Tetrahedron 68 (2012) 8875–8879

Contents lists available at SciVerse ScienceDirect

Tetrahedron

journal homepage: www.elsevier.com/locate/tet

Photochemical studies on acyclic alkyl aromatic ketones in the solid state: asymmetric induction and increased chemoselectivity

Manling Ma [a], Wei Feng [a], Fang Guo [a], Chao Yang [a,*], Wujiong Xia [a,b,*]

[a] The State Key Lab of Urban Water Resource and Environment & the Academy of Fundamental and Interdisciplinary Science, Harbin Institute of Technology, PO Box 3026, 2# Yikuang Street, Harbin, Heilongjiang, PR China
[b] State Key Lab of Applied Organic Chemistry, Lanzhou University, Lanzhou 730000, PR China

ARTICLE INFO

Article history:
Received 2 June 2012
Received in revised form 3 August 2012
Accepted 14 August 2012
Available online 21 August 2012

Keywords:
Acyclic
Photochemical investigation
Yang cyclization
Norrish type II
Chiral auxiliary

ABSTRACT

The acyclic alkyl aromatic ketones, 2-isobutyl-4-methyl-1-arylpentan-1-one derivatives were designed and synthesized for photochemical investigations. Irradiation of such compounds in acetonitrile solution led to the Yang cyclization and Norrish type II cleavage photoproducts with a ratio of 1:1, whereas the reaction conducted in the solid state using the ionic chiral auxiliary method led to only the Yang cyclization product with as high as 99% ee. Furthermore, the conformational transitions were first observed in the reaction.

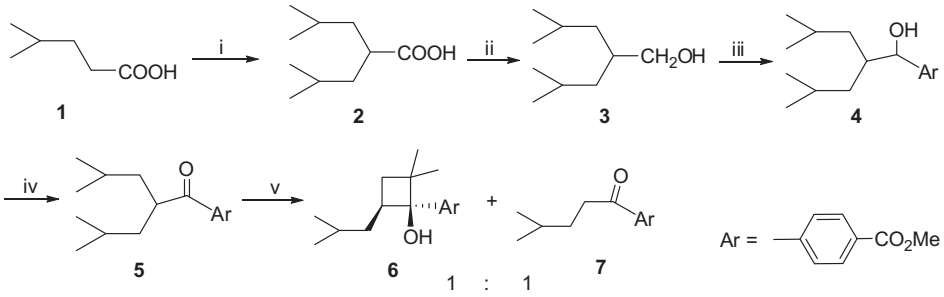
1. Introduction

The solid-state reaction has attracted widespread interest and attention owing to its several advantages compared to reactions conducted in solution: increased reaction selectivity, the opportunity to correlate chemical behavior with detailed structural information obtained through X-ray crystallography, simplicity in process, and handling, and low environmental impact.[1] Photochemical reactions are particularly well suited for study in the solid state because they can be conducted at ambient temperature or below, where the crystals do not melt, and light is able to penetrate deep within the crystal lattice.[2] One aspect of organic solid-state photochemistry that has received a great deal of attention recently concerns its use in asymmetric synthesis.[3] For example, in the past two decades, many research efforts were focused on the asymmetric studies on Norrish/Yang type II reactions and elegant advances were achieved on the asymmetric induction through the technique of zeolites,[4] host–guest assemblies,[5] as well as ionic chiral auxiliaries.[6] However, the substrates employed in the reactions were mono- and/or polycyclic compounds. The asymmetric study on acyclic substrates is still rare. This is because, for acyclic ketones, the reactive conformer is often a minor component of the equilibrium mixture present in solution, and in such cases, the ketones are unreactive in the solid state because they crystallize in thermodynamically more stable conformations that have the distance between carbonyl oxygen and γ-hydrogen more than 2.8±0.2 Å unfavorable for γ-hydrogen abstraction.[7] Therefore, it remains as a challenge for engineering acyclic ketones for solid-state photochemical investigation. With our long-term research on the organic photochemical reactions,[8] we are intrigued to design and synthesize 2-isobutyl-4-methyl-1-arylpentan-1-one derivatives based upon the molecular mechanics calculations to pursue such a goal through the ionic chiral auxiliary method.

