Enhanced Photodeamination of Prolyl Tripeptides

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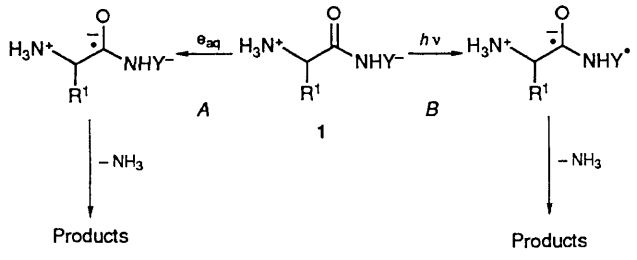
When compared with results from other tripeptides, high yields of ammonia in the aqueous photolyses of glycylprolylglycine and alanylprolylglycine suggest that the prolyl residue can promote peptide conformations favourable for long-range electron transfer.

The role of the peptide chain in long-range electron transfer within proteins has attracted much attention in recent years, but the picture remains unclear.[1] The prolyl residue has been a popular choice as a peptide spacer between redox centres in studies of model compounds[2–4] because its relative rigidity allows factors controlling the rate of electron transfer to be more readily evaluated. Two such investigations have prompted different conclusions, however; one suggests that the peptide group functions as would an equivalent saturated σ-bond spacer,[2] while the other emphasises the directional



a; Y = $CH(R^2)CO_2$
b; Y = $CH(R^2)CONHCH(R^3)CO_2$

Scheme 1

specificity of the peptide chain.[3] As part of a continuing study of the aqueous photochemistry of small peptides,[5,6] we have found that the inclusion of prolyl as the central residue in each of two tripeptides more than doubles the photolytic yield of ammonia, a product best explained by a pathway involving electron transfer from the carboxylate anion through two peptide groups.[6]

Aqueous solutions (0.03 mol dm^{-3}) of five HPLC-pure tripeptides were irradiated in the absence of oxygen using a medium-pressure mercury arc and quartz apparatus, giving the representative results in Table 1. Peptide photolysis was monitored by reversed-phase HPLC (typically: SP, 250 × 4.6 mm ODS; MP, 2% acetonitrile in 0.05 mol dm^{-3} KH_2PO_4 with 1.2×10^{-3} mol dm^{-3} sodium octanesulphonate; λ, 215 nm) and the release of ammonia by an ion-selective electrode. The distinctive values obtained with the prolyl peptides are accompanied by a more complex array of products in the photolysate, the other tripeptides giving principally the product of decarboxylation.[6]

Release of ammonia from a peptide signals one-electron reduction of the *N*-terminal peptide group. This sequence is well known in radiolysis[7] (Scheme 1*A*) and is also the final step of an efficient intramolecular electron transfer from carboxylate in the photolysis of aliphatic dipeptides[5] (**1a** in Scheme 1***B***). We have suggested that the small yield of ammonia in the photolysis of triglycine (**1b**, $R^1 = R^2 = R^3 = H$) reveals a minor pathway in which one or more lightly populated conformations allow an electron to be transferred through two peptide groups.[6] An alternative interpretation, in which a locally excited *N*-terminal peptide group oxidizes the carboxylate anion directly across space, requires a sterically crowded conformation, which also imposes simultaneous overlap of donor and acceptor orbitals with those of the intervening peptide group (approximate torsional angles:[8] $\phi_2 = -45°$ $\psi_2 = 90°$, $\phi_3 = 90°$, $\psi_3 = -45°$ or 135°). A through-bond mechanism,[9] requiring alignment of appropriate bonding and antibonding orbitals, is also conformation dependent.

The inclusion of a prolyl unit in a peptide introduces three potentially pertinent features: an accessible *cis* peptide configuration,[10] a more polarizable peptide bond[11] and severe constraints on conformation.[8] Models show readily that a *cis* *N*-terminal peptide group is conformationally less accessible to the other two π systems, and offers no obvious advantage in a through-bond mechanism. The present results are consistent with both the other features, however. Increased polarizability enhances electron accepting behaviour in the excited state and, as conformations favourable for π-orbital overlap fall within the limited range accessible with a central prolyl residue (*e.g.* $\phi_2 = -60 \pm 20°$), they form a higher proportion of those available than would be the case with other tripeptides. The small but significant increase in ammonia yield observed with triglycine, glycylvalylglycine and alanylglycylglycine at the higher temperature, but not with alanylprolylglycine, also accords with a conformational influence. Thus, peptide conformations included among those readily available to the prolyl residue may be a contributing factor in long-range electron transfer in some proteins.

Table 1 Yields (%) of ammonia at 20% photolysis of aqueous tripeptides.[a]

X	GlyXGly	AlaXGly
Gly	20(13)	25(18)
Val	22(17)	—
Pro	65(—)	56(59)

[a] Values, ±3%, from solutions at 50–55 °C and, in parentheses, at 25 °C.

While oligoproline spacers are useful in the study of some aspects of long-range electron transfer, their conformations are generally not representative of those within proteins[12] and, indeed, may hinder the detection of other influential properties of peptides in general, and of the prolyl residue in particular.

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