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Enantiospecific photochemical carbon skeletal rearrangement of Morita–Baylis–Hillman products in water

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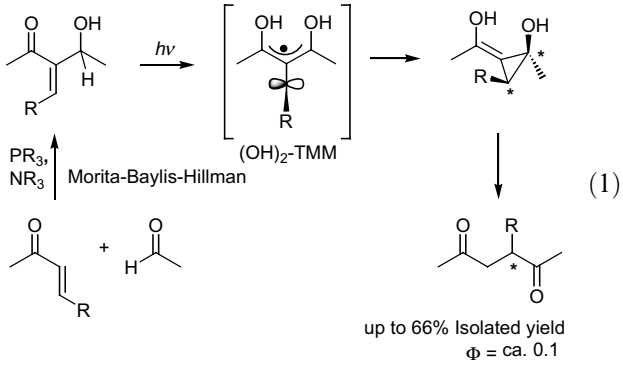
Abstract—Asymmetric carbon skeletal rearrangements of Morita–Baylis–Hillman products, α-hydroxymethylenones, under photochemical irradiation in water are described, wherein the asymmetric induction mechanism is discussed in detail.

During the past decades, thermal asymmetric syntheses have advanced to a great extent.[1] In sharp contrast, only modest progress has been made for asymmetric photochemical syntheses, for which circular polarized light (CPL) or chiral sensitizers have been employed.[2] Quite recently, γ-cyclodextrin (γ-CD)[3] has been used as a chiral supercage[4] to give 51% ee in the photochemical dimerization of anthracenecarboxylic acid under high pressure at low temperature.[5] We have reported the photochemical carbon skeletal reorganization[6] of the Morita–Baylis–Hillman product,[7] involving the C_s-symmetric dihydroxytrimethylenemethane ($(OH)_2$-TMM) as a common intermediate[8] (Eq. 1). This result suggested to us that the asymmetric desymmetrization[9] of the C_s-symmetric $(OH)_2$-TMM intermediates by matched C_2-symmetric chiral controllers, in the presence or absence of a chiral supercage, could provide an asymmetric route to the photochemical synthesis of 1,4-dicarbonyl compounds.[10] The enantiospecific carbon skeletal rearrangement through ternary complex of $(OH)_2$-TMM with C_2-symmetric chiral controllers and a chiral supercage (γ-CD) in water[11] is the subject of this communication.



(1)

The Morita–Baylis–Hillman product, α-hydroxyethylenone **1**, was irradiated by a high-pressure mercury lamp in benzene for 8 h, in the presence of chiral molecules such as C_2-symmetric chiral diamines and diols, to give 1,4-dicarbonyl compounds with α-aryl functionality, otherwise difficult to obtain.[12] However, only low levels of enantioselectivities and chemical yields were obtained with a variety of C_2-symmetric chiral controllers such as (*S*,*S*)-diaminocyclohexane (23%, 13% ee, the highest enantioselectivity obtained therewith (1 equiv rather than 0.5 or 2 equiv)), (*S*,*S*)-diphenylethylenediamine (DPEN)[13] (19%, 3% ee), and diethyl tartrate (30%, 4% ee). When CDs were employed as chiral supercages in water, γ-CD gave almost quantitative yield (93%) but only 2% ee. It is noted here that among cyclodextrins, only γ-CD effectively promotes the reaction in water. α- and β-CD could not form any inclusion complex with **1** and hence only low yields was obtained (38%, almost the same without CD). γ-CD was found to significantly

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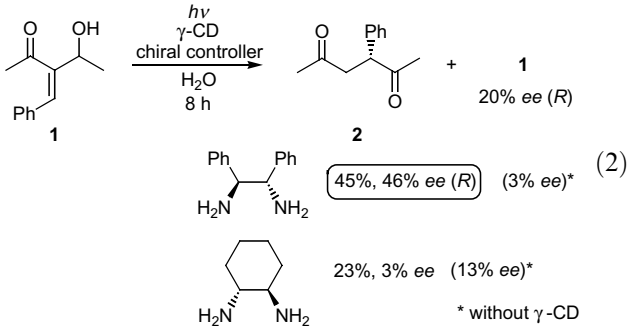
facilitate the photochemical carbon skeletal rearrangement to give 1,4-dicarbonyl compound **2** in higher (64%) isolated yield within 3 h (20% in the absence of γ-CD). Therefore, only 26% of starting material **1** was recovered even after 3 h (42% recovery without γ-CD). Retardation of the olefin isomerization was also observed (9% instead of 19% without γ-CD). Other Morita–Baylis–Hillman products also gave much higher isolated yields (79%: R = *o*-MeOPh; 49%: R = *iso*-Pr) when the reaction was carried out in the presence of γ-CD.

