



NITRATES IN THE
SYNTHESIS OF
AMINO ACID RADICALS.

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by

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"No formal education can prepare anybody for life. Only life can prepare you for what comes."

-Neil, *Thirty Five Up*, 1991.

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ABSTRACT

α -Amino acid radicals can be conveniently prepared through the β -scission of alkoxy radicals, which themselves can be formed either *via* the photolysis of O^{β} -nitro- β -hydroxy amino acid derivatives, or through their reaction with AIBN. The process of β -scission involves bond homolysis of an alkoxy radical to give a carbonyl species and a carbon centred radical, and competes with the process of hydrogen abstraction, which involves the direct transfer of a hydrogen atom from either the solvent or an alternative hydrogen source (for example, tributyltin hydride) to give the corresponding alcohol. The preparation of α -amino acid radicals *via* the process of β -scission provides information on the factors affecting their relative stability, as the rate of hydrogen abstraction is relatively independent of the nature of the alkoxy radical. Therefore, the ratio of the rate of β -scission to that of hydrogen abstraction (determined from the ratio of the two products formed *via* the respective processes) is a good measure of the efficiency of β -scission.

The studies contained in this thesis have shown the rate of β -scission to be dependent upon a number of factors, including steric effects on the initial alkoxy radical formed, the stability of the product carbonyl compound, and the stability of the product radical.

An increase in substitution at the amino acid β -position has been shown to increase the rate of β -scission by factors of > 6 , with this increase being attributed to steric effects on the alkoxy radical during the β -scission process. Further increases in the rate of β -scission are noticed if the transition state for β -scission is stabilised by the production of a conjugated carbonyl compound, such as benzaldehyde. A similar steric effect has also been observed through an increase in substitution at the amino acid α -position.

A study of the comparative effects of a benzamido group versus a phthalimido

group at the incipient radical centre has shown that the presence of a phthalimido group relative to a benzamido group causes a reduction in the rate of β -scission, due to the reduced stabilisation afforded by the phthalimido substituent.

Finally, it has been shown that the process of β -scission is enhanced by the presence of both the methoxycarbonyl and benzamido substituents at the incipient radical centre. Based on the proposal that the transition state for β -scission is highly polar with a δ^+ charge at the radical centre, it is proposed that the methoxycarbonyl substituent contributes to the polar effect, while the electron donating resonance effect of the benzamido substituent provides stabilisation of the δ^+ charge. In a comparison of the effects of the methoxycarbonyl and benzamido substituents, it has been found that the stabilisation afforded by the benzamido substituent on the electron deficient radical centre is significantly greater than that afforded by the methoxycarbonyl substituent.

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This work contains no material which has been accepted for the award of any other degree or diploma in any university or other tertiary institution, and, to the best of my knowledge, contains no material previously published or written by another person, except where due reference has been made in the text.

I give consent to this copy of my thesis, when deposited in the University Library, being available for loan and photocopying.

Craig Anthony Smith.

June 1996.