Enhanced nucleophilic character of the 1-adamantyl radical in chlorine atom abstraction and in addition to electron-poor alkenes and to protonated heteroaromatic bases. Absolute rate constants and relationship with the Gif reaction

Francesco Recupero, Anna Bravo, Hans-René Bjørsvik, Francesca Fontana, Francesco Minisci * and Mariella Piredda

Dipartimento di Chimica del Politecnico, via Mancinelli, 7; I-20131 Milano, Italy

The absolute rate constants for reactions of the 1-adamantyl radical with electron-deficient substrates have been measured by competition kinetics. Addition to electron-poor alkenes or to protonated heteroaromatic bases, as well as chlorine abstraction from CCl_4 and $CHCl_3$, are two to three orders of magnitude faster than the corresponding reactions of the *tert*-butyl radical. This behaviour is ascribed to the enhanced nucleophilic character of the 1-adamantyl radical compared to *generic* tertiary alkyl radicals; it is related to the particular stability of the 1-adamantyl cation and to the low oxidation potential of adamantane. These results contribute to the understanding of the Gif reaction mechanism; in this debate, adamantane oxidation was one of the most controversial aspects because the 1-adamantyl radical is trapped by pyridinium ions, while the 2-adamantyl radical is not. This behaviour is explained by the large difference in the reactivity of the two isomeric adamantyl radicals towards protonated pyridine.

Introduction

Adamantane and the 1-adamantyl radical (1-Ad$^\bullet$) are interesting species for what concerns free-radical reactivity. The selectivity for hydrogen abstraction between C^3–H and C^2–H of adamantane is little affected by the enthalpic effect: the bromine atom, which is highly sensitive to the C–H bond energies, shows very low selectivity.[1] This is not unexpected on the basis of the 1-Ad–H bond energy, evaluated as 3.7 kcal mol^{-1} greater than tertiary C–H bond energy in isobutane, and therefore quite close to secondary C–H bond energies of alkanes.[1] However, this hydrogen abstraction is greatly influenced by polar effects: Minisci chlorination[2] by $R_2NH^{\bullet+}$ radicals [reaction (1)]

$$\text{Ad–H} + R_2NH^{\bullet+} \longrightarrow [\overset{\delta+}{\text{Ad}}\cdots\text{H}\cdots\overset{\delta+}{\text{N}}HR_2]^{\ddagger} \longrightarrow \text{Ad}^\bullet + R_2\overset{+}{N}H_2 \quad (1)$$

and the oxidation by acylperoxyl radicals,[3] RCOOO$^\bullet$ [reaction (2)], are particularly sensitive to polar effects[4] and are highly

$$\text{Ad–H} + {}^\bullet\text{OOCOR} \longrightarrow [\overset{\delta+}{\text{Ad}}\cdots\text{H}\cdots\overset{\delta-}{\text{O}}\text{OCOR}]^{\ddagger} \longrightarrow \text{Ad}^\bullet + \text{HOOCOR} \quad (2)$$

selective.[1,3] Hydrogen abstraction by an electron-transfer process, which can be considered as the limiting case of a polar transition state, is also particularly sensitive [reaction (3)].[5]

$$\text{Ad–H} \longrightarrow [\text{Ad–H}]^{\bullet+} \longrightarrow \text{Ad}^\bullet + \text{H}^+ \quad (3)$$

This behaviour can be related to the considerably higher stability of the 1-Ad$^+$ cation with respect to its (secondary) 2-isomer[6] and to the oxidation potential of adamantane (E_{ox} = 2.72 V *vs.* SCE), which is considerably lower than that of 2,3-dimethylbutane (E_{ox} = 3.45 V *vs.* SCE).[5] These factors should contribute to an enhanced nucleophilic character (high charge-transfer character in the transition state) of the 1-Ad$^\bullet$ radical compared with simple tertiary alkyl radicals. We have qualitatively explained some anomalous behaviour of 1-Ad$^\bullet$ radical reactions, such as halogen abstraction from $CHCl_3$ and $CBrCl_3$, and the oxidation by peracids, as a consequence of this enhanced nucleophilicity.[3]

In this paper we report the absolute rate constants for the reactions of the 1-Ad$^\bullet$ radical with electron-deficient substrates ($CHCl_3$, CCl_4, electron-poor alkenes and protonated heteroaromatic bases), which emphasise the enhancement of its nucleophilic character. We believe that these results can also make a contribution to the dispute concerning the mechanism of the Gif reaction, in which the oxidation of adamantane was one of the most controversial aspects.

Results and discussion

The 1-Ad$^\bullet$ radical was formed by iodine abstraction from 1-iodoadamantane by $Bu^n_3Sn^\bullet$ and Ph$^\bullet$ radicals [reactions (4) and (5)], generated from Bu^n_3SnH and benzoyl peroxide. Reactions (4) and (5) are extremely fast (>10^9 M^{-1} s^{-1}) and selective.[7,8]

$$\text{1-Ad–I} + Bu^n_3Sn^\bullet \xrightarrow{k_4} \text{1-Ad}^\bullet + Bu^n_3SnI \quad (4)$$

$$\text{1-Ad–I} + \text{Ph}^\bullet \xrightarrow{k_5} \text{1-Ad}^\bullet + \text{PhI} \quad (5)$$

Another method for generating the 1-Ad$^\bullet$ radical involves the oxidative decarboxylation of the carboxylic acid, 1-AdCOOH, by $Pb(OAc)_4$ [reactions (6) and (7)]. Reaction (4) has been utilised under reducing conditions for the reductive alkylation of alkenes and for chlorine abstraction from chloromethanes, whereas reactions (5) and (7) were employed under oxidising conditions for the substitution of heteroaromatic bases.

