New synthetic methods *via* radical cation fragmentation

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Photoinduced single electron transfer followed by radical cation cleavage is a selective method for generating radicals and cations from unconventional substrates under unparalleled mild conditions. The versatility of the method and its synthetic significance are demonstrated through the discussion of selected examples involving alkyl radicals as the key species, such as nucleophilic aromatic substitution, addition to unsatured esters, nitriles and ketones, and reduction, as well as of an example of addition to cations.

1 An unconventional synthetic method

The basis of organic synthesis is the formation of the carbon–carbon bond. Available methods are based upon active species, such as carbanions, carbocations or radicals, in turn prepared through hetero- or homo-lytic cleavage of a bond. This introduces an intrinsic limitation as only relatively weak bonds, *e.g.* C–I, undergo homolytic cleavage under convenient conditions, while heterolytic cleavage requires the use of an aggressive reagent. For example, a strong base must be used for abstracting a proton (or another electrofugal group). Organic molecules derive their stability from being closed shell species; thus, another way of inducing fragmentation is to weaken first a molecule by subtracting, or adding, an electron. The resulting odd-electron species (a radical ion) is strongly destabilized, and often fragments [*e.g.* eqn. (1)].

$$R–X \xrightarrow{-e} R–X^{\bullet+} \rightarrow R^{\bullet} + X^{+} \qquad (1)$$

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How can such a redox activation be carried out? One may look to electrochemistry, or to the use of inorganic oxidants or reductants (which often operate *via* atom transfer, not electron transfer, however), certainly not to oxidation or reduction by another organic molecule. Undergraduate students may sometimes be puzzled by the fact that redox reactions [*e.g.* eqn. (2)] are one of the main topics in inorganic chemistry courses, while they never hear of redox reactions between organic molecules. This is because inorganic ions mostly have several closely spaced redox states, while in organic molecules the HOMO–LUMO gap is too large, and thus with a very few exceptions single electron transfer (SET) between any pair of organic molecules [*e.g.* eqn. (3)] would be largely endothermic.

$$M^{m+} + N^{n+} \longrightarrow M^{(m-1)+} + N^{(n+1)+} \quad (2)$$

$$A + R\text{–}X \longrightarrow A^{\bullet -} + R\text{–}X^{\bullet +} \quad (3)$$

However, precisely because of the HOMO–LUMO gap being so large, the situation is reversed with electronically excited states, and if SET is a rare event in ground state organic chemistry, it is quite common in photochemistry. Indeed, the method discussed below is based on the activation of a substrate by photoinduced single electron transfer (SET) to an acceptor A [see eqn. (3)] followed by fragmentation of the thus formed radical cations giving the carbon centred radicals or carbocations. It will be shown that:

- Photochemistry is a convenient method for generating radical cations in solution.
- Under such conditions strong bonds (*e.g.* C–H, C–C) are selectively cleaved, and in this way radicals and cations are generated from unconventional precursors under unparalleled mild conditions.
- The thus generated intermediates, in particular carbon-centred radicals, can be trapped for synthetically useful reactions *via* C–C bond formation.

2 Principles of the method

2.1 Photosensitised redox processes

Electronically excited states, while widely differing in their electronic structure, and thus in their chemical reactivity, share one common feature, *viz.* they are both stronger oxidants and stronger reductants than the corresponding ground states. This is because they can both easily donate the electron promoted in a vacant orbital and accept an electron in the vacancy created in an occupied orbital.[1] The realisation that such is the case was attained first in photophysical studies, but somewhat later, at the beginning of the 1970s, it was clearly demonstrated that some photochemical reactions involve SET as the primary step [eqn. (6)], and the bond-making and bond-breaking steps take place at the radical ion stage [eqn. (7)] rather than directly on the excited state surface [eqn. (5)].[1]

$$A + h\nu \longrightarrow A^* \quad (4)$$

$$A^* \longrightarrow \text{Products} \quad (5)$$

$$A^* + D \longrightarrow A^{\bullet -} + D^{\bullet +} \quad (6)$$

$$A^{\bullet -} \text{ and/or } D^{\bullet +} \longrightarrow \text{Products} \quad (7)$$

This area has expanded in the last two decades,[2–11] and the underlying motivation has changed. While it remains interesting to demonstrate that a specific photochemical reaction occurs *via* electron transfer, the use of photoinduced SET [eqns. (4), (6)] as an efficient and versatile method for generating radical ions has a much more general interest. The other methods available either have only a spectroscopic interest, as in the case of ionisation in the gas phase, or have intrinsic limitations, as with radiolysis (non-specific) or electrochemistry (a conducting salt is required, SET occurs at the electrode surface and is influenced by absorption phenomena).

In contrast, photochemistry allows us to carry out a redox process between organic molecules [eqn. (3)] in homogeneous solution. Therefore, this is often the method of choice for the unambiguous characterisation of radical ions and the assessment of their reactivity, *e.g.* through time-resolved spectroscopy. Such information may be used for supporting the intervention of a redox step in chemical or enzyme induced (or enzyme mimetic) reactions.

More importantly, photoinduced SET makes radical ions useful to the synthetic chemist. In fact, these are generated directly in organic solution in a way not requiring the addition of aggressive reagents or of inorganic salts and allowing a large choice in the experimental conditions. This gives further possibilities for controlling the course of the reaction, so that one can use 'synthetic' know-how and intuition for exploiting the chemistry of these unusual species, without bothering about the generation of the key intermediates which does not significantly limit the choice of experimental parameters. Furthermore, since excited states are extremely strong oxidants, the choice of oxidizable substrates by photoinduced SET is much larger than with thermal methods, as will be shown below with examples involving aliphatic radical cations generated from poor donors, for which non-photochemical methods are difficult to devise.

In the following part of this section the conditions for generating radicals and cations by this method are discussed, while their synthetic uses are discusssed in section 3.

