Pergamon

Tetrahedron Letters 40 (1999) 8737–8740

TETRAHEDRON
LETTERS

Linearly conjugated benzocyclohexadienone photochemistry in the solid state: ionic chiral auxiliary mediated asymmetric induction

Eugene Cheung, Matthew R. Netherton, John R. Scheffer * and James Trotter
Department of Chemistry, University of British Columbia, 2036 Main Mall, Vancouver, Canada V6T 1Z1

Received 22 July 1999; accepted 27 September 1999

Abstract

Asymmetric induction in the photochemistry of a linearly conjugated benzocyclohexadienone derivative has been achieved for the first time through the use of the solid state ionic chiral auxiliary method. Enantiomeric excesses as high as 70–80% at reasonable conversions are readily attainable. Crystal structures for both reactant and product are reported. © 1999 Elsevier Science Ltd. All rights reserved.

Keywords: asymmetric induction; ketones; photochemistry; $[\pi_2^a+\sigma_2^a]$ rearrangement.

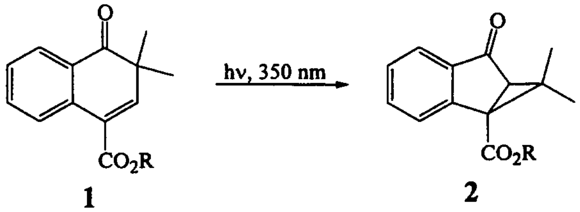
In this communication we report the application of the solid state ionic chiral auxiliary method of asymmetric synthesis[1] to a new type of reaction — the photochemical conversion of the achiral linearly conjugated benzocyclohexadienone derivative **1** into the chiral benzobicyclo[3.1.0]hexenone product **2** (Scheme 1).[2] The goal of this work was twofold: first, to demonstrate the viability and synthetic utility of the ionic chiral auxiliary method on as wide a spectrum of reactions as possible, and second, to test the method on a reactant that was conformationally unbiased. In most of the systems studied to date, some degree of conformational flexibility has been present in the reactant, thus allowing it to crystallize in a chiral conformation that favors formation of one enantiomer of the product over the other. With rigid or planar molecules, however, such biases are expected to be small. The origin of asymmetric induction in these cases may have less to do with the conformation of the reactant and may be more influenced by the availability of free space within the crystal lattice. Molecular modeling (HyperChem MM+) of methyl ester **1b** predicts a planar ring system, with the molecule possessing overall C_s symmetry. It was expected, therefore, that the benzocyclohexadienone moiety in salts formed between carboxylic acid **1a** and optically active amines should also be planar. With this in mind, we set out to see what effect this lack of conformational bias would have on the ability of the lattice to promote asymmetric induction in the crystalline state.[3]

Irradiation of carboxylic acid **1a**[4] in acetonitrile solution at 350 nm provided racemic photoproduct **2a** (87%) whose structure was confirmed by X-ray crystallography.[5] Attempts to trap a ketene intermediate

---

* Corresponding author. Tel: (604) 822-3496; fax: (604) 822-2847; e-mail: scheffer@chem.ubc.ca

PII: S0040-4039(99)01868-7



1 **2**

(a) R = H; (b) R = CH_3; (c) R = $H_3\overset{\oplus}{N}$-R*

Scheme 1. Linearly conjugated benzocyclohexadienone photochemistry

in this reaction with dimethylamine were unsuccessful, as were attempts to quench the formation of photoproduct **2a** with the triplet quencher, 2,5-dimethyl-2,4-hexadiene. These experiments are consistent with (but not proof of) a concerted process occurring through an excited singlet state. Quinkert has suggested that products such as **2a** (formally equivalent in terms of structure to those generated in the oxadi-π-methane photorearrangement) are formed in a $[\pi_2^a+\sigma_2^a]$ manner through $(\pi,\pi^*)^1$ excited states.[2b]

For solid state asymmetric induction studies, salts (**1c**) of carboxylic acid **1a** were formed with a variety of optically active amines (Table 1), and crystals of these salts were sandwiched between two Pyrex plates and irradiated under nitrogen at 350 nm (Rayonet photochemical reactor). Subsequent treatment of the irradiated crystals with ethereal diazomethane led to a mixture of unreacted starting material **1b** and photoproduct **2b**, which could be analyzed for enantiomeric excess and extent of reaction by chiral gas chromatography. The results of these solid state reactions are reported in Table 1.

