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Selective Photocyclization of Amino Acids in Dipeptides

Stephan Sauer, Christian Staehelin, Caroline Wyss, and Bernd Giese*

Abstract. Amino acids in dipeptides which are substituted at the N-atom by a benzoylalkyl group can be selectively photocyclized *via* a triplet biradical. With valine as amino acid the cyclization leads mainly to one product out of eight possible isomers.

During the last years it became clear that the same rules of stereoselectivity govern the reactions of radicals as well as of non-radicals [1]. In diffusion-controlled radical-radical reactions the stereoselectivity nearly disappears, but if the two radical centers establish a triplet state, its lifetime might be long enough for a selection between different reaction pathways.

Recently, we have shown that the interconversion between glycine and proline derivatives (**1** → **3**) *via* the triplet biradical **2**, is completely stereoselective when the chiral auxiliary **5** is used [2]. We have explained this by the transition-state structure **4** (Scheme 1).

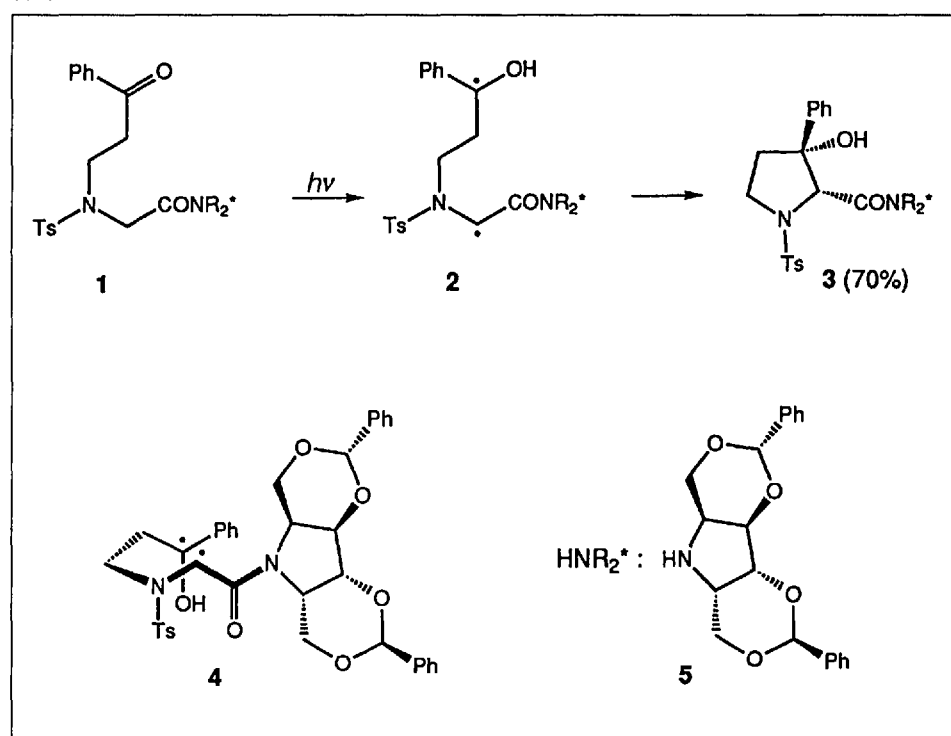
In order to learn whether stereochemical induction occurs also in the absence of

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Photolysis of dipeptides **10** occurred with high regioselectivity and simple diastereoselectivity as well as significant asymmetric induction [3]. From the eight possible isomers, the δ -lactams **11a** and **11b** are formed as major products (Scheme 3). The regioisomeric γ -lactams are not observed and *trans*-substituted δ -lactams are formed only in trace amounts (aprotic solvents).

