Electron-Transfer-Photosensitized Conjugate Alkylation

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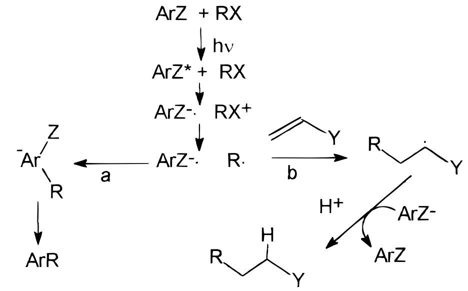
Photoinduced electron transfer (PET) from an aliphatic donor to a sensitizer and fragmentation of the radical cation leads to alkyl radicals. Radical alkylation of electron-withdrawing substituted alkenes and alkynes has been obtained in this way, and its scope has been explored. Effective sensitizers are tetramethyl pyromellitate (TMPM), 1,4-dicyanonaphthalene (in combination with biphenyl, DCN/BP), and 1,2,4,5-tetracyanobenzene. Radical precursors are tetraalkylstannanes, 2,2-dialkyldioxolanes, and, less efficiently, carboxylic acids. Steady-state and flash photolysis experiments show that escape out of cage of radical ions is the main factor determining the yield of radical formation. This is efficient with triplet sensitizers such as TMPM, while with singlet sensitizers, the use of a "cosensitizer" is required, as in the DCN/BP system. Radical cations containing primary alkyl radicals escape and fragment more efficiently than those containing tertiary radicals. The thus-formed radicals are trapped by electron-withdrawing substituted alkenes, and the relative efficiency is determined by the rate of radical addition, in accord with the proposed mechanism. Among the alkynes tested, only dimethyl acetylenedicarboxylate reacts, and the order of radical reactivity is different. It is suggested that a different mechanism operates in this case and involves assistance by the alkyne to the radical cation fragmentation.

The largely positive reduction potential of aromatic nitriles in their singlet excited state [$E_{\text{red.}}(\text{ArCN}^{1*}) = E_{\text{red.}}(\text{ArCN}) + E_{\text{exc}}(\text{ArCN}^{1*})$] makes photoinduced electron transfer (PET) a common occurrence upon irradiation of such substrates in the presence of a variety of donors.[1] Although back-electron transfer cuts down the lifetime of the thus-formed radical ion pair, fragmentation of the radical cation is sufficiently fast in a number of cases to give neutral alkyl radicals with a reasonable (0.1 or higher) quantum yield.[1,2] In turn, the radical is trapped by the long-lived nitrile radical anion, and aromatic substitution is the final result (Scheme 1, path a). However, the radical can also add to a neutral trap, and indeed, we recently showed that radicalic alkylation of electron-withdrawing substituted alkenes can be obtained under this condition, with the aromatic nitrile (or alternatively an aromatic ester, in this case via the triplet state) functioning as a nonconsumed sensitizer.[3] This reaction, as illustrated in Scheme 1, path b, represents a novel redox sequence for radicalic alkene alkylation in which the educt radical is generated through an oxidative step and the final product arises from the adduct radical via a reductive step.[3a] Therefore, the method may have preparative value. The present contribution is an exploratory study of the scope and the selectivity of this reaction, as well as an effort to establish the best conditions for this photosensitization and to demonstrate the mechanism involved. This has been obtained by using a variety of sensitizers, donors, and radical traps and comparing the efficiency and the selectivity of the observed addition processes in competition experiments.

Scheme 1



Results

Scope of the Reaction:Alkenes. In a typical experiment a PET sensitizer (0.005 or 0.01 M) was irradiated in the presence of a α,β-unsaturated ester (or a nitrile, 0.1 M) and an alkylstannane (0.05 M) in acetonitrile. The thus-formed alkylated derivatives were isolated by bulb-to-bulb distillation or by column chromatography. Extending the previously reported initial attempt,[3a] the reaction was tested with various alkenes, such as methyl

