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The use of ionic chiral sensitizers in the crystalline state: application to the di-π-methane photorearrangement of a benzonorbornadiene derivative

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Abstract

Simultaneous asymmetric induction and triplet–triplet energy transfer has been achieved in the di-π-methane photorearrangement of a benzonorbornadiene derivative through the use of 'ionic chiral sensitizers'. In this approach, salts formed between a reactant carboxylic acid and optically pure sensitizer amines are irradiated and the products monitored for optical activity following removal of the ionic auxiliary. In contrast to the results in solution, where only racemic products are formed, photolysis of the salts in the crystalline state leads to enantiomeric excesses as high as 91% at 100% conversion. © 1999 Elsevier Science Ltd. All rights reserved.

Keywords: ammonium salts; asymmetric induction; photochemistry; di-π-methane rearrangement.

The transformation of an achiral carboxylic acid **1** into an optically pure derivative (+)-**2** can be approached in two ways (Scheme 1).[1] The traditional approach would be to carry out a chemical reaction of **1** that produces a racemic mixture of **2**, and then resolve the racemate by the Pasteur procedure using an optically pure amine, (+)-**3**.[2] The maximum yield of (+)-**2** attainable by this procedure is 50%, and could be considerably lower depending on the efficiency of the resolution process.[3] An alternative approach would be to form a salt between compounds **1** and (+)-**3** and to carry out the chemical transformation of **1** to **2** on this material. Such reactions proceed through diastereomerically related *n* and *p* transition states (*n*=(−)-**2**/(+)-**3**; *p*=(+)-**2**/(+)-**3**),[4a] and given a sufficiently large difference in activation energy, one could in principle obtain a near-quantitative yield of a single desired enantiomer — in this case, (+)-**2**. This method has an obvious advantage over the Pasteur procedure in terms of yield.

The role of the optically active ammonium ion (+)-**3** in the second approach is that of an ionic chiral auxiliary, and previous work from our laboratory has demonstrated that high (>90%) enantiomeric excesses can be obtained when the process is carried out in the crystalline state.[4] In this and the following three communications we document further successful applications of the solid state ionic chiral auxiliary approach to asymmetric synthesis. The reactions are all photochemical in nature, but there is no reason

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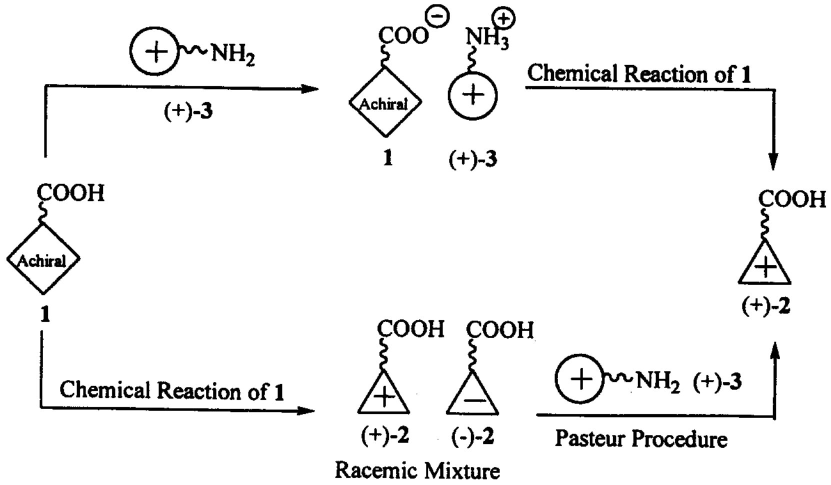
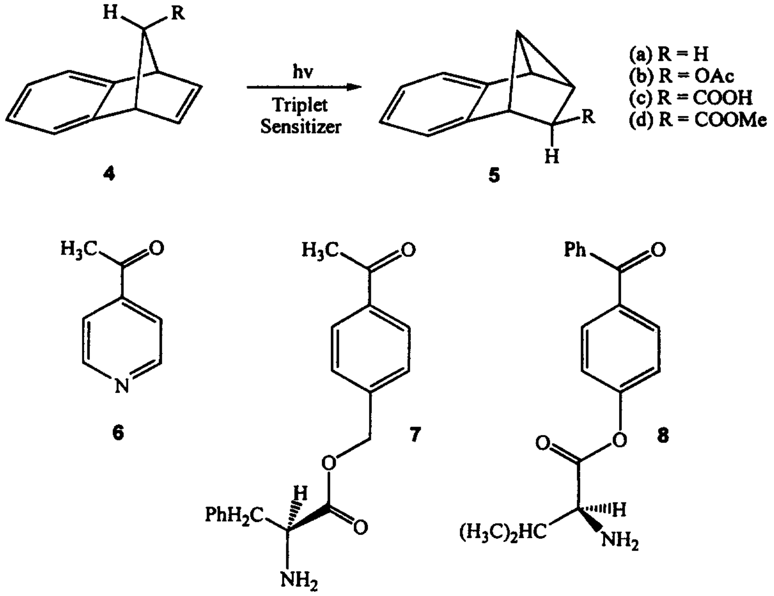