The substrate, 2-isobutyl-4-methyl-1-arylpentan-1-one derivative **5** chosen for investigation was synthesized from 4-methylpentanoic acid **1**, which was treated with LDA and 1-bromo-2-methylpropane in THF to afford compound **2** in 82% yield (Scheme 1). Reduction of compound **2** with $LiAlH_4$ in THF led to alcohol **3** in 95% yield, which was oxidized with pyridinium chlorochromate (PCC) in CH_2Cl_2 and sequentially reacted with Grignard reagent at low temperature to form the aromatic alcohol **4** in 56% yield. Oxidation of **4** with PCC in CH_2Cl_2 led to keto–ester **5**. Prior to the solid state studies, keto–ester **5** was photolyzed in acetonitrile, which afforded a 1:1 ratio of photoproducts **6** (Yang cyclization) and **7** (Norrish type II cleavage).[9] The stereochemistry of cyclobutanol **6** was established as *cis* (OH and ^{i}Bu *cis*) by NOE difference measurements; none of the *trans* cyclobutanol diastereomer could be detected by GC. For asymmetric synthesis,

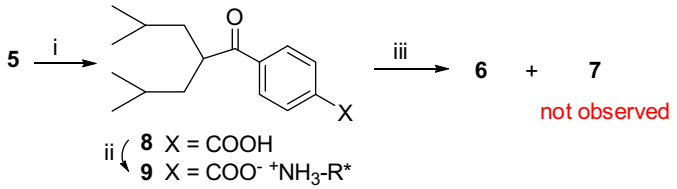
* Corresponding authors. Tel.: +86 451 86403193; fax: +86 451 86403760; e-mail addresses: xyyang@hit.edu.cn (C. Yang), xiawj@hit.edu.cn (W. Xia).

0040-4020/$ – see front matter © 2012 Elsevier Ltd. All rights reserved.
http://dx.doi.org/10.1016/j.tet.2012.08.040



Scheme 1. (i) LDA, DMPU, THF, 1-bromo-2-methylpropane, −78 °C; H_2SO_4 workup; 82% yield; (ii) $LiAlH_4$, THF; 95% yield; (iii) PCC, CH_2Cl_2; *p*-$IC_6H_4CO_2CH_3$, ^{i}PrMgBr, THF, −40 °C; 56% yield (two steps); (iv) PCC, CH_2Cl_2; 96% yield; (v) *hv*, CH_3CN.

keto−ester **5** was hydrolyzed to afford the corresponding keto−acid **8**, and this compound was treated with a series of optically pure amines to produce the corresponding ammonium carboxylate salts **9** (Scheme 2). Such salts are required to crystallize in chiral space groups (e.g., $P2_12_12_1$) under the influence of amines, which provide the asymmetric environment responsible for chiral induction. Crystals of the salts **9** (2−5 mg) were crushed between two microscope slides, and sealed in a polyethylene bag under nitrogen, and irradiated with a 450 W medium mercury pressure lamp. After irradiation, the photoproduct was treated with ethereal diazomethane to give the methyl esters, which were then analyzed by chiral HPLC to obtain enantiomeric excess values and by GC to give the conversions. The results are summarized in Table 1. Notably, only the cyclization product **6** was obtained in the reaction. Such a result represents one of the advantages of the solid-state reaction that usually high chemo-/regioselectivity might be achieved due to the molecules highly restricted in the crystals, in which the conformation is more favorable for the formation of one photoproduct than the other.



Scheme 2. (i) LiOH, THF/H_2O (1:1); HCl; (ii) NH_2-R*; (iii) *hv*, crystals; CH_2N_2 workup.

Table 1
Asymmetric studies on the irradiation of salts **9** in the solid state[a]

Amine	*T* (°C)	Time (hr)	Conv (%)[b]	ee (%)[c]	α[d]
(*S*)-(−)-1-Phenyl ethylamine	rt	1	62	31	−
	−25	1	24	44	
(*S*)-(−)-*N*-Methyl-1-phenyl ethylamine	rt	1	36	49	+
	−25	1	26	61	
(*S*)-(−)-1-*p*-Tolyl ethylamine	rt	3	100	88	−
	−25	1	48	96	
(*R*)-(+)-2-Phenyl-1-propylamine	rt	1	75	98	−
	−25	1	53	99	

[a] Samples were irradiated through Pyrex using a 450-W hanovia medium-pressure mercury lamp.
[b] Conversion % based on GC.
[c] ee % analyzed on chiral OD-H column with hexane:isopropanol=99:1 as the eluting solvent.
[d] Sign of rotation at the sodium D-line.

