1255, 1214, 1127, 1104, 974, 955, 940, 866, 789, 766, 735, 703, 547,531, 459 $cm^{-1}$; UV (methanol) 247 (16 000), 275 (sh, 1300), 322 (200) nm; MS (EI) *m*/*z* 299, 298 ($M^+$), 281, 253, 178, 159, 150, 149 (100), 148, 131, 121, 107, 93, 81, 79, 65, 55, 41; HRMS (EI) *m*/*z* 298.1562 (calcd for $C_{19}H_{22}O_3$, 298.1569). Anal. Calcd for $C_{19}H_{22}O_3$: C, 76.47; H, 7.44. Found: C, 76.35; H, 7.39.

**2-(*p*-Carbomethoxybenzoyl)-2-methyladamantane (5g).** This compound was synthesized from **5f** in 96% yield by a procedure identical to that used to convert ketone **1f** to **1g**. Recrystallization of the crude product from petroleum ether gave white plates: mp 90−92 °C; $^1$H NMR ($CDCl_3$) $\delta$ 8.10−8.00 (2H, d, $J$ = 8 Hz, ArH), 7.80−7.70 (2H, d, $J$ = 8 Hz, ArH), 3.94 (3H, s, $CO_2CH_3$), 2.32 (2H, m), 2.21−2.07 (2H, m), 1.93−1.73 (2H, m), 1.73−1.50 (8H, m), 1.52 (3H, s, $CH_3$); $^{13}$C NMR ($CDCl_3$) $\delta$ 23.78 (−), 26.95 (−), 27.16 (−), 32.44 (+), 33.95 (−), 35.04 (+), 37.99 (+), 52.33 (−), 53.33 (+), 127.71 (−), 129.23 (−), 131.85 (+), 143.10 (+), 166.37 (+), 210.10 (+); IR (KBr) 2911, 2859, 1727 (C═O), 1673 (C═O), 1457, 1438, 1402, 1285, 1255, 1218, 1107, 1017, 972, 954, 860, 791, 743, 709 $cm^{-1}$; UV (methanol) 247 (15 800), 275 (sh 1360), 323 (200) nm; MS (EI) *m*/*e* 312 ($M^+$), 297, 281, 253, 164, 163, 150, 149 (100), 135, 121, 107, 93, 79; HRMS (EI) *m*/*z* 312.1720 (calcd for $C_{20}H_{24}O_3$, 312.1725). Anal. Calcd for $C_{20}H_{24}O_3$: C, 76.88; H, 7.75. Found: C, 76.91; H, 7.84.

**Preparation of Salts.** Salts were prepared by dissolving equimolar amounts of keto acid (**1f** or **5f**) and amine in the solvents indicated. The initial precipitates were collected and recrystallized from the solvents given in Table 3; melting points and crystal morphologies are also given in Table 3. Satisfactory NMR, IR, and UV spectra were recorded for all salts. In the IR, salt formation resulted in a characteristic change in the carboxylic acid OH stretching band at ∼3500−2400 $cm^{-1}$, which was replaced by multiple combination bands for ammonium in the 3200−2200-$cm^{-1}$ region. In addition, the carboxylic acid carbonyl stretch at ∼1690 $cm^{-1}$ was replaced by two bands for the carboxylate anion: a strong absorption in the 1650−1550-$cm^{-1}$ region and a weaker one near 1400 $cm^{-1}$.

**(*S*)-(+)-Prolinol Salt of Keto Acid 1f (S1).** Keto acid **1f** (246 mg, 0.8 mmol) and 82 mg (0.8 mmol) of (*S*)-(+)-prolinol were mixed in 30 mL of acetone. The solution was heated until the solid dissolved, and after standing for 1 h at room temperature, the precipitated salt was collected by suction filtration (252 mg, 77%). MS (FAB, +LSIMS) *m*/*z* 404 ($M^+$ + 1), 391, 333, 305, 304, 303, 301, 286, 285, 229, 149 (100), 133, 102 (matrix: thioglycerol + methanol). Anal. Calcd for $C_{24}H_{37}O_4N$: C, 71.42; H, 9.25; N, 3.47. Found: C, 71.27; H, 9.26; N, 3.43.

**(1*S*,2*S*)-(+)-Pseudoephedrine Salt of Keto Acid 1f (S2).** Keto acid **1f** (202 mg, 0.67 mmol) and 111 mg (0.67 mmol) of (1*S*,2*S*)-(+)-pseudoephedrine were dissolved in 30 mL of ethanol. The solution was concentrated in vacuo to a volume of ∼5 mL and ether added until a white precipitate was observed. The precipitated salt was collected by suction filtration (293 mg, 94%). MS (FAB, +LSIMS) *m*/*z* 468 ($M^+$ + 1), 393, 380, 347, 304, 303, 285, 229, 167, 166 (100), 165, 149, 133 (matrix: thioglycerol + methanol). Anal. Calcd for $C_{29}H_{41}O_4N{\cdot}2H_2O$: C, 69.15; H, 9.01; N, 2.78. Found: C, 69.16; H, 8.86; N, 2.76.

**(*S*)-(+)-Arginine Salt of Keto Acid 1f (S3).** Keto acid **1f** (197 mg, 0.65 mmol) and 113 mg (0.65 mmol) of (*S*)-(+)-arginine in 2 mL of water were dissolved in 25 mL of ethanol. After standing for several hours at room temperature, the solution was concentrated to dryness in vacuo and the resulting white solid washed with ether, leaving 301 mg (97%) of the desired salt: MS (FAB, -LSIMS) *m*/*z* 475 ($M^-$ − 1), 445, 409, 407, 383, 317, 302, 301 (100), 285, 257, 229, 209, 173, 121, 120 (matrix, thioglycerol). Anal. Calcd for $C_{25}H_{40}O_5N_4$: C, 63.00; H, 8.46; N, 11.76. Found: C, 62.92; H, 8.52; N, 11.63.