It has turned out that this photocyclization is glycine-selective [4]. But if the length of the ether is reduced in one CH₂,

Scheme 1



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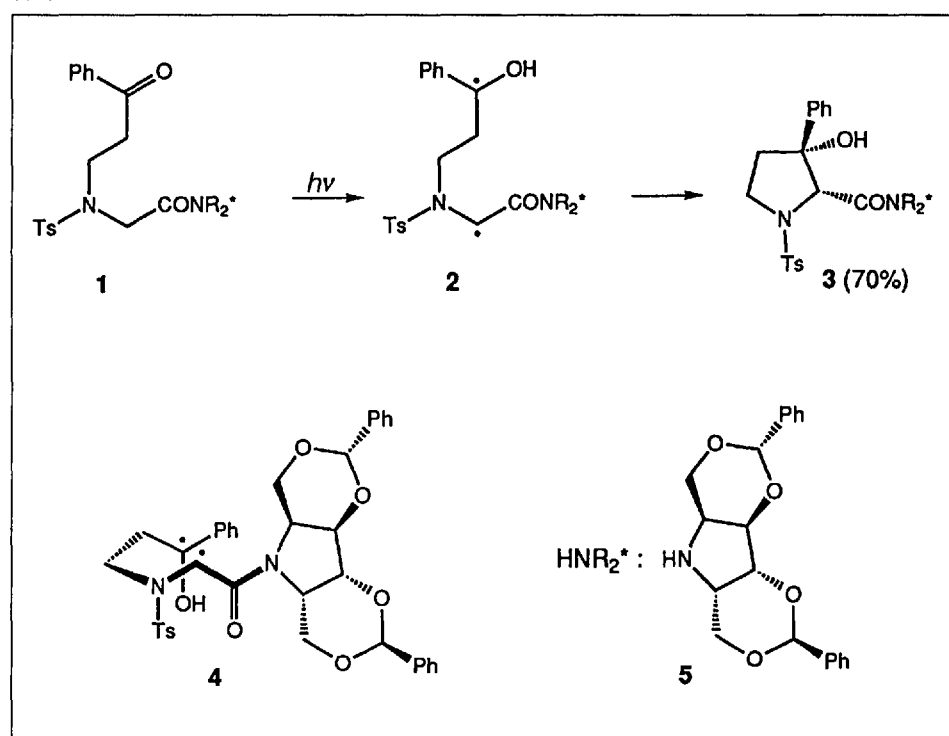
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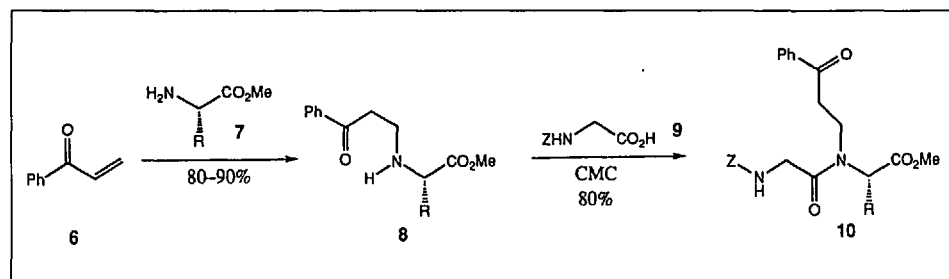
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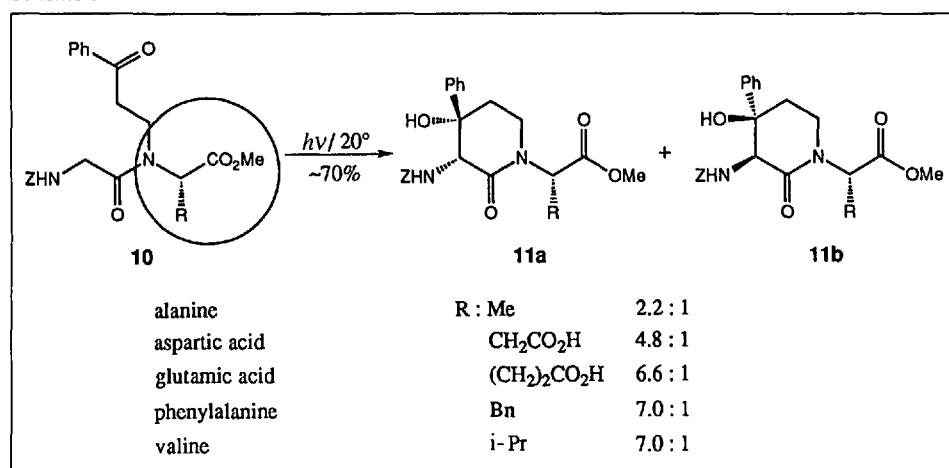


