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[8] Several geometrical isomers are possible for complexes **3**. In $CDCl_3$, **3** is a mixture of *trans-anti* and *trans-syn* isomers, which correspond to a *trans* arrangement of carbene moieties along the Pd ··· Pd axis and a relative *syn* or *anti* arrangement of the diethylamino groups relative to the coordination plane. The compound first formed is tentatively assigned (the assignment might be reversed) as *trans*-**3**, which (both isomers) slowly isomerizes to the *cis* (*syn* and *anti* isomers) and eventually undergoes hydrolysis when kept in solution for several days.
[9] Decomposition data for **3** (%) after seven days in $CDCl_3$ at room temperature: *trans*-**3** (25.9), *cis*-**3** (26.9), **5** (19.5), **7** (27.7).
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Asymmetric Baeyer – Villiger Reaction with Hydrogen Peroxide Catalyzed by a Novel Planar-Chiral Bisflavin**

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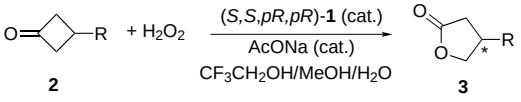
Metal-free organocatalytic reactions, especially enantioselective ones, have attracted increasing attention as a complement to metal-catalyzed and enzyme-catalyzed reactions.[1] Organocatalytic reactions have several advantages, for example, the availability of structural diversity of the catalysts in optically pure form and their stability under aerobic and aqueous conditions, and the catalysts are often more stable than enzymes.

In 1989 we demonstrated that 5-alkylated flavins can be used as organocatalysts for oxidations based on the precise kinetic study on the recycling step of flavoenzymes.[2] Thus, the flavin-catalyzed biomimetic oxidations of sulfides and amines with hydrogen peroxide occurs highly efficiently to give the corresponding sulfoxides and nitrones, respectively. A novel method for enantioselective oxidation with organocatalysts can be developed if one can design suitable chiral flavin catalysts. We report herein that a flavin-catalyzed asymmetric Baeyer – Villiger reaction of cyclobutanones can be performed with up to 74% *ee* [Eq. (1)].



2 3 (1)

Much attention has been focused on the asymmetric Baeyer – Villiger reaction, because this is the direct route to obtain optically active lactones from cyclic ketones.[3] Transition-metal catalysts in the asymmetric Baeyer – Villiger reactions of cyclic ketones have been studied extensively: copper with a combination of molecular oxygen and aldehyde,[4] platinum with H_2O_2,[5] titanium with *tert*-butyl hydroperoxide,[6] cobalt with urea · H_2O_2,[7] and magnesium[8] and aluminum[9] with cumene hydroperoxide; selectivities of up to 77% *ee* were observed. Enantioselective Baeyer – Villiger reactions have been also performed by using microbial whole cell cultures[10] as well as purified enzymes[11] with stoichiometric amounts of NADPH as a cofactor.

Catalytic Baeyer – Villiger reactions have been shown to occur in the presence of flavin catalyst,[12] which is similar to our catalyst.[2] Therefore, we wanted to design chiral flavin catalysts for enantioselective oxidation reactions. Planar-chiral flavins have been prepared and used for the asymmetric oxidation of sulfides.[13, 14] However, the synthesis of the catalysts is very tedious because of the need for optical resolution with preparative HPLC. To prepare chiral flavin catalysts simply without optical resolution, we designed planar-chiral C_2-symmetric bisflavinium perchlorate **1** (Scheme 1), in which each of the flavin moieties blocks one plane of the other flavin moiety. The bisflavin catalyst **1** was prepared in three steps without resolution. Treatment of (*S*,*S*)-1,2-diaminocyclohexane (**4**) with *o*-fluoronitrobenzene (**5**) gave (*S*,*S*)-1,2-bis[(2-nitrophenyl)amino]cyclohexane (**6**) in 77% yield. Catalytic hydrogenation of **6** over palladium on charcoal and subsequent treatment with 3-methylalloxan[15] gave C_2-symmetric bisflavin **7** in 90% yield [m.p. 223.5 – 224.6 °C; $[\alpha]_D^{25} = +401$ ($c = 0.20$ in $CHCl_3$)] in diastereomerically pure form. The stereochemistry was determined by difference NOE experiments of **7**;[16] irradiation of the H^b proton ($\delta = 8.38$ ppm) caused a 20% enhancement of the signal for H^a ($\delta = 7.30$ ppm) and caused no detectable enhancement of other signals on the cyclohexane ring, from