Scheme 1. Ionic chiral auxiliary-induced asymmetric induction

why the procedure should not work on ground state transformations, and efforts along these lines are underway in our laboratory.

In this communication we report our work with the achiral carboxylic acid **4c** (Scheme 2). This compound was selected because benzonorbornadiene itself (**4a**),[5] its 9-acetoxy derivative **4b**,[6] and a host of other derivatives[7] are known to undergo triplet-sensitized di-π-methane photorearrangement to afford chiral tetracyclo[5.4.0.0^{2,4}.0^{3,6}]undeca-1(7),8,10-trienes (**5**). Compound **4c** was expected to behave similarly. The triplet nature of the photoreaction meant that our ionic auxiliary would have to serve the dual role of asymmetric induction agent and triplet energy sensitizer. Chiral sensitizers have been used in solution with varying degrees of success[8] but never before in the solid state.[9]



Scheme 2. Di-π-methane photorearrangement of benzonorbornadienes

Table 1
Solid state irradiation of chiral triplet sensitizer salts[a]

Amine[b]	Irradiation Time	Percent Conversion	Enantiomeric Excess[c]
7	30 min (-20 °C)	4.5	70 (-)
	2 h (-20 °C)	19	66 (-)
	8 h (-20°C)	74	50 (-)
	5 min (room temp)	55	47 (-)
	15 min (room temp)	93	45 (-)
8	4 h (-20 °C)	100	91 (-)
	1 min (room temp)	58	84 (-)
	5 min (room temp)	100	82 (-)

[a]Conversions and enantiomeric excesses were determined by GC following diazomethane workup of the crude reaction mixtures to form photoproduct **5d**. [b]A third optically pure amine, the 4-benzoylbenzyl ester of L-valine, was also investigated, but failed to give enantiomeric excesses greater than 30%. [c]The sign of rotation of the major enantiomer at the sodium D line is given in parentheses.

The known carboxylic acid **4c** was prepared in good yield by a modification of the original method used by Buske and Ford.[10] A crystal structure confirmed the *anti* relationship between the benzo ring and the carboxylic acid group.[11] As expected, solution phase irradiation of acid **4c** and its methyl ester **4d** in the presence of triplet energy sensitizers (acetone, acetophenone, benzophenone) gave excellent yields of racemic **5c** and **5d**.[12] Low yields of these photoproducts were also formed upon direct irradiation, but the reaction was too inefficient to be of any practical importance.

One achiral and two optically pure amines were investigated as ionic triplet energy sensitizers for solid state studies. The achiral photosensitizer *p*-acetylpyridine (**6**) formed a crystalline 1:1 complex (mp 204–205°C) with acid **4c**,[13] and irradiation of this material at $\lambda \geq 330$ nm, where compound **4c** does not absorb, afforded racemic ester **5d** as the only product detectable by GC following diazomethane workup. The 4-acetylbenzyl ester of L-phenylalanine (**7**) and the 4-benzoylphenyl ester of L-valine (**8**) were synthesized as possible ionic chiral sensitizers.[14] Each of these amines afforded crystalline salts when mixed with carboxylic acid **4c**. The salt formed with amine **7** melted at 111–113°C, and that formed with amine **8** melted at 143–144°C. The infrared spectra of the salts clearly indicated that both were ionic in nature.