**(*S*)-(−)- and (*R*)-(+)-α-Methylbenzylamine Salts of Keto Acid 1f (S4 and S5).** A solution of 13.2 mg (0.11 mmol) of (S)-(−)-α-methylbenzylamine in 10 mL of ether was added to a solution of 32.6 mg (0.11 mmol) of keto acid **1f** in 20 mL of ether. The resulting precipitate was filtered and washed with ether to give 33 mg (71%) of salt: MS (FAB, +LSIMS) *m*/*z* 424 ($M^+$ + 1), 395, 377, 333, 304, 303, 285, 277, 241, 229, 214, 165, 149, 122 (100), 105 (matrix: glycerol + methanol). Anal. Calcd for $C_{27}H_{37}O_3N$: C, 76.55; H, 8.81; N, 3.31. Found: C, 76.69; H, 8.84; N, 3.44.

The (*R*)-(+)-α-methylbenzylamine salt was prepared analogously (78% yield) and also gave satisfactory MS and elemental analysis results.

**(1*R*,2*S*)-(−)-Ephedrine Salt of Keto Acid 1f (S6).** To a solution of 14.4 mg (0.09 mmol) of (1*R*,2*S*)-(−)-ephedrine in 10 mL of ether was added a solution of 26.4 mg (0.09 mmol) of keto acid **1f** in 20 mL of ether. Precipitate started to form within 1 min, and after 1 h, filtration and washing with ether afforded 33 mg (80%) of salt: MS (FAB, +LSIMS) *m*/*z* 468 ($M^+$ + 1), 452, 433, 395, 361, 331, 304, 303, 285, 258, 229, 167, 166 (100), 149, 148, 133 (matrix: glycerol + methanol). Anal. Calcd for $C_{29}H_{41}O_4N$: C, 74.48; H, 8.84; N, 3.00. Found: C, 74.12; H, 8.79; N, 2.97.

**(*S*)-(−)-Proline-*tert*-butyl Ester Salt of Keto Acid 1f (S7).** This salt was prepared in 87% yield by a procedure identical to that described for salts **S4**−**S6**: MS (FAB, +LSIMS) *m*/*z* 474 ($M^+$ + 1), 441, 409, 379, 371, 343, 304, 303, 301, 285, 229, 173, 172, 149, 133, 116 (100), 83, 70 (matrix, thioglycerol). Anal. Calcd for $C_{28}H_{43}O_5N$: C, 71.00; H, 9.15; N, 2.96. Found: C, 70.98; H, 8.91; N, 2.80.

**(1*R*,2*S*)-(−)-Norephedrine Salt of Keto Acid 1f (S8).** This salt was prepared in 97% yield by a procedure identical to that described for salts **S4**−**S6**: MS (FAB, +LSIMS) *m*/*z* 454 ($M^+$ + 1), 433, 395, 336, 304, 303, 285, 258, 244, 229, 166, 152 (100), 134, 118 (matrix: glycerol + methanol). Anal. Calcd for $C_{28}H_{39}O_4N$: C, 74.14; H, 8.67; N, 3.09. Found: C, 74.24; H, 8.54; N, 3.08.

**(*S*)-(−)-Prolinamide Salt of Keto Acid 1f (S9).** To a solution of 7.6 mg (0.07 mmol) of (*S*)-(−)-prolinamide in 2 mL of ethanol was added a solution of 20.2 mg (0.07 mmol) of keto acid **1f** in 5 mL of acetonitrile. The solution was allowed to stand until almost all of the solvent had evaporated. The remaining solvent was decanted and the solid material was washed with diethyl ether to give 27 mg (96%) of salt: MS (FAB, +LSIMS) *m*/*z* 417 ($M^+$ + 1), 395, 317, 304, 303, 285, 258, 244, 229, 215, 217, 166, 152, 134, 115 (100) (matrix: glycerol + methanol). Anal. Calcd for $C_{24}H_{36}O_4N_2$: C, 69.20; H, 8.71; N, 6.72. Found: C, 68.91; H, 8.80; N, 6.66.

**(1*S*)-(−)-2,10-Camphorsultam Salt of Keto Acid 1f (S10).** This salt was prepared in 84% yield by a procedure identical to that described for salts **S4**−**S6**: MS not obtained. Anal. Calcd for $C_{29}H_{43}O_5N_2S$: C, 67.28; H, 8.37; N, 2.71. Found: C, 67.18; H, 8.47; N, 2.69.

**(*S*)-(+)-Lysine Salt of Keto Acid 1f (S11).** This salt was prepared by combining a solution of 10.8 mg (0.07 mmol) of (*S*)-(+)-lysine in 0.5 mL of water and a solution of 22.3 mg (0.07 mmol) of keto acid **1f** in 6 mL of ethanol. After standing for several hours at room temperature, the solution was concentrated to dryness in vacuo and the resulting light yellow solid washed with ether, leaving 33 mg (100%) of the desired salt: MS (FAB, +LSIMS) *m*/*z* 449 ($M^+$ + 1), 433, 417, 383, 347, 341, 331, 315, 303, 293, 285, 261, 229, 215, 201, 169, 147 (100), 130, 91 (matrix, thioglycerol). Anal. Calcd for $C_{25}H_{40}O_5N_2$: C, 66.94; H, 8.99; N, 6.24. Found: C, 66.74; H, 9.08; N, 6.16.

**(*S*)-(+)-Prolinol Salt of Keto Acid 5f (S12).** This salt was prepared in 77% yield by a procedure identical to that described for salt **S1**: MS (FAB, +LSIMS) *m*/*z* 400 ($M^+$ + 1), 371, 358, 343, 316, 300, 299, 297, 281, 237, 203, 181, 149, 133, 131, 124, 103, 102 (100)

(matrix, thioglycerol). Anal. Calcd for $C_{24}H_{33}O_4N$: C, 72.15; H, 8.33; N, 3.51. Found: C, 72.32; H, 8.36; N, 3.55.

**(1*S*,2*S*)-(+)-Pseudoephedrine Salt of Keto Acid 5f (S13).** This salt was prepared in 94% yield by a procedure identical to that described for salt **S2**: MS (FAB, +LSIMS) *m*/*z* 464 ($M^+ + 1$), 448, 413, 388, 348, 331, 314, 299, 297, 281, 258, 225, 201, 167, 166 (100), 148, 133 (matrix, glycerol). Anal. Calcd for $C_{29}H_{37}O_4N$: C, 75.13; H, 8.04; N, 3.02. Found: C, 74.80; H, 8.02; N, 2.96.