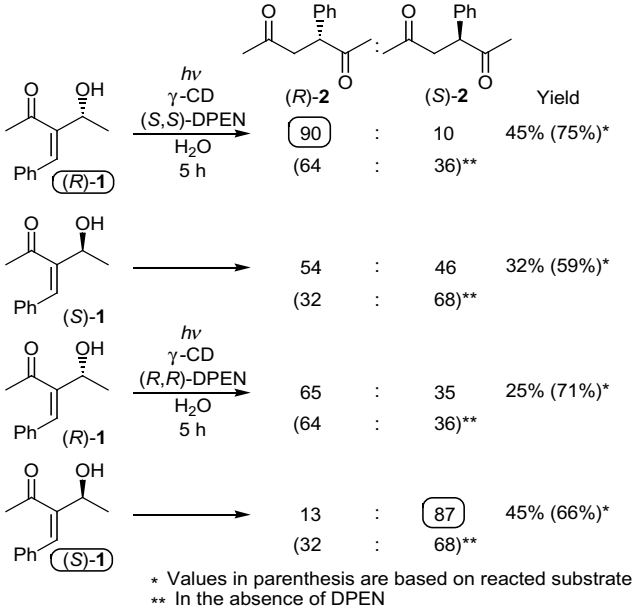
Although the highest enantioselectivity was obtained with diaminocyclohexane in the absence of γ-CD, the combined use gave only low yield and enantioselectivity (Eq. 2). Because diaminocyclohexane could not be included into the chiral supercage γ-CD in sharp contrast to DPEN. The use of (*S*,*S*)-DPEN with γ-CD afforded both higher yield and enantioselectivity (45%, 46% ee *R*)[14] as compared with those obtained in the absence of γ-CD (19%, 3% ee). Indeed, (*S*,*S*)-DPEN did form an inclusion complex with γ-CD. Since the recovered substrate was 20% ee (*R*), the relative reactivity between (*S*)- and (*R*)-**1** was calculated to be 3.3.[15]



(2)

The enantiospecific carbon skeletal rearrangement in the present asymmetric photochemistry of enantiopure **1** was then investigated by changing the chirality of DPEN.[14] A significantly high enantiospecifity was observed (Scheme 1); (*R*)-substrate **1**, in combination of (*S*,*S*)-DPEN and γ-CD, provided 90% (*R*)-selectivity for 1,4-dicarbonyl compound **2**. This 90% (*R*)-selectivity was significantly increased from 64% (*R*)-selectivity obtained without DPEN. By contrast, (*S*)-substrate **1** with (*R*,*R*)-DPEN and γ-CD provided the opposite (*S*)-**2** enantiomer in 87% selectivity. In the absence of DPEN, (*R*)- and (*S*)-**1** enantiospecifically gave (*R*)- and (*S*)-**2**, respectively, though in low level of enantiomeric excess (28% ee and 36% ee). These results suggest the importance of ternary complex formation with DPEN and CD in attaining high enantiospecificity. Indeed, the mixture of substrate (*R*)-**1** with (*S*,*S*)-DPEN and γ-CD in water gave a precipitate, which could be removed by filtration; further extraction with ethyl acetate of the filtrate afforded three separated fractions, composed of **1**, DPEN and γ-CD (1:1:1).

The chiral recognition through triple binding of **1** with DPEN in the chiral supercage, γ-CD bearing chiral secondary hydroxy groups is thus effective for the enantiospecific carbon skeletal rearrangement (Fig. 1).[16] The use of (*S*,*S*)-DPEN induced the changeover of the



Scheme 1.

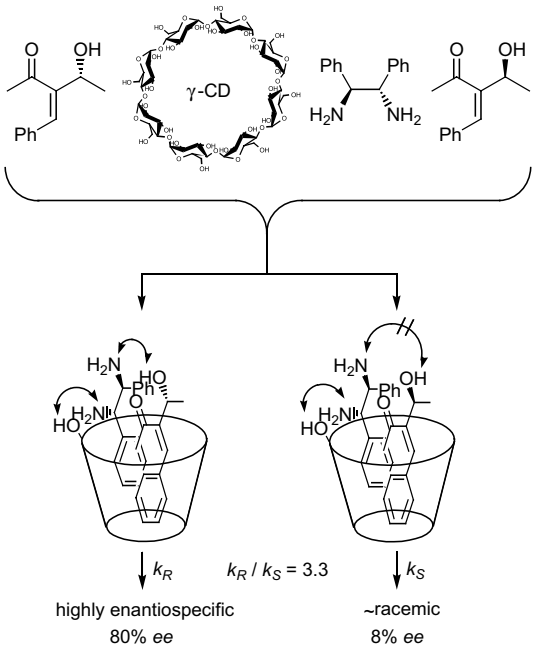


Figure 1.

sense of enantioselectivity of (*S*)-**1** to give (*R*)-**2** albeit in low selectivity (54% *R*; cf. 68% *S* without DPEN). Furthermore, the geometrical isomer (*E*)-**1** also provides only low (25% ee) enantioselectivity due to its mismatched geometry for the relatively inflexible bucket-shaped CD.

