Photocyclisation of Phenylglyoxylamides as Inclusion Complexes with an Optically Active Host Derived from Tartaric Acid: Delicate Dependence on the Substituent of the Host and Glyoxylamide

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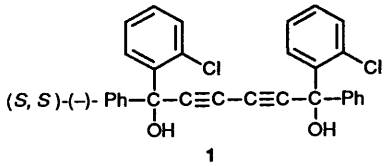
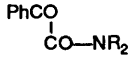
Optically active β-lactams and/or oxazolidinones have been obtained selectively by photoirradiation of a 1:2 inclusion complex of phenylglyoxylamide with an optically active host derived from tartaric acid. Delicate selectivity which is dependent on substituents in the phenylglyoxylamide and the host is described.

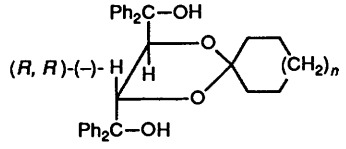
Two enantioselective photocyclisations of phenylglyoxylamides to β-lactam derivatives have been reported so far, namely, photoconversion of *N,N*-dimethylphenylglyoxylamide **2a** as an inclusion complex with optically active 1,6-bis(*o*-chlorophenyl)-1,6-diphenylhexa-2,4-diyne-1,6-diol **1**[1] and of *N,N*-diisopropylphenylglyoxylamide **2b** in its own chiral crystal[2] to the corresponding optically almost pure β-lactam.



1



2
a R = Me
b R = Pr^i

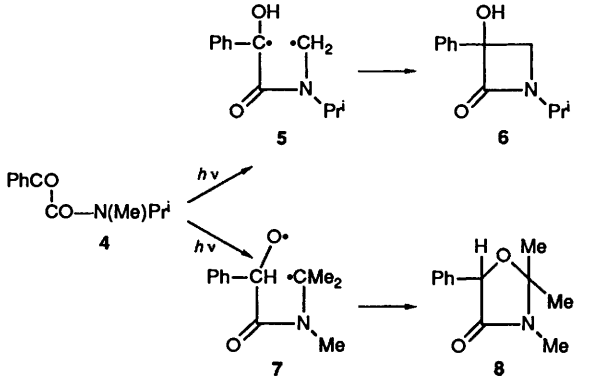


3
a *n* = 0
b *n* = 1

Recently we found that photocyclisation of the *N,N*-dialkylphenylglyoxylamides **2a**, **4**, **11**, **13** as inclusion complexes of the optically active hosts **3a** and **3b** derived from tartaric acid[3] is controlled by changing the substituents of the host and the phenylglyoxylamide.

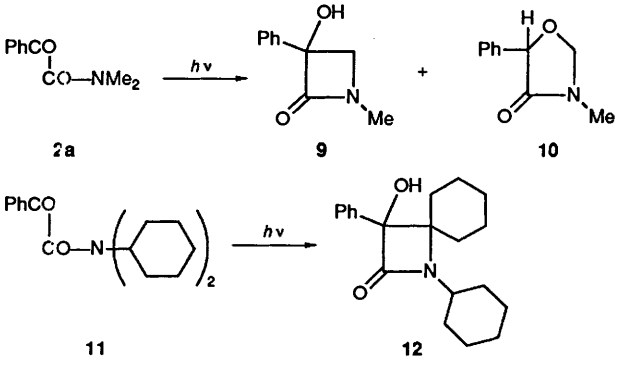
Host–guest inclusion complexes of **3a** and **3b** with phenylglyoxylamide were prepared by recrystallisation of the components from ether and benzene, respectively, since **3a** and **3b** form inclusion complexes with benzene and ether, respectively. All the inclusion complexes are colourless crystals with sharp melting points and a host–guest ratio of 2:1. For example, a solution of **3a** (2.37 g, 4.8 mmol) and **4** (0.48 g, 2.3 mmol) in ether (20 cm^3)–hexane (10 cm^3) was kept in the dark for 1 day to give a 2:1 inclusion complex of **3a** and **4** as colourless needles (1.52 g, 53%, m.p. 100–101 °C). Similarly, **3a** (1.5 g, 3 mmol) and **13b** (0.33 g, 1.5 mmol) in ether–hexane gave a 2:1 inclusion complex of **3a** and **13b** as colourless needles (1.28 g, 70%, m.p. 99–100 °C).

Powdered inclusion complexes of **2a**, **4** and **11** with **3** upon irradiation gave β-lactams and/or oxazolidinones in the optical and chemical yields shown in Table 1. In the case of **4**, the methyl and isopropyl groups are concerned only in the photoreaction leading to the β-lactam **6** and the oxazolidinone **8**, respectively (see Scheme 1). Enantiocontrol of the reaction was



Scheme 1

also achieved although the efficiency was not very high. For example, irradiation of the powdered 2:1 inclusion complex of **3a** and **4** (1.52 g) with a 400 W high-pressure Hg-lamp at room temperature for 50 h gave, after purification by column chromatography on silica gel, (−)-**6** of 100% ee {0.03 g, 11%, m.p. 105–107 °C, $[\alpha]_D$ −22† (*c* 0.195, MeOH)} and (−)-**8** of 39% ee {0.05 g, 20%, as an oil, $[\alpha]_D$ −21 (*c* 0.60, MeOH)}. On the other hand, photoirradiation of **4** in MeCN for 50 h gave *rac*-**8** (38%). Photoirradiation of **11** in the solid state and in MeCN for 12 and 50 h, respectively, gave *rac*-**12** in 53 and 11% yields, respectively.



