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AN ABNORMAL HYDROLYTIC C-N CLEAVAGE OF THE AMIDE GROUP IN N-SUBSTITUTED 4-CARBAMOYLTETRADECACHLOROTRIPHENYLMETHYL RADICALS, AND RELATED REACTIONS

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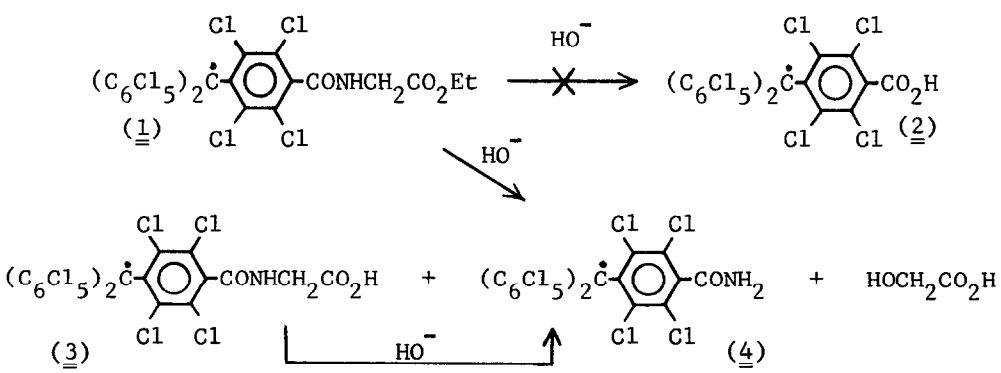
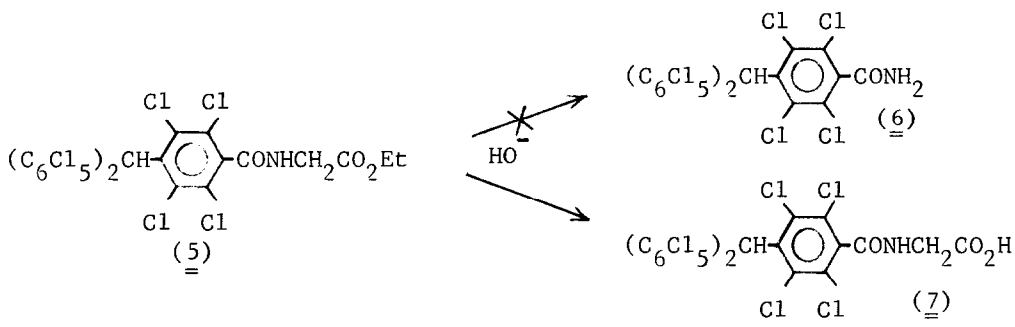
Summary: The alkaline hydrolysis of amides p-(RCH_2NHCO)-C_6Cl_4-$\dot{C}(C_6Cl_5)_2$ (R, CO_2Et or CO_2H) occurs via methylene-nitrogen bond cleavage. Under the given conditions, the amide group in the corresponding non-radical, triarylmethane species, and in 4-(benzylcarbamoyl)tetradecachlorotriphenylmethyl radical, does not undergo any hydrolysis. That abnormal cleavage is traced therefore to the radical character.

In connection with inert spin labelling of aminoacids with tetradecachloro--4-(chloroformyl)triphenylmethyl radical,[1,2] it has been found that the alkaline hydrolysis of radical tetradecachloro-4-(glycinoformyl)triphenylmethyl ethyl ester (1),[1,3] instead of resulting in the "expected" product, the 4-carboxytetradecachlorotriphenylmethyl radical (2),[4] leads surprisingly to 4-carbamoyltetradecachlorotriphenylmethyl radical (4)[3] by an abnormal C-N bond fission. In fact, radical 1 gives carbamoyl radical 4 (40%) and tetradecachloro-4-(glycinoformyl)triphenylmethyl radical (3)[1,3] (46%) when treated with NaOH in aqueous dioxane (room temp.; 24 h), a substantial proportion of glycollic acid being formed.



In that reaction, carbamoyl radical 4 arises, at least partly, from radical 3, since the latter, under similar conditions, undergoes also abnormal hydrolysis giving the former.

As far as non-radical species, it has been found that the amides αH-tetradecachloro-4-(glycinoformyl)triphenylmethane ethyl ester (5) -closely related to radical 1- and N-(pentachlorobenzoyl)glycine ethyl ester (8)[3] do not hydrolize at the amido group but give acids αH-tetradecachloro-4-(glycinoformyl)triphenylmethane (7) (94%) [needles, mp 271-7° (dec). IR (KBr) 1735 (C=O ester), 1665 (C=O amide) cm^{-1}. UV ($CHCl_3$) λ(ε) 293 (1845), 303 (2000) nm] (no amide αH-4--carbamoyltetradecachlorotriphenylmethane (6) has been detected) and N-(pentachlorobenzoyl)glycine (9)[3] (99%), respectively.