2.2 Generation of radical ions

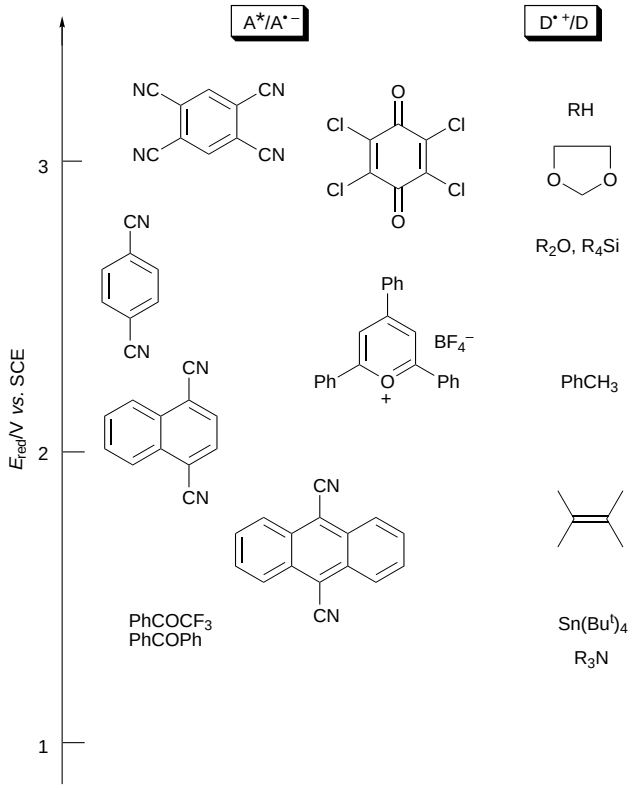
Several conditions must be met in order that a photoinitiated SET process occurs efficiently. The first one is that the SET step is exothemic or at least thermoneutral. The reduction potential of a molecule in an excited state is raised by an amount corresponding to the excitation energy, *viz.* by 2 to 4 eV.

$$E(A^*/A^{\bullet -}) = E(A/A^{\bullet -}) + E_{exc} \quad (8)$$

This is a dramatic change and poor electron acceptors in the ground state become extremely strong oxidants in the excited state, far superior to available inorganic oxidants. Ground state organic molecules all have largely negative reduction potentials, with only very good acceptors, *e.g.* chloranil, approaching $E(A/A^{\bullet -}) = 0$ *vs.* SCE. However, as Scheme 1 shows, excited states all have largely positive reduction potentials. 'Moderate' photoexcited acceptors, such as aromatic ketones [$E(A^*/A^{\bullet -}) = 1$ to 1.6 V *vs.* SCE] oxidise relatively good donors such as amines $E(R_3N^{\bullet +}/R_3N$ *ca.* 1.2 V). These are comparable to 'strong' inorganic oxidants [*e.g.* $E(Ce^{III}/Ce^{VI}) = 1.28$ V]. However, more effective photoexcited acceptors, such as quinones, heterocyclic (*e.g.* pyrrolinium and pyrylium) salts and aromatic nitriles have $E(A^*/A^{\bullet -}) > 2$ or even > 3 V, and thus oxidise even weak donors.

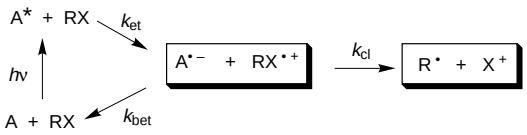
In recent years the research has progressed upward along the *y* axis of Scheme 1. The initial results were obtained with moderate donors, such as alkenes,[12] aromatic hydrocarbons[13] and stannanes. Later, the study was extended to compounds which would usually be regarded as oxidation resistant (and correctly so, if only thermal oxidants are considered), such as aliphatic ketals[14] and silanes[15] and even aliphatic hydrocarbons.[16] It was found that the corresponding radical cations were efficiently generated, provided that the photosensitiser was chosen in such a way that SET was exothermic (see Scheme 1).

A peculiarity of photoinduced SET is that the oxidant is the *in situ* generated, short-lived excited state ($\tau \leqslant 10^{-8}$ s for singlet excited states, and $\ll 10^{-6}$ s for triplet states), the steady state concentration of which is very low. This has two important consequences. First, the redox process is selective and little affected by impurities, since it is a bimolecular process between two species one of which is present at a very low concentration. Therefore, the rate will be significant only when the rate constant is high (k_{et}, see Scheme 2, approaches the diffusion



Scheme 1

controlled value, *ca.* 10^{10} dm^3 mol^{-1} s^{-1}, when the process is exothermic) and only for compounds present at a large enough concentration (on the other hand, using the reagent at a high concentration is desirable from the preparative point of view). Second, further SET steps involving the excited state and short-lived intermediates forming in the course of the reaction are usually too slow to matter. This is particularly important for alkyl radicals, since these have a low E_{ox}, and are often further oxidised when generated by means of inorganic reagents, obviously added at a large initial concentration, or by electrochemical methods (see section 3.3). Thus, photoinduced reactions usually involve a single SET step, while thermal reaction often leads to different products resulting from further oxidation of an intermediate.

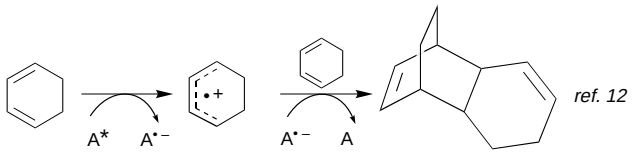


Scheme 2

2.3 Fragmentation of radical cations

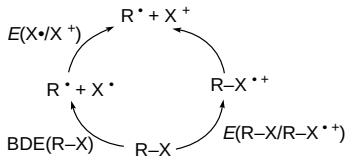
That radical cations fragment is well known being the principle of mass spectroscopy. When generated in the gas phase and with excess energy (usually 70 eV electron impact is used) these species undergo a variety of fragmentation processes. This is of course desirable in that case, since it gives more hints for structural identification. However, when radical cations are generated in solution by a mild method, a single mode of fragmentation is usually operating, and gives selectively a radical and a cation.