$$\text{1-Ad–COOH} + Pb(OAc)_4 \rightleftharpoons Pb(OAc)_3OCO\text{–Ad-1} + \text{AcOH} \quad (6)$$

$$Pb(OAc)_3OCO\text{–Ad-1} \longrightarrow Pb(OAc)_3 + CO_2 + \text{1-Ad}^\bullet \quad (7)$$

In order to measure the absolute rate constants for 1-Ad$^\bullet$ radical reactions, we have utilised reactions (8) and (9), which

$$R^\bullet + \text{H–SPh} \xrightarrow{k_8} \text{R–H} + {}^\bullet\text{SPh} \qquad k_8 \sim 1.3 \times 10^8 \text{ M}^{-1}\text{ s}^{-1} \text{ at 298 K} \quad (8)$$

$$R^{\bullet} + H\text{–}SnBu^{n}_{3} \xrightarrow{k_9} R\text{–}H + {}^{\bullet}SnBu^{n}_{3}$$

$$k_9 \sim 1.8 \times 10^6\ M^{-1}\ s^{-1} \text{ at } 300\ K \quad (9)$$

provide suitably non-selective hydrogen abstraction standards applicable to a broad variety of substituted alkyl radicals with little error due to the changes of enthalpic, polar and steric character.

The absolute rate constants for hydrogen abstraction by primary, secondary and tertiary alkyl radicals from thiophenol are clustered around $1.3 \times 10^8\ M^{-1}\ s^{-1}$ at 298 K.[9] The relative insensitivity of abstraction rates to the radical structure and the low temperature dependence make reaction (8) particularly useful as a standard for determining the values of the rate constants for other very fast alkyl radical reactions since, within reasonable limits, k_8 will not depend on the detailed structure of the alkyl radical.[9] These results could reflect a balance between enthalpic effect, decreasing from primary to tertiary alkyl radicals, and polar effect [reaction (10)], increasing from primary to tertiary radicals (the two effects are opposite).

$$R^{\bullet} + H\text{–}SPh \longrightarrow [\overset{\delta+}{R} \cdots H \cdots \overset{\delta-}{SPh}]^{\ddagger} \longrightarrow R\text{–}H + {}^{\bullet}SPh \quad (10)$$

On the other hand, the high value of the rate constants should minimise the small differences of these effects (reactivity–selectivity principle). Thus it appears reasonable to assume the value of k_8 also for 1-Ad$^{\bullet}$ radical. In any case, we could only expect a higher value of k_8 for 1-Ad$^{\bullet}$ radical compared to ordinary tertiary alkyl radicals for enthalpic (higher energy of the C–H bond), polar (lower oxidation potential of admantane and higher stability of 1-adamantyl cation) [reaction (10)] and steric reasons. In this case, the values of the rate constants for 1-Ad$^{\bullet}$ radical reactions would be minimal, by using reaction (8) as a standard.

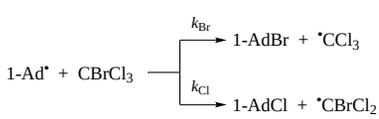
Reaction (9) is more intriguing; also in this case, the rate constants of primary, secondary and tertiary alkyl radicals with $Bu^{n}_{3}SnH$ are essentially equal at room temperature.[10] The enthalpic, steric and polar effects [reaction (11)], however, act in

$$R^{\bullet} + H\text{–}SnBu^{n}_{3} \longrightarrow [\overset{\delta-}{R} \cdots H \cdots \overset{\delta+}{SnBu^{n}_{3}}]^{\ddagger} \longrightarrow R\text{–}H + {}^{\bullet}SnBu^{n}_{3} \quad (11)$$

the same direction, decreasing from primary to tertiary alkyl radicals, due to the different electronegativity between Sn and S and the consequent opposite polarization of Sn–H and S–H bonds. In any case, reaction (9) has been applied as a standard to a variety of alkyl radical reactions, due to the lower value of k_9 compared with k_8. We have utilised both standards, when it was possible, and the agreement was satisfactory.

Chlorine abstraction from polychloromethanes

The reaction of the 1-Ad$^{\bullet}$ radical with $BrCCl_3$ leads to 1-bromo- and 1-chloro-adamantane in a 17 : 1 ratio[11] (Scheme 1);

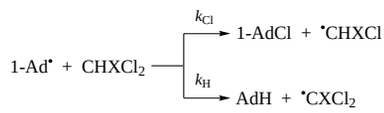


Scheme 1

this result conflicts with the behaviour of ordinary alkyl radicals (primary, secondary and tertiary, including the 2-Ad$^{\bullet}$ radical), in which bromine abstraction is the only detected process.[11,12] We have explained these results[3] by the fact that, though the enthalpic factor (lower energy of C–Br compared with the C–Cl bond) is generally dominant in halogen abstraction by alkyl radicals, the enhanced nucleophilic character of the 1-Ad$^{\bullet}$ radical [reaction (12)] also allows chlorine abstraction to take place to a significant extent.

$$1\text{-}Ad^{\bullet} + CBrCl_3 \longrightarrow [\overset{\delta+}{1\text{-}Ad} \cdots Cl \cdots \overset{\delta-}{CBrCl_2}]^{\ddagger} \longrightarrow 1\text{-}Ad\text{–}Cl + {}^{\bullet}CBrCl_2 \quad (12)$$

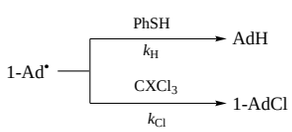
This behaviour prompted us to investigate the reaction of the 1-Ad$^{\bullet}$ radical with $CHCl_3$ and CH_2Cl_2, and also because 1-AdCl was always among the reaction products when the 1-Ad$^{\bullet}$ radical was generated in these solvents.[3] The reaction was carried out by decomposition of benzoyl peroxide in a mixture of benzene and $CHCl_3$ (or CH_2Cl_2) in the presence of 1-AdI; the 1-Ad$^{\bullet}$ radical was cleanly formed according to reaction (5) and abstracted both hydrogen and chlorine atoms from the chloromethanes (Scheme 2).