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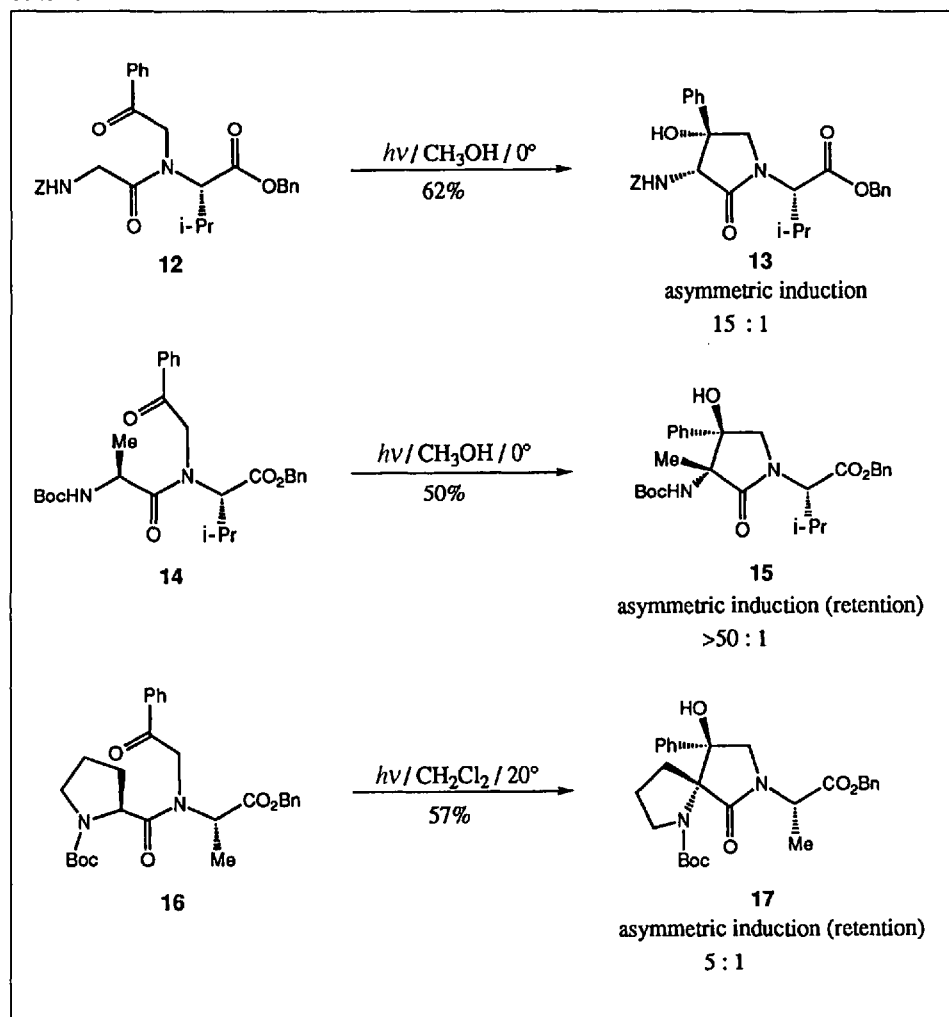
Scheme 2



Scheme 3



Scheme 4



group, cyclization takes place also into substituted amino acids. Thus, γ -lactam formation does not only occur with dipeptide **12** (\rightarrow **13**), which contains a glycine, but also with dipeptides like **14** (\rightarrow **15**) and **16** (\rightarrow **17**) (Scheme 4).

The goal of this work is to introduce the photolinker directly into oligopeptides, to carry out the photocyclization and study the effect of the γ -lactam formation on the conformation of the peptide.

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