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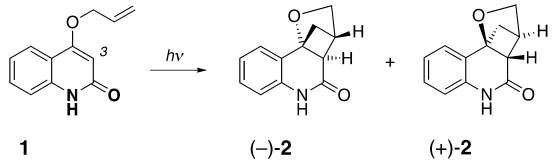
Enantioselective Intramolecular [2+2]-Photocycloaddition Reactions in Solution**

Thorsten Bach,* Hermann Bergmann, and Klaus Harms

Dedicated to Professor Horst Kessler on the occasion of his 60th birthday

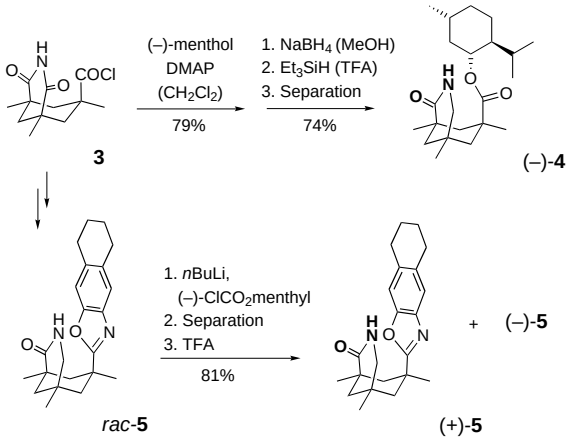
There are various approaches to obtain enantiomerically pure or enriched products from prochiral substrates by photochemical reactions in solution.[1] Whereas chiral auxiliaries which are covalently bound to one of the substrates have been successfully employed in many cases,[2, 3] chiral complexing agents which bind one substrate and thereby induce face discrimination have only been used to a limited extent.[4–8] Enantiomeric excess (*ee*) values achieved in C–C bond forming reactions based on the latter method have been moderate at best. In the solid phase however, complexes of an achiral substrate and a chiral complexing agent have been used more frequently and some excellent enantioselectivities have been recorded.[9, 10] We now report on [2+2]-photocycloaddition reactions in the presence of a chiral host, which proceeded in toluene with high enantioselectivity. Hydrogen bonds facilitate the binding of the prochiral substrate to the host and the transmission of the chiral information.

Our concept is based on the fact that prochiral lactams can coordinate to a chiral amide through their oxygen atom which acts as hydrogen acceptor and their nitrogen-bonded hydrogen atom which acts as hydrogen donor. We have recently shown that certain chiral amides derived from Kemp's triacid (1,3,5-trimethylcyclohexan-1,3,5-tricarboxylic acid) show low self-association and are therefore able to bind prochiral lactams efficiently.[11] A prochiral lactam bound to such a host is expected to undergo a stereoselective reaction. For our studies we have selected the 2-quinolone **1**, which upon irradiation with UV light cleanly yields the chiral cyclobutane (−)-**2** and its enantiomer (+)-**2** by an intramolecular [2+2]-photocycloaddition.[12] The simple diastereoselectivity of the reaction is high; only a single diastereoisomer is formed, as shown in Scheme 1.



Scheme 1. The intramolecular [2+2]-photocycloaddition reaction of the prochiral substrate **1**.

As host compounds, the bicyclic lactams (−)-**4** and (+)-**5** were prepared (Scheme 2). Association of compound **1** to the lactam unit through the atoms shown in bold would lead to an



Scheme 2. The synthesis of the enantiomerically pure host compounds (−)-**4**, (+)-**5**, and (−)-**5**. The transformation of acid chloride **3** into the racemic host *rac*-**5** is discussed in the text. (See also ref. [13]). DMAP = 4-dimethylaminopyridine, TFA = trifluoroacetic acid.

