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 \rightarrow 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 stereoechemical induction occurs also in the absence of auxiliary control, we synthesized dipeptides 10 by Michael addition (6 + 7 \rightarrow 8) and subsequent amide formation (8 + 9 \rightarrow 10) (Scheme 2).

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

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Selective Photocyclization of Amino Acids in Dipeptides

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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 regiosomeric 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
group, cyclization takes place also into substituted amino acids. Thus, \( \gamma \)-lactam formation does not only occur with dipeptide 12 (→ 13), which contains a glycine, but also with dipeptides like 14 (→ 15) and 16 (→ 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 \( \gamma \)-lactam formation on the conformation of the peptide.

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