$C_6Cl_5CONHCH_2CO_2Et \xrightarrow{HO^-} C_6Cl_5CONHCH_2CO_2H$

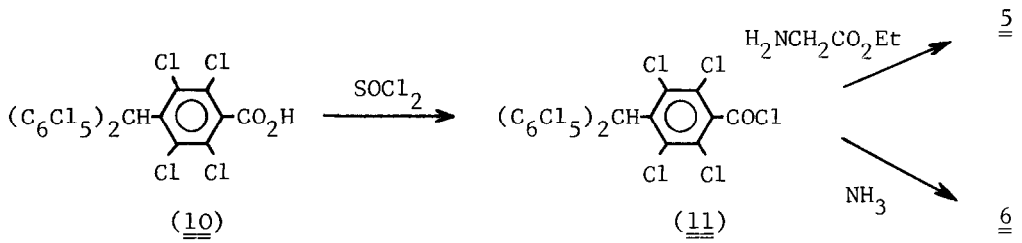
(8) (9)

The occurrence of the abnormal hydrolysis seems to be related therefore to the radical character. In this connection it is pointed out that the effect of such a character on the reactivity of a substituent in a radical has been well established in some clear-cut reactions ("reverse effect").[5]

Ethyl ester 5 [mp 163-5°. IR (KBr) 1760 (C=O ester), 1662 (C=O amide) cm^{-1}. PMR ($CDCl_3$) τ 2.97 (s, 1H, CH), 3.47 (broad band, 1H, NH), 5.74 (c, 2H, J 7 Hz, CH_2CH_3), 5.76 (d, 2H, J ~5 Hz, CH_2NH), 8.70 (t, 3H, J 7 Hz, CH_3)] was synthesized by reaction of αH-tetradecachlorotriphenylmethane-4-carboxylic acid (10)[4] with $SOCl_2$ (reflux temp.; 24 h) to give αH-tetradecachloro-4-(chloroformyl)triphenylmethane (11) (81%) [mp 336-47° (dec). IR (KBr) 1797 and 1777 (C=O) cm^{-1}. UV ($CHCl_3$) λ(ε) 294 (1920), 304 (2180) nm. PMR (CCl_4) τ 2.97 (s)], followed by condensation of 11 with glycine ethyl ester hydrochloride, in the presence of

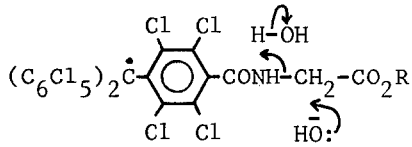
Et_3N, and in C_6H_6-H_2O (room temp.; 29 h) (71%).

αH-4-Carbamoyltetradecachlorotriphenylmethane (6), the would-be product of the abnormal hydrolyses of 5 and 7, was obtained from acid chloride 11 with NH_3 in $CHCl_3$ (room temperature; 3h) (90%) [mp 350°. IR (KBr) 1770 (C=O), 1600 (NH_2) cm^{-1}. UV ($CHCl_3$) λ(ε) 293 (1790), 303 (1920) nm].

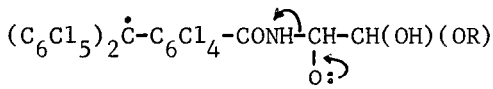


(10) (11)

The mechanism of the abnormal hydrolysis might be accounted for by assuming that anion $(C_6Cl_5)_2\dot{C}$-C_6Cl_4-$CONH^-$ behaves as a good leaving group abstracting a proton from H_2O in a concerted manner, either by an S_N2 reaction



or involving intermediate anion 12 formed through a simple sequence of prototropic changes from substrate 1. For a mechanistically related N-C bond cleavage involving a similar formation of an intermediate of type 12 see reference 6.



(12)

In connection with an S_N2 mechanism, the hydrolysis of 4-(benzylcarbamoyl)-tetradecachlorotriphenylmethyl radical (13) was attempted; it did not give any carbamoyl radical 4, but starting substrate instead in an almost quantitative yield. This negative result might be due to the lower electronic stabilization of the S_N2 transition state by the phenyl, in comparison with that afforded by the CO_2R group.

Radical 13 [mp 270-2°. IR (KBr) 1650 (C=O) cm^{-1}. UV-Vis ($CHCl_3$) λ(ε) 286 (6600), 381 (40 200), 507 (1230), 560 (1200) nm. EPR ($CHCl_3$) g, 2.0026±0.0003; singlet; computer simulation: width 1.1, a(α-^{13}C) 29.7, a(bridgehead-^{13}C) 12.9, a(o-^{13}C) 10.6 G. Magn. Suscep. χ_{dia} $-0.530 \cdot 10^{-6}$ emu, θ 7.8°K, Bohr magnetons 1.70 (96% pure), spins/mole $5.81 \cdot 10^{23}$] was obtained (80%) by condensation of radical tetradecachloro-4-(chloroformyl)triphenylmethyl,[1,2] with benzylamine, in the presence of Et_3N, and in C_6H_6 (room temp.; 24 h).

All new compounds gave correct elemental analyses.

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