X = H or Cl

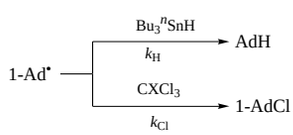
Scheme 2

It is interesting to note that chlorine abstraction by 1-Ad$^{\bullet}$ largely prevails over hydrogen abstraction with $CHCl_3$ ($k_{Cl}/k_H = 22.3$), whereas with Bu$^{t\bullet}$ radical hydrogen abstraction from $CHCl_3$ prevails ($k_H = 2.54 \times 10^2\ M^{-1}\ s^{-1}$ and $k_{Cl} = 1.84 \times 10^2\ M^{-1}\ s^{-1}$ at 310 K, $k_{Cl}/k_H = 0.72$).[13] With CH_2Cl_2, hydrogen and chlorine abstraction by 1-Ad$^{\bullet}$ radical occur with similar rates ($k_{Cl}/k_H = 0.84$), whereas with ordinary alkyl radicals hydrogen abstraction largely prevails. These results can be explained by the enhanced nucleophilic character of the 1-Ad$^{\bullet}$ radical with transition states similar to those of reaction (12). In order to measure the rate constants for chlorine abstraction from CCl_4 and $CHCl_3$ by the 1-Ad$^{\bullet}$ radical we utilised competition kinetics according to Schemes 3 and 4. The reactions were carried out in



X = H or Cl

Scheme 3



X = H or Cl

Scheme 4

benzene; the 1-Ad$^{\bullet}$ radical was generated according to reaction (4). The validity of the competition kinetics is related to the facts that reaction (4) is much faster than chlorine abstraction from CCl_4 or $CHCl_3$ by the $Bu^{n}_{3}Sn^{\bullet}$ radical and that hydrogen abstraction by alkyl radicals from PhSH is two orders of magnitude faster than from $Bu^{n}_{3}Sn\text{–}H$ and six orders of magnitude faster than from $CHCl_3$.

Adamantane and 1-chloroadamantane were the only reaction products from the 1-Ad$^{\bullet}$ radical; thus the quantitative analysis of these compounds in reactions carried out with a known excess of substrates (PhSH and $CXCl_3$ or $Bu^{n}_{3}Sn\text{–}H$ and $CXCl_3$) allowed the evaluation of the ratios k_{Cl}/k_H and therefore of k_{Cl}. With CCl_4 both standards, PhSH and $Bu^{n}_{3}Sn\text{–}H$ have been used, due to the value of the rate constant of chlorine abstraction, which is intermediate between k_8 and k_9. With $CHCl_3$, the rate of chlorine abstraction is lower and only $Bu^{n}_{3}Sn\text{–}H$ can be used as a standard in competition kinetics.

The rate constants are reported in Table 1 in comparison with the corresponding values for the Bu$^{t\bullet}$ radical. In both cases, CCl_4 and $CHCl_3$, the rate constants for chlorine abstraction by

Table 1 Absolute rate constants for chlorine abstraction from CCl_4 and $CHCl_3$ by 1-Ad$^{\bullet}$ and Bu$^{t\bullet}$

		k_{Cl}/M^{-1} s^{-1}		k_{Cl}/M^{-1} s^{-1}	
$CXCl_3$	Procedure[a]	(1-Ad$^{\bullet}$)	T/°C	(Bu$^{t\bullet}$[b])	T/°C
CCl_4	A	4.4×10^7	25	4.9×10^4	37
CCl_4	B	2.6×10^7	37	—	—
$CHCl_3$	A	6.4×10^4	25	1.8×10^2	37

[a] A—using Bu$^n_3$SnH as reference standard. B—using PhSH as reference standard. [b] Ref. 13.

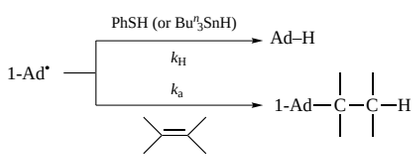
the 1-Ad$^{\bullet}$ radical are, at least, two orders of magnitude higher than those of the corresponding reactions by the Bu$^{t\bullet}$ radical.

We explain the enhanced reactivity of the 1-Ad$^{\bullet}$ radical mainly by the polar effect, as shown in reaction (12), due to the higher nucleophilicity of the 1-Ad$^{\bullet}$ radical compared to tertiary alkyl radicals. In agreement with this explanation the rate constant for chlorine abstraction from CCl_4 by the 2-Ad$^{\bullet}$ radical has been evaluated at 1.2×10^4 M^{-1} s^{-1} by the same method (Bu$^n_3$Sn–H has been used as standard).

Addition to electron-poor alkenes

Polar effects can play an important role in the addition of free radicals to alkenes. Alternating addition of alkyl radicals to pairs of alkenes with opposite polar character (electron-poor and electron-rich alkenes) in the presence of metal salt redox systems is a significant synthetic application[14] of the polar effect. The absolute rate constants for the addition of several alkyl radicals to a great variety of alkenes have been extensively investigated by Fischer.[15] It was, therefore, interesting to determine the absolute rates of addition of the 1-Ad$^{\bullet}$ radical to alkenes in order to compare them with the rate constants of other alkyl radicals, in view of the enhanced nucleophilic character claimed[3] for the 1-Ad$^{\bullet}$ radical.

Fischer's data[15] suggested that we could use PhSH or Bu$^n_3$Sn–H as standards for determining the values of the rate constants by competition kinetics with alkenes conjugated with electron-withdrawing groups. Thus we have applied the competitive method to acrylonitrile, ethyl fumarate and maleate, maleic anhydride and ethyl crotonate according to Scheme 5.



