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Photochemical Synthesis

# A Polymer-Bound Chiral Template for Enantioselective Photochemical Reactions**

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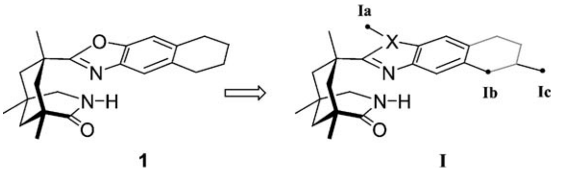
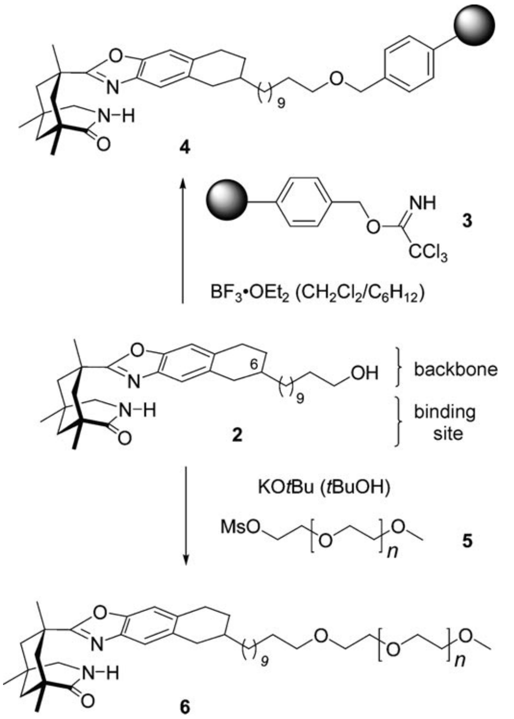
Polymer-bound reagents[1] and catalysts[2] offer significant advantages over the analogous low-molecular-weight compounds, for example, in streamlining product purification and simplifying re-isolation. There are numerous methods to immobilize compounds on a polymeric support,[3] the crucial prerequisite being that the desired reactivity and selectivity of the low-molecular-weight reagent or catalyst are retained upon immobilization. Immobilized catalysts and reagents have so far played a minor role in organic photochemistry,[4–6] which does not come as a big surprise, because light is by definition the reagent of photochemistry. In connection with our studies on enantioselective photochemical reactions in solution, which led to the development of the highly selective chiral complexing agent **1**[7–9] (Scheme 1), we also focused on the immobilization of this template. We report herein on a successful modification of **1**, which allows for its grafting onto a polymeric support. High enantioselectivities were consistently achieved in several cycles of a photochemical test reaction.[10]



***Scheme 1.*** Possible positions **Ia**–**Ic** to attach a linker for the immobilization of chiral complexing agent **1**.

Scheme 1 depicts three options for attaching a linker to template **1**. The connection at a nitrogen atom (X = N) with retention of the tetrahydronaphthalene system (**Ia**) was examined as well as the attachment of the linker to either the reduced benzoxazole scaffold (X = O, **Ib**) or to the complete backbone (X = O, **Ic**). The first two alternatives gave poorer results than the parent compound **1** with regard to enantioselective photochemistry. Consequently, option **Ic** was selected; in this preparatively most complex route the linker is attached to the carbon atom C6 of the tetrahydronaphthalene. The choice led to alcohol **2** (Scheme 2), which was prepared in a multistep sequence starting from Kemp's triacid[11] and a methoxytetralone (see the Supporting Information). As the epimers at C6 could not be separated, we used compound **2** in enantiomerically pure form as a mixture of diastereoisomers. The influence of the stereogenic center at C6 on the stereoselectivity of the planned photochemical reaction was minimal (see below). Indeed, enantioselectivities achieved with **1** and related complexing agents rest on two key elements: 1) efficient binding of a substrate to the NHCO-binding motif of the 2-oxo-3-azabicyclo[3.3.1]nonane ring and 2) complete enantioface differentiation through the action of the 5,6,7,8-tetrahydronaphtho[2,3-*d*]oxazole as a steric "shield" for any incoming reagent.



***Scheme 2.*** Alcohol **2** and its immoblization on a Wang resin (**3**) and on a MPEG 2000 polymer (**5**) to give products **4** and **6**.

The immobilization was conducted in two different ways. On the one hand, template **2** was grafted on a Wang resin[12] by treatment of commercially available trichloroacetimidate **3** (200–400 mesh) with an excess of alcohol **2** in the presence of $BF_3{\cdot}OEt_2$. The loading of polymer **3** with active template

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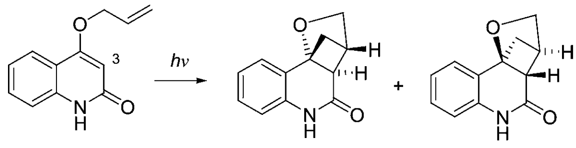
was determined to be 0.17 mmol g$^{-1}$ by elemental analysis. The Wang resin was chosen as the solid support because of its anticipated photochemical stability, the high loading, and its good swelling properties in nonpolar solvents.[13] On the other hand, alkylation of alcohol **2** with mesylate **5** yielded template **6** bound to methoxypolyethylene glycol (MPEG)[14] with an average molecular mass of 2000 Da (MPEG 2000).