**(*S*)-(−)- and (*R*)-(+)-α-Methylbenzylamine Salts of Keto Acid 5f (S14 and S15).** The (*S*)-(−)-salt was prepared in 71% yield by a procedure identical to that described for salts **S4**−**S6**: MS (FAB, +LSIMS) *m*/*z* 421, 420 ($M^+ + 1$), 391, 327, 300, 299, 297, 282, 281, 253, 214, 201, 165, 152, 149, 122 (100), 105 (matrix: glycerol + methanol). Anal. Calcd for $C_{27}H_{33}O_3N$: C, 77.29; H, 7.93; N, 3.34. Found: C, 77.35; H, 7.89; N, 3.23.

The (*R*)-(+)-α-methylbenzylamine salt was prepared analogously (78% yield) and also gave satisfactory MS and elemental analysis results.

**(1*R*,2*S*)-(−)-Ephedrine Salt of Keto Acid 5f (S16).** This salt was prepared in 80% yield by a procedure identical to that described for salts **S4**−**S6**: MS (FAB, +LSIMS) *m*/*z* 465, 464 ($M^+ + 1$), 429, 391, 350, 331, 314, 300, 299, 297, 282, 281, 258, 225, 167, 166 (100), 149, 148, 133, 105 (matrix: glycerol + methanol). Anal. Calcd for $C_{29}H_{37}O_4N$: C, 75.13; H, 8.04; N, 3.02. Found: C, 75.17; H, 8.07; N, 3.19.

**(1*R*,2*S*)-(−)-Norephedrine Salt of Keto Acid 5f (S17).** This salt was prepared in 97% yield by a procedure identical to that described for salts **S4**−**S6**: MS (FAB, +LSIMS) *m*/*z* 451, 450 ($M^+ + 1$), 429, 391, 334, 304, 303, 300, 299, 297, 281, 244, 225, 153, 152 (100), 149, 134, 118 (matrix, glycerol). Anal. Calcd for $C_{28}H_{35}O_4N$: C, 74.80; H, 7.85; N, 3.12. Found: C, 74.76; H, 7.89; N, 3.21.

**Photochemical Procedures.** All photolyses were performed using a 450-W Hanovia medium-pressure mercury lamp placed in a water-cooled immersion well. For small-scale solution-phase and solid-state photolyses, the sample in a Pyrex tube or an NMR tube was degassed by several freeze−thaw−pump cycles, sealed under nitrogen, and suspended ∼10 cm from the immersion well. A minimum of three samples was irradiated, and for each photolysis, at least three GC runs were performed. GC detector responses were calibrated with appropriate internal standards and compounds to be detected. Average results are reported. For preparative-scale liquid-phase photolyses, the solution was purged with nitrogen for at least 30 min prior to photolysis. Workup consisted of solvent removal in vacuo followed by silica gel column or radial chromatograpy. For larger scale solid-state photolyses, the sample was placed between two Pyrex microscope slides, and by sliding the top and bottom plates back and forth, the sample was distributed over the surface in a thin, even layer. The sample plates were then Scotch-taped together at the top and bottom ends, placed in a polyethylene bag, and thoroughly degassed with nitrogen. The bag was then sealed under a positive pressure of nitrogen with a heat-sealing device and suspended ∼10 cm from the immersion well. Low-temperature solid-state photolyses were performed by placing the bags as close to the immersion well as possible in a cooled ethanol/water bath (Neslab Cryocool CC-100 II). Temperatures were maintained within ±2 °C of the designated value.

**Photoproduct Identification.** X-ray crystal structures were obtained for photoproducts **2i** and **6d**. A detailed comparison (including 2D-COSY, NOE, HMQC, and HMBC correlations) of the 400- and/or 500-MHz NMR spectra of these compounds with the corresponding spectra of the other photoproducts allowed unambiguous structural assignments to be made.

**Photolysis of Ketone 1a.** The solution-phase photochemistry of this compound has been reported by Lewis et al.;[12] our results agree with theirs. In the solid state, ketone **1a** was found to be photochemically inert.

**Photolysis of Ketone 1b.** Ketone **1b** (108 mg, 0.4 mmol) in 10 mL of benzene was irradiated through Pyrex for 2 h, during which time the solution turned orange. GC indicated a 24% conversion, and chromatography of the crude reaction mixture (5% ether/hexanes) afforded 23 mg of 1-(*p*-Fluorophenyl)-5-*tert*-butyl-6-hepten-1-one (4b): mp 31−34 °C; $^1$H NMR ($CDCl_3$) $\delta$ 7.98−7.92 (2H, m, ArH)), 7.15−7.06 (2H, m, ArH), 5.60−5.49 (1H, m, vinyl CH), 5.08−4.88 (2H, m, vinyl $CH_2$), 2.97−2.80 (2H, m), 1.70−1.60 (1H, m), 1.83−1.70 (1H, m), 1.60−1.45 (2H, m), 1.25−1.10 (1H, m), 0.88 (9H, s, $C(CH_3)_3$); $^{13}$C NMR ($CDCl_3$) $\delta$ 23.20 (+), 27.82 (−), 28.60 (+), 32.60 (+), 38.36 (+), 55.40 (−), 115.25 and 115.69 ($^2J_{C-F}$ = 22 Hz, −ve), 116.42 (+), 130.66 and 130.84 ($^3J_{C-F}$ = 9 Hz, −ve), 134.07 and 134.00 ($^4J_{C-F}$ = 4 Hz, +ve), 140.25 (−), 168.50 and 163.50 ($^1J_{C-F}$ = 252 Hz, +ve), 198.88 (+); IR (KBr) 3080, 2970, 2912, 2870, 1682 (C=O), 1597, 1504, 1477, 1459, 1407, 1364, 1345, 1318, 1291, 1269, 1233, 1197, 1155, 1095, 1008, 998, 985, 917, 851, 819, 745, 601, 568 cm$^{-1}$; UV (hexane) 241 (15 600), 268 (1285), 273 (1040) nm; MS (EI) *m*/*z* 263, 262 ($M^+$), 247, 229, 207, 206, 205, 191, 177, 165, 152, 151, 139, 138 (100), 123, 109, 95, 75, 67, 58, 57, 56, 41; HRMS (EI) *m*/*z* 262.1726 (calcd for $C_{17}H_{23}OF$, 262.1733). Anal. Calcd for $C_{17}H_{23}OF$: C, 77.82; H, 8.84. Found: C, 77.91; H, 9.00.

