Letters in Organic Chemistry, **2009**, *6*, 41-43

Photochemical Studies on Benzonorbornene Derivatives: Medium Effects and Asymmetric Induction

Chao Yang, Wujiong Xia*, Qian Chen, Xiao Zhang, Bing Li and Baoquan Gou

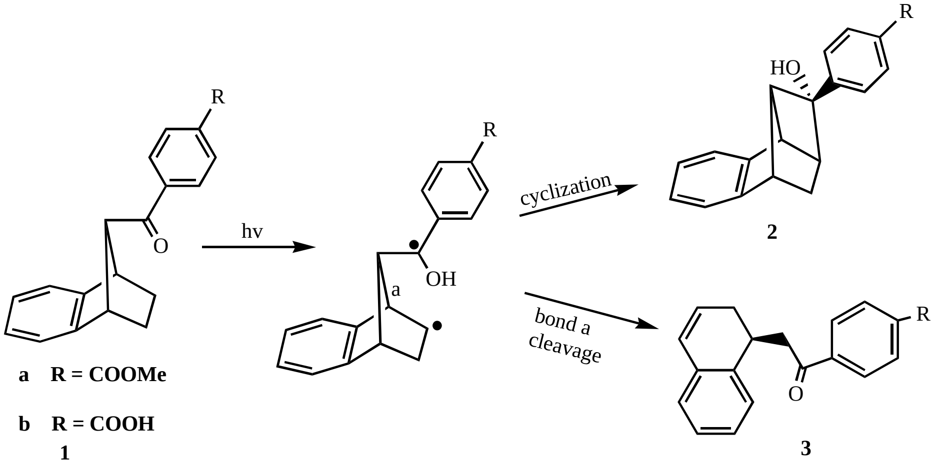
The Academy of Fundamental and Interdisciplinary Science, Harbin Institute of Technology, Harbin, Heilongjiang, 150080, State Key Laboratory of Applied Organic Chemistry, Lanzhou, Gansu, 730000, P. R. China

Received March 03, 2008: Revised September 30, 2008: Accepted October 09, 2008

Abstract: The photochemical behaviors of benzonorbornene derivatives were investigated in the solid state as well as in the solution. In acetonitrile solution, benzonorbornene derivatives underwent the Norrish type II reaction affording a ratio of 1:1 of cyclization and cleavage products, whereas in the solid state, the sole cyclization product was obtained. The stereochemistry of the photoproducts was identified by the X-ray crystallography. Enantiomeric excesses of up to 97% can be achieved through the use of the solid-state ionic chiral auxiliary method of asymmetric synthesis.

Keywords: Benzonorbornene, solid state, Norrish type II, enantiomeric excesses, asymmetric synthesis.

Unlike reactions in solution, atomic and molecular motions in the solid state are highly restricted imposed by the crystal lattice which makes it possible to get high enantioselectivies, and the differentiation in chemical behavior compared with the reaction in solution. During the course of our investigations on the solid-state photochemical reactions [1], the benzonorbornene derivative **1** was synthesized and its photochemical behavior was studied in the solution as well as in the solid state. In acetonitrile solution, benzonorbornene derivative **1a** was shown to undergo the Norrish type II reaction affording a ratio of 1:1 of cyclization and cleavage products [2]. However, the cyclobutanol **2b** was obtained as the sole product when benzonorbornene derivative **1b** was photolyzed in the solid state (Scheme **1**). These reactions, which convert achiral reactants into chiral products, appeared to be ideal for studying asymmetric induction in organic photochemistry, and motivated by the paucity of general methods of asymmetric photochemical synthesis, we embarked on a program designed to achieve this goal.



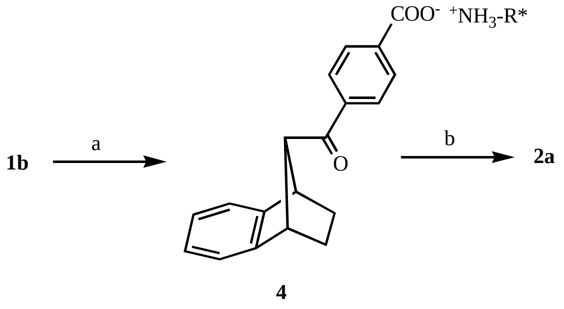
Scheme 1.