Scheme 5

The reactions were carried out in benzene solution and the 1-Ad$^{\bullet}$ radical was generated according to reaction (4). Adamantane and the compounds of reductive adamantylation of alkenes were the only reaction products from the 1-Ad$^{\bullet}$ and the quantitative analysis of these compounds in reactions carried out with a known excess of substrates (PhSH and alkene or Bu$^n_3$Sn–H and alkene) allowed us to measure k_a/k_H and therefore k_a. The results are reported in Table 2 and compared with the corresponding values known for the Bu$^{t\bullet}$ radical.

The absolute rate constants obtained in this way are in satisfactory agreement with the relative rates determined by the competitive adamantylation of pairs of alkenes (Table 3). In all cases, the rate constants for the addition of the 1-Ad$^{\bullet}$ radical to electron-poor alkenes are significantly higher than those of the corresponding reactions by the Bu$^{t\bullet}$ radical, supporting the enhanced nucleophilicity of the 1-Ad$^{\bullet}$ radical, which is reflected in transition states with substantial charge-transfer character [reaction (13)].

$$1\text{-Ad}^{\bullet} + CH_2{=}CH{-}CN \longrightarrow [1\text{-Ad}^{+}(CH_2{-}\dot{C}H{-}CN)^{\bullet -}]^{\ddagger} \longrightarrow 1\text{-Ad}{-}CH_2{-}\dot{C}H{-}CN \quad (13)$$

Table 2 Absolute rate constants for the addition of 1-Ad$^{\bullet}$ and Bu$^{t\bullet}$ radicals to alkenes at 25 °C

		k_a/M^{-1} s^{-1}	
Alkene	Procedure[a]	1-Ad$^{\bullet}$	Bu$^{t\bullet}$[b]
Acrylonitrile	A	2.2×10^8	5.2×10^6
Acrylonitrile	B	5.3×10^7	—
Maleic anhydride	A	2.3×10^8	—
Ethyl fumarate	B	1.2×10^8	5.3×10^5
Methyl maleate	A	2.1×10^7	2.1×10^5
Methyl maleate	B	2.7×10^7	—
Methyl crotonate	A	2.4×10^6	6.9×10^3

[a] A—using Bu$^n_3$SnH as reference standard. B—using PhSH as reference standard. [b] Ref. 15.

Table 3 Relative rates for the addition of the 1-Ad$^{\bullet}$ radical to alkenes at 25 °C

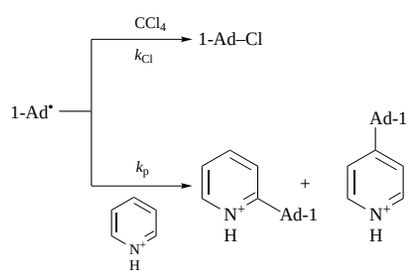
Alkene	Relative rates[a]	Relative rates from Table 2
Ethyl crotonate	1	1
Methyl maleate	23	20
Ethyl fumarate	106	100
Acrylonitrile	183	167
Maleic anhydride	201	192

[a] Determined by competition of pairs of alkenes.

When electron-rich alkenes, such as cyclohexene and hex-1-ene, reacted with the 1-Ad$^{\bullet}$ radical and Bu$^n_3$Sn–H, adamantane was the only reaction product and no detectable attack on the alkene was observed at a 20:1 ratio between alkene and Bu$^n_3$Sn–H; this means that the rate constant for the addition of 1-Ad$^{\bullet}$ radical to these alkenes is $<10^3$ M^{-1} s^{-1}, which supports the important role of the polar effect.

Substitution of protonated heteroaromatic bases by the 1-adamantyl radical and the relationship with the Gif reaction

Polar effects play a dominant role in the addition of nucleophilic carbon-centred radicals to protonated heteroaromatic bases.[16] It was of great interest to determine the absolute rate constants for the addition of the 1-adamantyl radical to these substrates in order to evaluate the importance of the suggested enhanced nucleophilic character of this radical. The absolute rate constants for hydrogen abstraction from PhSH and Bu$^n_3$SnH were not suitable standards in this case because the heteroaromatic substitution requires an oxidising medium. Thus we have used chlorine abstraction from CCl_4 as a standard for determining the rate constants for the addition of the 1-Ad$^{\bullet}$ radical to protonated heteroaromatic bases (Scheme 6).



Scheme 6

Pyridine, 4-cyanopyridine and quinoline have been used as heteroaromatic bases; we had previously[17] measured the rate constants for the addition of the Bu$^{t\bullet}$ radical to 4-cyanopyridine and quinoline.

The 1-Ad$^{\bullet}$ radical was generated, according to reaction (5), from 1-Ad–I and benzoyl peroxide in benzene solution. 1-AdCl and the adamantylpyridine derivatives were the only reaction products from the reaction of the 1-Ad$^{\bullet}$ radical and the quantitative analysis of these compounds allowed us to evaluate k_p.

Table 4 Absolute and relative rate constants for the addition of 1-Ad$^{\bullet}$ and Bu$^{t\bullet}$ radicals to protonated pyridine derivatives at 57 °C

Pyridine derivative	Procedure[a]	k_p/M^{-1} s^{-1} (1-Ad$^{\bullet}$)	Relative rate from k_p	Relative rate from direct competition	k_p/M^{-1} s^{-1} (Bu$^{t\bullet}$[b])	Relative rate
Pyridine	A	2.1×10^6	1	1	3.3×10^4[c]	1
Pyridine	B	2.3×10^6	—	—	—	—
Quinoline	A	1.4×10^8	818	913	4.1×10^6	124
Quinoline	B	2.2×10^8	—	—	—	—
4-Cyanopyridine	A	2.5×10^8	1273	1196	6.3×10^7	1910
4-Cyanopyridine	B	3.1×10^8	—	—	—	—

[a] A—1-Ad–I and B—1-Ad–COOH as radical sources. [b] Ref. 23. [c] Evaluated by the relative rates.