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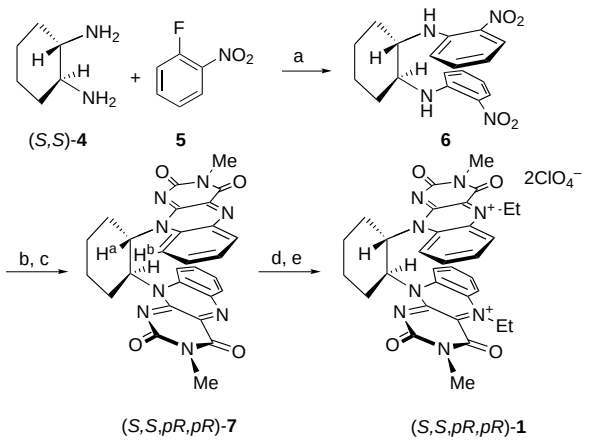

Scheme 1. Synthesis of **1**. a) K_2CO_3, EtOH, reflux, 36 h, 77%; b) H_2, Pd/C, AcOH, room temperature, 3 h; c) 3-methylalloxan, $B(OH)_3$, AcOH, 10 h, 90% over two steps; d) CH_3CHO, $NaBH_3CN$, $Na_2S_2O_4$, DMF, 60 °C, 3 h; e) $HClO_4$, $NaNO_2$, $NaClO_4$, H_2O, 1 h, 80% over two steps. DMF = *N*,*N*-dimethylformamide.

which the (*S*,*S*,*pR*,*pR*) stereochemistry can be deduced. This diastereomer (of three possibilities) was obtained exclusively as a result of rotational restriction between two flavin moieties. The energy minima of the three possible diastereomers were calculated by the semi-empirical molecular-orbital method (AM1).[17] The energy of (*S*,*S*,*pR*,*pR*)-**7** is the lowest and is 4.6 and 6.5 kcal mol^{-1} lower than that of (*S*,*S*,*pS*,*pS*)-**7** and (*S*,*S*,*pR*,*pS*)-**7**, respectively. The violet catalyst **1** was obtained upon treatment of **7** with ethanal and $NaBH_3CN$ and subsequent treatment with $HClO_4$, $NaNO_2$, and $NaClO_4$ [m.p. 220 °C (dec.)].[18] The antipode (*R*,*R*,*pS*,*pS*)-**7** was also prepared from (*R*,*R*)-**4** in a similar manner.

Treatment of 3-phenylcyclobutanone (**2a**; R = Ph) with a solution of hydrogen peroxide (30%) in the presence of bisflavin (*S*,*S*,*pR*,*pR*)-**1** (10 mol%) at −30 °C gave optically active 3-phenyl-γ-butyrolactone (**3a**). The *S* configuration of **3a** was confirmed by comparison of the optical rotation with that reported in the literature.[19] The enantiomeric excess of **3a** was determined by HPLC analysis with a chiral column (Daicel Chiralpak AS).