Prolonged irradiation of a benzene solution of ketone **1b** resulted in a complex mixture of products and a decrease in the amount of photoproduct **4b**. *p*-Fluoroacetophenone could be detected in this mixture (GC comparison with an authentic sample). Photolysis of ketone **1b** In the solid state led to no detectable photoproducts.

**Photolysis of Ketone 1c.** In agreement with the report of Lewis et al.,[12] photolysis of ketone **1c** in benzene was found to afford cyclobutanol **2c** (an oil) in >95% yield. The same compound was the only detectable product when ketone **1c** was irradiated in the crystalline state (sample melting at higher conversions).

**Photolysis of Ketone 1d.** A solution of 208 mg (0.75 mmol) of ketone **1d** in 20 mL of benzene was photolyzed through Pyrex for 3 h (solution turns light red). GC analysis indicated the complete consumption of starting material and the presence of two products in a 94:6 ratio. After three Chromatotron separations (3% ether/hexanes), 152 mg (73%) of cyclobutanol **2d**, 7 mg (3%) of cyclobutanol **3d**, and 46 mg (22%) of a mixture of **2d** and **3d** were obtained.

***endo*-Arylcyclobutanol 2d**: oil; $^1$H NMR ($C_6D_6$) $\delta$ 7.16−7.11 (2H, m, ArH), 6.76−6.71 (2H, m, ArH), 2.85−2.79 (2H, m), 2.02−1.95 (1H, m), 1.85−1.78 (1H, m), 1.67−1.61 (1H, m), 1.39−1.23 (2H, m), 1.22 (1H, s, OH), 1.03 (3H, s, $CH_3$), 1.00−0.97 (1H, d, $J$ = 8 Hz), 0.63 (9H, s, $C(CH_3)_3$); $^{13}$C NMR ($C_6D_6$) $\delta$ 19.73 (−), 20.41 (+), 28.72 (−), 32.70 (+), 37.09 (+), 46.66 (+), 47.13 (+), 47.49 (−), 54.48 (−), 80.39 (+), 114.58 and 114.41 ($^2J_{C-F}$ = 21 Hz, −ve), 129.63 and 129.57 ($^3J_{C-F}$ = 8 Hz, −ve), 142.09 and 142.06 ($^4J_{C-F}$ = 4 Hz, +ve), 163.17 and 161.21 ($^1J_{C-F}$ = 247 Hz, +ve); IR (film) 3424 (OH), 2951, 2866, 1605, 1510, 1472, 1365, 1229, 1157, 1052, 1012, 909, 839, 814 cm$^{-1}$; MS (EI) *m*/*z* 277, 276 ($M^+$), 275, 274, 258, 243, 219, 201, 187, 178, 177, 165, 163, 161, 153, 152, 151, 147, 138, 137, 123 (100), 109, 97, 95, 84, 83, 82, 81, 69, 57, 55, 43, 41; HRMS (EI) *m*/*z* 276.1893 (calcd for $C_{18}H_{25}OF$, 176.1889). Anal. Calcd for $C_{18}H_{25}OF$: C, 78.22; H, 9.12. Found: C, 78.48; H, 9.18.

***exo*-Arylcyclobutanol 3d**: oil; $^1$H NMR ($C_6D_6$) $\delta$ 7.17−7.12 (2H, m, ArH), 6.80−6.74 (2H, m, ArH), 1.76−1.65 (1H, m), 1.59−1.52 (1H, m), 1.28−1.20 (2H, m), 1.10−0.99 (2H, m), 1.08 (3H, s, $CH_3$), 0.95 (9H, s, $C(CH_3)_3$), 0.89−0.80 (2H, m), 0.19−0.15 (1H, t, $J$ = 7 Hz); $^{13}$C NMR ($C_6D_6$) $\delta$ 18.86 (+), 19.88 (+), 23.52 (−), 27.37 (−), 28.68 (−), 33.85 (+), 35.04 (+), 35.20 (+), 46.20 (−), 68.65 (+), 114.88 and 114.71 ($^2J_{C-F}$ = 21 Hz, −ve), 133.73 and 133.66 ($^3J_{C-F}$ = 9 Hz, −ve), 140.18 and 140.16 ($^4J_{C-F}$ = 3 Hz, +ve), 163.08 and 161.04 ($^1J_{C-F}$ = 244 Hz, +ve); IR (film) 3467 (OH), 2955, 2866, 1636, 1510, 1472, 1457, 1397, 1364, 1229, 1157, 1052, 1012, 987, 949, 909, 840, 816, 733, 602, 546, 474 cm$^{-1}$; MS (EI) *m*/*z* 277, 276 ($M^+$), 261, 259, 258, 243, 233, 221, 220, 219, 205, 202, 201, 191, 187, 178, 177, 166, 165, 163, 161, 154, 153, 152, 151, 148, 147, 139, 138, 137, 133, 124, 123, 122, 109, 97, 96, 95, 94, 83, 81, 71, 69, 57 (100), 55, 43, 41; HRMS (EI) *m*/*z* 276.1892 (calcd for $C_{18}H_{25}OF$, 176.1889). Anal. Calcd for $C_{18}H_{25}OF$: C, 78.22; H, 9.12. Found: C, 78.33; H, 8.99.

Regardless of the extent of conversion, *endo*-arylcyclobutanol **2d** was shown by GC and $^1$H NMR to be the sole product resulting from irradiation of crystals of ketone **1d**.