Again, this is due to kinetic selection. Photoinduced SET leads to a radical ion pair. Thus, the thermodynamically favoured back electron transfer regenerating the reagents in their ground state (k_{bet} > 10^8 dm^3 mol^{-1} s^{-1})[11] always competes with any chemical reaction of the radical ions (Scheme 2), and introduces a second requirement for the success of the overall process. Fortunately, most radical cations react at a rate comparable with k_{bet}, since ionisation strongly destabilizes the molecule. The reaction may be a non-fragmentative process, such as a rearrangement or an addition reaction; as an example, with alkenes and dienes single electron oxidation may be considered as a more powerful method for obtaining the Umpolung of the molecule than *e.g.* complexation with Lewis acids, and leads to very fast ionic addition or cycloaddition (*e.g.* see Scheme 3).[12,17]



Scheme 3

More often, cleavage to yield a neutral radical and a charged fragment dominates (see k_{cl}, Scheme 2). This may be expected, since SET injects a large amount of energy into the substrate, *ca.* 1–3 eV, 22 to 70 kcal mol^{-1} (1 cal = 4.184 J), approaching the order of magnitude of chemical bond energy. This depends on which bond is cleaved, and the labilization occurring upon ionisation can be evaluated through the appropriate thermochemical cycle (Scheme 4), which leads to eqn. (9).[2,4,8,18]



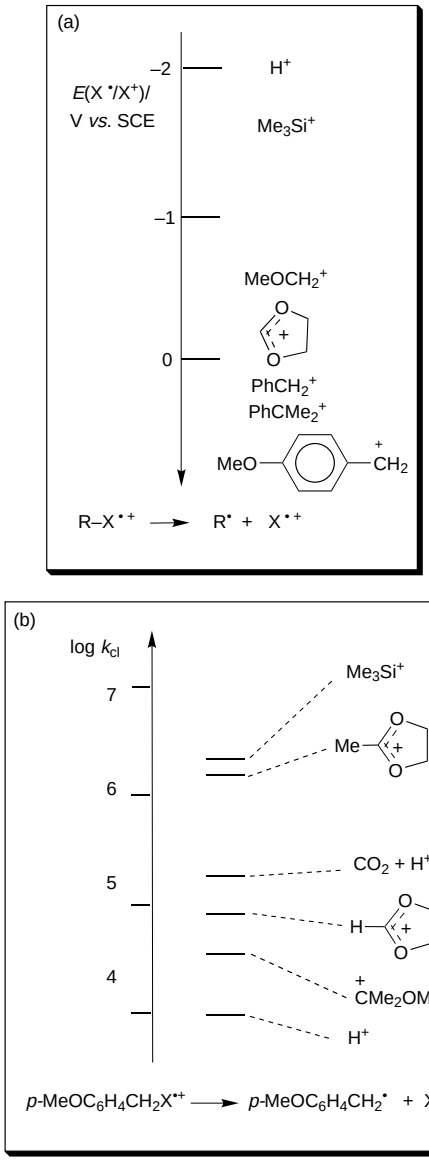
$$BDE(R–X^{\bullet+}) = BDE(R–X) - [E(R–X/R–X^{\bullet+}) - E(X^{\bullet}/X^{+})] \quad (9)$$

Scheme 4

Notice that the quantity indicated in square brackets is always positive since radicals are oxidised at a lower potential than neutral molecules, and thus BDE(R–X$^{\bullet+}$) < BDE(R–X). In other words, all bonds are weakened. However, the effect is different for different bonds, since it depends both on its strength [the BDE(R–X) term] and on how good an electrofugal group is X [E(X$^{\bullet}$/X^{+})]. If the second term has a small positive or, even better, a negative value, bond weakening is substantial. Indeed, such thermochemical calculations show that the barrier for dissociation of some radical cations is reduced to a few kcal mol^{-1}, and only in that case can fragmentation compete with back electron transfer (see below for further limitations).

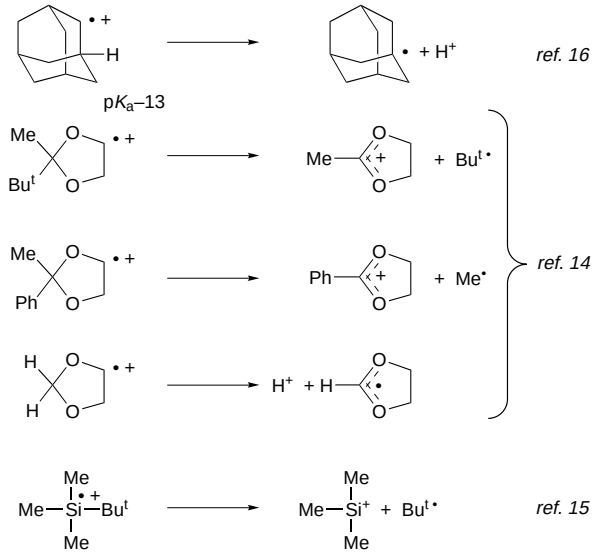
Some knowledge has now accumulated about radical cations fragmentation in solution, and the main characteristics can be summarized as follows.

- Fragmentation in solution is often efficient. As seen above, efficiency is limited by competition with back electron transfer. Actual quantum yields, $\Phi_{react} \approx k_{cl}/(k_{cl} + k_{bet})$, range from less than 1% to *ca.* 40%. Obviously, the most synthetically interesting cases are those at the higher limit of this interval, and there is quite a number of them.
- While homolytic cleavage in neutral molecules is restricted to weak bonds, *e.g.* carbon–iodine, fragmentation of radical ions has a more extensive scope. Certainly, a relatively weak bond, such as the C–Sn bond, cleaves upon ionisation, and formation of carbon centred radicals by destannylation of aliphatic organostannanes by photoinduced (as well as thermal) SET works well.[9,19,20] However, fragmentation of strong σ bonds (C–C, C–H) can also be obtained. In particular, this applies to weak donors: the more difficult is the substrate to oxidise [the larger is the E(R–X/R–X$^{\bullet+}$) term], the more energy is accumulated in the radical cation, and thus the easier will it be to cleave a strong bond.