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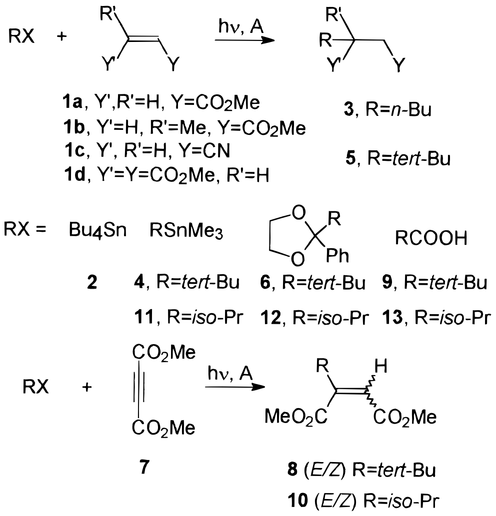
Table 1. Products Formed in the PhotoSensitized Alkylation of Alkenes and Alkynes[a]

	alkene			alkylating reagent	sensitizer[b]	products (% isol yield)
	Y′	Y	R′			
1a	H	CO$_2$Me	H	**2**, Bu$_4$Sn	TMPM	**3a** (27)
1a				**4**, *t*-BuSnMe$_3$	TMPM	**5a** (30)
1b	H	CO$_2$Me	Me	**2**	TMPM	**3b** (36)
1b				**4**	TMPM	**5b** (20)
1c	H	CN	H	**2**	TMPM	**3c** (50)
1c				**4**	TMPM	**5c** (40)
1d	CO$_2$Me	CO$_2$Me	H	**2**	TMPM	**3d** (80)
1d				**4**	TMPM	**5d** (85)
1d				**6**, *t*-BuPhCO(CH$_2$)$_2$O	TCB	**5d** (50)
	alkyne					
7	CO$_2$Me	CO$_2$Me		**4**	TMPM	**8** (50)
7				**6**	TCB	**8** (61)
7				**9**, *t*-BuCO$_2$H	TCB	**8** (22)
7				**11**, *i*-PrSnMe$_3$	TMPM	**10** (55)
7				**12**, *i*-PrPhCO(CH$_2$)$_2$O	TCB	**10** (45)
7				**13**, *i*-PrCO$_2$H	TCB	**10** (15)

[a] By irradiating 15 h in the setup described in the Experimental Section. [b] Concentration of the sensitizers: TCB 0.005 M, TMPM, 0.01 M. TMPM can be substituted, with similar product yield and often shorter reaction times, by the DCN (0.005 M)−BP (0.1 M) pair.

Scheme 2



acrylate (**1a**), methyl crotonate (**1b**), acrylonitrile (**1c**), and dimethyl maleate (**1d**). Under these conditions irradiation with tetrabutylstannane (**2**) gave the corresponding alkylated derivatives **3a**−**d** in medium to good yield (Scheme 2). Various sensitizers (or sensitizer/"cosensitizer" pairs) were tested (see below). It was found that product distribution depended only marginally on the sensitizer chosen, but the reaction rate changed considerably. Complete reaction required a few hours to 2 days. A convenient reaction was generally obtained by using tetramethyl pyromellitate (TMPM) as the sensitizer, as reported in Table 1. Equally well worked the 1,4-naphthalenedicarbonitrile (DCN)/biphenyl (BP) pair, which in some cases required a shorter irradiation time, while the reaction was slower or the sensitizer was consumed faster in the other cases. Representative examples are reported in Table 1.

Similar results were obtained with *tert*-butyltrimethylstannane (**4**) as the alkylating agent, which gave products **5a**−**d** from the same alkenes (see Table 1). Previously, it had been demonstrated that alkyl radicals could also be obtained from different donors, in particular with 2,2-disubstituted 1,3-dioxolanes provided that 1,2,4,5-benzenetetracarbonitrile, TCB, was the sensitizer.[4a] Using 2-*tert*-butyl-2-phenyldioxolane (**6**) as the radical source, we now found that **1d** gave **5d** (Table 1) in a moderate yield, although with the other alkenes tested no significant alkylation took place.

Alkynes. Extension of the reaction to alkynes as substrates was then explored. Irradiation of various sensitizers and either **2** or **4** resulted in only a minimal alkylation of methyl propiolate, methyl 2-butynoate, or phenylacetylene. However, dimethyl acetylenedicarboxylate (**7**) was successfully *tert*-butylated by **4** to give product **8** as a mixture of *E* and *Z* isomers. When the primary stannane **2** was used, a very poor alkylation was also obtained with this alkyne.

The alkylation of **7** to give **8** could be effected with various sensitizers (see below). The reaction took place similarly, although at a different rate. Likewise, other alkylating agents could be used. Thus, **6** proved effective for obtaining **8** from **7**, while pivalic acid (**9**) gave a poor yield. Furthermore, although addition of a primary radical was unsuccessful, the reaction occurred with a secondary radical. Thus, **7** was converted to **10** (the *E* isomer was isolated, the *Z* isomer was present in the mixture) by using both isopropyltrimethylstannane (**11**) and 2-isopropyl-2-phenyl-1,3-dioxolane (**12**), as well as, although with a lower yield, isobutyric acid (**13**). These reactions could be carried out up to complete consumption of **7**, and the alkylation did not proceed further. Separate experiments with the trisubstituted alkene **8** showed that no further alkylation occurred at a reasonable rate under any of the conditions above.