**Photolysis of Ketone 1e.** A solution of 79 mg (0.28 mmol) of ketone **1e** in 10 mL of benzene was photolyzed through Pyrex for 4 h. GC indicated the presence of a single photoproduct, and column chromatography of the crude photolyzate using 5% ether/hexanes afforded 74 mg (94%) of ***endo*-arylcyclobutanol 2e** as a white powder.

Recrystallization from acetonitrile gave colorless prisms: mp 181−183 °C; $^1$H NMR ($C_6D_6$) $\delta$ 7.01−6.96 (4H, m, ArH), 2.76−2.69 (2H, m), 1.89−1.82 (1H, m), 1.78−1.69 (1H, m), 1.60−1.54 (1H, m), 1.37−1.25 (1H, m), 1.16 (1H, br s, OH), 1.10−1.00 (1H, m), 0.93 (3H, s, $CH_3$), 0.93−0.91 (1H, d, $J$ = 8 Hz), 0.53 (9H, s, $C(CH_3)_3$); $^{13}$C NMR ($C_6D_6$) $\delta$ 19.59 (−), 20.49 (+), 28.59 (−), 32.62 (+), 36.78 (+), 46.44 (+), 46.88 (+), 47.86 (−), 54.30 (−), 80.33 (+), 111.40 (+), 118.82 (+), 128.36 (−), 131.33 (−), 150.47 (+); IR (KBr) 3482 (OH), 2968, 2950, 2906, 2863, 2227, 1605, 1475, 1456, 1393, 1361, 1057, 1016, 986, 977, 950, 910, 853, 835, 576, 551, 521, 502 cm$^{-1}$; MS (EI) *m*/*z* 284, 283 ($M^+$), 282, 268, 266, 265, 250, 228, 227, 226, 222, 214, 213, 212, 210, 209, 208, 204, 199, 198, 196, 195, 194, 193, 186, 185, 184, 173, 172, 171, 170, 169, 168, 154, 153, 145, 144, 131, 130 (100), 116, 109, 103, 102, 97, 95, 83, 81, 69, 57, 55, 41; HRMS (EI) *m*/*z* 283.1936 (calcd for $C_{19}H_{25}NO$, 283.1936). Anal. Calcd for $C_{19}H_{25}NO$: C, 80.52; H, 8.89; N, 4.94. Found: C, 80.46; H, 8.89; N, 4.86.

*endo*-Arylcyclobutanol **2e** was also found to be the sole product resulting from irradiation of crystals of ketone **1e** (GC, $^1$H NMR).

**Photolysis of Ketone 1f.** A solution of 5 mg of keto acid **1f** in 3 mL of acetone was irradiated through Pyrex for 2 h. The solvent was removed in vacuo and the residue dissolved in ether and treated with excess diazomethane. GC analysis showed that keto acid **1f** was completely absent and that two photoproducts were present in a 94:6 ratio. The GC retention times of these peaks were the same as those of the products formed by photolysis of keto ester **1g** (i.e., the *endo*- and *exo*-arylcyclobutanols **2g** and **3g**, respectively). Irradiation of crystals of keto acid **1f** followed by diazomethane workup gave a single photoproduct which had the same GC retention time as *endo*-arylcyclobutanol **2g**. The characterization of this material is described below.

**Photolysis of Ketone 1g.** A solution of 125 mg (0.40 mmol) of keto ester **1g** in 20 mL of acetone was photolyzed through Pyrex for 2 h. GC showed the presence of a small amount of starting material plus two photoproducts in a 94:6 ratio. Silica gel column chromatography using 5% ether/hexanes as eluent afforded 15 mg (12%) of recovered starting material plus a mixture of photoproducts **2g** and **3g**. Further column and radial chromatography (3% ether/hexanes) gave 81 mg (65%) of pure **2g** (white powder) and 30 mg (23%) of a mixture of **2g** and **3g**; a pure sample of photoproduct **3g** could not be obtained. Recrystallization of **2g** from various solvents returned only white powder.

***endo*-Arylcyclobutanol 2g**: mp 114−115 °C; $^1$H NMR ($C_6D_6$) $\delta$ 8.07−8.03 (2H, m, ArH), 7.34−7.30 (2H, m, ArH), 3.52 (3H, s, $OCH_3$), 2.86−2.80 (2H, m), 2.06−2.00 (1H, m), 1.84−1.76 (1H, m), 1.67−1.60 (1H, m), 1.41−1.22 (2H, m), 1.40 (1H, br s, OH), 1.05 (3H, s, $CH_3$), 1.00−0.96 (1H, m), 0.61 (9H, s, $C(CH_3)_3$); $^{13}$C NMR ($C_6D_6$) $\delta$ 19.79 (−), 20.62 (+), 28.71 (−), 32.69 (+), 37.04 (+), 46.63 (+), 47.11 (+), 47.94 (−), 51.55 (−), 54.54 (−), 80.67 (+), 127.94 (−), 129.27 (−), 129.48 (+), 151.02 (+), 166.54 (+); IR (KBr) 3492 (OH), 2983, 2946, 2866, 1703 (C═O), 1608, 1568, 1472, 1456, 1440, 1407, 1363, 1332, 1282, 1225, 1197, 1182, 1111, 1052, 1015, 986, 964, 946, 911, 860, 830, 778, 720, 530, 509 cm$^{-1}$; MS (EI) *m*/*z* 317, 316 ($M^+$), 301, 285, 260, 259, 258, 257, 241, 227, 205, 203, 201, 192, 173, 169, 165, 164, 163 (100), 159, 153, 152, 149, 146, 145, 143, 141, 136, 135, 131, 129, 128, 115, 105, 104, 103, 97, 95, 94, 91, 83, 81, 77, 69, 59, 57, 55; HRMS (EI) *m*/*z* 316.2039 (calcd for $C_{20}H_{28}O_3$, 316.2038). Anal. Calcd for $C_{20}H_{28}O_3$: C, 75.91; H, 8.92. Found: C, 75.72; H, 8.88.