Scheme 5

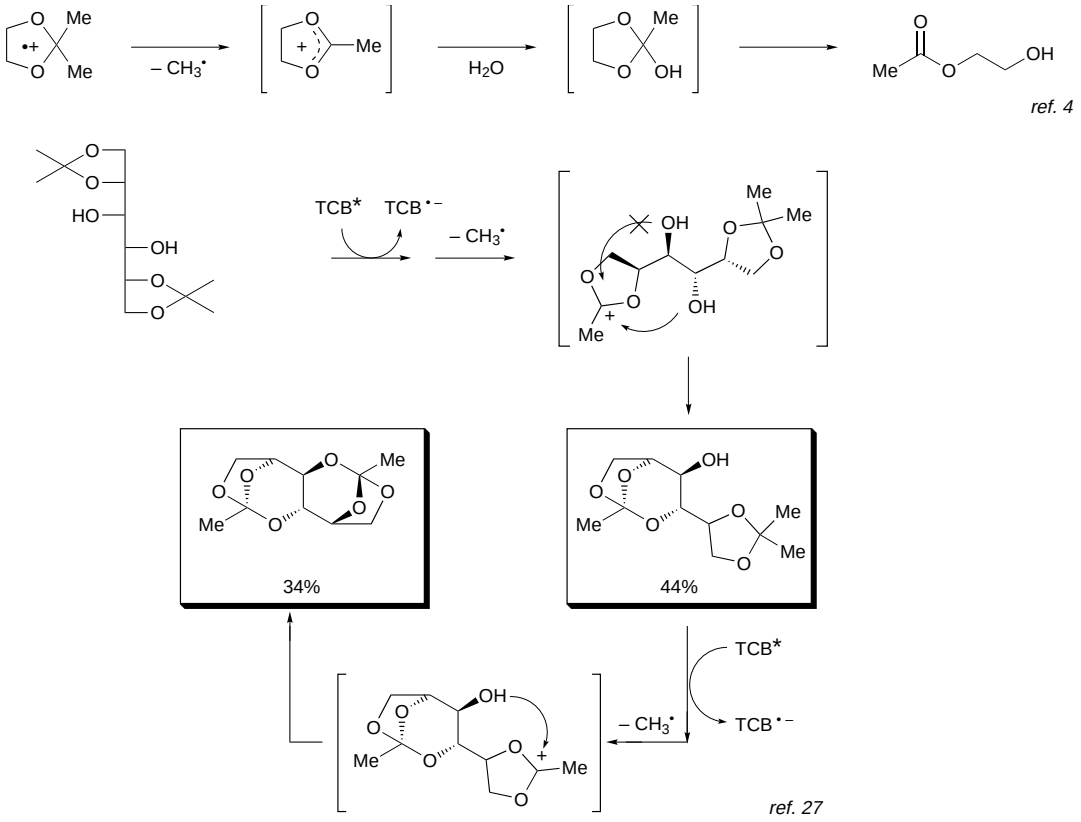
- Fragmentation is highly selective. Furthermore, the preferred fragmentation can be predicted. A first indication is given by eqn. (9), and in particular by the electrofugacity scale of leaving cations: the more shifted towards negative potentials is $E(X\cdot/X^+)$ (see Scheme 5(*a*)], the more weakened is the R–X bond. Deprotonation is predicted to be a facile process, despite the strength of the C–H bond, since in acetonitrile, where the experiments referred to here are usually carried out, the redox pair H/H$^+$ equilibrium has a very negative potential,[21] and desilylation comes near to it [Scheme 5(*a*)]. Deprotonation is slower than expected from the thermochemical calculations, apparently because there is a 'kinetic overhead'. This corresponds to the relevant internal and external reorganisation energy involved in the transfer of a proton to the solvent from a σ_{C-H} bond non-polarised in the starting radical cation (since the radical cation in general has lower-lying MOs where the charge resides). This process is fast when assisted by a nucleophile, which may be an added species, *e.g.* an alcohol, or the radical anion when this has a nucleophilic character (*e.g.* in the case of a ketone).[6,22,23] Reorganisation is less expensive when the electrofugal group is larger or more delocalised. Acetonitrile, often the solvent used in such a reaction, is a sufficiently good nucleophile for assisting the detachment of a trialkylsilyl cation. With a non-nucleophilic radical anion (*e.g.* an aromatic nitrile) in acetonitrile the experimental electrofugacity scale places the silyl group in the first position.[24] As an example, the rates of fragmentation measured for α-substituted *p*-methoxybenzyl radical cations are reported in Scheme 5(*b*).[25] The rate constants change greatly with different substrates; in particular all reactions will be much faster with less stabilized radical cations. However, the order of the leaving groups remains the same, and Scheme 5(*b*) reasonably represents an 'electrofugacity' scale for radical cations in acetonitrile. What is important for synthetic purposes is that leaving groups are well differentiated in this scale, and indeed observed fragmentations are > 90% selective. As an example with xylyl radical cations of the type $XCH_2C_6H_4CH_2Y^{\bullet+}$, the rates of cleavage of group X$^+$ to yield a benzyl radical are in the order k_{cl} (Me_3Si^+) > 10 k_{cl} (CO_2 + H$^+$) > 10 k_{cl} (H$^+$).
- Selectivity is also observed within a given type of bond. As eqn. (6) shows, a BDE difference in the neutral substrate translates without change in the radical cation. Thus, all other factors being equal, the rate of fragmentation follows the order of homolytic strength. As an example, with adamantane deprotonation from the radical cation occurs selectively (≈ 100 : 1) from the bridgehead (tertiary) position (Scheme 6).[16] Likewise, with ketals or silanes alkyl radicals are generated with marked (≈ 10 times) tertiary > secondary > primary selectivity.