The starting material **1** chosen for study was synthesized from commercially available 1-bromo-2-fluorobenzene and freshly cracked cyclopentadiene. The [4π + 2π] cycloaddition of the above two compounds led to the benzonorbornadiene, which was, according to the procedure we reported in the previous paper, treated with bromine, KH/diisopropylamine and *tert*-Butyl Lithium/CO_2 sequentially to give the carboxylic acid [3]. The target compounds **1a** and **1b** were obtained by conversion of the carboxylic acid to the Weinreb amide [4], followed by addition of the Grinard reagents respectively. A solution of ketone **1a** (267 mg, 0.87 mmol) in acetonitrile (40 mL) was purged with N_2 and irradiated (Pyrex filter, 450 W Hanovia lamp) for 4.5 hours. Gas chromatography indi-

---

*Address correspondence to this author at the Academy of Fundamental and Interdisciplinary Science, Harbin Institute of Technology, Harbin, Heilongjiang, 150080, P. R. China; Fax: (86) 451 86403193;
Email: xiawj@hit.edu.cn

1570-1786/09 $55.00+.00



Scheme 2.

cated that the reaction had proceeded to 91% conversion, producing two primary photoproducts: **2** (46%) and **3** (52%). The structure and the stereochemistry of the photoproducts was identified by 1D, 2D NMR, IR, EI analysis, and further by X-ray crystallographic method (Fig. **1a**). Gas chromatography with a mass selective detector confirmed the presence of small amounts of naphthalene and *p*-carboxymethylacetophenone resulting from Norrish type II cleavage of ketone **3** in a secondary photoreaction. When conducting the solid state photolysis, 2-3 milligrams of the crystalline ketone **1b** were crushed between two glass microscope slides and sealed under a nitrogen atmosphere within a polyethylene bag. After irradiation, the photoproducts were treated with ethereal diazomethane and converted into the corresponding methyl esters as **2** (>99%) and **3** (trace) [5]. We speculated that there are two main factors on the differentiation in the results obtained both in solution and solid state. First, molecular conformation as well as the conjugative effect with benzo- group has the equal effect in the product formation, leading to the ratio of 1:1 of cyclization and cleavage products; while in the solid state, the ketone was recrystallized in a conformation in which cyclization is the preferred mode of reaction of the biradicals formed by photolysis. Therefore, molecular conformation rather than conjugative effect affects the production formation in the solid state.

Now we turn to the asymmetric study aspect of the work. The salts **4** for study were prepared by treatment of carboxylic acid **1b** with a variety of optically pure amines at the molar ratio of 1:1. Salts were photolyzed in the crystalline state in the same manner as the ketone **1b** (Scheme **2**). Following photolysis, the photoproducts were treated with ethereal diazomethane, and the resulting methyl esters were analyzed by chiral HPLC to obtain the enantiomeric excess (ee) values and GC for the conversions. The results of the enantiomeric excess determinations are summarized in Table **1**.

As can be seen in Table **1**, the enantiomeric excess was obtained as high as 97%. The poor enantioselectivity observed for the salt of (*1S*,*2S*)-(+)-2-amino-1-phenyl-1,3-propandiol can be attributed in part to conformational enantiomerism since, in the crystalline state, the enantiomeric conformations exist as diastereomers and may therefore have different rates of reactivity. Although the salt of (*R*)-(+)-β-methylphenethylamine was seen to give no observable photoreaction, there are some features of the crystal structure deserving mention. From Fig. (**1b**), it is clearly seen that the carbonyl oxygen atom lies closer to one of the two diastereotopic γ-hydrogens (the closer has been Ha, the further Hb [6]). It is reasonable to assume that all of the salts showing optical selectivity following solid state photolysis crystallize in a similar manner. Therefore, the observed enantioselectivity is due to a conformational effect during crystallization rather than a direct influence of the chiral auxiliary upon the reaction, or even the chiral cavity created by the neighbouring molecules. Work is ongoing in our laboratory to provide evidence for the chiral auxiliary method being applied in synthetically useful compounds.

ACKNOWLEDGEMENTS

We thank Dr. C. Scott and Brian O. Patrick for X-ray crystallographic analysis. C.Y. and W.X. thank the financial support from the New Century Excellent Talent Program of Chinese Ministry of Education (No.NCET-06-0341 and NCET-07-0242). W. X. thanks the financial support from Science Foundation of Harbin City (No. 01310800), program of excellent Team in HIT, China NSFC (No. 20802013) and CSCSE (No. 01311065).

Table 1. Asymmetric studies on salts 4 in the solid state[a]

Amine	Conversion (%)[b]	Ee (%)[c]	α[d]
(*R*)-(+)-1-phenylethylamine	24	97	B
	66	92	
(*S*)-(-)-1-phenylethylamine	17	96	A
	99	93	
(*S*)-(-)-phenylalanine	99	84	A
(*1R*,*2R*)-(-)-pseudoephedrine	42	86	B
(*1S*,*2S*)-(+)-2-amino-1-phenyl-1,3-propandiol	21	12	B
(*R*)-(+)-β-methylphenethylamine	3	-	-

[a] Samples were irradiated through Pyrex using a 450-W Hanovia medium-pressure mercury lamp. [b] Conversion % based on GC. [c] Enantiomeric excesses were determined using a Chiralpak® AS® HPLC column. [d] A refers to the first peak eluted in the HPLC analysis as the predominant enantiomer, B to the second.