*endo*-Arylcyclobutanol **2g** was also found to be the sole product resulting from irradiation of crystals of ketone **1g** (GC, $^1$H NMR).

**Photolysis of Ketone 1h.** A solution of 69 mg (0.25 mmol) of ketone **1h** in 10 mL of benzene was photolyzed through Pyrex for 2 h. GC indicated an 85% conversion and the presence of a single photoproduct. Column chromatography of the crude photolyzate using 5% ether/hexanes afforded 54 mg of ***endo*-arylcyclobutanol 2h** as a white powder. Recrystallization from various solvents returned only white powder: mp 59−61 °C; $^1$H NMR ($C_6D_6$) $\delta$ 7.30−7.26 (2H, m, ArH), 6.95−6.91 (2H, d, $J$ = 8 Hz, ArH), 2.93−2.88 (2H, m), 2.20−2.13 (1H, m), 2.10 (3H, s, $ArCH_3$), 1.92−1.84 (1H, m), 1.73−1.67 (1H, m), 1.55−1.46 (1H, m), 1.46−1.38 (1H, m), 1.36 (1H, br s, OH), 1.14 (3H, s, $CH_3$), 1.06−1.01 (1H, m), 0.68 (9H, s, $C(CH_3)_3$); $^{13}$C NMR ($C_6D_6$) $\delta$ 19.94 (−), 20.61 (+), 21.07 (−), 28.86 (−), 32.77 (+), 37.34 (+), 46.78 (+), 47.29 (+), 47.62 (−), 54.71 (−), 80.92 (+), 127.90 (−), 128.46 (−), 136.68 (+), 143.45 (+); IR (KBr) 3432 (OH), 3600−3200, 2948, 2864, 1514, 1470, 1396, 1365, 1327, 1304, 1217, 1052, 1011, 984, 948, 908, 820, 760 cm$^{-1}$; MS (EI) *m*/*z* 273, 272 ($M^+$), 254, 239, 226, 215, 198, 197, 184, 183, 182, 181, 171, 170, 169, 167, 165, 161, 157, 156, 155, 153, 152, 143, 142, 141, 129, 128, 121, 119, 117, 115, 106, 105 (100), 91, 83, 81, 79, 77, 69, 67, 57, 55; HRMS (EI) *m*/*z* 272.2141 (calcd for $C_{19}H_{28}O$, 272.2140). Anal. Calcd for $C_{19}H_{28}O$: C, 83.77; H, 10.36. Found: C, 83.84; H, 10.25.

*endo*-Arylcyclobutanol **2h** was also found to be the sole product resulting from irradiation of crystals of ketone **1h** (GC, $^1$H NMR).

**Photolysis of Ketone 1i.** Photolysis of 90 mg (0.31 mmol) of ketone **1i** in 10 mL of benzene through Pyrex for 4 h led to the formation of two products in a 94:6 ratio as determined by GC. Silica gel chromatography using 5% ether/hexanes as eluent afforded 10 mg (11%) of recovered starting material, 60 mg (67%) of photoproduct **2i**, and 19 mg (21%) of a mixture of photoproducts **2i** and **3i**; despite repeated chromatography, a pure sample of compound **2i** could not be obtained. Recrystallization of ***endo*-arylcyclobutanol 2i** from 5% ether/hexanes afforded colorless prisms: mp 73−76 °C; $^1$H NMR ($C_6D_6$) $\delta$ 7.32−7.28 (2H, d, $J$ = 8 Hz, ArH), 6.73−6.69 (2H, d, $J$ = 8 Hz, ArH), 3.32 (3H, s, $OCH_3$), 2.95−2.89 (2H, m), 2.19−2.12 (1H, m), 1.93−1.86 (1H, m), 1.74−1.68 (1H, m), 1.56−1.47 (1H, m), 1.47−1.39 (1H, m), 1.31 (1H, s, OH), 1.15 (3H, s, $CH_3$), 1.05−1.02 (1H, d, $J$ = 7 Hz), 0.69 (9H, s, $C(CH_3)_3$); $^{13}$C NMR ($C_6D_6$) $\delta$ 19.91 (−), 20.55 (+), 28.85 (−), 32.78 (+), 37.39 (+), 46.79 (+), 47.34 (+), 47.53 (−), 54.67 (−), 54.68 (−), 80.76 (+), 113.19 (−), 129.04 (−), 138.53 (+), 159.17 (+); IR (KBr) 3516 (OH), 2942, 2863, 1608, 1511, 1473, 1456, 1362, 1242, 1177, 1033, 1013, 985, 908, 834, 817, 792, 605, 555 cm$^{-1}$; MS (EI) *m*/*z* 289, 288 ($M^+$), 287, 271, 270, 257, 232, 231, 213, 199, 186, 177, 175, 173, 171, 164, 150, 137, 136, 135 (100), 121, 115, 109, 107, 105, 95, 92, 91, 81, 79, 77, 69, 57, 55, 43, 41; HRMS (EI) *m*/*z* 288.2091 (calcd for $C_{19}H_{28}O_2$, 288.2089). Anal. Calcd for $C_{19}H_{28}O_2$: C, 79.12; H, 9.78. Found: C, 79.33; H, 9.85.

Irradiation of crystals of ketone **1i** (74 mg, 0.26 mmol) for 4 h through Pyrex gave a 58% conversion to a single product, shown by GC and $^1$H NMR to be *endo*-arylcyclobutanol **2i**.