enantioface differentation in the course of the photocycloaddition, favoring enantiomer (−)-**2** (*Re* attack at carbon atom C-3). For the synthesis of host (−)-**4**, acid chloride **3**[13] was treated with enantiomerically pure (−)-menthol. Diastereoselective reduction of one carbonyl group and subsequent separation of diastereoisomers yielded compound (−)-**4** in enantiomerically pure form. The racemic benzoxazole *rac*-**5** was prepared from chloride **3** in 71 % yield by employing the corresponding *ortho*-aminophenol 3-amino-5,6,7,8-tetrahydro-2-naphthol[14] as the nucleophile according to a known procedure.[13] The resolution of enantiomers was performed by chromatographic separation of the corresponding *N*-menthyloxycarbonyllactam and its diastereoisomer. Removal of the chiral alkoxycarbonyl group yielded the enantiomerically pure host (+)-**5**[15] and its enantiomer (−)-**5**.

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Irradiation experiments with the substrate **1** in the presence of the host molecules depicted in Scheme 2 gave product **2** whose *ee* value was determined by HPLC (Table 1).[16] Host (−)-**4** was suitable for induction of enantioselectivity but the

Table 1. Intramolecular [2+2]-Photocycloaddition Reactions of **1** (Scheme 1) in the Presence of Chiral Host Compounds.[16]

Entry	Host	Equiv[a]	T [°C][b]	Yield [%]	*ee* [%][c]
1	(−)-**4**	2.1	30	74	11
2	(−)-**4**	2.3	−15	89	37
3	(+)-**5**	1	30	76	28
4	(−)-**5**	1	−15	77	−78
5	(−)-**5**	2.1	30	73	−39
6	(+)-**5**	2.6	−15	79	84
7	(−)-**5**	2.6	−60	77	−93

[a] Equivalents of chiral host. The host compounds were recovered almost quantitatively (>90%). [b] Irradiation temperature. Irradiation source at 30°C: Rayonet RPR 3000 Å. Irradiation source at −15°C and at −60°C: Original Hanau TQ 150. [c] The *ee* values were determined by chiral HPLC.

ee values remained low (entries 1, 2). As anticipated, product (−)-**2** was the predominant enantiomer formed. We suspected that the nonplanarity of the menthol ring was responsible for a comparably weak association and insufficient face differentiation. Indeed, the crystal structure of compound (−)-**4** revealed that the methyl group at the menthyl ring might interact unfavorably with an associated substrate (Figure 1).[17] The almost planar tetrahydronaphthalenoxazole

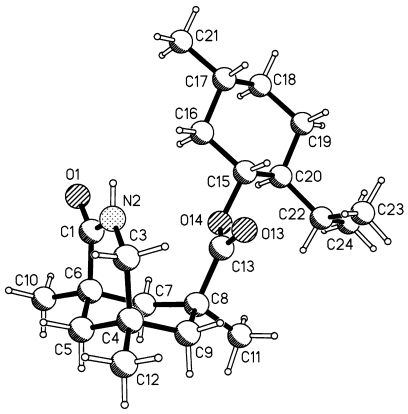
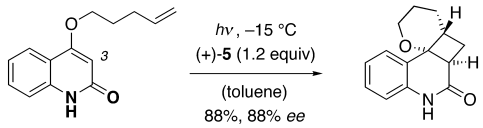


Figure 1. Structure of host (−)-**4** as a crystal.

moiety of compounds (+)-**5** and (−)-**5** should not encounter this problem. Indeed, host **5** proved superior to (−)-**4**. If employed stoichiometrically the *ee* value achieved in the photocycloaddition at −15°C was remarkably high (entry 4). Increased association can be forced by the use of more than one equivalent of the host. This led to an improvement of the *ee* values, both at 30°C (entries 3 and 5) and at −15°C (entries 4 and 6). The best value recorded so far was obtained at −60°C (entry 7). The absolute configuration of (+)-**2** (obtained by irradiation in the presence of (−)-**5**) was proven by single-crystal X-ray crystallography of its *N*-menthyloxycarbonyl derivative.[18]

The application of the enantioselective photocycloaddition is not restricted to the formation of the crossed photocycloaddition product **2**. A high enantiomeric excess was also recorded in the photocycloaddition of substrate **6**[12] which was converted enantioselectively into cyclobutane (−)-**7** (Scheme 3). The product (88% *ee*) was isolated in 88% yield. Its absolute configuration was assigned based on the assumption of *Re* attack at C-3.