Scheme 6

3 Synthetic use of radical cation fragmentation

It has been shown above that heterolytic cleavage of an organic molecule is efficiently obtained under unparalleled mild conditions through photoinduced single electron oxidation and selective fragmentation of the radical cation. Unusual precursors (π, σ, or n donors) can thus be used for generating neutral radicals and cations. As an example, alkyl radicals were conveniently and selectively generated from aliphatic stannanes, silanes or silyl ethers (*via* cleavage of a carbon–metal bond),[13] aliphatic ketals (C–C cleavage),[14] carboxylic acids (deprotonation followed by CO_2 loss),[26] or alkanes (C–H deprotonation),[16] provided that in each case the appropriate photochemical oxidant is chosen (see Scheme 6). This versatility should be useful for synthetic applications, since one should be able to choose the most convenient functionality as the precursor of the radical in view of other groups present in the donor and of the structure of the electron acceptor as well as of the desired radical trap.



Scheme 7

3.1 Nucleophilic addition onto the cation

Both species generated, the cation and the radical, can be exploited. The cation is trapped by a nucleophile, *e.g.* by moisture present in the solvent (in most cases acetonitrile) or an added alcohol. Photosensitized fragmentation of an aliphatic acetal gives an α,α-dioxy carbocation and an ortho-acid (or ester) from it (Scheme 7).[4] This realizes a mild conversion of a ketone to an ester function. The intramolecular application of such a scheme is of some interest in view of the possible selectivity. A representative case is that of 1,2;5,6-di-*O*-isopropylidene-D-mannitol diacetonide (Scheme 7), where the cation formed from the fragmentation undergoes selective addition by the hydroxy group in position 4 to give a bicylic orthoester (the process can be repeated to give a bis orthoester). This reaction can be considered as a method for protecting group exchange and has been extended to some carbohydrate derivatives.[27]

3.2 Radical addition to the acceptor: aromatics, ketones

From the point of view of synthetic planning, the most appealing side of the above method is certainly the generation of carbon-centred radicals, and thus the use of photoinduced SET for carbon–carbon bond forming reactions through this path. Generation of radicals through oxidative procedures is obviously largely precedented. However, comparison with reported thermal reactions shows that photochemical initiation is much broader with respect to the radical precursors. Thus, thermal oxidants such as Mn^{III} or Ce^{IV} oxidize only good donors, such as conjugated alkenes, enamines and (tautomeric) enols,[28] while excited states have a more positive E_{red} and also oxidize poor donors, including alkanes.

Photochemical sensitization has further important differences; as it appears from Scheme 2, in this method radicals are generated in the presence of radical anions, and of course coupling between two odd-electron species is fast.

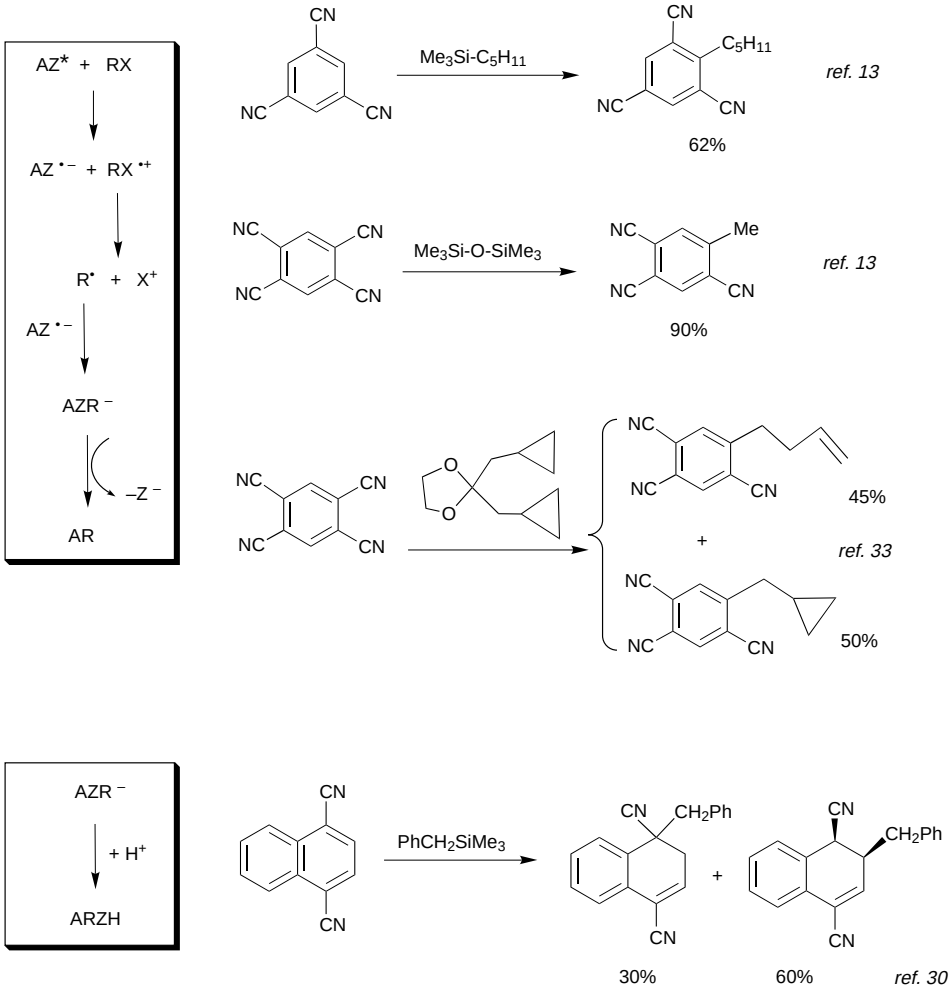
When aromatic nitriles are used as the acceptors, the corresponding radical anions are persistent, non-nucleophilic species, which can build up to a relatively high steady state concentration, and these couple with the alkyl radical (Scheme 8).[29] This gives an unconventional method for aromatic alkylation.[30] Benzonitrile—and better polycyanobenzene which are stronger acceptors—undergoes alkylation when irradiated in the presence of a variety of substrates, ranging from *tert*-butyl esters[26] to siloxanes,[6] ethers,[31] alkylaromatics,[13,32] and alkanes.[16] The reaction proceeds as shown in Scheme 8, and addition of the alkyl radical to the radical anion is regioselective (the position with the largest spin in the radical anion is always attacked, independently of whether it is substituted or not). As a result, substitution of an alkyl for a cyano group takes place with *o*- and *p*-dicyanobenzene as well as with tetracyanobenzene, while alkylation at an unsubstituted position occurs with *m*-dicyano and 1,3,5-tricyanobenzene.[13] When cyanated naphthalenes are used, the reaction proceeds in the same way up to the anion adduct, but this protonates instead of rearomatizing by cyanide ion loss and gives an alkyldihydro derivative (such compounds undergo easy base-catalysed dehydrocyanation, however).[30]