Table 1
Solid state photolysis results for chiral salts of carboxylic acid **1a**

Chiral Auxiliary	Temp (°C)	Conversion (%)	ee of **2b** (%)[a]	GC Peak[b]
(S)-(-)-α-methylbenzylamine	room temp	25	81.0	2
	room temp	80	70.6	
	-78	30	86.5	
(R)-(+)-*p*-methyl-α-methyl-benzylamine	room temp	09	50.1	1
	room temp	28	27.8	
	-78	15	47.6	
(1R,2R)-(-)-pseudoephedrine	room temp	11	38.1	1
	room temp	67	29.1	
$(DHQD)_2PYR$[c]	room temp	36	35.6	2
	room temp	69	36.7	
	-78	53	52.5	
(1R,2S)-(-)-ephedrine	room temp	17	30.6	1
	room temp	61	30.5	
	-78	68	32.7	
brucine	room temp	15	20.2	2
		49	21.9	
		76	25.2	

[a] Enantiomeric excesses measured by chiral GC (β-Dex 350/1701, 20 m, SUPELCO). [b] Peak 1 indicates major enantiomer is first peak eluted from chiral GC. [c] Hydroquinidine 2,5-diphenyl-4,6-pyrimidinediyl diether (Aldrich). This base forms a salt with two equivalents of acid **1a**.

As can be seen from the data in Table 1, only one ionic chiral auxiliary — α-methylbenzylamine — gave a respectable enantiomeric excess (ca. 80%). The others gave ees in the

20–50% range, and some (not shown in Table 1) gave even lower enantioselectivities. In three of the six salts studied, there was a decline in photoproduct optical purity with increasing conversion. This is a frequently observed feature of the ionic chiral auxiliary method (see preceding three papers in this issue, as well as earlier work cited) and stems from the breakdown of order in the crystal lattice as product replaces starting material. Performing the photolyses at low temperatures had little effect on product ee, except in the case of the $(DHQD)_2PYR$ salt. In this instance an increase in ee of ca. 17% was realized when the reaction temperature was lowered from ambient to −78°C. Irradiation of the salts in chloroform solution gave only racemic photoproduct, this despite the fact that the ^{13}C NMR spectra of some of the salts in $CDCl_3$ show two distinct methyl signals for the anion of acid **1a**.[6] In all our ionic chiral auxiliary work we have yet to observe any enantioselectivity resulting from photolysis of the salts in solution.

Of the salts of acid **1a** investigated to date, only the brucine salt formed crystals suitable for X-ray diffraction. The stoichiometry of this salt is two parts acid to one part base, and the crystal structure[7] shows that one of the acid molecules has protonated the brucine nitrogen atom while the second acid molecule forms a hydrogen bond to the first. In agreement with the molecular mechanics prediction, both acids possess ring systems that deviate very little from planarity. The hydrogen bonding motif is shown in Fig. 1. The two acid moieties are chemically and crystallographically independent and reside in different chiral environments. It seems likely that this is what is responsible for the low enantioselectivity observed in this case (ca. 20%), where one acid reacts to give predominantly one enantiomer of photoproduct **2** while the other affords primarily its optical antipode.[8] Absolute configuration correlation studies coupled with computer simulations of the solid state reaction are planned in order to identify the specific lattice interactions responsible for the observed enantioselectivities.

