New Frontier in Enone Photoreaction: Enantiospecific Rearrangement of Morita-Baylis-Hillman Products



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Photochemical reactions

- 1. Photochemistry of Alkene
- 2. Photochemistry of Carbonyl Group
- 3. Photoreaction of Enone
- 4. Photoreaction of Morita-Baylis-Hillman Product
- 5. Asymmetric Photoreaction of Morita-Baylis-Hillman Product

The instrument

UV-sources:

Low-pressure Hg-lamp (1 atm) Mid-pressure Hg-lamp (10 atm) High-pressure Hg-lamp (200 atm) 254 nm 313;366;405 nm polychromatic

Cutoff filters:

Pyrex 300 nm Quartz 200 nm

Interaction with Light



Planck Law: $\Delta E = hv$

Franck-Condon Principle: The nuclei do not move during the transition

Wigner spin conservation: The total spin is unchanged

Spin Multiplicities



Modification of Energy Levels



Lifetime of Excited States

Steady-state kinetics approximation:



Time Scales



Triplet quenching

Photochemistry of Alkenes: Isomerization



Asymmetric Isomerization



B. Feringa, J. Am. Chem. Soc. 2005, 127, 14208

Electrocyclization



Suprafacial [1,3]Sigmatropic Shifts



40% (+50% SM)

A.D. Rodriguez, J. Org. Chem. 1998, 63, 420



P.A. Wender, J. Am. Chem. Soc. 1992, 114, 5878

cf. Thermally: Antarafacial: J.A. Berson, Acc. Chem. Res. '68, 1, 15

Di-p-methane Rearrangement



Additions



Asymmetric Additions



sens* = aromatic menthyl ester

via radical cation of the alkene. up to 58% ee

Y. Inoue et al. J. Photochem. Photobiol. A:Chem 2001, 145, 53-60.

Photosensitized lactonization



triplet states -> low ee's

M. Alvaro, H. Garcia, E. Palomares, M.J. Sabater, J. Org. Chem. 2002, 67, 5184.

[2+2] Cycloadditions













Diastereoselective [2+2] cycloadditions

with a chiral auxiliary: K. Langer, J. Mattay J. Org. Chem. 1995, 60, 7256-7266.



Chiral ligands in the [2+2] cycloaddition



(+/-)

< 5% ee



R=*i*Pr, Et

K. Langer, J. Mattay J. Org. Chem. 1995, 60, 7256-7266.

Other Cycloadditions



Y. Kubo, J. Am. Chem. Soc. 1992, 114, 7660.

Arene-Olefin Cycloaddition: Cedrene



P. A. Wender, J.J. Howbert, J. Am. Chem. Soc. 1981, 103, 688-690.

Photochemistry of Carbonyl Group: Norrish-I



Chiral solvents



D. Seebach et al., Chem. Ber. 1977, 110, 2316-2333.

Photochemistry of Carbonyl Group: Norrish-II

3) intramolecular hydrogen abstraction



4) [2 + 2] cycloaddition



Norrish-II

Abstraction of hydrogen in the γ position.



Cycloaddition



The reaction is faster with electon-rich alkenes

D.C: Neckers, *J. Org. Chem.* **1997**, *6*2, 564. Review: T. Bach, *Synlett* **2000**, *1*2, 1699.



S.L. Schreiber, J. Am. Chem. Soc. 1984, 15, 4186.

Paterno-Büchi reaction

Photoreaction of Enones

1) α -hydrogen abstraction



2) [2 + 2] cycloaddition



[2+2] Cycloaddition: Longifolene



W. Oppolzer, T. Godel, J. Am. Chem. Soc. 1978, 100, 2583-2584.

[2+2] Cycloaddition

First example of asymmetric [2+2] cycloaddition





88% (88% ee)

T. Bach, Angew. Chem. Int. Ed. 2000, 39, 2302

[2+2] Cycloaddition: Isocomene



M.C. Pirrung, J. Am. Chem. Soc. 1979, 101, 7130-7131.

[2+2] Cycloadditon: Ingenol



J.D. Winkler, M.B. Rouse, M.F. Greany, S.J. Harrison, Y.T. Jeon, *J. Am. Chem. Soc.* **2002**, *124*, 9726-9728.

Photoreaction of Enones

3) rearrangement



Use of circularly polarized light: *E*/Z isomerization



Y. Inoue et al., 1st Osaka Intl. Symp. Asym. Photochem. 2001, L 106.

Diastereoselective enolization/protonation



Piva, O. *J. Org. Chem.* **1995**, *60*, 7879-7883. Bargiggia, F.; Dos Santos, S.; Piva, O. *Synthesis* **2002**, 427-437. Bach, T.; Höfer, F. *J. Org. Chem.* **2001**, *66*, 3427-3434.

