A new direct homolytic iodination reaction of alkanes by perfluoroalkyl iodides

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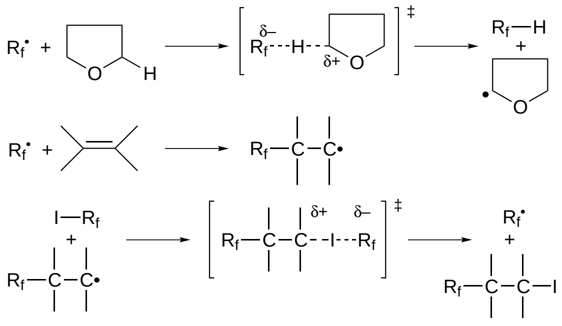
A new method for the direct free-radical chain iodination of alkanes by perfluoroalkyl iodides is described.

The direct free-radical iodination of alkanes by iodine, unlike the other halogens, is not feasible owing to its large positive enthalpy of hydrogen abstraction [eqn. (1)]. The rates of hydrogen abstraction from C–H bonds [eqn. (2)] by perfluoroalkyl radicals ($R_f^{\cdot}$) are $> 10^3$ times larger than those of the analogous hydrocarbon radicals.[1] Enthalpic (the higher energy of R_f–H compared to R–H bonds) and polar (the electrophilic character of $R_f^{\cdot}$) effects influence the rates of hydrogen abstraction. Thus, the rate of hydrogen abstraction by $C_7F_{15}^{\cdot}$ from THF, whose α-position is particularly activated by both enthalpic and polar [eqn. (3)] factors, has been evaluated[1] at $6.1 \times 10^5\ \mathrm{M}^{-1}\ \mathrm{s}^{-1}$. On the other hand, alkyl radicals easily abstract iodine atom from R_f–I, as shown by the effective free-radical addition of R_f–I to alkenes[2] [eqns. (4) and (5)], with the polar effect playing a significant role.

$$\mathrm{R{-}H} + \mathrm{I}^{\bullet} \longrightarrow \mathrm{R}^{\bullet} + \mathrm{H{-}I} \qquad \Delta H \sim 20\text{–}33\ \mathrm{kcal\ mol^{-1}} \qquad (1)$$

$$\mathrm{R{-}H} + \mathrm{R_f}^{\bullet} \longrightarrow \mathrm{R}^{\bullet} + \mathrm{R_f{-}H} \qquad (2)$$



(3)

(4)

(5)

$$\mathrm{R_f}^{\bullet} + \mathrm{H{-}R} \longrightarrow \mathrm{R_f{-}H} + \mathrm{R}^{\bullet} \qquad (6)$$

$$\mathrm{R}^{\bullet} + \mathrm{I{-}R_f} \longrightarrow \mathrm{R_f}^{\bullet} + \mathrm{R{-}I} \qquad (7)$$

$$\mathrm{Bu^tOOH} + \mathrm{Fe^{III}} \longrightarrow \mathrm{Bu^tO}^{\bullet} + \mathrm{OH}^{-} + \mathrm{Fe^{IV}} \qquad (8)$$

$$\mathrm{Bu^tO}^{\bullet} \longrightarrow \mathrm{CH_3}^{\bullet} + \mathrm{MeC(O)Me} \qquad (9)$$

$$\mathrm{C_4F_9{-}I} + \mathrm{CH_3}^{\bullet} \longrightarrow \mathrm{C_4F_9}^{\bullet} + \mathrm{CH_3{-}I} \qquad (10)$$

$$\mathrm{Bu^tOOH} + \mathrm{Fe^{III}} \longrightarrow \mathrm{Bu^tOO}^{\bullet} + \mathrm{H}^{+} + \mathrm{Fe^{II}} \qquad (11)$$

Thus, the conditions of alkane iodination according to the radical chain of eqns. (6) and (7) appeared to be fulfilled.

