Photoinduced SET for the Functionalization of Alkanes

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Thermochemical cycles show that deprotonation of alkane radical cations is an exothermic process, and indeed photoinduced SET between several alkanes and 1,2,4,5-tetracyanobenzene (TCB) is followed by efficient deprotonation of the radical cation with tertiary > secondary > primary selectivity; the alkyl radical is trapped by TCB$^{\cdot -}$ or, when present, by oxygen; when tetrachloro-*p*-benzoquinone is used in the place of TCB, the radical is further oxidized to the cation.

Selective and efficient activation of the C–H bond in alkanes remains a difficult task, despite the variety of methods employed,[1–3] which include reactions with radicals,[3] excited states,[4] and strong organic,[5] inorganic,[6] or organometallic[7] oxidants. This is obviously due to the strength and the apolar character of this bond. A solution to this problem would be single electron transfer (SET) oxidation of the alkane followed by deprotonation [eqns. (2), (3) rather than eqn. (1)] and in this communication we show that *photoinduced* SET is indeed an appealing possibility.

$$\text{R–H} \rightarrow \text{R}^{\cdot} + \text{H}^{\cdot} \qquad (1)$$

$$\text{R–H} \xrightarrow{-e} \text{R–H}^{+\cdot} \qquad (2)$$

$$\text{R–H}^{\cdot +} \rightarrow \text{R}^{\cdot} + \text{H}^{+} \qquad (3)$$

Recent literature has shown that SET dramatically increases the acidity of C–H bonds.[8,9] Direct measurements have been limited to strongly stabilized radical ions, *e.g.* fluorenyl or α-amino derivatives.[8] However, the oxidation potential of some unsubstituted alkyl radicals has been recently measured,[10] and this allows the evaluation of the free energy change for the deprotonation of the radical cations of simple alkanes through a thermochemical cycle.[10,11]

We carried out such a calculation for some alkanes (Table 1) and found that the weakening of the $\sigma_{\text{C–H}}$ bond is conspicuous [*ca.* 100 kcal mol^{-1} (1 cal = 4.184 J)] compared to 50–60 kcal mol^{-1} for stabilized radicals, *e.g.* deprotonation from α-amino or benzylic position,[8e,f] so that deprotonation of the radical cation of unsubstituted alkanes [eqn. (3)] was exergonic in every case [see $\Delta G(3)$ in Table 1], with a marked selectivity for the formation of the more stable radical.

Of course, this requires that the alkane is firstly oxidized [eqn. (2)]. Alkanes have been anodically oxidized in 'inert' solvents such as acetonitrile, but overoxidation of the initially formed alkyl radical to the carbocation cannot be avoided.[11] However, recent experiments have shown that a mild and efficient way to carry out SET in homogeneous solution is now available, by exploiting the strong oxidizing properties of the excited state of organic molecules.[12]

Typical representatives of strong photochemical oxidants (A) are 1,2,4,5-tetracyanobenzene [TCB, $E_{\text{red}}(\text{S}_0)$ −0.66 V *vs.* SCE, $E_{\text{red}}(\text{S}_1)$ 3.44 V] and chloranil [Chl, $E_{\text{red}}(\text{S}_0)$ 0.02 V, $E_{\text{red}}(\text{T}_1)$ 3.33 V]. Consideration of the Weller equation shows that the oxidation of most alkanes according to eqn. (4) is feasible [see $\Delta G(4)$ in Table 1].

$$\text{R–H} + \text{A}^{*} \rightarrow \text{R–H}^{\cdot +} + \text{A}^{\cdot -} \qquad (4)$$

Indeed, we found that the fluorescence of TCB was quenched by adamantane **1a**. Preparative irradiation of a deaerated acetonitrile solution of 5×10^{-3} mol dm^{-3} TCB and 1×10^{-2} mol dm^{-3} **1a** afforded 5-(adamantan-1-yl)benzene-1,2,4-tricarbonitrile **2a** in good chemical and quantum yield, while the corresponding adamant-2-yl derivative was not found in detectable amounts (Scheme 1 and Table 1). This reaction was obviously related to the previously studied alkylation of TCB with better donors,[13] where the radical cation formed by photoinduced electron transfer underwent fragmentation to yield a neutral radical and this coupled with the acceptor radical anion (see Scheme 2). Fragmentation competed efficiently with back electron transfer, as shown by the relatively high quantum yield.