Photoreaction of Morita-Baylis-Hillman Product



Modification of Enone: Morita-Baylis-Hillman Reaction



Photoreaction of Morita-Baylis-Hillman Product



\mathbb{R}^1	R^2	yield (%) ^a	R^1	R^2	yield (%) ^a
Me	Ph	53	Ph	Ph	53
	<i>p</i> -MeOPh	41 (43)		Me	62
	<i>p</i> -MePh	55 (57)		Et	50
	<i>p</i> -CIPh	66 (82)	MeO	Ph	decomp.
	<i>p</i> −CF ₃ Ph	34 (41)			

^a Value in parenthesis is based on recovery of substrates



Mechanism of Photoreaction of Baylis-Hillman Product



Mechanism of Photoreaction of Baylis-Hillman Product



Photoreaction of Cyclic Baylis-Hillman Product



Photoreaction of Vinylogous Baylis-Hillman Product







		Yield	Yield (%)	
R	R'	1	2	
C_6H_5	Н	63	-	
CH_3	Н	26	-	
CH_3CH_2	Н	30	-	
CH ₃	C_6H_5	17	27	

Strategy of Asymmetric Photoreaction of Baylis-Hillman



Asymmetric Photoreaction of Baylis-Hillman Product





Asymmetric Supercage





Photoderacemization with chiral sensitizers

Photoderacemization unique to photochemistry (otherwise forbidden by thermodynmics !)

Only significant examples: allenes and sulfoxides:



H.B. Kagan, J.C. Fiaud, Top. Stereochem. 1978, 10, 175-285.

Absolute asymmetric synthesis: the anisotropy factor

Some chiral molecules absorb left-handed and right-handed circularly polarized light (CPL) with different extinction coefficients. This can be measured by the CIRCULAR DICHROISM. One can define the ANISOTROPY FACTOR: g



At the photostationary state (equilibrium), the asymmetric induction **cannot** *exceed* the g factor ! Balavoine, G.; Moradpour, A.; Kagan, H. B. J. Am. Chem. Soc. **1974**, *96*, 5152-5158.

Circularly polarized light can be produced by using special optical devices:

How to make circularly polarized light?



Figure 1. CPL irradiation apparatus: (a) lamp house (Model UI502Q, Ushio); (b) 500 W ultrahigh pressure Hg lamp (Model USH-500SC, Ushio); (c) collimator lens; (d) water layer (quartz cell, path (l) = 2 cm, transmittance at λ = 313 nm (Tr) = ca. 100%); (e) interference filter for 313 nm (Model BPF313 JASCO, FWHM = 11 nm, Tr = 60%) or 290–390 nm solution filter (l = 2 cm, Tr = 17%, see ref 7); (f) polarizing filter (Model SPFU-30C, Sigma Koki, Tr = 17%); (g) quarter-wavelength plate (JASCO, Tr = 90%, 99% CPL at λ = 313 nm); (h) reaction vessel (Model S15-SQ-10, GL Science, 1 × 1 × 4.5 cm³, Tr = 85%); (i) photometric measurement of 313 nm CPL (>1.0 mW/cm²) was performed at this point using a photodiode (Model PD300-UV-SH, OPHIR as the head with a NOVA-II powermeter for λ = 313 nm).

Kawasaki, T.; Sato, M.; Ishiguro, S.; Saito, T.; Morishita, Y.; Sato, I.; Nishino, H.; Inoue, Y.; Soai, K. *J. Am. Chem. Soc.* **2005**, *127*, 3274-3275.

Hybrid Strategy of Asymmetric Photoreaction



"High yield & enantioselectivity"

Asymmetric Photoreaction of Baylis-Hillman Product



Effect of Chiral Controller



1) Yield was determined by ¹H NMR using cyclohexene as an internal standard

Complexation of Chiral Controller in γ **-CD**



Asymmetric Photoreaction induced by (S,S)-DPEN / γ-CD



1)This number is obtained from the following equation: recovered substrate $ln[(1-c)(1-ee_{recov})]/ln[(1-c)(1+ee_{recov}), c=ee_{recov}/(ee_{recov}+ee_{prod}) k_S / k_R^{-1} = 3.3$

Triple Chiral Recognition Model



Enantiospecific Photoreaction by (S,S)-DPEN / γ-CD



Enantiospecific Photoreaction by (*R*,*R*)-DPEN / γ-CD



*Based on reacted substrates

Enantiospecific Photoreaction of Baylis-Hillman Product



Photoreaction of Baylis-Hillman Product

