Enantioselective Intramolecular [2 + 2] Photocycloaddition Reaction of *N*-Allyl-3-oxo-1-cyclohexenecarboxamides in Inclusion Crystals with Chiral Host Compounds

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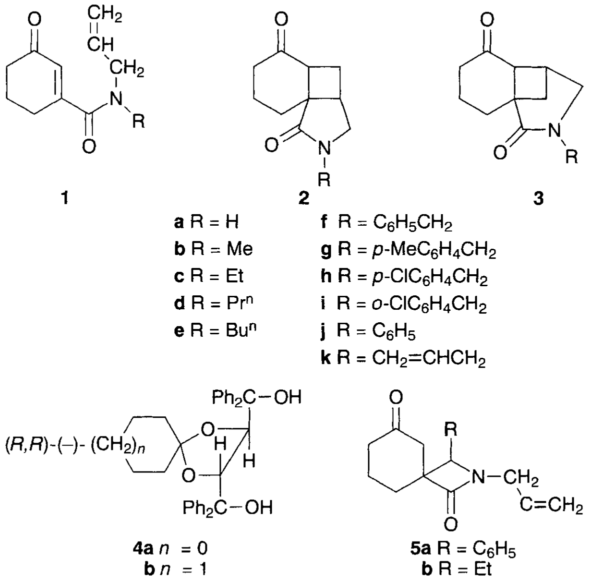
Photoirradiation of powdered inclusion crystals of the title compounds with chiral host compounds derived from tartaric acid in a water suspension give the optically active [2 + 2] photocyclisation products.

It has been reported that photoirradiation of *N*-allyl-3-oxo-1-cyclohexenecarboxamides **1** in MeCN gives the intramolecular [2 + 2] photocyclisation product 3-azatricyclo-$[5.4.0.0^{1,5}]$undecane-3,4-dione **2**, which is an important synthon of various products.[1] However, photoreaction of the *N*-methyl (**1b**) and *N*-allyl (**1k**) derivatives of **1a** gave the corresponding regioisomers, *N*-methyl- (**3b**) and *N*-allyl-3-azatricyclo-$[4.4.1.0^{1,6}]$undecane-2,7-dione (**3k**), respectively, along with **2b** and **2k**.[1]



In order to carry out the reaction not only regioselectively but also enantioselectively, we studied the photoreactions of inclusion crystals of **1** with the chiral hosts **4**, derived from tartaric acid. We found that the photoirradiation of *N*-alkyl derivatives of **1b–i** in (*R*,*R*)-(−)-*trans*-2,3-bis(hydroxydiphenylmethyl)-1,4-dioxaspiro[4.4]nonane **4a** and (*R*,*R*)-(−)-*trans*-2,3-bis(hydroxydiphenylmethyl)-1,4-dioxaspiro[5.4]decane **4b**[2] proceeds regio- and enantio-selectively to give optically active **2b–i**. In particular, the enantioselectivities of the photocycloaddition reactions of *N*-benzyl derivatives of **1f–i** were very high and the corresponding optically pure products **2f–i** were obtained.

A powdered 1 : 2 inclusion crystal of the *N*-benzyl derivative of **1a** (**1f**) with **4a** (2.33 g), prepared by recrystallisation of both components from diethyl ether as colourless crystals (mp 115–118 °C),† was suspended in water (120 ml) containing alkyl sulfate (0.1 g) as a surfactant, and the suspension was irradiated by a 100 W high pressure Hg lamp with stirring at room temperature for 10 h. The reaction mixture was filtered, dried, and column chromatographed on silica gel using AcOEt–hexane (1 : 1) as eluent to give (−)-**2f** of 100% e.e. (0.45 g, 90% yield, mp 73–74 °C, $[\alpha]_D$ −115 (*c*. 0.4, MeOH)). The structure of **2f** was elucidated by X-ray analysis.[3]‡ The optical purity was determined by HPLC using a column containing the chiral solid phase Chiralcel OD.§ Similar photoirradiation of a 1 : 2 inclusion compound of **1f** with **4b** gave (−)-**2f** of 100% e.e. in 87% yield (Table 1).¶ These highly selective photoreactions of **1f** in the inclusion crystal with **4** are valuable, since photoirradiation of **1f** in MeCN gives a mixture of *rac*-**2f** and the *rac*-spiramic β-lactam, *N*-allyl-2-aza-3-phenylspiro[3.5]nonane-1,6-dione **5a**.[1]

In the inclusion crystal of **1f** with **4**, the allyl group of **1f** would be arranged above (or below) the cyclohexenone ring, and the [2 + 2] photocycloaddition reaction occurs at the upside