In oxygen saturated solution, the overall quantum yield was unchanged, while the main product was 1-adamantanol **3** along with small amounts of adamantan-2-one **4** and **2a**. Apparently, the alkyl radical was trapped by O_2 (Scheme 2, path ii) and TCB mainly functioned as a non-consumed sensitizer.[†] The alcohols probably arose from the corresponding hydroperoxides (a little 1-adamantanyl hydroperoxide was indeed obtained); the somewhat lower tertiary *vs.* secondary selectivity in this case may be due to concurrent hydrogen abstraction by alkoxy or peroxy radicals formed from the hydroperoxides.

Irradiation of Chl and **1a** in dearated MeCN caused reduction of the former to the hydroquinone ChlH$_2$ and oxidation of the latter to *N*-(adamant-2-yl)acetamide **5** as the main product, accompanied by a small amount of the isomeric 2-adamantyl derivative **6**; the phenyl ethers **7** and **8** were identified as minor products. Again, in the presence of oxygen adamantan-1-ol and adamantan-2-one were also formed (and ChlH· was reoxidized).

The process differed from that observed with TCB in two ways. Firstly, the acceptor radical anion had here nucleophilic properties, contrary to the case of arenenitriles,[15] and the proton was transferred to Chl$^{\cdot -}$ yielding a pair of neutral radicals. The second difference with TCB lay in the redox potentials (see

Table 1

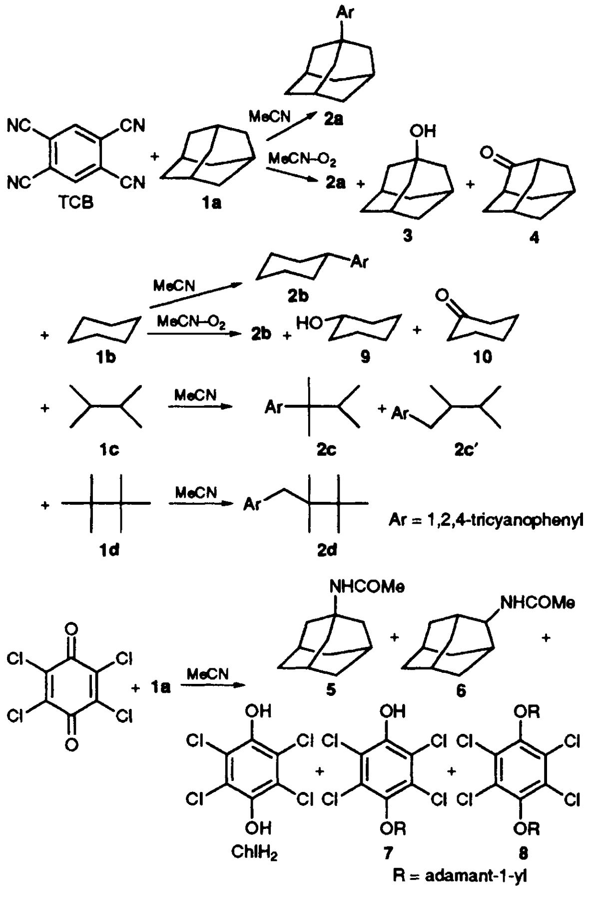
Donor	Acceptor	$\Delta G(4)$/ kcal mol^{-1}	$\Delta G(3)^{a}$/ kcal mol^{-1}	K_{SV}/ mol^{-1}	$\Phi^{b,c}$	Photochem. products (% Yield)^{c}	Selectivity^{a} (stat. corr.)
1a	TCB	−17	t −11.5 s −8.0	110	0.06	**2a**(81)	t/s > 100
1a	Chl	−14			0.05	**5**(32), **6**(2), **7** + **8**(25), ChlH$_2$(37)	t/s 45
1b	TCB	−14	−9.9	6	0.04	**2b**(70)	
1c	TCB	−9	t −14.1 p −8.1	2	0.005	**2c**(70), **2c′**(7)	t/p 60
1d	TCB			1	0.005	**2d**(80)	
1a	TCB				0.06	**2a**(9), **3**(60), **4**(18)^{d}	
1a	Chl				0.01	**3**(24), **4**(13), **5**(25), ChlH$_2$(10)^{d}	
1b	TCB				0.04	**2b**(6), **9**(21), **10**(59)^{d}	