Quantum Yield Measurements. The quantum yield of the photosensitized reaction of some of the above donors in the presence and in the absence of the radical trap was measured. Irradiation of DCN in the presence of BP and stannanes **2** or **4** (0.015 M) rapidly consumed the sensitizer and gave a mixture of 3- and 4-alkyl-1-cyanonaphthalenes. The reaction occurred with moderate quantum yield (see Table 2). Addition of the above conjugated esters (0.1 M) virtually suppressed the alkylation of the nitrile and led instead to alkylation of such substrates with roughly the same quantum yield as the above substitution. Noteworthy, when BP was omitted,

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Table 2. Quantum Yields

substrates (M)	Φ_{-DCN}	Φ_{-DCN}[a]	Φ_{3d}[a]
DCN (0.005), **2** (0.015)	0.02	0.35	
DCN (0.005), **2** (0.015), **1d** (0.1)		<0.01	0.4
			Φ_{5d}[a]
DCN (0.005), **4** (0.015)	0.02	0.5	
DCN (0.005), **4** (0.015), **1d** (0.1)		<0.01	0.25
	Φ_{-TMPM}	Φ_{3d}	
TMPM (0.01), **2** (0.015), **1d** (0.1)	≪0.01[b]	0.04	
		Φ_{5d}	
TMPM (0.01), **4** (0.015), **1d** (0.1)	≪0.01[b]	0.04	

[a] In the presence of 0.1 M BP. [b] Φ_{-TMPM} ≪0.01 also in the absence of **1d**.

neither DCN photosubstitution nor DCN-sensitized alkylation occurred at a reasonable rate.

Irradiation of the ester TMPM in the presence of the stannanes showed only a minimal consumption of the sensitizer (see Table 2; the products were not identified); when the stannane **2** was used the solution became yellow. In the presence of the above electron-withdrawing substituted alkenes, photosensitized alkylation took place. In the case of dimethyl maleate, the measured quantum yield was 0.04 (Table 2).

Sensitizers and Medium Effects. Various sensitizers (or sensitizer/cosensitizer pairs) were examined. These included aromatic nitriles (DCN, TCB) or esters (dimethyl phthalate, DMP, TMPM) in some cases in combination with biphenyl (BP) or phenathrene (PH). Representative examples of the results obtained in the alkylation of acetylenedicarboxylate **7** to give **8** are given in Table 3. With the stannane **4** as the donor, DCN and DMB acted as sensitizers only in the presence of BP or PH, respectively, while the tetranitrile TCB and the tetraester TMPM did not require such additives. With the dioxolane **6**, on the other hand, only TCB was active. Further sensitizers tested (besides nitriles and esters) included 1,3-dinitrobenzene (DNB) and 2,4,6-tetraphenylpyrylium tetrafluoborate (TPPT), both with poor results: in the first case the reaction was slow, in the latter one the sensitizer was rapidly consumed. The PH/DNB pair worked somewhat better.

In Table 3, the ratio between the moles of alkylated product **8** formed and the moles of sensitizing acceptor consumed is reported as the "turnover number". To allow the discussion of the process observed, the relevant redox data for the sensitizers are also reported in the Table 3.

Further exploratory studies concerned the medium effect. Thus, addition of 0.1 M Et_4NClO_4 did not significantly affect product distribution or rate of reaction.

Carrying out the reaction in acetonitrile containing 0.1 M D_2O led to substantial deuterium incorporation in the α position in the alkylation of **1d** by both **4** and **6**. On the other hand, deuterium incorporation took place only to a small degree (<10%) in the reaction of **7** with the same reagents. The alkylation of **7** was tested also in CD_3CN and showed no significant deuterium incorporation.

Competitive Alkylations. The relative rate of the alkyl radical addition to the substrate considered was determined in competition experiments. A sensitizer (both the DCN/BP pair and TMPM were used, see Table 4A and B) was irradiated in the presence of either **2** or **4**, and equimolecular amounts of two α,β-unsaturated esters (compounds **1a**,**b**,**d** and **7** were considered). The results, see Table 4, showed a variation over a large span in the case of TMPM; in particular, maleate **1d** reacted more efficiently than acrylate **1a**. The variation with DCN/BP was less pronounced, with **1d** being about as efficient as **1a** and crotonate **1b** markedly less efficient.

