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INERT FREE RADICALS AS SPIN LABELS. I. REACTIONS WITH GLYCINE AND L-ALANINE

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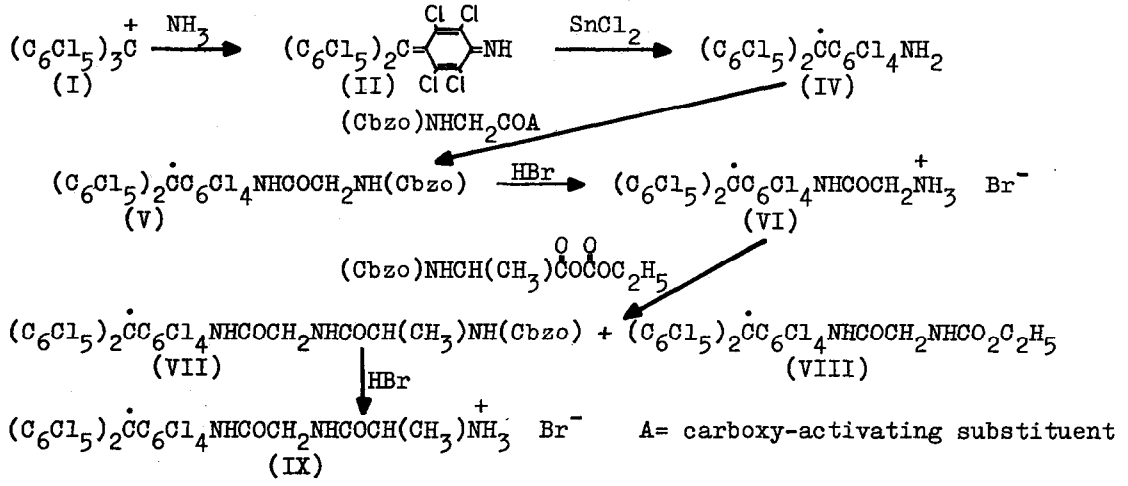
Some nitroxide radicals, in spite of their sensitivity, have extensively and successfully been used as spin labels for structural elucidation in Organic Chemistry and Biochemistry,[1] including synthetic polymers, haemoglobin, RNA, ADP, ATP, and membranes. With the discovery of the Inert Free Radicals,[2] which withstand extremely aggressive chemical species and high temperatures, the possibility of synthesizing "inert" spin labels was opened.

Perchlorotriphenylcarbonium hexachloroantimonate[3] (I) reacts immediately with ammonia in CH_2Cl_2 at room temperature to give NH-tetradecachlorofuchsonimine (II; 85%). II includes hexane of crystallization, as occurs in some other highly chlorinated compounds. II hydrolyses slowly to perchlorofuchsone (III), even on standing in the air. Its reduction with $SnCl_2$ in ethyl ether (12h; room temp.) yields 4-aminotetradecachlorotriphenylmethyl radical (IV; 82%), mp 285° (dec.). epr (C_2Cl_4) g, 2.0027 ± 0.0003; singlet with central inflexion; computer simulation: width 0.92, a_H 0.63, a_N 1.00, a (α-^{13}C) 27.9, a(bridgehead-^{13}C) 11.1, a(o-^{13}C) 9.8 gauss. Magn. suscept. χ_{dia} $-0.470\cdot10^{-6}$, θ -1.5°K, Bohr magnetons 1.73, spins/mole $6.04\cdot10^{23}$ (99.7%). IV reverts to II with NaClO in aqueous dioxane.

Condensation of IV with benzyloxycarbonylglycine, activated with Palomo's reagent ($SOCl_2$, DMF),[4] (3 d; room temp.) gives N-(benzyloxycarbonylglycyl)-4-aminotetradecachlorotriphenylmethyl radical (V; 76%), red needles mp 231-3° (dec.). epr (dioxane) g 2.0026 ± 0.0003; distorted, centrosymmetrical doublet; computer simulation: width 0.75, a_H 1.5, a_N 0.42, a(α-^{13}C) 29.55, a(bridgehead-^{13}C) 12.65, a(o-^{13}C) 10.4 gauss. Magn. suscept. χ_{dia} $-0.500\cdot10^{-6}$, θ -3.8°K, Bohr magnetons 1.76, spins/mole $6.23\cdot10^{23}$ (102.7%). V reacts with HBr in dioxane (1 h; room temp.) yielding the N-glycyl-4-aminotetradecachlorotriphenylmethyl radical hydrobromide (VI; 100%), red microcrystalline powder dec. 226°. epr (dioxane) g 2.0027 ± 0.0003; distorted, centrosymmetrical doublet; computer simulation: width 0.88, a_H 1.49, a_N 0.44, a(α-^{13}C) 29.4, a(bridgehead-^{13}C) 12.6, a(o-^{13}C) 10.1 gauss. Magn. suscept. χ_{dia} $-0.590\cdot10^{-6}$, θ -0.4°K, Bohr magnetons 1.73, spins/mole $6.01\cdot10^{23}$ (99.3%).

VI with N-benzyloxycarbonyl-O-ethoxycarbonyl-L-alanine (from ethylchloroformate and N-benzyloxycarbonyl-L-alanine) (4.5 h; 5° → room temp.) gives a mixture of N-(benzyloxycarbonyl-L-alanylglycyl)-4-aminotetradecachlorotriphenylmethyl radical (VII; 64%), deep-red needles mp 218-21° (dec.), and N-(ethoxycarbonylglycyl)-4-aminotetradecachlorotriphenylmethyl radical (VIII; 8%), red needles mp 277-9° (dec.). VII: epr (dioxane) g 2.0027 ± 0.0003; distorted, centrosymmetrical doublet; computer simulation: width 0.75, a_H 1.5, a_N 0.42, a(α-^{13}C) 29.6, a(bridgehead-^{13}C) 12.65, a(o-^{13}C) 10.4 gauss. Magn. suscept. χ_{dia} $-0.470\cdot10^{-6}$, θ -0.2°K, Bohr magnetons 1.71, spins/mole $5.92\cdot10^{23}$ (97.6%). VIII: epr (dioxane) g 2.0027 ± 0.0003; distorted, centrosymmetrical doublet; computer simulation: width 0.75, a_H 1.5, a_N 0.42, a(α-^{13}C) 29.55, a(bridgehead-^{13}C) 12.65, a(o-^{13}C) 10.4 gauss. Magn. suscept. χ_{dia} $-0.490\cdot10^{-6}$, θ 0.6°K, Bohr magnetons 1.69, spins/mole $5.79\cdot10^{23}$ (95.6%). VII with HBr in dioxane (1h; room temp.) gives N-(alanylglycyl)-4-aminotetradecachlorotriphenylmethyl radical hydrobromide (IX; 100%), red microcrystalline powder dec. 215°. epr (dioxane) g 2.0026 ± 0.0003; distorted, centrosymmetrical doublet; computer simulation: width 0.88, a_H 1.49, a_N 0.44, a(-^{13}C) 29.4, a(bridgehead-^{13}C) 12.6, a(o-^{13}C) 10.1 gauss. Magn. suscept. χ_{dia} $-0.545\cdot10^{-6}$, θ 1.4°K, Bohr magnetons 1.72, spins/mole $5.96\cdot10^{23}$ (98.3%).



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