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Photochemical studies on *exo*-bicyclo[2.1.1]hexyl and bicyclo[3.1.0]hexyl aryl ketones: two approaches for synthesis of enantiomerically enriched cyclopentene derivatives

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ABSTRACT

Two approaches for the photochemical synthesis of cyclopentene derivatives through the Norrish type II cleavage reaction were described. Asymmetric studies using ionic chiral auxiliaries afforded enantiomeric excesses of up to 98% at the conversion of 85%. The results were rationalized by single X-ray crystal structures.

1. Introduction

Enantiomerically enriched cyclopentene derivatives have been found to be crucial building blocks in the synthesis of naturally occurring products, which are widely distributed throughout the animal, bacterial, and plant kingdoms. Consequently, the syntheses of such compounds have attracted the interest from organic chemists.[1] The general efficient methods involve intramolecular carbon–hydrogen insertions of alkylidenecarbenes[2], organocatalytic [3+2] cyclizations,[3] RCM reaction of the acyclic precursors[4] and carbonyl allylation with cyclic allyl halide.[5] Among them stoichiometric amounts of metal catalysts should be first prepared in multiple synthetic steps and/or halides were employed in the reaction. For example, in the [3+2] annulation reaction, the planar chiral 2-phospha[3]ferrocenophanes were synthesized in five steps and expensive reagents were involved. Therefore, room exists for developing environmentally friendly approaches for synthesis of enantiomerically enriched cyclopentenes, a feature that has been embodied in the synthesis of natural products.[6] As part of research interest in solid-state organic photochemistry,[7] we found that such a goal can be achieved through a typical Norrish type II cleavage process using the ionic chiral auxiliary method. The ionic chiral auxiliary concept, developed by Scheffer and coworkers, has proven to be a reliable method of asymmetric studies on 1,4-hydroxybiradical behavior.[8] We extended this method to the asymmetric synthesis of cyclopentene derivatives owing to its features that make this particular method attractive in terms of general applicability: 1) it makes use of a large pool of commercially available, inexpensive, optically pure amines; 2) the auxiliary is easily attached and removed through acid–base chemistry; 3) ionic solids are generally high melting, giving robust crystals (essential for studying reactions in the solid state). In this paper, we present what we have achieved in asymmetric photochemical studies on *exo*-bicyclo[2.1.1]hexyl and bicyclo[3.1.0]hexyl aryl ketones.

2. Results and discussion

Our strategy for synthesis of the above ketones **2** and **9** was started from norbornene **1** and bicyclo[2.2.1]heptadiene **6**, respectively. As shown in Schemes 1 and 2, according to the reported procedures[7c,9], norbornene **1** was converted to the ketone **2** through a straightforward pathway. Irradiation of **2a** in acetonitrile solution with a 450 W medium mercury pressure lamp under N_2 for 24 h gave the cyclization product **5** in 30% yield and the cleavage product **4** in 66% yield.[10] In this reaction, compound **5** containing a plane of symmetry is an achiral molecule, which is not suitable for