Another procedure we employed for generating the 1-Ad$^{\bullet}$ radical under oxidising conditions involves reactions (6) and (7) in benzene solution. When this procedure was used, significant amounts of 1-AdOAc were also formed, clearly arising from the oxidation of 1-Ad$^{\bullet}$ radical by $Pb(OAc)_4$ [reaction (14)].

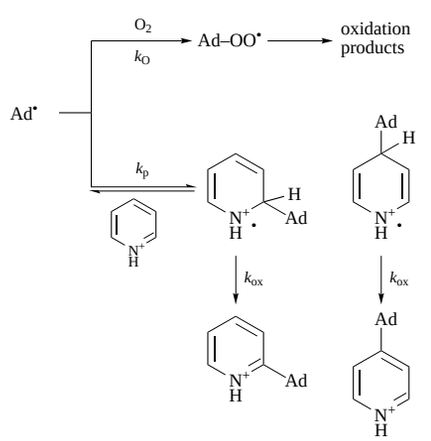
$$1\text{-Ad}^{\bullet} + Pb(OAc)_4 \longrightarrow 1\text{-Ad–OAc} + Pb(OAc)_3 \qquad (14)$$

Since $Pb(OAc)_4$ is used in small amounts and it reacts completely during the competition process, it was not possible to exactly evaluate the rate constant for reaction (14), which, however, appears to be very fast (>10^8 M^{-1} s^{-1}) because it competes with chlorine abstraction and heteroaromatic addition. This high oxidation rate further supports the enhanced nucleophilic character of the 1-Ad$^{\bullet}$ radical, but it does not affect the validity of the competition kinetics for evaluation of k_p (Scheme 6). The agreement of the rate constants obtained by the two procedures is satisfactory (Table 4). In the case of pyridine, the rate constant for the reaction of the Bu$^{t\bullet}$ radical was not known, but it could be deduced from the relative rates of reaction with quinoline and 4-cyanopyridine.

With 4-cyanopyridine, the increase in the rate constant for the addition of the 1-Ad$^{\bullet}$ radical with respect to pyridine is less marked compared to the Bu$^{t\bullet}$ radical; a possible explanation is the incomplete protonation of the less basic cyanopyridine under the conditions of the competition kinetics (protonation enhances the addition rates of nucleophilic alkyl radicals to heteroaromatic bases by three to four orders of magnitude).[16] The reaction is not completely selective in the α-position; in addition to the prevailing formation of 2-adamantyl-4-cyanopyridine (82.8%), the 3-adamantyl isomer is also formed (17.2%); with the Bu$^{t\bullet}$ radical under the same conditions, the substitution is more selective (94.5% of the 2-isomer and 5.5% of the 3-isomer).

The limit of this kinetic evaluation is related to the reversibility of the alkyl radical addition to protonated pyridines,[18] whereas chlorine abstraction from CCl_4 is irreversible. Thus the rate constants reported in Table 4 must be considered as lower limit values. We have also explained[18] the different regioselectivities observed in the homolytic alkylation of 4-cyanopyridine as an effect of this reversibility. When the kinetic approach depicted in Scheme 6 was applied to the 2-adamantyl radical, the rate constant determined for the reaction with pyridine was 1.3×10^4 M^{-1} s^{-1}, which is two orders of magnitude lower than the value obtained for the 1-adamantyl radical. The only reasonable explanation for this high increase in reactivity is given by the polar effect (the enhanced nucleophilic character of the 1-adamantyl radical) because enthalpic and steric effects must be substantially similar for both radicals (1-Ad–H and 2-Ad–H bonds have the same energies and this is very likely true also for Ad–C bonds). On the other hand, the complete selectivity in the α- and γ-positions in the substitution of the pyridine and quinoline rings is very strong evidence of the dominant polar effect. We believe that these results contribute to the understanding of the debated[19–21] Gif reaction mechanism, in which adamantane oxidation was one of the most controversial aspects. According to Barton,[21] 'Gif chemistry' is based on a Fe^{III}/Fe^{V} non-radical-producing manifold with formation of iron–carbon bonds at both positions of adamantane; in the tertiary case the bond is so weak that spontaneous fragmentation to the carbon radical takes place and only this radical is trapped by pyridine, whereas the 2-Ad–Fe intermediate is oxidised. We,[19] as well as Perkins,[20] suggested that this behaviour can be explained by the different reactivity of 1-Ad$^{\bullet}$ and 2-Ad$^{\bullet}$ radicals towards protonated pyridine; till now this was only a reasonable hypothesis, which is now clearly confirmed by the results in Table 4.

Barton's argument[21,22] was based on the different behaviour observed in the 'Gif oxidation' of adamantane compared to adamantyl radicals generated from Barton esters under reduced oxygen pressure. Thus at 4% oxygen pressure the ratio of oxidised products to pyridine-trapped products was 4.3 for the secondary adamantyl radical and 0.74 for the tertiary one, when they were generated from Barton esters. During Gif oxidation at 4% oxygen in nitrogen the ratio of oxidation to pyridine trapping for the secondary position was 94, but it was only 0.03 for the tertiary position; the conclusion was that the radicals behave completely differently from what is seen in the Gif chemistry. However, Barton neglects an essential feature of the homolytic alkylation of pyridine, namely, the above mentioned[18] reversibility of the addition of alkyl radicals to the pyridine ring. If 1-Ad$^{\bullet}$ and 2-Ad$^{\bullet}$ radicals are generated in protonated pyridine, which contains dissolved oxygen, we expect competition between the reversible addition to the large excess of pyridine and the irreversible peroxyl radical formation (Scheme 7), due to the low concentration of oxygen.