Iodocyclohexane was obtained in 70% yield, based on C_4F_9I, by refluxing a solution of cyclohexane and C_4F_9I in acetic acid in the presence of catalytic amounts of Bu^tOOH and $Fe(OAc)_3$. The reaction is explained by the radical chain of eqns. (6) and (7), initiated by a redox system [eqns. (8)–(10)] and represents a new simple, direct iodination of alkanes; we believe[3] eqn. (8) to be operating in this case, rather than eqn. (11).

In order to probe the reactivity–selectivity relationship of the reaction, an investigation was carried out with heptane, adamantane and 1-chlorohexane; heptane gave a mixture of all the iodoheptane isomers (Table 1, including a comparison with chlorination by *N*-chloroamines).

Enthalpic and steric effects contribute to the regioselectivity: the CH_2 groups in positions 3 and 4 have substantially the same reactivity, while the CH_2 in position 2 is more reactive due to steric factors and the methyl group is less reactive for enthalpic reasons. The behaviour is qualitatively similar to that for chlorination by protonated *N*-chloroamines[4] (Minisci chlorination),[5] in which the selectivity is determined by hydrogen abstraction by $R_2NH^{+\cdot}$.

The free-radical reactivity of adamantane is interesting because the selectivity of hydrogen abstraction is little affected by enthalpic factors, but it is greatly influenced by polar effects[6] (high selectivity with $R_2NH^{+\cdot}$[6] and $ArC(O)OO^{\cdot}$[7] radicals and in electron-transfer processes[8]). The yields obtained according to eqns. (6) and (7) (84.7% 1-iodo- and 15.3% 2-iodo-ada-

Table 1 Iodination of heptane

Iodinating agent	Iodination per hydrogen (%)[a] 1-iodo	2-iodo	3-iodo	4-iodo
C_4F_9I	1 (4.1)	18.7 (51.0)	11.1 (30.3)	10.7 (14.6)
Me_2NHCl^+	1	75.8	39.5	39.0
Bu^i_2NCl	1	75.3	26.4	26.1

[a] Figures in brackets indicate the yield of each isomer.

Table 2 Iodination of 1-chlorohexane

Iodinating agent	Iodination per hydrogen (%)[a] 1-iodo	2-iodo	3-iodo	4-iodo	5-iodo	6-iodo
C_4F_9I	0.2 (2.1)	0.3 (3.5)	1 (12.0)	2.2 (26.7)	4.2 (50.0)	0.3 (5.7)
Me_2NHCl^+	—	—	1	2.9	10.5	0.2
Cl_2	0.09	0.4	1	1.1	1.2	0.5

[a] Figures in brackets indicate the yield of each isomer.

mantane) confirm the expected influence of the polar effect, due to the electrophilic character of $C_4F_9^{\cdot}$, the higher stability of 1-adamantyl$^+$ with respect to its (secondary) 2-isomer[9] and the oxidation potential of adamantane (E_{ox} = 2.72 V *vs*. SCE), which is lower than that of 2,3-dimethylbutane (E_{ox} = 3.45 V *vs*. SCE).[8]

The iodination of 1-chlorohexane, reported in Table 2 and compared with chlorination by Me_2NHCl^+ and Cl_2, further supports our ideas about the influence of enthalpic and polar effects in hydrogen abstraction by $C_4F_9^{\cdot}$.

The σ-inductive and field effects of the chlorine atom in 1-chlorohexane are significant in the iodination, but they are lower than in chlorination by Me_2NHCl^+. This result suggests that the increase in hydrogen abstraction rates for $R_f^{\cdot}$ compared to the analogous hydrocarbon radicals must be mainly ascribed to the enthalpic effect (higher energy of the R_f–H bonds), the polar effect being a significant but minor factor.

We have recently[10] reached the same conclusion concerning the increase in addition rates of $R_f^{\cdot}$ to aromatic substrates, compared to addition of alkyl radicals, which is due mainly to the enthalpic effect, with a significant but minor polar contribution.

Footnote and References

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