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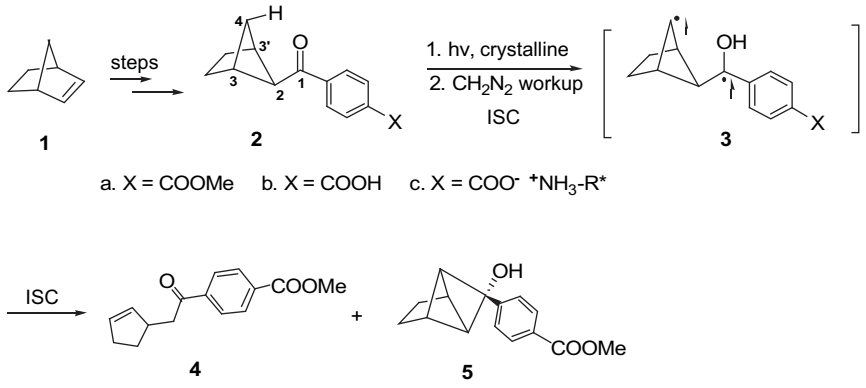
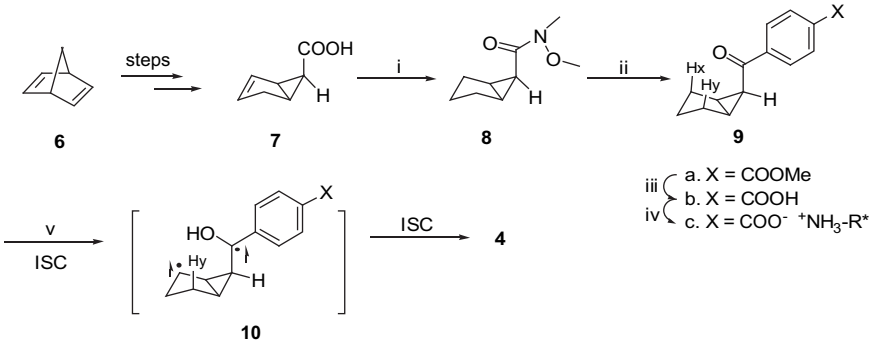


Scheme 1.



Scheme 2. (i) PtO_2, H_2, ethyl acetate; CDI, MeO(Me)NH.HCl, CH_2Cl_2; (ii) $IC_6H_4CO_2CH_3$, ^iPrMgBr, THF; (iii) Na_2CO_3, THF/H_2O (1:5); 10% HCl; (iv) R^*NH_2, Et_2O; (v) *hv*, solid state; CH_2N_2 workup.

asymmetric studies, whereas the formation of cyclopentene **4** is the conversion of achiral reactants to chiral products, which is ideal for asymmetric photochemical studies. Therefore, the carboxylic ester **2a** was hydrolyzed with LiOH in THF/H_2O followed by conc. HCl workup to give the carboxylic acid **2b** in quantitative yield. The compound **2b** was then treated with a variety of optically pure amines to form the corresponding ammonium carboxylate salts **2c**. Such salts are required to crystallize in chiral space groups, which provide the asymmetric environment responsible for chiral induction. Crystals of the salts **2c** (3–5 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.

As it can be seen in Table 1, the enantiomeric excess (*ee*) as high as 98% was obtained in the solid state. To rationalize the results observed, the X-ray single crystal structure of the (*S*)-(-)-1-phenylethyl amine salt of the keto acid **2b** was determined and presented in

Table 1
Asymmetric studies on the irradiation of salts **2c** and **9c** in the solid state[a]

Amine	**2c**					**9c**[f]			
	T (°C)	conv[b] (%)	ee[c] (%)	[α][d]	5:4[e]	*T* (°C)	conv[b] (%)	ee[c] (%)	[α][d]
(*S*)-(-)-1-phenylethylamine	−20	85	98	−	23:74	−20	59	76	+
	rt	21	>98	−	20:79	rt	70	66	+
	rt	53	98	−	21:77	rt	96	43	+
(*R*)-(+)-1-phenylethylamine	−20	27	92	+	20:79	−20	41	90	−
	rt	74	77	+	22:75	rt	79	67	−
	rt	51	81	+	21:77	rt	95	55	−
(*R*)-(-)-1-Cyclohexylethylamine	rt	97	91	−	23:75	−20	32	60	+
	−20	53	93	−	22:77	rt	25	55	+
	rt	31	92	−	21:77	rt	57	25	+
(1*S*,2*R*)-(-)-*cis*-1-amino-2-indanol	−20	48	72	+	21:77	−20	67	74	+
	rt	67	60	+	20:79	rt	89	67	+
	rt	91	53	+	22:76	rt	95	64	+

[a] Samples were irradiated through Pyrex using a 300-W hanovia medium-pressure mercury lamp.
[b] Conversion % based on GC.
[c] Ee % analyzed on chiral OD-H column with hexane:isopropanol=99.5:0.5 as the eluting solvent.
[d] Sign of rotation at the sodium D-line.
[e] Based on GC analysis.
[f] **9c** was the sole photoproduct if no prolonged time was employed.