Table 1 summarizes the results obtained when each of the chiral sensitizer salts was irradiated at $\lambda \geq 330$ nm in the crystalline state. From the Table it is clear that amine **8** is a better chiral sensitizer than **7**, both in terms of the enantiomeric excess in which photoproduct **5d** is produced and in terms of reaction efficiency. An enantiomeric excess of 91% at 100% conversion is an excellent result for any asymmetric induction, ground state or photochemical. Serving to highlight the importance of crystal lattice-enforced preorganization of reactant and ionic auxiliary, irradiation of the salts in acetonitrile solution gave only racemic product. The exact nature of the stereoelectronic factors responsible for energy transfer and high enantioselectivity in the solid state must remain unspecified for the moment, however, since we were unable to obtain X-ray crystal structures of any of the salts investigated in this work. Related questions having to do with the exact nature of the enantiodifferentiating step and the absolute steric course of the photorearrangement must also await the preparation of crystalline samples suitable for X-ray diffraction.

Acknowledgements

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References

1. The sign of rotation given for compounds **2** and **3** is arbitrary and used for illustrative purposes only.
2. Pasteur, L. *C. R. Acad. Sci.* **1853**, *37*, 162.
3. (a) Jacques, J.; Collet, A.; Wilen, S. H. *Enantiomers, Racemates and Resolutions*; Wiley: New York, 1981; (b) Eliel, E. L.; Wilen, S. H. *Stereochemistry of Organic Compounds*; Wiley: New York, 1994; Chapter 7; (c) Collet, A. *Angew. Chem., Int. Ed. Engl.* **1999**, *37*, 3239.
4. (a) Cheung, E.; Netherton, M. R.; Scheffer, J. R.; Trotter, J. *J. Am. Chem. Soc.* **1999**, *121*, 2919; (b) Leibovitch, M.; Olovsson, G.; Scheffer, J. R.; Trotter, J. *J. Am. Chem. Soc.* **1998**, *120*, 12755; (c) Gamlin, J. N.; Jones, R.; Leibovitch, M.; Patrick, B.; Scheffer, J. R.; Trotter, J. *Acc. Chem. Res.* **1996**, *29*, 203.
5. Edman, J. R. *J. Am. Chem. Soc.* **1966**, *88*, 3454; *ibid*, **1969**, *91*, 7103.
6. Tufariello, J. J.; Rowe, D. W. *J. Org. Chem.* **1971**, *36*, 2057.
7. Paquette and co-workers have studied the solution phase photochemistry of a variety of aryl, bridgehead and vinyl-substituted benzonorbornadiene derivatives: Paquette, L. A.; Burke, L. D. *J. Org. Chem.* **1987**, *52*, 2674 and references cited therein.
8. (a) Hammond, G. S.; Cole, R. S. *J. Am. Chem. Soc.* **1965**, *87*, 3256; (b); Inoue, Y.; Matsushima, E.; Wada, T. *J. Am. Chem. Soc.* **1998**, *120*, 10687.
9. For an example of the use of an achiral ionic triplet energy sensitizer in the crystalline state, see: Gamlin, J. N.; Olovsson, G.; Pitchumani, K.; Ramamurthy, V.; Scheffer, J. R.; Trotter, J. *Tetrahedron Lett.* **1996**, *37*, 6037. Recently, Ramamurthy et al. have shown that modest (ca. 15% ee) levels of asymmetric induction can be generated in photoproduct **5a** by irradiation of benzonorbornadiene in the zeolite TlY containing ephedrine hydrochloride. See: Joy, A.; Robbins, R. J.; Pitchumani, K.; Ramamurthy, V. *Tetrahedron Lett.* **1997**, *38*, 8825.
10. Buske, G. R.; Ford, W. T. *J. Org. Chem.* **1976**, *41*, 1998.
11. Cheung, E.; Trotter, J. Unpublished results.
12. All new compounds described in the present paper gave spectroscopic data and elemental analyses completely in accord with their assigned structures. Details will be provided in a subsequent full paper.
13. It is likely that this material is a hydrogen bonded complex, since *p*-acetylpyridine is not sufficiently basic to remove a proton from carboxylic acid **4c**.
14. The chiral sensitizers **7** and **8** were synthesized by DCC coupling of the appropriate *N*-carbobenzyloxy-protected amino acid to *p*-acetylbenzyl alcohol or *p*-hydroxybenzophenone, followed by deprotection with HBr in acetic acid.