Scheme 7

This occurs for both 1-Ad$^{\bullet}$ and 2-Ad$^{\bullet}$ radicals, but the essentially diffusion-controlled reaction with oxygen has about the same rate constant for both radicals; on the other hand, the reaction rate of the 1-Ad$^{\bullet}$ radical with the pyridinium ion is much greater than that of the 2-Ad$^{\bullet}$ radical. This means that the reversibility of the 1-Ad$^{\bullet}$ radical addition to pyridine is lower than that for 2-Ad$^{\bullet}$, because the enthalpy is similar and the polar effect is dominant. This mechanistic picture (Scheme 7) implies that the ratio of oxidation products to pyridine-

trapped products is largely determined by the rate of the rearomatisation step (k_{ox}). Now the Gif^{IV} system (Zn^0–O_2–Fe^{II}) is very poorly effective in rearomatisation, the latter taking place either by electron- or by hydrogen-transfer, including disproportionation.[16,18,23] This explains why, under Gif^{IV} conditions, the 2-Ad$^{\bullet}$ radical, which is more reversible in the pyridinium addition than the tertiary one, is mostly oxidised, whereas the same radical, when generated from Barton esters, gives significant amounts of pyridine-trapped products. In this latter case, rearomatisation of the radical adduct is more effective through an induced radical chain homolysis of the Barton esters.[23] Thus, Barton's results are, in our opinion, consistent with the intermediate formation of 1-Ad$^{\bullet}$ and 2-Ad$^{\bullet}$ radicals in the Gif oxidation of adamantane.

In conclusion, 1-Ad$^{\bullet}$ radical appears to be a very peculiar alkyl radical, because it is more reactive than ordinary tertiary alkyl radicals, for enthalpic reasons (higher energy of the 1-Ad–H bond, similar to the energy of secondary C–H bonds and, very likely, also higher energy of the 1-Ad–C bond), as well as for polar reasons (more nucleophilic than tertiary alkyl radicals and therefore also than secondary and primary alkyl radicals). For 'ordinary' alkyl radicals, in the absence of polar substituents, the two effects are opposite: bond energies decrease from primary to tertiary alkyl bonds, whereas the nucleophilic character increases from primary to tertiary alkyl radicals.

Experimental

General methods

GLC analyses were performed on a Dani 8610 capillary gas chromatograph, equipped with a 30 m × 0.25 mm id CP SIL 5CB fused silica column (0.25 μm film thickness), hydrogen as carrier gas, PTV injector and flame ionization detector.

^{1}H NMR spectra were recorded on a Bruker ARX400 instrument. GLC–MS spectra were performed on a GLC–MS HP5972 instrument, using a HP5890 series II gas chromatograph, equipped with DB-5 fused silica column (30 m × 0.25 m id, 0.25 μm film thickness) and helium as carrier gas.

All the reagents were obtained from commercial sources and were used without further purification.

Reaction of the 1-adamantyl radical with $CHCl_3$

A mixture of 0.5 mmol of 1-Ad–I and 0.5 mmol of benzoyl peroxide in 4 ml of $CHCl_3$ and 6 ml of benzene was refluxed for 4 h. The solution was directly analysed by GLC and GLC–MS. The conversion of 1-Ad–I was 49%; 1-AdCl and 1-AdH were formed in relative amounts of 95.7 and 4.3%, respectively. The reaction products were identified by comparison with authentic commercial samples.

Reaction of the 1-adamantyl radical with CH_2Cl_2

The reaction was carried out by refluxing for 8 h a solution of 0.5 mmol of 1-Ad–I and 0.5 mmol of benzoyl peroxide in 4 ml of CH_2Cl_2 and 6 ml of benzene. The conversion of 1-Ad–I was 22%; 1-AdCl and 1-AdH were formed in relative amounts of 45.7 and 54.3%, respectively.

Absolute rate constants for chlorine abstraction from CCl_4 and $CHCl_3$ by the 1-adamantyl radical by competition kinetics

General procedures. (*a*) A solution of CCl_4 or $CHCl_3$ and Bu^n_3SnH (the ratios between CCl_4 and Bu^n_3SnH were in the range 1:5–1:10, while the ratios between $CHCl_3$ and Bu^n_3SnH were in the range 10:1–40:1), 1-Ad–I (10% of CCl_4 or 10% of Bu^n_3SnH in the reactions with $CHCl_3$) and AIBN (10% of Ad–I) in benzene was refluxed for 30 min. GLC and GLC–MS analyses revealed the presence of adamantane and 1-Ad–Cl as the only reaction products from 1-Ad–I. The quantitative analysis of adamantane and 1-Ad–Cl and the known amounts of CCl_4 or $CHCl_3$ and Bu^n_3SnH used have allowed us to evaluate the values of the ratio k_{Cl}/k_H of Scheme 4 and therefore the value of k_{Cl} by assuming a value of 1.5×10^6 M^{-1} s^{-1} at 25 °C for hydrogen abstraction from Bu^n_3SnH by the 1-adamantyl radical, taking into account the known Arrhenius parameters of reaction (9). The results are reported in Table 1 in comparison with the corresponding known values for the *tert*-butyl radical. (*b*) A solution of CCl_4 and PhSH (ratios in the range 5:1–10:1), equimolar amounts of 1-Ad–I and Bu^n_3SnH (0.2 mol per mol of PhSH) and AIBN (0.05 mol per mol of 1-Ad–I) in benzene was refluxed for 30 min. The analysis was carried out as in (a) with the purpose of evaluating the ratio k_{Cl}/k_H of Scheme 3 and therefore k_{Cl}, by assuming a value of 1.3×10^8 M^{-1} s^{-1} at 25 °C for hydrogen abstraction from PhSH by the 1-adamantyl radical. The results are reported in Table 1, taking into account the known Arrhenius parameters for reaction (8).