Free radicals have a significant lifetime, since radical–radical anion coupling is a second-order process involving two species both at a low steady-state concentration. When using rearranging radicals ('radical clocks'), we found that the radical incorporated is partially rearranged, to an extent which depends on the substrate chosen and the medium used (*e.g.* added salts; see the cyclopropylmethyl derivative in Scheme 8).[33]

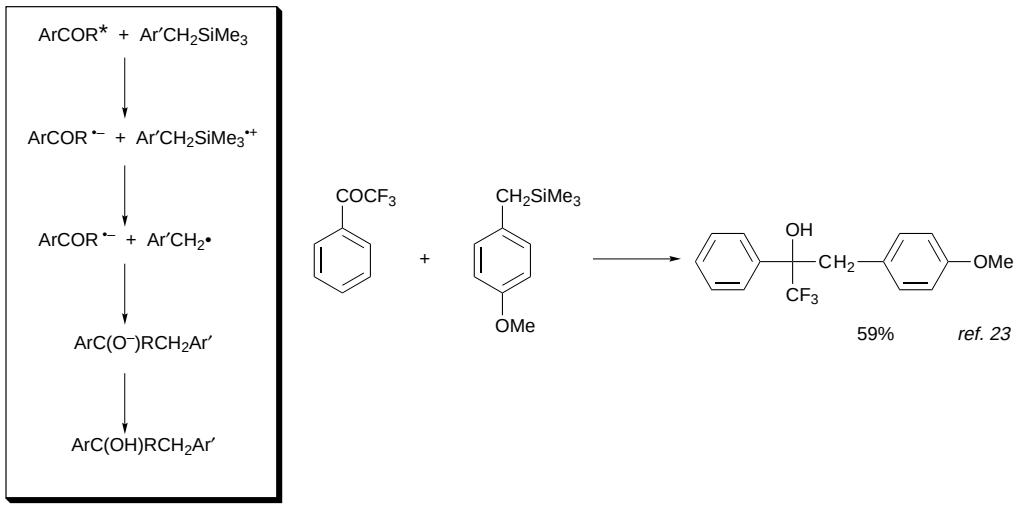
With ketones related reductive alkylations have been observed, but at the moment the process is limited to benzylic donors, where the heterocoupling (Scheme 9) is accompanied by homocoupling to give $Ar'CH_2CH_2Ar'$.[23]

3.3 Sensitized radical addition to C–C multiple bond

The above direct alkylation of the acceptor may be of some interest, *e.g.* alkylated aromatic nitriles are intermediates for the synthesis of phthalogenines. However, a more general issue uses photoinduced SET and radical cation fragmentation for



Scheme 8



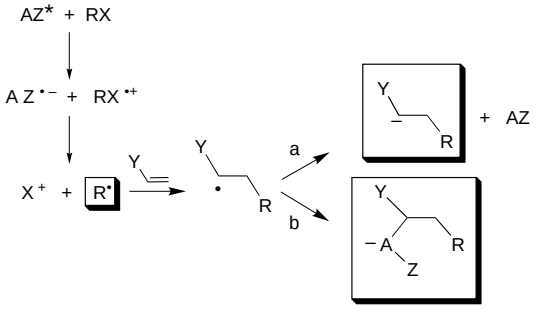
Scheme 9

generating the radicals and uses these for alkylating an added substrate, limiting the role of the acceptor to that of a regenerated photosensitizer, rather than that of a reagent.

For such intermolecular trapping two further conditions must be met, besides those mentioned above. First, the radical must diffuse out of the cage and live long enough as a 'free' species to be trapped by an added reagent rather than coupling in the cage with the acceptor radical anion. That radicals do diffuse is indicated by the above 'radical clocks' experiments, where it is shown that radical–radical anion coupling at least in part involves diffusion and re-encounter.[33] In view of the nucleophilic character of alkyl radicals, one may expect that carrying out the irradiation in the presence of an electron-withdrawing substituted alkene, radicals may be trapped, and indeed photosensitized addition to such substrates occurs satisfactorily under appropriate conditions. Second, the radical anion of the

acceptor must be re-oxidized to the starting material at some stage of the process in order to participate in further sensitization cycles.