Table 1 Photocyclisation reaction of **1** in a 1 : 2 inclusion compound with **4** in a water suspension

Host 4	Guest 1	Mp of inclusion compound[a] /°C	Irradiation time/h	Product	Yield (%)	$[\alpha]_D$ (*c*, MeOH)	Optical purity[b] (% ee)
4a	**1a**	—	—	—	—	—	—
4b	**1a**	—	—	—	—	—	—
4a	**1b**	129–131	10	(−)-**2b**	32	−26 (0.2)	65
4b	**1b**	164–167	10	(−)-**2b**	17	−25 (0.3)	68
4a	**1c**	127–129	100	(−)-**2c**	40	−7 (1.4)	14
4b	**1c**	149–152	100	(−)-**2c**	30	−18 (1.2)	67
4a	**1d**	115–117	10	(−)-**5b**	38	−20 (0.4)	64
4b	**1d**	138–140	10	(−)-**5b**	69	−31 (0.5)	97
4a	**1e**	111–113	10	(−)-**2e**	13	−27 (0.3)	28
4b	**1e**	131–133	10	(−)-**2e**	25	−95 (0.7)	53
4a	**1f**	115–118	10	(−)-**2f**	90	−115 (0.4)	100
4b	**1f**	158–160	10	(−)-**2f**	87	−110 (0.8)	100
4b	**1g**	154–156	10	(−)-**2g**	56	−102 (3.2)	100
4b	**1h**	148–150	10	(−)-**2h**	42	−78 (1.6)	100
4a	**1i**	101–103	10	(−)-**2i**	53	−89 (0.6)	100
4a	**1j**	96–98	20		0	—	—
4b	**1j**	121–122	20		0	—	—

[a] All guest–host inclusion compounds are formed in a 1 : 2 guest : host ratio. [b] Optical purities were determined by HPLC using a column containing the optically active solid phase Chiralcel OD.§

(or downside) of the cyclohexenone ring. The arrangement of **1f** is controlled by the chirality of host **4**. These will be clarified by X-ray analytical studies in the future.

Similar irradiation of powdered 1 : 2 inclusion compounds of **1g–i** with **4** in a water suspension gave the corresponding optically pure products **2g–i** in the yields given in Table 1. Although phenyl-substituted derivative **1j** also formed 1 : 2 inclusion compounds with **4a** and **4b**, these were inert to the photoreaction.

However, the [2 + 2] photocyclisation reaction of **1b,c** and **1e** (which are substituted by an alkyl group on the nitrogen atom) in a 1 : 2 inclusion crystal with **4** again gave optically active **2b,c** and **2e**, respectively, although the enantioselectivities were relatively low compared with those of **1f–i** (Table 1). Interestingly, photoirradiation of a 1 : 2 inclusion compound of **1d** (which is substituted with propyl group) and **4** gave the spiramic β-lactam **5b**. In the case of a 1 : 2 inclusion compound of **1d** and **4b**, (−)-**5b** of 97% e.e. was produced in 69% yield by photoirradiation for 10 h (Table 1). The structure of **5b** was elucidated by ^{1}H NMR, which shows the CH_3 protons of the ethyl group at δ 0.9 as a triplet signal (*J* 7 Hz) and CH_2=CH protons of the allyl group at δ 5.4 as a complex multiplet signal. It is not clear why **1d** is special and gives the spiramic β-lactam **5b** but not the tricyclic compound **2d**. This also should be clarified by an X-ray structural analysis of the 1 : 2 inclusion crystal of **1d** with **4**.

In all cases, the chiral host **4** was recovered unchanged and was used again. This method is very economical.

The unsubstituted derivative on the nitrogen atom, **1a**, did not form an inclusion compound with **4**. Even if an inclusion compound of **1a** with any other host is formed, photocycloaddition reaction would not be expected since it has been reported that **1a** is inert to photoirradiation in MeCN.[1]

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Footnotes

† Satisfactory elemental analyses were obtained for all new host–guest inclusion complexes and photocyclisation products. Host : guest ratios were also determined by measurement of ^{1}H NMR spectra of the inclusion complexes.

‡ Although the absolute configuration and stereochemistry of **2** and **5** are not determined, these will be clarified by X-ray structural analyses in the near future.

§ Chiralcel OD is available from Daicel Chemical Co. Ltd., Himeji, Japan.

¶ The mechanism of the highly enantioselective photocyclisation reaction of **1** in the inclusion crystal with **4** will be studied by X-ray structural analysis of the inclusion complex in the near future.

References

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