As can be seen in Table 1, the enantiomeric excess (ee) was obtained as high as 99% in the solid state. To rationalize the results observed, the X-ray single crystal structure of the (*R*)-(+)-2-phenyl-1-propylamine salt of the keto acid **8** was determined and presented in Fig. 1. A significant finding was that the carboxylate anion of the (*R*)-(+)-2-phenyl-1-propylamine salt of the keto acid **8** contained equal amounts of two independent conformers in the crystal lattice when the crystal data was collected at −78 °C (Fig. 1i), whereas at 10 °C, the same crystal contained a single conformational enantiomer of the reactant (Fig. 1ii). Such a phenomenon was first observed in this work and termed as *conformational transitions*. In addition, the DSC analysis showed that the transition took place between −25 °C and −40 °C. Unlike the reported conformational enantiomerism, in which the two independent conformers are in mirror-image relation in the crystal lattice usually led to the racemate or low ee,[3d,10] the two conformers shown in Fig. 1(i) react in the crystal to afford the same enantiomer of the cyclobutanol **6**, thereby leading to a high enantioselectivity.

As shown in Fig. 1, the enantioselectivity of the asymmetric studies on salts **9** in the crystalline state was attributed to conformational factors. Under the influence of the ionic chiral auxiliary, the carboxylate reactant crystallizes in a homochiral conformation, in which the carbonyl oxygen is closer to one γ-hydrogen than to the other (e.g., in a, 3.102 Å vs 4.607 Å; in a′, 3.062 Å vs 3.266 Å; in b, 3.029 Å vs 3.364 Å; Fig. 1). As a result, one of the γ-hydrogens is abstracted preferentially, affording a 1,4-biradical that leads to one enantiomer of the final cyclobutanol photoproduct. Finally, a control experiment was conducted by irradiation of the salts **9** in methanol, which led to racemic product **6** as well as the cleavage product **7**. This is typical and highlights the critical importance of carrying out the reactions in the solid state and avoiding conditions that could lead to crystal softening or melting. Therefore, the enantioselectivity is the result of preorganization of the reactant in a homochiral conformation favorable for the formation of a single enantiomer of the product.

2. Conclusion

In summary, the photochemical behavior of the acyclic alkyl aromatic ketones was investigated in acetonitrile solution and in the solid state. The solid-state reaction exhibited the high chemoselectivity, in which only the cyclization product was formed. Asymmetric studies through the utilization of ionic chiral auxiliary method led to as high as 99% ee. Furthermore, the

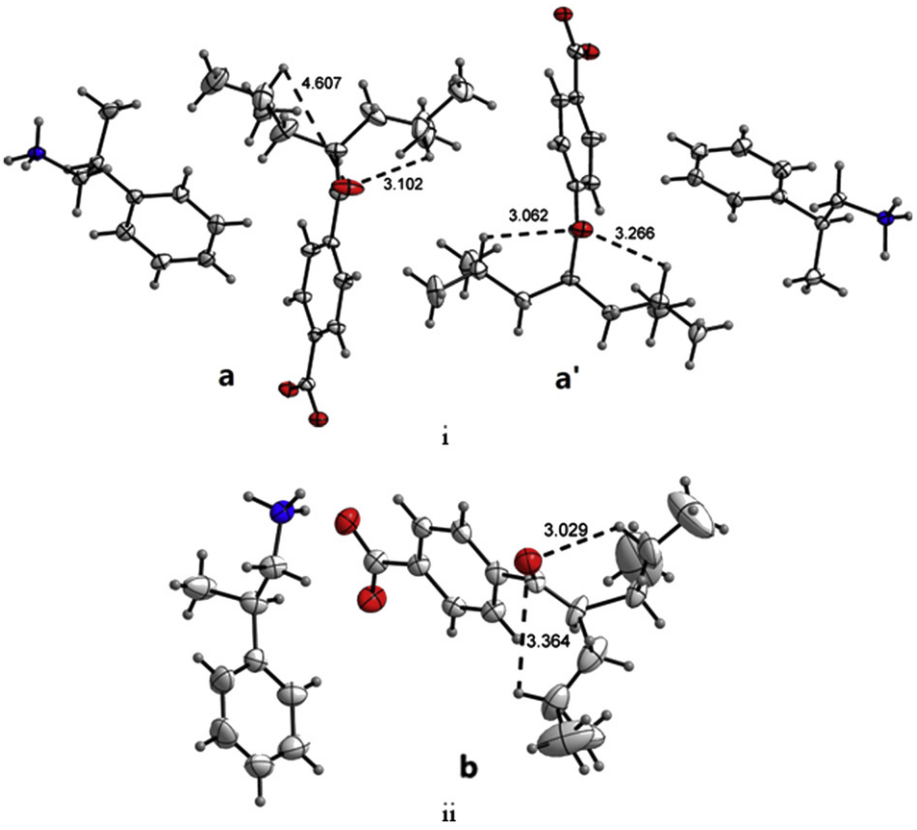


Fig. 1. X-ray crystal structure of (*R*)-(+)-2-phenyl-1-propylamine salt of the keto acid **8**, (i) crystal data was collected at −78 °C; (ii) crystal data was collected at 10 °C.