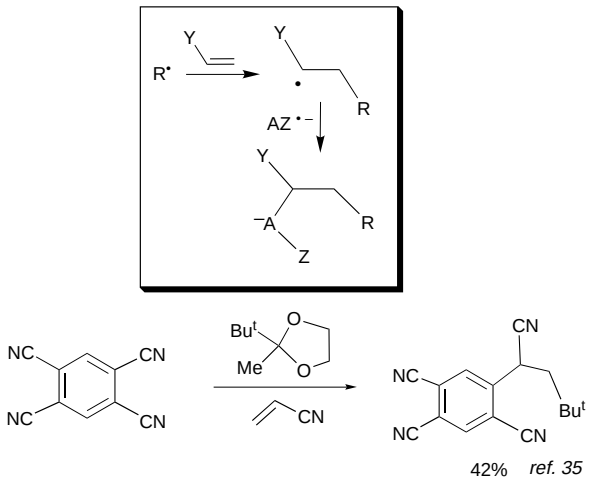
The conditions for obtaining such photosensitized addition (see Schemes 10 and 11) have been explored. The probability that the radical escapes coupling with the radical anion of the acceptor and is trapped by the alkene depends on the structure of the acceptor, of the donor (in particular of the electrofugal group in it) and on the structure of both radical and trapping olefin. Thus, *e.g.* triplet state acceptors such as aromatic esters work better in this reaction than singlet state acceptors such as aromatic nitriles, since diffusion of the radical ions is faster in the first case; alkyl radicals produced by C–C cleavage in ketals or C–Sn cleavage in stannanes are easier to trap than radicals arising from the deprotonation of alkane radical cations; more stabilised tertiary radicals are better trapped than primary radicals; the trapping ability of mono- and di-substituted olefins depends on the balance between electronic activation and steric hindrance.[34,35]



Scheme 10

The following course of the reaction is characterized, as it is typical of this kind of chemistry, by the copresence of several radical species. Trapping of the originally formed ('educt') radical by the alkene leads to a new ('adduct') radical. This in turn interacts with $A^{\bullet -}$. The electron withdrawing group makes the adduct radical more stable and more easily reducible than the educt radical, and two paths are possible: it can be reduced by $A^{\bullet -}$ [Scheme 10(a)] or add to it (path b).[34,35]

In the latter case, which has been studied with aromatic nitriles as the acceptor, both alkylation and arylation of the double bond occur and the final product results from a three-component combination with formation of two C–C bonds (Scheme 11).[35]



Scheme 11

In the other instance, the second SET closes the cycle, regenerating the sensitiser (typically, turnover numbers of 30 to 50 are observed). The combination of the two redox steps establishes a photosensitised radical addition where the educt radical is generated through an oxidation step (in this case it is the reduction potential of the *excited* acceptor which matters) and the adduct radical is converted to the final product *via* a reduction step (and in this case it is the reduction potential of the *ground state* acceptor that matters) (see Scheme 12). Since one can usually choose between different acceptors, where $E_{red}(A)$ and $E_{red}(A^*)$ change in a different way, it is possible to drive the reaction either way, towards the three-component addition [Scheme 10(a)] or towards the photosensitised radical addition (path b). The latter process is the more interesting one from the preparative point of view and can be satisfactorily carried out with a variety of C–C multiple bonds, provided that the acceptor–donor combination is properly chosen.[27,34]

This photosensitized addition has been tested with several alkenes, the relative reactivity of which is the same as that observed in conventional 'free' radical alkylation. As for alkynes, those with two activating substituents in positions 1,2 react, and the reaction cleanly stops at the double bond level due to the increased steric hindrance in the product.[27] A further convenient alkylation is that of 'push–pull' alkenes.[27]

Radical benzylation can be obtained starting directly from the hydrocarbons. In some cases addition of benzyl radicals to the alkene is inefficient, since π-interaction between donor and acceptor slows down diffusion out of cage. However, this can be overcome by adding a protic cosolvent which weakens the complex and allows us to obtain the efficient benzylation of alkenes.[27]

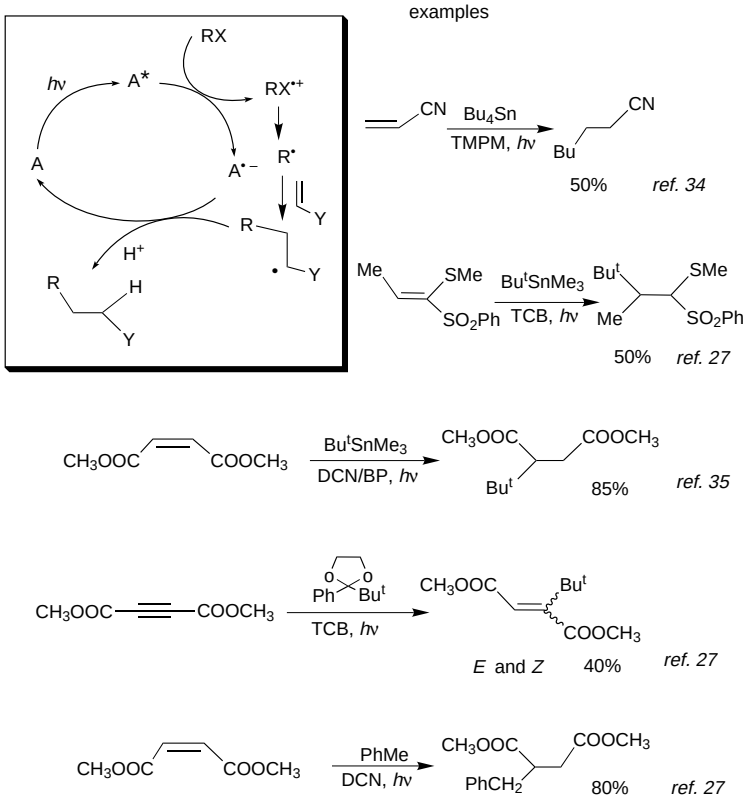
It is too early to estimate the synthetic potential of this method in comparison to classic free radical alkylation. Some key points should be stressed, however. First, new radical precursors are used, which pertain to neither of the categories classically used, *viz.* neither have a homolytically weak bond, nor are good donors (such as could be oxidized thermally). Second, all of these reactions are carried out by simple irradiation in neat acetonitrile, under neutral conditions, with the photosensitizer (typically 10^{-3}–10^{-2} mol dm^{-3}) as the only added (and recovered) chemical. Third, this method differs from thermal redox initiated reactions in that the radical adduct is not oxidized, as usually happens in that case, but rather reduced, as has been shown above, and thus the final products are different. A likely limitation is that, precisely because excited states are such strong oxidants, the method may be scarcely tolerant of other functions present in the substrates, which may undergo competitive redox processes.