Absolute rate constants for chlorine abstraction from CCl_4 by the 2-adamantyl radical

The general procedure (*a*), used for 1-Ad–I, was also used for 2-Ad–I,with a Bu^n_3SnH–CCl_4 ratio of 1:40. Adamantane and 2-Ad–Cl were obtained in 75.6 and 24.4% yield, respectively.

Reductive adamantylation of alkenes

General procedure. 5 mmol of alkene, 2.5 mmol of 1-Ad–I, 2.5 mmol of Bu^n_3SnH and 0.2 mmol of AIBN in 15 ml of benzene were refluxed for 1 h. The solution was qualitatively analysed by GLC–MS. No quantitative analysis was carried out, but the pure products of reductive adamantylation of the alkenes were isolated by flash chromatography (hexane–ethyl acetate 9:1) and identified by NMR and MS analysis. The pure compounds were used for identification and quantitative analysis in the competition kinetics.

Ethyl maleate. *m*/*z* 308 (M^+), 265, 235, 173, *135*, 107, 79; δ($CDCl_3$) 4.15 (4H, q, 2 CH_2CH$_3$), 2.72 (1H, –C*H*CO), 2.42 (2H, –CH_2CO), 2.10 (3H, tertiary position of adamantane), 1.76 (6H, 3 CH_2 of adamantane, close to the substituent), 1.58 (6H, 3 CH_2 of adamantane), 1.25 (6H, t, 2 CH_3CH$_2$–).

Methyl fumarate. *m*/*z* 280 (M^+), 248, 221, 179, 145, *135*, 107, 79; δ($CDCl_3$) 3.67 (6H, s, 2 CH_3O), 2.70 (1H, –C*H*CO), 2.42 (2H, –CH_2CO), 2.08 (3H, tertiary position of adamantane), 1.76 (6H, 3 CH_2 of adamantane, close to the substituent), 1.58 (6H, 3 CH_2 of adamantane).

Maleic anhydride. *m*/*z* 234 (M^+), 206, 177, 162, *135*, 107, 79; δ($CDCl_3$) 2.96 (1H, –C*H*CO), 2.42 (2H, –CH_2CO), 2.08 (3H, tertiary position of adamantane), 1.76 (6H, 3 CH_2 of adamantane, close to the substituent), 1.58 (6H, 3 CH_2 of adamantane).

Acrylonitrile. *m*/*z* 189 (M^+), 171, 155, *135*, 107, 79; δ($CDCl_3$) 2.30 (2H, t, –CH_2CN), 2.02 (3H, tertiary position of adamantane), 1.65 (6H, 3 CH_2 of adamantane, close to the substituent), 1.45 (6H, 3 CH_2 of adamantane, and 2H, CH_2CH_2CN).

Ethyl crotonate. *m*/*z* 250 (M^+), 205, 163, *135*, 107, 79; δ($CDCl_3$) 4.15 (2H, q, OCH_2CH$_3$), 2.50 (1H, dd, –CH_2CO), 1.96 (3H, tertiary position of adamantane and 1H, –CH_2CO), 1.65 (6H, 3 CH_2 of adamantane and 1H, CH$_3$C*H*–), 1.48 (6H, 3 CH_2 of adamantane), 1.22 (3H, t, CH_3CH$_2$O), 0.88 (3H, d, CH_3CH–).

Absolute rate constants for the addition of the 1-adamantyl radical to alkenes

General procedures. (*a*) A solution of alkene and Bu^n_3SnH (typically 30 mmol), 1-Ad–I (1 mmol) and AIBN (0.2 mmol) in 15 ml of benzene was refluxed for 30 min. The ranges of the ratios between alkene and Bu^n_3SnH were fixed by preliminary explorative experiments for an approximate evaluation of the reactivity of the alkenes in order that adamantane and the product of reductive adamantylation of the alkene (the only reaction products from 1-Ad–I) according to Scheme 5 were formed in the most suitable amounts from an analytical standpoint. These ranges were: for ethyl crotonate 1:2–2:1; for methyl maleate 5:1–10:1; for acrylonitrile 7:1–12:1; for ethyl

fumarate 10:1–20:1; for maleic anhydride 10:1–20:1. The quantitative GLC analyses of adamantane and of the product of reductive adamantylation of the alkene by using the pure products to check the gas chromatographic response, allowed the evaluation of the values of k_a/k_H for reactions in Scheme 5 and therefore the values of k_a, by assuming a value of 1.5×10^6 M^{-1} s^{-1} at 25 °C for hydrogen abstraction from Bu^n_3SnH by the 1-adamantyl radical, taking into account the known Arrhenius parameters of reaction (9). The results are reported in Table 2 in comparison with the corresponding known values for the *tert*-butyl radical. (*b*) A solution of alkene and PhSH (typically 20 mmol), 1 mmol of 1-Ad–I, 2 mmol of Bu^n_3SnH and 0.2 mmol of AIBN in 15 ml of benzene was refluxed for 30 min. The ranges of the ratios between PhSH and alkene were 1:3–2:1 for acrylonitrile, 1:5–1:10 for methyl maleate and 1:2–2:1 for ethyl fumarate. Adamantane and the product of reductive adamantylation of the alkenes were the only reaction products from 1-Ad–I. Their quantitative analysis, as in (a), allowed the evaluation of k_a. The results are reported in Table 2. When the competition reaction was carried out with electron-rich alkenes, *e.g.* hex-1-ene or cyclohexene, by using a 20:1 ratio between alkene and Bu^n_3SnH, adamantane was the only reaction product.