phenomenon of conformational transitions was first observed in the reaction. Remarkably, it should be pointed out that the formed cyclobutanol photoproduct has the potential application in organic synthesis.[11]

Crystallographic data for the structures in this paper have been deposited with the Cambridge Crystallographic Data Centre as supplementary publication nos. CCDC 798458, 798459. Copies of the data can be obtained, free of charge, on application to CCDC, 12 Union Road, Cambridge CB2 1EZ, UK, (fax: +44-(0)1223-336033 or e-mail:deposit@ccdc.cam.ac.uk).

3. Experimental

3.1. General methods

Commercial spectral grade solvents were used for photochemical experiments unless otherwise stated. Infrared spectra were recorded on a Perkin–Elmer 1710 Fourier transform spectrometer. Melting points were determined on a Fisher–Johns apparatus. Low-resolution mass spectra were obtained from a Kratos MS 50 instrument using electron impact (EI) ionization at 70 eV. ^{1}H NMR spectra were obtained at 400 MHz on Bruker AV-400 instrument. ^{13}C NMR spectra were recorded at 100 MHz.

*3.1.1. Methyl 4-(1-hydroxy-2-isobutyl-4-methylpentyl)benzoate (**4**).* 2-Isobutyl-4-methylpentan-1-ol (1.5 g, 9.5 mmol) prepared from the reduction of 2-isobutyl-4-methylpentanoic acid was dissolved in 120 mL of methylene chloride. To this solution, PCC (3.08 g, 14.3 mmol) and Celite (6 g) ground homogeneously in mortar were added. The mixture was stirred at room temperature overnight, filtered with silica gel column, and rinsed with diethyl ether. The solvent was then removed in vacuo, and the residue 2-isobutyl-4-methylpentanal was used for next step without purification (GC detected the purity is 98%, which is pure enough for next step).

To the solution of methyl *p*-iodobenzoate (2.5 g, 9.5 mmol) in 50 mL of dried THF precooled at −40 °C was added isopropyl magnesium chloride (2 M, 4.75 mL), dropwise. After addition, the mixture was stirred for 1 h at this temperature. To this solution, 2-isobutyl-4-methylpentanal was dissolved in dry THF (10 mL) and added slowly. The solution was stirred at −40 °C for 4 h. Saturated ammonium chloride solution (30 mL) was added quickly and the solution was extracted with diethyl ether (3×50 mL), and the combined organic layer was washed with saturated brine solution (2×30 mL). The solvent was removed in vacuo after being dried over magnesium sulfate, and the residue was purified by chromatography (20% pet ether/diethyl ether) to give the alcohol **4** as an oil (1.55 g, 56% yield). ^{1}H NMR (400 MHz, $CDCl_3$): δ 8.02 (d, J=8.0 Hz, 2H), 7.40 (d, J=8.0 Hz, 2H), 4.88 (d, J=3.5 Hz, 1H), 3.93 (s, 3H), 1.84 (m, 1H), 1.69 (m, 1H), 1.50 (m, 1H), 1.40 (m, 1H), 1.10 (m, 1H), 1.06 (m, 2H), 0.94 (d, J=6.3 Hz, 3H), 0.92 (d, J=6.3 Hz, 3H), 0.82 (d, J=6.5 Hz, 3H), 0.65 (d, J=6.5 Hz, 3H). ^{13}C NMR (100 MHz, $CDCl_3$): δ 167.1 (+), 149.3 (+), 129.3 (−), 128.7 (+), 126.0 (−), 75.1 (−), 52.0 (−), 40.4 (+), 40.3 (−), 38.0 (+), 25.4(−), 25.2(−), 23.5(−), 23.3(−), 22.5(−), 21.9(−). IR (neat) ν_{max}: 3477, 2955, 1726, 1708, 1611, 1282, 1115, 869, 759, 712 cm^{-1}. LRMS (EI): 292 [M$^+$], 261, 245, 166, 151, 134, 106, 91, 77, 57. HRMS (EI) for $C_{14}H_{16}O_3$: calcd 232.1099; found 232.1095.