**Photolysis of Ketone 5c.** A solution of 88 mg (0.35 mmol) of ketone **1h** in 10 mL of benzene was photolyzed through Pyrex for 1.5 h. GC indicated the presence of a single photoproduct. Column chromatography of the crude photolyzate using 5% ether/hexanes afforded 2 mg of recovered starting material plus 85 mg (97%) of ***endo*-arylcyclobutanol 6c**: oil; $^1$H NMR ($C_6D_6$) $\delta$ 7.18−7.11 (3H, m, ArH), 7.09−7.01 (2H, m, ArH), 2.94−2.90 (1H, m), 2.65−2.61 (1H, t, $J$ = 6 Hz), 2.02−1.97 (1H, m), 1.85−1.80 (1H, m), 1.80−1.72 (2H, m), 1.70−1.60 (2H, m), 1.60−1.53 (3H, m), 1.53−1.49 (1H, m), 1.32 (3H, s, $CH_3$), 1.04 (1H, s, OH), 0.80−0.75 (1H, d, $J$ = 11 Hz); $^{13}$C NMR ($C_6D_6$) $\delta$ 18.96 (−), 25.88 (−), 29.40 (−), 31.16 (+), 34.22 (+), 35.15 (+), 35.95 (+), 37.25 (−), 37.54 (−), 46.54 (−), 49.99 (+), 83.20 (+), 124.52 (−), 125.11 (−), 126.88 (−), 129.21 (−), 129.43 (−), 147.36 (+); IR (film) 3413 (OH), 2911, 2850, 1617, 1485, 1448, 1369, 1335, 1056, 1015, 976, 950, 904, 787, 772, 701, 580 cm$^{-1}$; MS (EI) *m*/*z* 255, 254 ($M^+$, 100), 253, 236, 221, 211, 197, 193, 179, 167, 159, 150, 149, 145, 134, 120, 115, 105, 93, 91, 77, 67, 55, 41; HRMS (EI) *m*/*z* 254.1670 (calcd for $C_{18}H_{22}O$, 254.1671). Anal. Calcd for $C_{18}H_{22}O$: C, 84.99; H, 8.72. Found: C, 84.79; H, 8.72.

*endo*-Arylcyclobutanol **6c** was also found to be the sole product resulting from irradiation of crystals of ketone **5c** (GC, $^1$H NMR).

**Photolysis of Ketone 5d.** A solution of 127 mg (0.47 mmol) of ketone **5d** in 10 mL of benzene was photolyzed through Pyrex for 2 h. GC indicated the presence of a single photoproduct. Column chromatography of the crude photolyzate using 5% ether/hexanes afforded 9 mg of recovered starting material plus 118 mg (93%) of ***endo*-arylcyclobutanol 6d**. Recrystallization from petroleum ether gave colorless prisms: mp 96−98 °C; $^1$H NMR ($C_6D_6$) $\delta$ 6.95−6.90 (1H, m, ArH)), 6.84−6.76 (3H, m, ArH), 2.87−2.82 (1H, m), 2.54−2.50 (1H, t, $J$ = 6 Hz), 1.93−1.88 (1H, m), 1.78−1.73 (1H, m), 1.70−1.45 (8H, m), 1.23 (3H, s, $CH_3$), 1.09 (1H, br s, OH), 0.78−0.73 (1H, d, $J$ = 11 Hz); $^{13}$C NMR ($C_6D_6$) $\delta$ 18.79 (−), 25.81 (−), 29.29 (−), 31.11 (+), 34.19 (+), 35.03 (+), 35.91 (+), 37.14 (−), 37.58 (−), 46.56 (−), 49.92 (+), 82.55 (+), 115.83 and 116.00 ($^2J_{C-F}$ = 21 Hz, −ve),

116.16 and 116.33 ($^2J_{C-F}$ = 21 Hz, −ve), 125.99 and 126.05 ($^3J_{C-F}$ = 8 Hz, −ve), 126.81 and 126.87 ($^3J_{C-F}$ = 8 Hz, −ve), 143.19 and 143.22 ($^4J_{C-F}$ = 4 Hz, +ve), 161.60 and 163.01 ($^1J_{C-F}$ = 245 Hz, +ve); IR (KBr) 3596 (OH), 2906, 2868, 2847, 1600, 1504, 1483, 1445, 1392, 1368, 1354, 1338, 1210, 1149, 1095, 1056, 1014, 998, 975, 953, 911, 839, 810, 582 cm$^{-1}$; MS (EI) *m*/*z* 273, 272 ($M^+$), 271, 254, 239, 229, 215, 211, 197, 185, 177, 163, 150, 149 (100), 138, 134, 123, 107, 105, 95, 93, 79, 67, 55, 41; HRMS (EI) *m*/*z* 272.1571 (calcd for $C_{18}H_{21}OF$, 272.1577). Anal. Calcd for $C_{18}H_{21}OF$: C, 79.38; H, 7.77. Found: C, 79.55; H, 7.77.

*endo*-Arylcyclobutanol **6d** was also found to be the sole product resulting from irradiation of crystals of ketone **5d** (GC, $^1$H NMR).

**Photolysis of Ketone 5e.** A solution of 60 mg (0.21 mmol) of ketone **5e** in 10 mL of benzene was photolyzed through Pyrex for 3 h. GC indicated the presence of a single photoproduct. Column chromatography of the crude photolyzate using 5% ether/hexanes afforded 2 mg of recovered starting material plus 58 mg (97%) of ***endo*-arylcyclobutanol 6e**. Recrystallization from various solvents gave only a white powder: mp 168−170 °C; $^1$H NMR ($C_6D_6$) $\delta$ 7.10−7.00 (2H, m, ArH), 6.84−6.75 (1H, m, ArH), 6.69−6.59 (1H, m, ArH), 2.82−2.71 (1H, m), 2.45−2.37 (1H, t, *J* = 6 Hz), 1.85−1.65 (2H, m), 1.65−1.27 (8H, m), 1.14 (3H, s, $CH_3$), 0.95 (1H, br s, OH), 0.76−0.65 (1H, d, *J* = 13 Hz); $^{13}$C NMR ($C_6D_6$) $\delta$ 18.66 (−), 25.61 (−), 28.95 (−), 30.85 (+), 33.91 (+), 35.27 (+), 35.61 (+), 36.80 (−), 37.40 (−), 46.26 (−), 49.69 (+), 82.49 (+), 111.02 (+), 116.69 (+), 124.90 (−), 125.51 (−), 132.87 (−), 133.00 (−), 151.36 (+); IR (KBr) 3495 (OH), 2911, 2855, 2232, 1683, 1638, 1456, 1407, 1375, 1345, 1281, 1250, 1211, 1191, 1171, 984, 868, 547 cm$^{-1}$; MS (EI) *m*/*z* 280, 279 ($M^+$), 278, 261, 251, 236, 218, 206, 204, 181, 170, 159, 150, 149 (100), 134, 130, 107, 102, 93, 79, 67, 55, 41; HRMS (EI) *m*/*z* 279.1617 (calcd for $C_{19}H_{21}NO$, 279.1623). Anal. Calcd for $C_{19}H_{21}NO$: C, 81.67; H, 7.58; N, 5.02. Found: C, 81.55; H, 7.59; N, 4.99

*endo*-Arylcyclobutanol **6e** was also found to be the sole product resulting from irradiation of crystals of ketone **5e** (GC, $^1$H NMR).