The enantioselectivity is strongly dependent on the solvent used. Representative results of the solvent effect on the catalyzed oxidation of **2a** are summarized in Table 1. Higher enantioselectivities were obtained when a protic solvent was used. The reaction in MeOH or a MeOH/water mixture (2:1) gave the lactone (*S*)-**3a** with 35 and 45% *ee*, respectively, in lower yields, because of the formation of the dimethyl ketal of **2a** (Table 1, entries 3 and 4). The reaction in trifluoroethanol or 1,1,1,3,3,3-hexafluoro-2-propanol gave (*S*)-**3a** with low enantioselectivity, because the noncatalyzed reaction with hydrogen peroxide occurs fast.[20] When a mixture of solvents (CF_3CH_2OH/MeOH/water 6:3:1) was used, both noncatalyzed reaction and ketalization were retarded, and higher enantioselectivity (55% *ee*) was observed (Table 1, entry 7). Furthermore, a catalytic amount of AcONa was added to trap perchloric acid, which is formed from the reaction of the flavin catalyst with hydrogen peroxide.[21] Thus, the oxidation of **2a** with hydrogen peroxide in the presence of bisflavin **1**

Table 1. Effect of solvent on the bisflavin-catalyzed asymmetric Baeyer–Villiger reaction of **2a** with H_2O_2.[a]

Entry	Solvent	Yield [%]	*ee* [%][b]
1	CH_2Cl_2	13	8 (*S*)
2	MeCN	61	22 (*S*)
3	MeOH	15	35 (*S*)
4	MeOH/H_2O (2:1)	17	45 (*S*)
5	CF_3CH_2OH	89	8 (*S*)
6	CF_3CH_2OH[c]	81	31 (*S*)
7	CF_3CH_2OH/MeOH/H_2O (6:3:1)	52	55 (*S*)
8	CF_3CH_2OH/MeOH/H_2O (6:3:1)[c]	67	63 (*S*)
9	CF_3CH_2OH/MeOH/H_2O (6:3:1)[c,d]	64	62 (*R*)

[a] A mixture of **2a** (0.2 mmol), (*S*,*S*,*pR*,*pR*)-**1** (0.02 mmol), and H_2O_2 (0.3 mmol) in solvent (1 mL) was stirred at −30 °C for 6 days. [b] Determined by HPLC analysis with a chiral stationary phase (Daicel Chiralpak AS, hexane/2-propanol 9:1). [c] AcONa (0.05 mmol) was added. The reaction was carried out in 0.5 mL of solvent. [d] (*R*,*R*,*pS*,*pS*)-**1** was used as catalyst.

(10 mol%) and AcONa (25 mol%) gave (*S*)-**3a** in 67% yield with 63% *ee* (Table 1, entry 8). Without the catalyst **1** no oxidation occurred. The opposite enantiomer (*R*)-**3a** was obtained when (*R*,*R*,*pS*,*pS*)-**1** was used as a catalyst (Table 1, entry 9). A protic solvent is essential to obtain higher enantioselectivity, which indicates that the hydrophobic π–π stacking between the aromatic ring of the catalyst **1** and that of a substrate seems to play an important role in asymmetric induction.[22, 23] Such a solvent effect is not observed for the metal-catalyzed asymmetric Baeyer–Villiger reaction.[7]

Various 3-aryl-substituted cyclobutanones can be oxidized enantioselectively by using the novel chiral flavin catalyst **1** in the presence of AcONa. Representative results are summarized in Table 2. The enantioselectivity was slightly influenced by the electronic effect of the 3-arylcyclobutanones **2**. The cyclobutanone bearing *p*-bromophenyl group was converted into the lactone **2d** with 68% *ee*. 3-(4-Fluorophenyl)-γ-butyrolactone (**3f**) was obtained with 74% *ee* at −50 °C.

Table 2. Asymmetric Baeyer–Villiger reaction of 3-arylcyclobutanones catalyzed by (*S*,*S*,*pR*,*pR*)-**1**.[a]

Entry	**2**	R	Yield [%][b]	*ee* [%][c]
1	**b**	4-$MeOC_6H_4$	67	61 (+)
2	**c**	4-MeC_6H_4	53	62 (+)
3	**a**	Ph	67	63 (*S*)
4	**d**	4-BrC_6H_4	28	68 (+)
5	**e**	4-ClC_6H_4	34	66 (*S*)
6	**f**	4-FC_6H_4	55	65 (+)
7	**f**	4-FC_6H_4	17[d]	74 (+)

[a] A mixture of substrate **2** (0.6 mmol), **1** (0.06 mmol), AcONa (0.15 mmol), and H_2O_2 (0.9 mmol) in CF_3CH_2OH/MeOH/H_2O (6:3:1, 1.5 mL) was stirred at −30 °C for 6 days. [b] Determined by HPLC analysis with a chiral stationary phase, Daicel Chiralpak AS. [c] The absolute configuration was determined by comparison with reported data.[19] [d] The reaction was carried out at −50 °C.