*3.1.2. Methyl 4-(2-isobutyl-4-methylpentanoyl)benzoate **5**.* To a solution of alcohol **4** (1.0 g, 3.42 mmol) in 30 mL of anhydrous methylene chloride were added PCC (1.10 g, 5.13 mmol) and Celite (2 g). The mixture was stirred at room temperature overnight and diethyl ether (20 mL) was added. The solution was then filtered through a silica gel column and rinsed with diethyl ether. The solvent was removed in vacuo and the residue purified by column chromatography (10% pet ether/diethyl ether) to give keto–ester **5**

as a colorless crystal (953 mg, 96% yield). Mp 56–58 °C. ^{1}H NMR (400 MHz, $CDCl_3$): δ 8.17 (d, J=8.4 Hz, 2H), 8.04 (d, J=8.4 Hz, 2H), 3.98 (s, 3H), 3.62 (m, 1H), 1.74 (m, 2H), 1.61 (m, 2H), 1.37 (m, 2H), 0.92 (d, J=6.4, 6H), 0.89 (d, J=6.4 Hz, 6H). ^{13}C NMR (100 MHz, $CDCl_3$): δ 204.3 (+), 166.2 (+), 140.8 (+), 133.6 (+), 129.9 (−), 128.0 (−), 52.4 (−), 42.7 (−), 41.7 (+), 26.1 (−), 22.8 (−), 22.7 (−). IR (KBr) ν_{max}: 2954, 2868, 1724, 1670, 1280, 1108, 828, 785, 730 cm^{-1}. LRMS (EI): 290 [M$^+$], 275, 259, 234, 191, 163, 135, 104, 76, 55. Anal. calcd for $C_{18}H_{26}O_3$: C, 74.45; H, 9.02. Found: C, 74.78; H, 9.17.

*3.1.3. Irradiation of compound **5** in acetonitrile.* The solution of **5** (60 mg, 0.21 mmol) in acetonitrile (20 mL) was purged with N_2 for 15 min and irradiated with 450 W medium mercury pressure lamp under N_2 for 1.0 h. After irradiation, the solvent was removed in vacuo and the residue was purified by chromatography (10% pet ether/diethyl ether) to give photoproduct **6** (25 mg, 43%) and **7** (24 mg, 41%).

Photoproduct **6**. ^{1}H NMR (400 MHz, C_6D_6): δ 8.15 (d, J=6.7 Hz, 2H), 7.28 (d, J=6.7 Hz, 2H), 3.52 (s, 3H), 2.83 (m, 1H), 1.66 (m, 1H), 1.45 (m, 1H), 1.27 (m, 1H), 1.20 (s, 3H), 1.14 (m, 1H), 0.88 (d, J=6.6 Hz, 3H), 0.85 (d, J=6.6 Hz, 3H), 0.66 (s, 3H). ^{13}C NMR (100 MHz, C_6D_6): δ 166.6 (+), 149.5 (+), 129.8 (−), 129.5 (−), 126.4 (−), 81.6 (+), 51.6 (−), 41.5 (+), 38.0 (+), 37.8 (+), 35.1 (−), 26.6 (−), 26.3 (−), 23.5 (−), 23.0 (−), 22.3 (−). IR (KBr) ν_{max}: 3502, 2954, 2868, 1724, 1711, 1610, 1280, 1112, 851, 772, 725 cm^{-1}. LRMS (EI): 290 [M$^+$], 275, 259, 234, 219, 206, 191, 178, 159, 131. HRMS (EI) for $C_{18}H_{26}O_3$: calcd 290.1882; found 290.1885.

Photoproduct **7**. ^{1}H NMR (400 MHz, $CDCl_3$): δ 8.17 (d, J=8.4 Hz, 2H), 8.04 (d, J=8.4 Hz, 2H), 3.97 (s, 3H), 3.60 (m, 2H), 1.74 (m, 2H), 1.61 (m, 1H), 0.92 (d, J=6.4, 6H). ^{13}C NMR (100 MHz, $CDCl_3$): δ 202.3 (+), 166.2 (+), 140.6 (+), 133.4 (+), 129.8 (−), 128.1 (−), 52.2 (−), 42.3 (−), 40.9 (+), 26.0 (−), 22.8 (−). IR (KBr) ν_{max}: 2956, 2864, 1724, 1670, 1270, 824, 780, 730 cm^{-1}. LRMS (EI): 234 [M$^+$], 219, 203, 191, 163, 135, 104, 55. HRMS (EI) for $C_{14}H_{18}O_3$: calcd 234.1256; found 234.1260.