In summary, we have uncovered the enantiospecific carbon skeletal reorganization of the Morita–Baylis–Hillman product. Through triple binding by C_2-symmetric chiral DPEN controller in chiral γ-CD supercage

in water, the asymmetric route has thus been set for the photochemical synthesis of 1,4-dicarbonyl compounds.

References and notes

1. Comprehensive review: Gawley, R. E.; Aube, J. *Principles of Asymmetric Synthesis*; Pergamon: London, 1996.
2. Excellent reviews: (a) Bochet, C. *J. Chem. Soc. Perkin 1* **2002**, 125; (b) Pete, J. P. *Adv. Photochem.* **1996**, *21*, 135; (c) Inoue, Y. *Chem. Rev.* **1992**, *92*, 741; (d) Ramamurthy, V.; Venkatesan, K. *Chem. Rev.* **1987**, *87*, 433; (e) Rau, H. *Chem. Rev.* **1983**, *83*, 535; Chiral auxiliaries: (f) Buschmann, H.; Scharf, H. D.; Hoffmann, N.; Esser, P. *Angew. Chem., Int. Ed. Engl.* **1991**, *30*, 477; Chiral host-guest assembly: (g) Joy, A.; Ramamurthy, V. *Chem. Eur. J.* **2000**, *6*, 1287; (h) Bach, T.; Bergmann, H.; Harms, K. *Angew. Chem., Int. Ed.* **2000**, *39*, 2302; Bach, T.; Bergmann, H.; Harms, K. *J. Am. Chem. Soc.* **1999**, *121*, 10650; (i) Toda, F. *Acc. Chem. Res.* **1995**, *28*, 480; Chiral ionic auxiliaries: (j) Gamlin, J. N.; Jones, R.; Leibovitch, M.; Patrick, B.; Scheffer, J. R.; Trotter, J. *Acc. Chem. Res.* **1996**, *29*, 203.
3. (a) Bender, M. L.; Komiyama, M. *Cyclodextrin Chemistry*; Springer: Berlin, 1978; (b) Szejtli, T. *Cyclodextrin and their Inclusion Complexes* Akademiai: Kiado, 1982. Szejtle, T. *Comprehensive Supramolecular Chemistry*; Pergamon: UK, 1996; Vol. 3, p 189.
4. We have employed some cage molecules as hosts, such as cyclodextrins (usually called 'cavity' though), zeolite, and Fujita's Pd-nanocage, which might be totally called 'supercage' molecules.
5. Nakamura, A.; Inoue, Y. *J. Am. Chem. Soc.* **2003**, *125*, 966.
6. (a) Matsumoto, S.; Okubo, Y.; Mikami, K. *J. Am. Chem. Soc.* **1998**, *120*, 4015; (b) Matsumoto, S.; Mikami, K. *Synlett* **1998**, 469; (c) Mikami, K.; Okubo, Y. *Synlett* **2000**, *4*, 491; (d) Mikami, K.; Okubo, Y. *Synlett* **2000**, *8*, 1135; (e) Mikami, K.; Matsumoto, S.; Tanaka, S. *J. Synth. Org. Chem. Jpn.* **2004**, *62*, 598.
7. (a) Morita, K.; Suzuki, Z.; Hirose, H. *Bull. Chem. Soc. Jpn.* **1968**, *41*, 2815; (b) Baylis, A. B.; Hillman, M. E. D. *Ger. Offen.* **1972**, *2*, 113–115; (c) Drewes, S. E.; Roos, G. H. P. *Tetrahedron* **1988**, *44*, 4653; (d) Ciganek, E. *Org. React.* **1997**, *51*, 201; (e) Iwabuchi, Y.; Hatakeyama, S. *J. Synth. Org. Chem. Jpn.* **2002**, *60*, 4.
8. For reviews on trimethylenemethane, see: (a) Doering, W. E.; Roth, H. D. *Tetrahedron* **1970**, *26*, 2825; (b) Dowed, P. *Acc. Chem. Res.* **1972**, *5*, 242; (c) Berson, J. A. In *Rearrangements in Ground and Excited States*; de Mayo, P., Ed.; Academic: New York, 1980; Vol. 1, p 334; (d) *Rearrangements in Ground and Excited States*; Diradical Borden, W. T., Ed.; Wiley: New York, 1982; (e) Little, R. D. *Chem. Rev.* **1986**, *86*, 875.
9. For reviews, see: (a) Ward, R. S. *Chem. Soc. Rev.* **1990**, *19*, 1; (b) Poss, C. S.; Schreiber, S. L. *Acc. Chem. Res.* **1994**, *27*, 9; (c) Magnuson, S. R. *Tetrahedron* **1995**, *51*, 2167; (d) Mikami, K.; Yoshida, A. *J. Synth. Org. Chem. Jpn.* **2002**, *60*, 732.