The reaction can be rationalized by assuming the mechanism shown in Scheme 2.[2] The enantioselectivity is induced by face selectivity in the formation of the Criegee adduct. Since one face of the catalyst is completely blocked, the substrate would be attacked by the opposite side of the other

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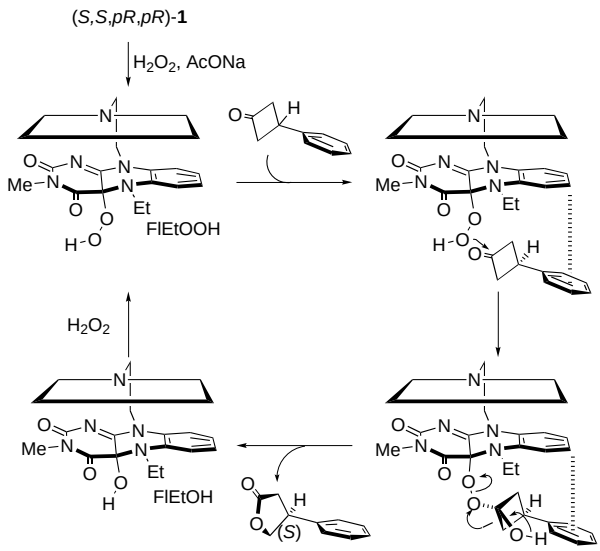

Scheme 2. Mechanism for the bisflavin-catalyzed asymmetric Baeyer–Villiger reaction.

flavin group. The asymmetric induction seems to be induced by hydrophobic $\pi-\pi$ stacking between the phenyl ring of the substrate and that of the catalyst to fix the direction of the substrate. Nucleophilic attack of the hydroperoxyflavin at the carbonyl group of the substrate occurs from the opposite side of the phenyl group of the substrate. Thus intramolecular rearrangement occurs antiperiplanar to the leaving group[3b] to give the (*S*)-γ-butyrolactone.

In conclusion, we demonstrated that novel planar-chiral bisflavinium perchlorate **1** catalyzes the asymmetric Baeyer–Villiger reaction of cyclobutanones with hydrogen peroxide to give the corresponding optically active lactones with up to 74% *ee*. This is the first demonstration that organic chiral compounds can catalyze asymmetric Baeyer–Villiger reactions, and will become a trigger to provide future environmentally friendly, clean organocatalytic oxidation reactions.

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Formation of High-Quality CdS and Other II–VI Semiconductor Nanocrystals in Noncoordinating Solvents: Tunable Reactivity of Monomers**

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Semiconductor nanocrystals are of great interest for both fundamental research and industrial development.[1, 2] The lack of adequate synthetic methods for nanocrystals of the desired quality is currently a bottleneck in this field.[3] The relatively successful approaches, including the organometallic approach[4–8] and its alternatives,[9–13] are exclusively performed in coordinating solvents. Evidently, only a few compounds can act as the coordinating solvents,[11] and this makes it extremely challenging to identify a suitable reaction system for growing high-quality nanocrystals in most cases. Here we show that noncoordinating solvents not only are compatible with the synthesis of semiconductor nanocrystals, but also provide tunable reactivity of the monomers by simply varying the concentration of ligands in the solution. The tunable reactivity of the monomers provides a necessary balance between nucleation and growth, which is the key for control over the size and size distribution of the resulting nanocrystals.[5] In practice, such tunability has great potential to promote the synthesis of various semiconductor nanocrystals to the level of that of the well-developed CdSe

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