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INERT FREE RADICALS AS SPIN LABELS. II. REACTIONS OF 4-HYDROXYTETRADECACHLOROTRIPHENYLMETHYL RADICAL WITH ALANINE, PHENYLALANINE, VALINE AND PROLINE

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In a recent communication[1] the first results on the synthesis of *inert spin labels* were reported. To develop this concept further it was decided to attach 4-hydroxytetradecachlorotriphenylmethyl radical (I) to some aminoacids by familiar reactions within the peptide synthesis, such as the mixed carboxylic-anhydride method.[2]

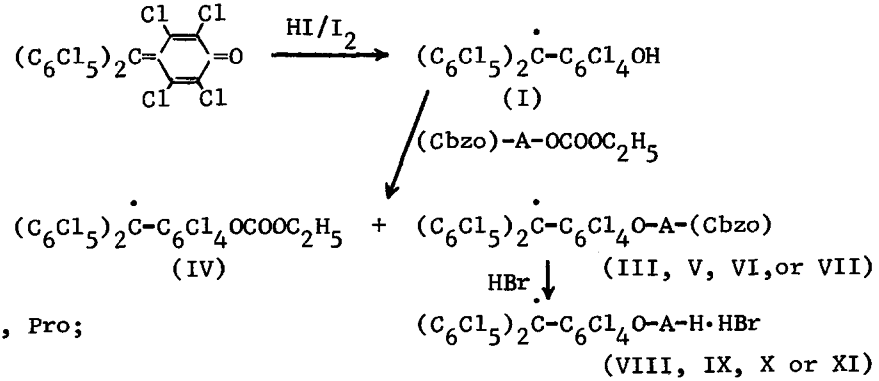
The reduction of perchlorofuchsone[3] (II) with HI/I_2 in C_6H_6 (room tem.; 24 h) yields 4-*hydroxytetradecachlorotriphenylmethyl radical*[*] (I; 100%), *mp* 318-20° (dec.). *epr* (CCl_4) g, 2.0026 ± 0.0003; singlet, width 1.2; a(α-^{13}C) 29.3, a(bridgehead-^{13}C) 12.2, a(*o*-^{13}C) 10.8 G. *Magn. suscept.* χ_{dia} $-0.585\cdot10^{-6}$, θ $-4.8^{o}K$, Bohr magns. 1.73 (100.2% pure). I reverts easily to II.

Condensation of *N*-benzyloxycarbonylalanine and ethyl chloroformate (8 min.; 0°) with (I) in presence of $(C_2H_5)_3N$ in $CHCl_3$ (45 min; 0° ⟶ reflux) gives a mixture of 4-(N-*benzyloxycarbonylalanyloxy)tetradecachlorotriphenylmethyl radical* (III; 80%), *mp* 128-30°, and 4-*(ethoxycarbonyloxy)tetradecachlorotriphenylmethyl radical* (IV; 11.2%), *mp* 161-3°. III: *epr* (CCl_4) g, 2.0028 ± 0.0003; singlet, width 1.24; a(α-^{13}C) 29.1, a(bridgehead-^{13}C) 12.2, a(*o*-^{13}C) 10.4 G. *Magn. suscept.* χ_{dia} $-0.627\cdot10^{-6}$, θ $-18.1^{o}K$, Bohr magns. 1.74 (101% pure). IV *epr* (CCl_4) g, 2.0028 ± 0.0003; singlet, width 1.04; a(α-^{13}C) 29.0, a(bridgehead-^{13}C) 12.4, a(*o*-^{13}C) 10.4 G. *Magn. suscept.* χ_{dia} $-0.714\cdot10^{-6}$, θ $-7.6^{o}K$, Bohr magns. 1.76 (103% pure).

With the same procedure 4-(N-*benzyloxycarbonyl*-L-*phenylalanyloxy)tetradecachlorotriphenylmethyl radical* (V; 76%), *mp* 109-11°, 4-(N-*benzyloxycarbonyl*-L-*valyloxy)tetradecachlorotriphenylmethyl radical* (VI; 59%), *mp* 176-8°, and 4-(N-*benzyloxycarbonyl*-L-*prolyloxy)tetradecachlorotriphenylmethyl radical* (VII, 53%), *mp* 122-3°, are obtained. V: *epr* (CCl_4) g, 2.0026 ± 0.0003; singlet, width 1.12; a(α-^{13}C) 29.2, a(bridgehead-^{13}C) 12.4, a(*o*-^{13}C) 10.25 G. *Magn. suscept.* χ_{dia}

$-0.528\cdot10^{-6}$, θ -2.7°K, Bohr magns. 1.74 (101% pure). VI: epr (CCl_4) g 2.0025 ± 0.0003; singlet, width 1.1; a(α-^{13}C) 29.4, a(bridgehead-^{13}C) 12.5, a(o-^{13}C) 10.3 G. Magn. suscept. χ_{dia} $-0.646\cdot10^{-6}$, θ -2.8°K, Bohr magns. 1.73 (100% pure). VII: epr (CCl_4) g 2.0026 ± 0.0003; singlet, width 1.22; a(α-^{13}C) 29.0, a(bridgehead-^{13}C) 12.4, a(o-^{13}C) 10.2 G. Magn. suscept. χ_{dia} $-0{,}536\cdot10^{-6}$, θ 2.7°K, Bohr magns. 1.73 (101% pure). By-product IV is also isolated (17, 23 and 27%, respectively).

With HBr in dioxane (1h; room temp.), III, V, VI and VII give hydrobromides VIII (98%) mp 271° (dec.), IX (91%) mp 162-4° (dec.), X (92.5%) mp 184-5° (dec.) and XI (91%) mp 184-5° (dec.), respectively. VIII: epr (dioxane g 2.0027 ± 0.0003; singlet, width 1.36; a(α-^{13}C) 31.2, a(bridgehead-^{13}C) 12.4, a(o-^{13}C) 10.2 G. Magn. suscept. χ_{dia} $-0.457\cdot10^{-6}$, θ 2.1°K, Bohr magns. 1.65 (91% pure).[†] IX: epr (dioxane) g 2.0024 ± 0.0003; singlet, width 1.16; a(α-^{13}C) 32.2, a(bridgehead-^{13}C) 12.7, a(o-^{13}C) 10.3 G. Magn. suscept. χ_{dia} $-0.533\cdot10^{-6}$, θ 1.7°K, Bohr magnetons. 1.66 (92% pure).[†] X: epr (dioxane) g 2.0027 ± 0.0003; singlet, width 1.18; a(α-^{13}C) 29.1, a(bridgehead-^{13}C) 12.65, a(o-^{13}C) 10.3 G. Magn. suscept. χ_{dia} $-0.499\cdot10^{-6}$, θ 1.0°K, Bohr magns. 1.68 (94% pure).[†] XI: epr (dioxane) g 2.0025 ± 0.0003; singlet, width 1.26; a(α-^{13}C) 29.7, a(bridgehead-^{13}C) 12.95, a(o-^{13}C) 10.6 G. Magn. suscept. χ_{dia} $-0.568\cdot10^{-6}$, θ 1.0°K, Bohr magns. 1.66 (92% pure).[†]



A= Ala, Phe, Val, Pro;
Cbzo= $C_6H_5CH_2OCO$

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2) J. P. Greenstein and M. Winitz, "Chemistry of the Amino Acids", Wiley (1961), vol. 2, p. 978.
3) M. Ballester, J. Riera, A. Rodríguez-Siurana, Tetrahedron Lett., 1970, 3615.

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[*] Previously obtained in impure state by A. Rodríguez-Siurana, this Institute.

[†] Low values due to anomalous magnetic behavior.