6 (−)-**7**

Scheme 3. The intramolecular [2+2]-photocycloaddition reaction of the prochiral substrate **6**.

In summary, the first highly enantioselective [2+2]-photocycloaddition reactions in solution have been described. 2-Quinolones **1** and **6** yield the corresponding photocycloaddition products (−)-**2** and (−)-**7** in the presence of the chiral host compound (+)-**5**. The use of this host in related photochemical reactions of lactams is likely to yield similarly high enantioselectivities. Experiments along these lines are currently under way in our laboratory.

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[15] The absolute configuration of the tetrahydronaphthalenoxazole derivative (+)-**5** was concluded from comparison of its optical rotation ($[\alpha]_D^{20} = +7.4$; $c = 1$ in $CHCl_3$) with the analogous benzoxazole derivative[13] ($[\alpha]_D^{20} = +7.4$; $c = 2$ in $CHCl_3$) and by the absolute configuration of the irradiation product **2**.
[16] The reactions were conducted at the indicated temperature with toluene as the solvent (0.15 M solution of **1**). Further details regarding the irradiation procedure can be found in: T. Bach, J. Schröder, *J. Org. Chem.* **1999**, *64*, 1265 – 1273. The *ee* values ($ee = [(-)\text{-}\mathbf{2} - (+)\text{-}\mathbf{2}]/[(-)\text{-}\mathbf{2} + (+)\text{-}\mathbf{2}]$) were determined by HPLC analysis (column: Chiracel OD; eluent: hexane/2-propanol, 92/8) of the crude product mixture. The separation of host and product is possible by flash chromatography (pentane/*tert*-butylmethylether, 1/2). Both enantiomers of the host **5** were employed. Naturally, the direction of the face discrimination changes if (+)-**5** is replaced by (−)-**5**.
[17] Crystal data of host (−)-**4** ($C_{22}H_{37}NO_3 \cdot CH_2Cl_2$, $M_r = 448.45$): crystal size $0.3 \times 0.3 \times 0.15$ mm^3, orthorhombic, space group $P2_12_12_1$, $a = 852.0(1)$, $b = 1212.3(1)$, $c = 2410.5(1)$ pm, $V = 2489.9(4)$ Å^3, $\rho_{calcd} = 1.196$ g cm^{-3}, $Z = 4$, $F(000) = 968$, $\mu = 2.516$ mm^{-1}, Enraf-Nonius-CAD4 diffractometer, $\lambda = 1.54178$ Å, ω-scans, 4875 measured reflections ($-h, +k, \pm l$), $\Theta_{max} = 65°$, 4245 independent and 3575 observed reflections [$F \geq 4\sigma(F)$], 272 refined parameters, $R = 0.0608$, $wR^2 = 0.2080$, max. residual electron density 0.22 e Å^{-3}, direct methods, carbon-bound hydrogen atoms calculated, N–H atom refined. Crystallographic data (excluding structure factors) for the structure reported in this paper have been deposited with the Cambridge Crystallographic Data Centre as supplementary publication no. CCDC-142268. Copies of the data can be obtained free of charge on application to CCDC, 12 Union Road, Cambridge CB2 1EZ, UK (fax: (+44) 1223-336-033; e-mail: deposit@ccdc.cam.ac.uk).
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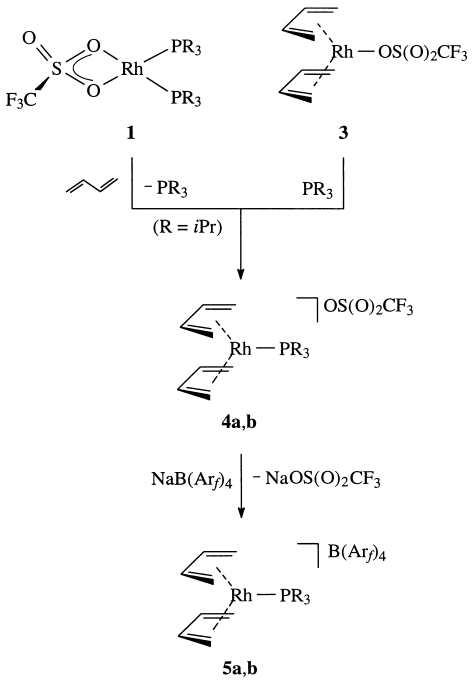
The Rhodium-Catalyzed Cyclotetramerization of Butadiene: Isolation and Structural Characterization of an Intermediate**