*3.1.4. 4-(2-Isobutyl-4-methylpentanoyl)benzoic acid **8**.* To a solution of keto–ester **5** (950 mg, 3.28 mmol) in THF (30 mL) and H_2O (15 mL) was added LiOH (1.5 g, 62 mmol). The mixture was stirred at room temperature for 4 h and then diethyl ether (40 mL) was added. The organic layer was washed with water (3×25 mL) and the aqueous layers were combined and acidified with concd HCl. The solution was then extracted with diethyl ether (4×40 mL) and the combined organic layer was washed with water (3×20 mL) and dried over $MgSO_4$. Removal of solvent in vacuo gave a white solid, which was recrystallized from methanol to afford keto–acid **8** as a white solid (896 mg, 99% yield). Mp 95–96 °C. ^{1}H NMR (400 MHz, $CDCl_3$): δ 8.25 (d, J=8.4 Hz, 2H), 8.06 (d, J=8.4 Hz, 2H), 3.63 (m, 1H), 1.73 (m, 2H), 1.61 (m, 2H), 1.38 (m, 2H), 0.94 (d, J=6.8 Hz, 6H), 0.90 (d, J=6.8 Hz, 6H). ^{13}C NMR (100 MHz, $CDCl_3$): δ 204.3 (+), 170.4 (+), 141.6 (+), 132.6 (+), 130.6 (−), 128.1 (−), 42.6 (−), 41.7 (+), 26.2 (−), 22.9 (−), 22.7(−). IR (KBr) ν_{max}: 3319, 3068, 2956, 2672, 2552, 1683, 1290, 872, 782, 725 cm^{-1}. LRMS (ESI, infusion @ 10 μL/min in MeOH −ve mode): 275.2 [M$^+$−1]. Anal. calcd for $C_{17}H_{24}O_3$: C, 73.88; H, 8.75. Found: C, 73.89; H, 8.45.

3.2. General procedure for synthesis of salts 9

To the solution of keto–acid **8** (100 mg, 0.36 mmol) in diethyl ether (5 mL) was added an equivalent of optically pure amine. Upon the addition, the precipitate formed immediately. The resulted suspension was filtered by suction to give the salt, which was then recrystallized from methanol.

*3.2.1. (S)-(−)-1-Phenylethylamine salt of keto–acid **8**.* Mp 146–148 °C (Methanol). ^{1}H NMR (400 MHz, CD_3OD): δ 7.92 (d, J=8.5 Hz, 2H), 7.86 (d, J=8.5 Hz, 2H), 7.33 (m, 2H), 7.28 (m, 3H), 4.33 (q, J=6.9 Hz, 1H), 3.59 (m, 1H), 1.54 (m, 2H), 1.51 (d, J=6.9 Hz, 3H), 1.43 (m, 2H), 1.19 (m, 2H), 0.79 (d, J=6.5 Hz, 6H), 0.78 (d, J=6.5 Hz, 6H). ^{13}C NMR (100 MHz, CD_3OD): δ 206.8 (+), 173.9 (+), 143.5 (+), 140.1 (+), 140.0 (+), 130.5 (−), 130.2 (−), 130.1 (−), 128.8 (−), 127.6 (−), 52.3 (−), 43.5 (−), 43.3 (+), 27.4 (−), 23.3 (−), 23.1 (−), 20.9 (−). IR (KBr) ν_{max}: 3420, 2955, 2553, 2201, 1673, 1635, 1582, 1391, 793, 732, 700 cm^{-1}. LRMS (ESI): 398 [M$^+$+1], 122, 105. Anal. calcd for $C_{25}H_{35}NO_3$: C, 75.53; H, 8.87; N, 3.52. Found: C, 75.90; H, 8.78; N, 3.55.

*3.2.2. (S)-(−)-N-Methyl-1-phenylethylamine salt of keto–acid **8**.* Mp 83–85 °C (Methanol). ^{1}H NMR (400 MHz, CD_3OD): δ 7.93 (d, J=8.5 Hz, 2H), 7.86 (d, J=8.5 Hz, 2H), 7.33 (m, 5H), 4.16 (q, J=6.9 Hz, 1H), 3.59 (m, 1H), 2.43 (s, 3H), 1.54 (d, J=6.9 Hz, 3H), 1.52 (m, 2H), 1.43 (m, 2H), 1.20 (m, 2H), 0.79 (d, J=6.6 Hz, 6H), 0.78 (d, J=6.5 Hz, 6H). ^{13}C NMR (100 MHz, CD_3OD): δ 206.8 (+), 173.9 (+), 143.3 (+), 140.0 (+), 138.1 (+), 130.6 (−), 130.5 (−), 130.4 (−), 128.8 (−), 128.6 (−), 60.5 (−), 43.5 (−), 43.3 (+), 31.6 (−), 27.4 (−), 23.3 (−), 23.1 (−), 19.4 (−). IR (KBr) ν_{max}: 2954, 2777, 2378, 2129, 1672, 1552, 1382, 877, 795, 735, 700 cm^{-1}. LRMS (ESI): 412 [M$^+$+1], 136, 105, 79. Anal. calcd for $C_{26}H_{37}NO_3$: C, 75.87; H, 9.06; N, 3.40. Found: C, 76.00; H, 9.24; N, 3.50.