10. (a) Trost, B. M. *Chem. Soc. Rev.* **1982**, *11*, 141; (b) Texier-Boullet, F.; Klein, B.; Hamelin, J. *Synthesis* **1986**, 409.
11. (a) *Organic Synthesis in Water*; Grieco, P. A., Ed.; Blackie Academic & Professional: London, 1998; (b) Li, C.-J.; Chen, T.-H. *Organic Reactions in Aqueous Media*; Wiley: New York, 1997.
12. Quite recently, the asymmetric α-arylation of ketone enolates has been reported: (a) Moradi, W. A.; Buchwald, S. L. *J. Am. Chem. Soc.* **2001**, *123*, 7996; (b) Hamad, T.; Chieffi, A.; Åhman, J.; Buchwald, S. L. *J. Am. Chem. Soc.* **2002**, *124*, 1261; (c) Spielvogel, D. J.; Buchwald, S. L. *J. Am. Chem. Soc.* **2002**, *124*, 3500; (d) Jorgensen, M.; Lee, S.; Liu, X.; Wolkowski, J. P.; Hartwig, J. F. *J. Am. Chem. Soc.* **2002**, *124*, 12557; (e) Culkin, D. A.; Hartwig, J. F. *Acc. Chem. Res.* **2003**, *36*, 234.
13. (a) Corey, E. J.; Jardine, P. D.; Virgil, S.; Yuen, P. W.; Connell, R. D. *J. Am. Chem. Soc.* **1989**, *111*, 9243; (b) Mangeney, P.; Tejero, T.; Alexakis, A.; Grosjean, F.; Normant, J. F. *Synthesis* **1988**, 255.
14. Typical asymmetric photoreaction of Morita–Baylis–Hillman products: To a mixture of (*Z*,*S*)-3-benzylidene-4-hydroxy-pentane-2-one (19.0 mg, 0.10 mmol), (*S*, *S*)-DPEN (25.5 mg, 0.12 mmol) and γ-CD (389.1 mg, 0.3 mmol) at room temperature in Pyrex vessel was added H_2O (3 mL) and stirred for 14 h to provide the ternary complex at that temperature. Then the mixture of this suspension was irradiated with high-pressure mercury lamp for 5 h with stirring. The resultant mixture was poured into brine and extracted with ethyl acetate. The organic layer was dried over Na_2SO_4. The solution was filtrated and concentrated under reduced pressure. The residue was purified by neutral silica gel chromatography to give 3-phenylhexane-2,5-dione in 45% yield. ^{1}H NMR (300 MHz, $CDCl_3$) δ 2.12 (s, 3H), 2.16 (s, 3H), 2.57 (dd, $J = 4.2$, 18.0 Hz, 1H), 3.45 (dd, $J = 9.9$, 18.0 Hz, 1H), 4.23 (dd, $J = 3.9$, 10.4 Hz, 1H), 7.19–7.36 (m, 5H). The enantiomeric excess of the product was determined by HPLC (Chiracel OD-H, hexane/2-propanol = 97:3, flow rate 0.7 mL/min, detection UV 220 nm, column temperature 15 °C t_R of 21.2 min, t_R of 34.9 min). GC (CP-Chirasil-Dex CB, i.d. 0.25 mm × 25 m, CHROMPACK; carrier gas, nitrogen 75 kPa; column, 110 °C; injection temp. 135 °C), t_R of (*R*)-isomer 42.4 min, t_R of (*S*)-isomer 44.1 min. cf. $[\alpha]_D$ −130.4 (*c* 1.5, $CHCl_3$): 33% ee (*R*).
15. For the equation to calculate the relative reactivity, see: (a) Wang, Y.-F.; Chen, C.-S.; Girdaukas, G.; Sih, C. J. *J. Am. Chem. Soc.* **1984**, *106*, 3695; (b) Martin, V. S.; Woodard, S. S.; Katsuki, T.; Yamada, Y.; Ikeda, M.; Sharpless, K. B. *J. Am. Chem. Soc.* **1981**, *103*, 6237; (c) Mikami, K.; Narisawa, S.; Shimizu, M.; Terada, M. *J. Am. Chem. Soc.* **1992**, *114*, 6566.
16. For strict hydrogen bonding with CDs bearing primary and secondary hydroxy groups, see: Miyake, K.; Yasuda, S.; Harada, A.; Sumaoka, J.; Komiyama, M.; Shigekawa, H. *J. Am. Chem. Soc.* **2003**, *125*, 50.