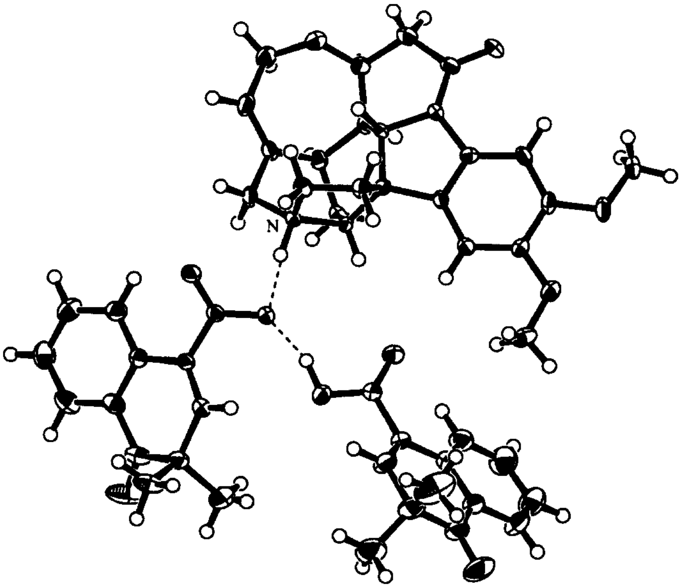


Figure 1. Hydrogen bond motif in brucine salt of acid **1a**

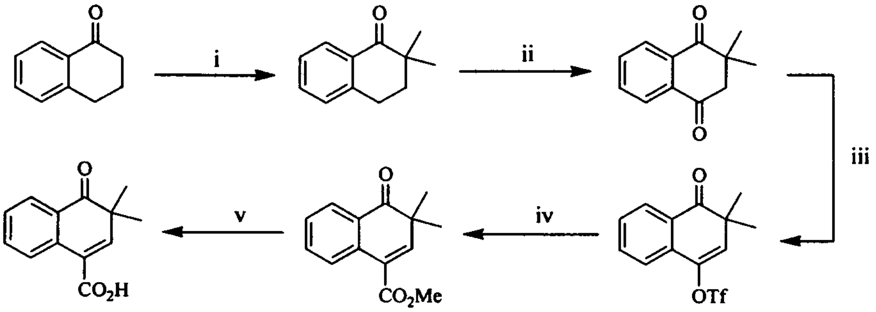
In summary, the results presented in this and the preceding three communications clearly demonstrate the wide applicability of the solid state ionic chiral auxiliary approach to asymmetric synthesis in organic photochemistry. While not all ionic chiral auxiliaries give high enantiomeric excesses, it has always been possible to find at least one that does. α-Methylbenzylamine, which can be purchased in both enantiomeric forms, has consistently out-performed all others.

Acknowledgements

Acknowledgment is made to the donors of the Petroleum Research Fund, administered by the American Chemical Society, for partial support of this research. Financial support by the Natural Sciences and Engineering Research Council of Canada is also gratefully acknowledged.

References

1. See preceding three articles in this issue and references cited therein.
2. For a review of the photochemistry of linearly conjugated cyclohexadienones, see: (a) Schultz, A. G. In *CRC Handbook of Organic Photochemistry and Photobiology;* Horspool, W. M.; Song, P.-S., Eds.; CRC Press: Boca Raton, 1991; Chapter 58; (b) Quinkert, G. *Pure Appl. Chem.* **1973**, *33*, 285.
3. The first paper in the present series of four articles also deals with the application of the solid state ionic auxiliary method of asymmetric synthesis to a conformationally rigid molecule.
4. Keto-acid **1a**, a new compound, was synthesized as shown below. 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.



Reagents: i) KH, MeI, THF, 89%; ii) tBuOOH, cat. CrO_3, CH_2Cl_2-H_2O, 4 days, 69%; iii) LDA then $PhNTf_2$, -78°-25°C, THF, 90%; iv) 10 mol% $Pd(OAc)_2$, PPh_3, CO, MeOH, DIPEA, DMF, 70%; v) LiOH, MeOH-H_2O, 98%.

5. Acid **2a**: $P2_1/c$; a=10.874(2) Å, b=9.182(1) Å, c=11.247(2) Å; β=95.72°; Z=4; R=4.4%.
6. The *gem*-dimethyl groups are diastereotopic as a result of close contact between the chiral cation and achiral anion in the solvated ion pair.
7. Brucine salt of acid **1a**: $P2_12_12_1$; a=9.569(1) Å, b=14.204(4) Å, c=29.98(1) Å; Z=4; R=4.1%.
8. A similar situation has been observed for a salt that crystallizes in a disordered structure containing two differing conformations of the reacting species. See: Cheung, E.; Netherton, M. R.; Scheffer, J. R.; Trotter, J. *J. Am. Chem. Soc.* **1999**, *121*, 2919.