*3.2.3. (S)-(−)-1-p-Tolylethylamine salt of keto–acid **8**.* Mp 162–164 °C (Methanol). ^{1}H NMR (400 MHz, CD_3OD): δ 7.89 (d, J=8.5 Hz, 2H), 7.83 (d, J=8.5 Hz, 2H), 7.19 (d, J=8.0 Hz, 2H), 7.10 (d, J=8.0 Hz, 2H), 4.26 (q, J=6.9 Hz, 1H), 3.56 (m, 1H), 2.20 (s, 3H), 1.51 (m, 2H), 1.47 (d, J=6.9 Hz, 3H), 1.41 (m, 2H), 1.18 (m, 2H), 0.76 (d, J=6.5 Hz, 6H), 0.75 (d, J=6.5 Hz, 6H). ^{13}C NMR (100 MHz, CD_3OD): δ 206.7 (+), 174.0 (+), 143.5 (+), 140.1 (+), 139.9 (+), 136.9 (+), 130.8 (−), 130.5 (−), 128.8 (−), 127.6 (−), 52.0 (−), 43.5 (−), 43.3 (+), 27.4 (−), 23.3 (−), 23.1 (−), 21.2 (−), 20.8 (−). IR (KBr) ν_{max}: 2957, 2869, 2546, 2187, 1674, 1648, 1581, 1392, 1245, 816, 792, 727 cm^{-1}. LRMS (ESI): 412 [M$^+$+1], 349, 312, 271, 136, 119. Anal. calcd for $C_{26}H_{37}NO_3$: C, 75.87; H, 9.06; N, 3.40. Found: C, 76.00; H, 9.20; N, 3.46.

*3.2.4. (R)-(+)-2-Phenyl-1-propylamine salt of keto–acid **8**.* Mp 115–116 °C (Methanol). ^{1}H NMR (400 MHz, CD_3OD): δ 7.89 (d, J=8.5 Hz, 2H), 7.82 (d, J=8.5 Hz, 2H), 7.18 (m, 2H), 7.12 (m, 3H), 3.55 (m, 1H), 2.98 (d, J=7.0 Hz, 2H), 2.92 (m, 1H), 1.49 (m, 2H), 1.39 (m, 2H), 1.18 (d, J=6.8 Hz, 3H), 1.15 (m, 2H), 0.75 (d, J=6.5 Hz, 6H), 0.73 (d, J=6.5 Hz, 6H). ^{13}C NMR (100 MHz, CD_3OD): δ 206.8 (+), 174.0 (+), 143.5 (+), 143.4 (+), 140.0 (+), 130.5 (−), 130.1 (−), 128.8 (−), 128.5(−), 128.2 (−), 46.9 (+), 43.6 (−), 43.5 (+), 39.8 (−), 27.4 (−), 23.3 (−), 23.1 (−), 19.9 (−). IR (KBr) ν_{max}: 2961, 2698, 2198, 1674, 1582, 1532, 1385, 1209, 836, 794, 759, 732 cm^{-1}. LRMS (ESI): 412 [M$^+$+1], 136, 105, 79. Anal. calcd for $C_{26}H_{37}NO_3$: C, 75.87; H, 9.06; N, 3.40. Found: C, 76.10; H, 9.30; N, 3.45.

3.3. General procedure for irradiation of salts 9 in the solid state

The salt crystals (2–5 mg) were crushed between two Pyrex microscope slides and sealed in a polyethylene bag under a positive pressure of nitrogen. The sample was irradiated from both sides with a 450 W medium pressure mercury lamp. After irradiation, the salt crystals were suspended in an excess of ethereal diazomethane solution and allowed to stand until dissolution was complete. Ether and excess diazomethane were removed in vacuo and the residue was taken up in methylene chloride and passed through a short plug of silica gel to remove the chiral auxiliary. The residue was then submitted to HPLC analysis to give the enantiomeric excesses and GC analysis to give the conversions.

Acknowledgements

We are grateful for the financial supports from China NSFC (Nos. 21002018 and 21072038), the Fundamental Research Funds for the

Central Universities (No. HIT.BRET2.2010001), and ZJSTP (No. 2011C23116).