3.4 Radical addition to α,β-unsatured ketones

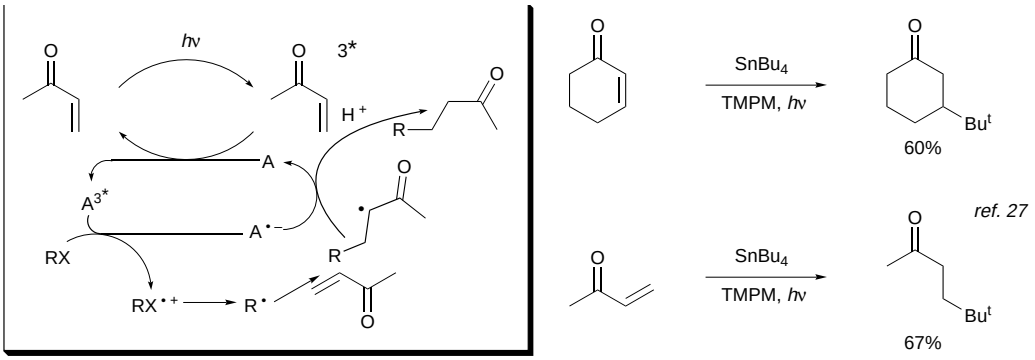
Differently from the previously considered unsaturated esters, nitriles and sulfones, α,β-unsaturated ketones absorb efficiently in the near UV and intersystem cross to the corresponding triplet states. These are reduced by good donors such as amines, and Mariano has demonstrated that this can be exploited for obtaining a convenient aminoalkylation.[6] On the other hand, adding an unsubstituted alkyl radical through a similar path poses a problem, since suitable precursors, *e.g.* tetraalkylstannanes, are too weak donors for reducing these triplets. This limitation is overcome in a system where the first step is energy transfer to an additive which has similar triplet energy to—but is a better electron acceptor than—the unsatured ketone, such as a pyromellitate ester.[27] This exploits photoinduced SET in a different cycle (see Scheme 13), showing how photosensitization can be conveniently tuned by taking into account both energy and redox potential of excited states. In this way, an efficient alkylation is obtained with both cyclic and acyclic ketones, provided that they are not β,β-disubstituted (since these are too hindered).

3.5 Radical reduction

When easily reducible (*e.g.* benzyl) radicals are generated by this method, reverse SET from $A^{\bullet -}$ takes place and is followed



Scheme 12

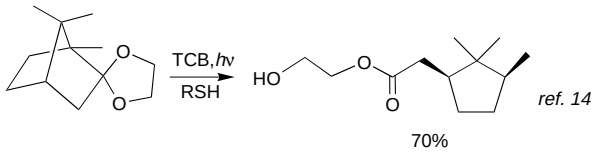


Scheme 13

by protonation to yield a hydrocarbon. In this way, hydrolysis of substituted bibenzyl and some related derivatives have been obtained [eqn. (10)].[3,32]

$$\mathrm{ArCR_2CR_2Ar'} \xrightarrow{h\nu,\ \mathrm{Sens},\ -\mathrm{e}} \mathrm{ArCR_2^{\bullet}} + \mathrm{Ar'CR_2^{+}} \xrightarrow{+\mathrm{e},\ +\mathrm{H_2O}} \mathrm{ArCR_2H} + \mathrm{Ar'CR_2OH} \qquad (10)$$

Alkyl radicals are less easily reduced than benzyl radicals, and in this case electron transfer from $A^{-}\cdot$ does not take place. However, when the bond fragmented in the radical cation is part of a ring, a distonic radical cation is formed. Such an intermediate is longer lived and the radical centre, while hindered toward addition, is activated toward hydrogen abstraction. Thus, reduction of the radical centre takes place, *via* atom transfer rather than electron transfer, while the cationic centre undergoes nucleophilic addition (*cf.* section 3.1). The final result is hydrolysis (or solvolysis) of an unactivated C–C bond under mild conditions (Scheme 14). Interestingly, with suitable substrates, hydrogen transfer is stereoselective.[14,27]



Scheme 14

4 Conclusion and outlook

Recent work has shown that, probably contrary to what most chemists think, radical cations are not only the key intermediates in mass spectroscopy, but can also be taken down from the gas phase to solution and they are useful synthetic intermediates. Photoinduced SET is a convenient method for preparing such species characterized by the mild conditions under which it is carried out and the great potential, enabling oxidation even of very weak donors. Radical cations often undergo a selective (and predictable) cleavage, and this is a new

method for preparing radicals and carbocations from unconventional substrates. In the third section of this review, we have demonstrated that this cleavage can be exploited for synthetic purposes, in particular for carbon–carbon forming reaction with neutral radicals as the key intermediates. The complex sequence involved differs largely from thermal methods *via* radicals. The final output, both in terms of efficiency and product selectivity, depends on several competitions at various stages of the process, which have been rationalised and can be controlled.

In a sense, the present stage of the study of radical ions recalls the development of homolytic radical chemistry, where synthetic applications were greatly accelerated only after the underlying mechanism was understood. We believe that the results obtained so far give only a hint of the synthetic possibilities offered by radical ions chemistry. In particular, the scope of photochemical SET is larger than its chemical counterpart and there are more possibilities to control the process by changing the conditions. Several efficient and selective reactions have been developed. Apart from this, the fact that photoinduced SET is essentially independent of experimental conditions enables us to obtain a more complete knowledge of radical ions chemistry. This offers new elements (and *bona fide* probes) for evaluating the role of electron transfer in thermal and biological processes.

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