The test reaction depicted in Scheme 3, an intramolecular [2+2] photocycloaddition first described by Kaneko et al.,[15] was used to estimate the enantioselectivity induction of immobilized templates **4** and **6**. 4-Allyloxyquinolone (**7**) undergoes a clean [2+2] photocycloaddition to give products **8** and *ent*-**8** upon irradiation with light of wavelength $\lambda >$ 300 nm. Other stereoisomers or side products are not formed, which makes the progress of this reaction easy to monitor. The absolute configurations could be assigned to the individual enantiomers as the specific rotation of **8** and *ent*-**8** and their chromatographic properties (HPLC on a chiral stationary phase) are known.[8c] The reaction proceeds presumably via the corresponding ππ* triplet state, which is populated by a rapid intersystem crossing (ISC) from the lowest excited singlet state of quinolone **7**.[16]



**7** **8** *ent*-**8**

***Scheme 3.*** Intramolecular [2+2] photocycloaddition of 4-allyloxyquinolone (**7**) to give products **8** and *ent*-**8**.

The photochemical reactions were conducted in toluene at −74 °C in single batches (see the Supporting Information). After each individual run the immobilized template was filtered off and weighed, and employed without any further treatment in the next reaction cycle. Table 1 summarizes the performance of immobilized template **4** in these reactions. The enantioselectivity was consistently high and did not deteriorate even after the catalyst had been recycled four times. The incomplete conversion after 4 hours is presumably because the Wang resin is not transparent and the penetration depth of the light remains low. The experiments were conducted in a glass tube with a diameter of 10 mm. The template could be fully recovered and apparently did not decompose under the conditions of the photochemical reaction.

***Table 1:*** Intramolecular [2+2] photocycloaddition of 4-allyloxyquinolone (**7**) in the presence of immobilized template **4**.

| Run[a] | e.r.[b] | Recovery yield [%][c] | Conv. [%] |
|---|---|---|---|
| 1 | 93:7 | 99 | 31 |
| 2 | 93:7 | 91 | 25 |
| 3 | 93:7 | 96 | 27 |
| 4 | 92:8 | 96 | 24 |
| 5 | 93:7 | 96 | 27 |

[a] A 1.5 mM solution of the substrate in toluene was irradiated (Rayonet RPR 3000 Å, Duran filter) at −74 °C in toluene for 4 h. [b] The enantiomeric ratio (**8**/*ent*-**8**) was determined by HPLC (Daicel Chiralpak AD-H, 250×4.6, hexane/*i*PrOH 95:5). [c] The recovery yield of **4** relative to the preceding run was determined after filtration and evaporation to dryness.

Experiments conducted with template **6** (Table 2)—with MPEG 2000[14] representing a transparent support—proved that high conversions are readily achieved at a consistently high level of enantioselection. The reactions were complete after 4 h. In this series a homogeneous solution was irradiated, as the polymer is soluble in toluene. Compound **6** readily precipitated upon addition of diethyl ether and could be recovered by filtration. Recovery yields were close to perfect, which is testimony to the high photochemical stability of the template.

***Table 2:*** Intramolecular [2+2]-photocycloaddition of 4-allyloxyquinolone (**7**) in the presence of immobilized template **6**.

| Run[a] | e.r.[b] | Recovery yield [%][c] | Conv. [%] |
|---|---|---|---|
| 1 | 95:5 | 99 | 96 |
| 2 | 95:5 | 99 | 98 |
| 3 | 96:4 | 97 | 97 |
| 4 | 96:4 | 98 | 99 |
| 5 | 96:4 | 97 | 96 |

[a] A 1.5 mM solution of the substrate in toluene was irradiated (Rayonet RPR 3000 Å, Duran filter) at −74 °C in toluene for 4 h. [b] The enantiomeric ratio (**8**/*ent*-**8**) was determined by HPLC (Daicel Chiralpak AD-H, 250×4.6; hexane/*i*PrOH 95:5). [c] The recovery yield of **6** relative to the preceding run was determined after precipitation with diethyl ether, filtration, and evaporation to dryness.

As mentioned above, the enantioface differentiation can be explained by the association of a substrate–template complex **7**·**4** or **7**·**6** through hydrogen bonds and by an efficient steric shielding through the tetrahydronaphthalene backbone. A major conclusion of this study is consequently that the key properties of the original template **1** are indeed retained if the linker and its position are appropriately chosen. In possible applications polymer-bound chiral templates could be employed in a continuous-flow system for enantioselective photochemical reactions as a continuous process.

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