Marco Bosch, Maurice S. Brookhart, Kerstin Ilg, and Helmut Werner*

We have recently shown that the square-planar sulfonatorhodium(I) complex *cis*-[Rh{η^2-$O_2S(O)CF_3$}($PiPr_3$)$_2$][1] (**1**) is an active catalyst for the polymerization of butadiene.[2] A remarkable side product of this process was found to be 1,5,9,13-cyclohexadecatetraene. Although in the initial studies the overall yield of this cyclotetramer was rather low (< 5 %), we became interested to find out whether there could be a relationship between this reaction and the well known, "naked-nickel"-catalyzed, cyclo*tri*merization of butadiene discovered by Wilke et al.[3, 4] Since a key step in the reaction leading to *all-trans*-1,5,9-cyclododecatriene is the oxidative coupling of two butadiene ligands in the coordination sphere of nickel(0) to give the labile octadienediylnickel(II) derivative [Ni(η^3:η^3-C_8H_{12})],[4] we focused our efforts on detecting or, if possible, even isolating a related rhodium complex containing a C_8H_{12} ligand.

In a first attempt to elucidate the mechanism of the rhodium-catalyzed cyclo*tetra*merization of butadiene, we treated the triflate [Rh{μ-$O_2S(O)CF_3$}(C_8H_{14})$_2$]$_2$ (**2**) with C_4H_6 and isolated the neutral bis(butadiene)rhodium(I) complex [Rh{η^1-$OS(O)_2CF_3$}(*s-cis*-η^4-C_4H_6)$_2$] (**3**) in almost quantitative yield.[5] Since it was known that the addition of one equivalent of tricyclohexylphosphane to the nickel(0) compound [Ni(*s-cis*-η^4-C_6H_{10})$_2$] induces the coupling of the two coordinated 2,3-dimethylbutadiene ligands to generate the substituted octadienediylnickel(II) complex [Ni(η^1:η^3-$C_{12}H_{20}$)(PCy_3)],[6] we also treated compound **3** with PCy_3. However, under the conditions used (acetone, 5 min, 25 °C), instead of a C–C coupling a substitution of the coordinated triflate occurred and the ionic product [Rh(*s-cis*-η^4-C_4H_6)$_2$(PCy_3)]OTf (**4b**) was formed (Scheme 1, $OS(O)_2CF_3$ = OTF). The triisopropylphosphane analogue **4a**, which like **4b** is a white, moderately air-stable solid, is accessible in a similar way.[5] Salt metathesis of **4a** and **4b** with $NaB(Ar_f)_4$ (Ar_f = 3,5-bis(trifluoromethyl)phenyl) affords the corresponding compounds **5a** and **5b** in 83 and 86 % yield, respectively.

Although both **4a** and **4b** are stable in solution at room temperature and thus can be characterized by ^{1}H, ^{13}C{^{1}H},



Scheme 1. **a**: R = *i*Pr; **b**: R = Cy.

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