In the case of **2a**, the photoreaction was controlled more efficiently. Irradiation of the complex of **2a** with **3a** gave (−)-**12** of 67% ee and (−)-**10** of 100% ee in 40 and 55% yields, respectively (Table 1). However, similar irradiation of the

† $[\alpha]_D$ Values recorded in units of 10^{-1} deg cm^2 g^{-1}.

Table 1 Photoreaction of the phenylglyoxylamides **2**, **4** and **11** as inclusion complexes with the host **3**

Host	Amide	Reaction time/h	Product					
				Yield (%)	% ee		Yield (%)	% ee
3a	**4**	50	(−)-**6**	11	100	(−)-**8**	20	39
3b	**4**	12	(+)-**6**	17	61	(−)-**8**	71	43
3a	**2a**	27	(−)-**9**	40	67	(−)-**10**	55	100
3b	**2a**	30	(−)-**9**	40	100	—	—	—
3b	**11**	60	(+)-**12**	21	54	—	—	—

Table 2 Photoreaction of the phenylglyoxylamides **13** as inclusion complexes with the host **3**[a]

Host	Amide	Product								
		14	Yield (%)	% ee	**15**	Yield (%)	% ee	**16**	Yield (%)	% ee
3a	**13a**	(+)-**14a**	32	44	(+)-**15a**	17	96	(−)-**16a**	28	95
3b	**13a**	(+)-**14a**	34	95	(+)-**15a**	15	100	(−)-**16a**	9	52
3a	**13b**	—	—	—	—	—	—	(−)-**16b**	100	100
3b	**13b**	—	—	—	—	—	—	(−)-**16b**	100	100

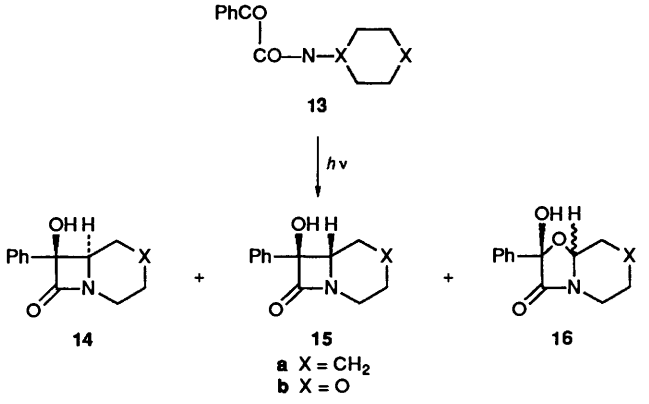
[a] All the photoreactions were carried out for 50 h.

complex of **2a** with **3b** gave (−)-**9** of 100% ee selectively. The complex of **11** with **3b** also gave (−)-**11** selectively upon the irradiation, although enantioselectivity was not high. However, **3a** did not form a complex with **11**.

More interesting selectivity was observed for the photocyclisation of the phenylglyoxylamides **13a** and **13b** which were derived from piperidine and morpholine, respectively. Photoirradiation of the complex of **13a** with **3a** for 50 h gave a mixture of *cis*-[(+)-**14a**] and *trans*-β-lactam [(+)-**15a**], and oxazolidinone [(−)-**16a**] in the optical and chemical yields shown in Table 2. Since the photoreaction of a 1:1 inclusion complex of **13a** with **1** gives **14a** of 62.5% ee and **15a** of 95% ee,[4] the present photoreaction is relatively non-selective. However, photoreaction of **13b** as an inclusion complex both with **3a** and **3b** proceeded very selectively and gave **16b** of 100% ee in quantitative yield (Table 2). For example, irradiation of the powdered 2:1 inclusion complex of **3a** and **13b** (1.28 g) for 50 h at room temperature gave (−)-**16b** of 100% ee as colourless prisms (0.33 g, 100% yield, m.p. 118–120 °C, $[\alpha]_D$ −5.0 [*c* 0.65, MeOH]. Although the *cis* and *trans* stereochemistry of **16a** and **16b** was not determined each was isolated as a single pure product. Photoreaction of a 1:1 complex of **13b** with **1** gives **14b** of 55.8% ee and **15b** of unknown optical purity.[4]

It is curious that the photoreaction of **13** is changed dramatically upon replacement of the cyclohexyl group by a morpholino group. This constitutes an interesting example of delicate molecular recognition in an inclusion complex and will be further investigated by an X-ray crystal structure analysis.

Nevertheless, it is very clear that the host **3** controls the photoreaction so as to produce more of the oxazolidinone **16** rather than β-lactam **14** and **15**, since **13a** and **13b** give *cis*-β-lactam **14a** and **14b**, respectively, upon direct irradiation in the solid state. For example, irradiation of powdered **13a** and **13b** in the solid state for 50 h gave only *rac*-**14a** (50%) and *rac*-**14b** (47%), respectively in the yields shown in parentheses.



Acknowledgements

The authors are grateful to the Ministry of Education, Science and Culture, Japanese Government for the Grant-in-Aid for Co-operative Research (A) No. 03303002.

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Paper 2/01619B
Received 27*th March* 1992
Accepted 13*th April* 1992