Relative rates for the addition of the 1-adamantyl radical to alkenes by competition kinetics

A solution of a pair of alkenes (20 mmol on the whole), 1-Ad–I (1 mmol), Bu^n_3SnH (1 mmol) and AIBN (0.1 mmol) in 15 ml of benzene was refluxed for 1 h. The following molar ratios were used for the pairs of alkenes: for ethyl crotonate–methyl maleate 3:1 methyl maleate–acrylonitrile 3:1, acrylonitrile–ethyl fumarate 2:1 and ethyl fumarate–maleic anhydride 1:1. The quantitative GLC analyses of the reductive adamantylation of alkenes allowed evaluation of the relative rates. The results are reported in Table 3 with the relative rates evaluated from Table 2.

Homolytic adamantylation of protonated pyridine derivatives

General procedures. A solution of 3 mmol of pyridine derivative, 6 mmol of CF_3COOH, 1 mmol of 1-Ad–I and 1 mmol of benzoyl peroxide in 10 ml of benzene was refluxed for 4 h. The adamantyl derivatives of pyridine were isolated by flash chromatography and analysed by NMR and MS analysis.

Pyridine. The α- and γ-(1-adamantyl)pyridines were obtained in a 15:1 ratio; the two isomers were isolated by flash chromatography (hexane–ethyl acetate 9:1) and identified by comparison of GLC–MS with authentic samples.[22] Isomer α: *m*/*z* 213 (M^+), 198, 184, 170, 156, 130, 117, 93, 78. Isomer γ: *m*/*z* 213 (M^+), 198, 184, 170, 156, 135, 120, 93, 79.

4-Cyanopyridine. The α-adamantyl isomer was obtained in 82.8% yield and the β-isomer in 17.2% yield. Isomer α: *m*/*z* 238 (M^+), 223, 209, 195, 181, 169, 155, 142, 131, 118, 103, 91, 77; $\delta(CDCl_3)$ 8.75 (1H, d, in position 6 of the pyridine ring), 7.50 (1H, s, in position 3 of the pyridine ring), 7.32 (1 h, d, in position 5 of the pyridine ring), 2.12 (3H, tertiary position of adamantane), 1.95 (6H, 3 CH_2 of adamantane, close to the pyridine ring), 1.75 (6H, 3 CH_2 of adamantane far from the pyridine ring). Isomer β: *m*/*z* 238 (M^+), 223, 209, 195, 181, 169; $\delta(CDCl_3)$ 8.77 (1H, s, in position 2 of the pyridine ring), 8.62 (1H, d, in position 6 of the pyridine ring), 7.52 (1H, d, in position 5 of the pyridine ring), 2.21 (9H, 3H tertiary and 6H at the secondary position of adamantane), 1.81 (6H, 3 CH_2 or adamantane, far from the pyridine ring).

(1-Adamantyl)quinoline. It was the only isomer obtained with quinoline. *m*/*z* 263 (M^+), 248, 234, 220, 206, 194, 180, 156, 143, 128; $\delta(CDCl_3)$ 8.10 (1H, d, in position 4 of quinoline), 8.04 (1H, d, in position 8 of quinoline), 7.5–7.8 (4H, m, positions 3, 5, 6 and 7 of quinoline), 2.18 (3H, tertiary position of adamantane, 2.10 (6H, 3 CH_2 of adamantane, close to the quinoline ring), 1.82 (6H, 3 CH_2 of adamantane, far from the quinoline ring).

Absolute rate constants for the addition of the 1-adamantyl radical to protonated pyridines

(*a*) A solution of the pyridine derivative and CCl_4 (20 mmol on the whole), CF_3COOH (2 mmol for mol of pyridine derivative), 1 mmol of 1-Ad–I and 1 mmol of benzoyl peroxide in 15 ml of benzene was refluxed for 4 h. The following ratios between CCl_4 and the pyridine derivatives were used: pyridine (1:8), quinoline (3:1), 4-cyanopyridine (4:1). 1-Chloroadamantane and the adamantylation products of pyridine derivatives were the only reaction products from 1-Ad–I. Their qualitative GLC analysis has allowed to evaluate k_p/k_{Cl} of Scheme 6 and therefore the values of k_a by assuming the value of 2.8×10^7 M^{-1} s^{-1} at 57 °C for k_{Cl}. The results are reported in Table 4 and compared with the corresponding values for the *tert*-butyl radical. (*b*) The reaction was carried out as in (a) by using 1 mmol of 1-AdCOOH and 1 mmol of $Pb(OAc)_4$ instead of 1-AdI and benzoyl peroxide. The results are reported in Table 4, in comparison with the corresponding values for the *tert*-butyl radical.

Absolute rate constants for the addition of the 2-adamantyl radical to protonated pyridine

The general procedure (*a*), utilised for 1-Ad–I, was also utilised for 2-Ad–I, with a pyridine–CCl_4 ratio of 1:1. 1-Ad–Cl and the α- and γ-adamantyl pyridines were obtained in 48% and 52% yield, respectively.

Relative rates for the addition of the 1-adamantyl radical to protonated heteroaromatic bases by competition kinetics

A solution of a pair of pyridine derivatives (20 mmol on the whole), 40 mmol of CF_3COOH, 1 mmol of 1-Ad–I and 1 mmol of benzoyl peroxide in 15 ml of benzene was refluxed for 4 h. The following ratios of the pyridine derivative were used: pyridine–quinoline 9:1, pyridine–4-cyanopyridine 10:1, pyridine–quinoline 1:1. The reaction solution was directly analysed by GLC by using 2-cyclohexylpyridine as internal standard. The results are reported in Table 4.

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