References and notes

1. (a) *Photochemistry in Organized and Constrained Media*; Ramamurthy, V., Ed.; VCH: New York, NY, 1991; (b) *Molecular and Supramolecular Photochemistry*; Ramamurthy, V., Schanze, K. S., Eds.; Marcel Dekker: New York, NY, 2000; Vol. 5, Chapter 6; (c) Scheffer, J. R.; Xia, W. *Top. Curr. Chem.* **2005**, *254*, 233.
2. (a) Everitt, S. R. L.; Inoue, Y. In *Molecular and Supramolecular Photochemistry*; Ramamurthy, V., Schanze, K. S., Eds.; Marcel Dekker: New York, NY, 1999; Vol. 3, p 71; (b) Pete, J. P. *Adv. Photochem.* **1996**, *21*, 135; (c) Inoue, Y. *Chem. Rev.* **1992**, *92*, 471; (d) Buschmann, H.; Scharf, H. D.; Hoffmann, N.; Esser, P. *Angew. Chem., Int. Ed. Engl.* **1991**, *30*, 477; (e) Rau, H. *Chem. Rev.* **1983**, *83*, 535.
3. (a) Scheffer, J. R. *Can. J. Chem.* **2001**, *79*, 349; (b) Xia, W.; Yang, C.; Patrick, B. O.; Scheffer, J. R.; Scott, C. *J. Am. Chem. Soc.* **2005**, *127*, 2725; (c) Yang, C.; Xia, W.; Scheffer, J. R.; Botoshansky, M.; Kaftory, M. *Angew. Chem., Int. Ed.* **2005**, *44*, 5087; (d) Xia, W.; Scheffer, J. R.; Botoshansky, M.; Kaftory, M. *Org. Lett.* **2005**, *7*, 1315; (e) Yang, C.; Xia, W.; Scheffer, J. R. *Tetrahedron* **2007**, *63*, 6791; (f) Zhao, G.; Yang, C.; Chen, Q.; Jin, J.; Zhang, X.; Zhao, L.; Xia, W. *Tetrahedron* **2009**, *65*, 9952.
4. (a) Joy, A.; Ramamurthy, V. *Chem.—Eur. J.* **2000**, *6*, 1287; (b) Sivaguru, J.; Natarajan, A.; Kaanu-malle, L. S.; Shailaja, J.; Uppili, S.; Joy, A.; Ramamurthy, V. *Acc. Chem. Res.* **2003**, *36*, 509.
5. (a) Toda, F.; Tanaka, K.; Miyamoto, H. In *Molecular and Supramolecular Photochemistry*; Ramamurthy, V., Schanze, K. S., Eds.; Marcel Dekker: New York, NY, 2001; Vol. 8, Chapter 6; (b) Tanaka, K.; Toda, F. In *Organic Solid-state Reactions*; Toda, F., Ed.; Kluwer: 2002; p 109.
6. (a) Gamlin, J. N.; Jones, R.; Leibovitch, M.; Patrick, B.; Scheffer, J. R.; Trotter, J. *Acc. Chem. Res.* **1996**, *29*, 203; (b) Yang, C.; Xia, W. *Chem.—Asian. J.* **2009**, *4*, 1774.
7. Scheffer, J. R.; Scott, C. In *CRC Handbook of Organic Photochemistry and Photobiology*, 2nd ed.; Horspool, W. M., Lenci, F., Eds.; CRC: Boca Raton, FL, 2004, Chapter 54.
8. (a) Xia, W.; Shao, Y.; Gui, W.; Yang, C. *Chem. Commun.* **2011**, 11098; (b) Shao, Y.; Yang, C.; Gui, W.; Liu, Y.; Xia, W. *Chem. Commun.* **2012**, 3560.
9. Cyclobutanol formation in the Norrish type II reaction, now referred to as Yang photocyclization, was first reported by Yang, N. C.; Yang, D. H. *J. Am. Chem. Soc.* **1958**, *80*, 2913.
10. The conformational enantiomerism was previously reported in (a) Cheung, E.; Kang, T.; Netherton, M. R.; Scheffer, J. R.; Trotter, J. *J. Am. Chem. Soc.* **2000**, *122*, 11753; (b) Natarajan, A.; Wang, K.; Ramamurthy, V.; Scheffer, J. R.; Patrick, B. *Org. Lett.* **2002**, *4*, 1443.
11. Ziadi, A.; Martin, R. *Org. Lett.* **2012**, *14*, 1266.