[a] Deprotonation from a tertiary (t), secondary (s), or primary (p) position. [b] Overall quantum yield (sensitizer + alkane consumption) in saturated alkane solution in acetonitrile. [c] By irradiation of a 0.005 mol dm^{-3} solution of TCB (or Chl) with 0.01 mol dm^{-3} **1a**. In the other cases 0.01 mol dm^{-3} TCB with 0.1 mol dm^{-3} alkane. [d] In oxygen saturated solution.

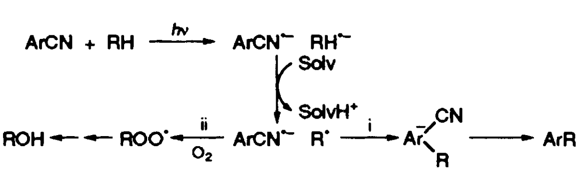
above). Thus, while these two molecules have the same E_{red} in the excited state, Chl is also a reasonable oxidant in the ground state, and thus oxidation of the alkyl radical to the cation (followed by trapping by the solvent) competed favourably with chemical trapping by Chl$^{\cdot -}$ (to give **8**), ChlH$^{\cdot}$ (to give **7**) or O_2 (Scheme 3). As a result, the main reaction was an overall two-electron transfer.

The photoinduced reaction between 0.01 mol dm^{-3} TCB and 0.1 mol dm^{-3} cyclohexane **1b** also proceeded efficiently yielding the alkylated trinitrile **2b** and, in the presence of oxygen, cyclohexanol **9** and cyclohexanone **10**.

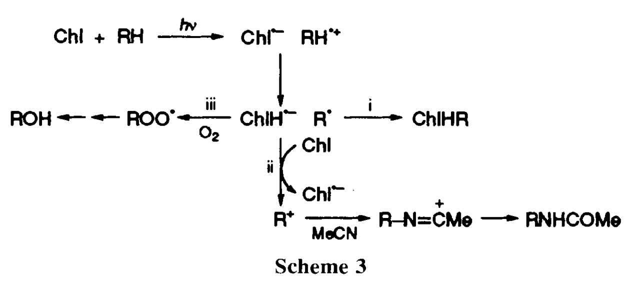
With 2,3-dimethylbutane **1c**, both possible alkylation products (**2c** and **2c′**) were formed, with statistical corrected tertiary *vs.* primary selectivity of 60: Even in the case of 2,2,3,3-tetramethylbutane the moderate quenching of TCB^{1*} was sufficient to promote alkylation and to yield **2d**.



Scheme 1



Scheme 2



Scheme 3

These findings can be summarized by stating that photoinduced electron transfer is a viable path for obtaining alkyl radicals from alkanes‡ under unusually mild conditions and with selectivities related to the thermodynamic stability of the radicals. The method is both generally applicable and flexible, as it allows *e.g.* trapping of the radical by oxygen or shifting from radical to carbocation chemistry by choosing the appropriate acceptor.

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Footnotes

† Oxidation of TCB$^{\cdot -}$ by O_2 is slightly endothermic.[14] However, in this case it occurs efficiently since back electron transfer is precluded by fast radical cation cleavage.

‡ We considered the possible intervention of other mechanisms, *e.g.* that hydrogen abstraction from the alkanes was a secondary reaction due to primary radicals formed by oxidation of the solvent. However, the good correlation of K_{SV} and chemical reactivity with the oxidation potential shows that with **1a–b**, direct oxidation of the alkane is involved, although the other mechanisms may compete with less easily oxidized alkanes such as **1c–d**.

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