**Photolysis of Ketone 5f.** A solution of 8 mg of keto acid **5f** in 3 mL of benzene was irradiated through Pyrex for 2 h. The solvent was removed in vacuo and the residue dissolved in ether and treated with excess diazomethane. GC analysis showed the absence of starting material and the presence of a single photoproduct, whose retention time was the same as that of the product formed by photolysis of keto ester **5g** (i.e., the *endo*-arylcyclobutanol **6g**). Irradiation of crystals of keto acid **5f** followed by diazomethane workup gave a single photoproduct which had the same GC retention time as *endo*-arylcyclobutanol **6g**. The characterization of this material is described below.

**Photolysis of Ketone 5g.** A solution of 96 mg (0.31 mmol) of ketone **5e** in 10 mL of benzene was photolyzed through Pyrex for 3 h. GC indicated the presence of a single photoproduct. Column chromatography of the crude photolyzate using 5% ether/hexanes afforded 9 mg of recovered starting material plus 87 mg (91%) of ***endo*-arylcyclobutanol 6g**. Recrystallization from petroleum ether gave colorless prisms: mp 141−143 °C; $^1$H NMR ($C_6D_6$) $\delta$ 8.15−8.07 (2H, d of q, *J* = 2 and 9 Hz, ArH), 7.13−7.06 (1H, d of d, *J* = 2 and 9 Hz, ArH), 7.00−6.93 (1H, d of d, *J* = 2 & 9 Hz, ArH), 3.53 (3H, s, $OCH_3$), 2.87−2.82 (1H, m), 2.55−2.50 (1H, t, *J* = 6 Hz), 1.94−1.88 (1H, m), 1.76−1.70 (1H, m), 1.70−1.45 (8H, m), 1.22 (3H, s, $CH_3$), 1.06 (1H, s, OH), 0.79−0.72 (1H, d, *J* = 12 Hz); $^{13}$C NMR ($C_6D_6$) $\delta$ 18.79 (−), 25.77 (−), 29.17 (−), 31.02 (+), 34.07 (+), 35.31 (+), 35.79 (+), 37.01 (−), 37.50 (−), 46.49 (−), 50.02 (+), 51.58 (−), 82.80 (+), 124.47 (−), 125.11 (−), 129.17 (+), 130.86 (−), 130.96 (−), 151.95 (+), 166.59 (+); IR (KBr) 3458 (OH), 2912, 2849, 1693 (C═O), 1609, 1439, 1310, 1294, 1248, 1174, 1112, 1058, 1015, 1004, 951, 860, 791, 721 cm$^{-1}$; MS (EI) *m*/*z* 313, 312 ($M^+$), 297, 294, 281, 269, 255, 254, 253, 235, 228, 214, 192, 178, 164, 163, 150, 149 (100), 135, 119, 107, 105, 93, 91, 79, 67, 55, 41; HRMS (EI) *m*/*z* 312.1718 (calcd for $C_{20}H_{24}O_3$, 312.1725). Anal. Calcd for $C_{20}H_{24}O_3$: C, 76.88; H, 7.75. Found: C, 76.72; H, 7.74.

*endo*-Arylcyclobutanol **6g** was also found to be the sole product resulting from irradiation of crystals of ketone **5g** (GC, $^1$H NMR).

**Photolysis of Salts S1−S17.** Crystals of salts **S1−S17** (1−2 mg) were photolyzed between Pyrex microscope slides for varying lengths of time and at different temperatures (see Table 4) as described under Photochemical Procedures. The solid mixtures were removed from the slides with ethyl acetate and treated with excess ethereal diazomethane to convert the acids to the corresponding methyl esters. After washing with water, drying, and removal of solvent in vacuo, the mixtures were chromatographed on silica gel using 3% ether/hexanes as eluent. The solid materials obtained after evaporation of the eluent were analyzed by GC and chiral HPLC to determine conversions and enantiomeric excesses of the only photoproducts observed, *endo*-arylcyclobutanols **2g** and **6g**.

**Quantum yields** were performed on thiophene-free benzene (purified by successive washes with concentrated sulfuric acid, drying, and distillation over sodium metal) or *tert*-butyl alcohol solutions containing 0.014−0.040 M ketone (Table 2), ∼0.003 M internal standard (docosane, eicosane, heneicosane, or nonadecane), and 0 to ∼1.5 M 2,5-dimethyl-2,4-hexadiene as quencher. Equal volumes (2.8 mL) of each solution (including actinometer, see below) were placed in specially cleaned 13 × 100 mm Pyrex culture tubes, degassed by four freeze−pump−thaw cycles, and sealed. Irradiations were conducted at 20 ± 3 °C in a merry-go-round apparatus[17] with a 450-W Hanovia medium-pressure mercury lamp housed in an immersion well. The 313-nm mercury line was isolated by a filter combination of 7-54 Corning glass plates and an aqueous solution of 0.002 M $K_2CrO_4$ containing 5% $K_2CO_3$ by weight circulated through a Pyrex cooling jacket. Quantum yields of photoproduct formation were determined by quantitative GC relative to acetophenone formation (<10%) from parallel runs on 0.1 M valerophenone in benzene containing 1.000 g/mL of tetradecane as internal standard ($\Phi$ = 0.33).[15] GC detector response factors were calculated from three injections of accurately prepared solutions containing starting ketone, photoproduct, and internal standard. Internal standards were chosen so that their peaks would not overlap with any other peaks and yet have retention times close to those of the photoproducts.

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