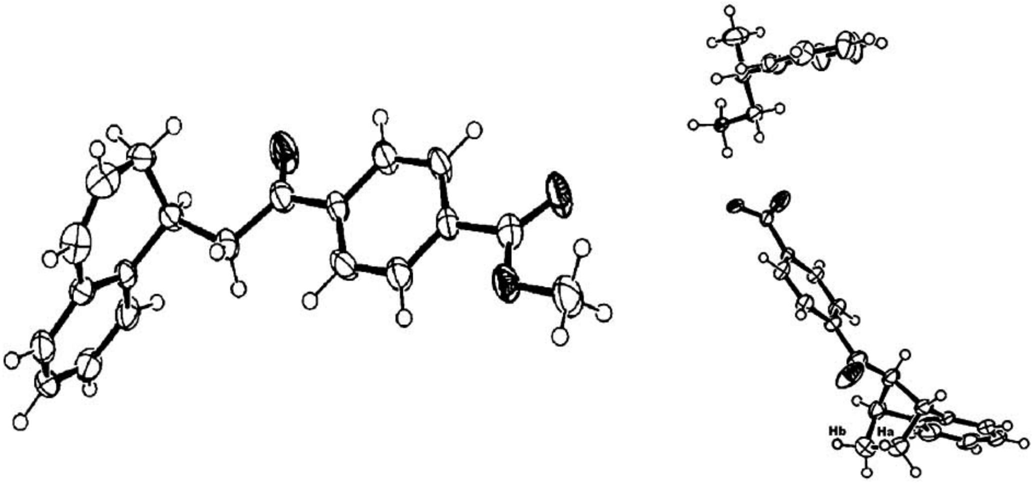


Fig. (1).

REFERENCES AND NOTES

[1] (a) Yang, C.; Xia, W.; Scheffer, J.R. *Tetrahedron*, **2007**, *63*, 6791; (b) Xia, W.; Yang, C.; Patrick, B. O.; Scheffer, J. R.; Scott, C. *J. Am. Chem. Soc*., **2005**, *127*, 2725; (c) Scheffer, J.R.; Xia,W. *Top. Curr. Chem.,* **2005**, *254*, 233; (d) Yang, C.; Xia, W.; Scheffer, J. R.; Botoshansky, M.; Kaftory, M. *Angew. Chem. Int. Ed.*, **2005**, *44*, 5087; (e) Xia, W.; Scheffer, J. R.; Botoshansky, M.; Kaftory, M. *Org. Lett.*, **2005**, *7*, 1315; (f) Xia, W.; Scheffer, J. R.; Patrick, B.O. *Cryst. Eng. Comm.*, **2005**, *7*, 728; (g) Xia, W.; Yang, C.; Scheffer, J. R.; Patrick, B.O. *Cryst. Eng. Comm.*, **2006**, *8*, 388.

[2] (a) For a general review of the Norrish type II reaction, see: Wagner, P.; Park, B.-S. In *Organic Photochemistry*; Padwa, A., Ed.; Marcel Dekker: New York, **1991**; Vol. *11*, Chapter 4; (b) Yang, N.C.; Yang, D.H. Cyclobutanol products in Norrish type II photochemistry. *J. Am. Chem. Soc.,* **1958**, *80,* 2913.

[3] (a) Buske, G. R.; Ford, W.T. *J. Org. Chem.,* **1976**, *41*, 1998; (b) Wittig, G.; Knauss, E. *Chem. Ber*., **1958**, *91*, 895; (c) Cristol, S. J.; Natchigall, G.W. *J. Org. Chem.,* **1967**, *32*, 3727; (d) Wilt, J. W.; Gutman, G.; Ranus, W.J., Jr.; Zigman, A. R. *J. Org. Chem.*, **1967**, *32*, 893.

[4] (a) Nahm, S.; Weinreb, S.M. *Tetrahedron Lett.,* **1981**, *22*, 3815; (b) Jones, T.K.; Mills, S.G.; Reamer, R.A.; Askin, D.; Desmond, R.; Volante, R.P.; Shinkai, I. *J. Am. Chem. Soc.,* **1989**, *111*, 1157.

[5] Braga, D.; Chen, S.; Filson, H.; Maini, L.; Netherton, M.R.; Patrick, B.O.; Scheffer, J. R.; Scott, C.; Xia, W. *J. Am. Chem. Soc.*, **2004**, *126*, 3511.

[6] For photochemical reactions involving intramolecular hydrogen atom abstraction, this requires a conformation in which the carbonyl oxygen is within approximately 2.7 ±0.2 Å of a γ-hydrogen atom. See: Xia, W.; Scheffer, J.R.; Botoshansky, M.; Kaftory, M. *Org. Lett*., **2005**, *7*, 1315-1318 and references therein.