In separate experiments, either TMPM or the DCN/BP was irradiated in the presence of the same unsaturated derivatives and equimolecular amounts of stannanes **2** and **4**, and the ratio of *n*-butylated vs *tert*-butylated derivatives was measured. As it appears from Table 4, this ratio was ca. 1.5 with the first sensitizer and ca. 2 with the latter one whenever an alkene was used as the trap. However, with both sensitizers, the ratio was much lower (<0.1) with alkyne **7**.

Quenching Constants. The mechanism of initial electron transfer in these systems was tested by the appropriate steady-state and transient measurement. The aromatic nitriles DCN and DCA were strongly fluorescent, and the emission was quenched by the stannanes. Quenching rate constants (calculated from steady-state Stern–Volmer constants) are reported in Table 5. In the case of DCA, nanosecond laser flash photolysis experiments were also carried out. When this nitrile was flashed in the presence of the stannane no transient was detected. On the other hand, flashing a DCA/BP solution led to an apparent absorption in the visible region, as has been shown by Gould et al.,[4b] this corresponded to the superimposition of two transients, the radical anion of DCA and the radical cation of BP. When an oxygen-purged rather than an argon-purged solution was flashed, only the latter transient was detected (λ_{max} 680 nm). Addition of the stannanes led to quenching of this absorption (see Table 5 for the rate constants).

The ester TMPM fluoresced weakly, and addition of the stannanes up to 0.1 M caused no measurable change. Flash photolysis of a degassed solution revealed an

Table 3. Alkylation of Dimethyl Acetylenedicarboxylate (7) with Different PhotoSensitizers[a]

donor (0.05 M) $E_{ox.}$, V	acceptor, A (0.005 M) $E_{red.}$, V	cosens. (0.1 M)	$E_{red.}$ (A), V	oxidizing species $E_{red.}$, V	irradn time, h	yield of **8**, %	turnover no.
4 (1.60)	TCB	BP	−0.65	$A^{1*}(3.15) + BP^{\bullet+}(1.8)$	15	61	6
4	DCN	BP	−1.28	$A^{1*}(2.17) + BP^{\bullet+}(1.8)$	5	50	18
4	DMP	PH	−2.07	$PH^{\bullet+}(1.58)$	15	16	>50
4	DNB	PH	−0.9	$PH^{\bullet+}(1.58)$	15	12	
4	TPPT		−0.39	$A^{1*}(2.5)$	5	3	0.25
4	TMPM		−1.31	$A^{3*}(1.73)$	15	60	25
6 (2.20)	TCB			$A^{1*}(3.15)$	15	62	6

[a] DCN, TCB, DMP, TPPT 0.005M; TMP, DNB, 0.01 M; BP, PH 0.1 M. Redox potential in MeCN vs SCE. Excited-state redox potentials are obtained by adding the excitation energy (see text).

Table 4. Relative Efficiencies for the Alkylation of Unsaturated Esters Obtained from Competition Experiments

A. Sensitizer, DCN/BP

	alkene or alkyne			alkylating agent		ratio
	Y′	Y	R′	Bu_4Sn	t-$BuSnMe_3$	n-Bu/t-Bu
1a	H	CO_2Me	H	1	1	2
1b	H	CO_2Me	Me	0.1	0.15	2.3
1d	CO_2Me	CO_2Me	H	1.6	0.7	1.7
7	CO_2Me	CO_2Me		low	2.85	<0.1

B. Sensitizer, TMP

	alkene or alkyne			alkylating agent		
	Y′	Y	R′	Bu_4Sn	t-$BuSnMe_3$	
1a	H	CO_2Me	H	1	1	1.3
1b	H	CO_2Me	Me	1.3	0.6	1.6
1d	CO_2Me	CO_2Me	H	11.0	5.9	1.6
7	CO_2Me	CO_2Me		low	16.2	<0.1

Table 5. Quenching Rate Constants in Acetonitrile

species quenched	$k_r(Bu_4Sn)$, $M^{-1}\ s^{-1}$	$k_r(t\text{-}BuSnMe_3)$, $M^{-1}\ s^{-1}$
DCN^{1*}	8.6×10^9	9.5×10^9
DCA^{1*}	3.5×10^9	5×10^9
$TMPM^{3*}$	2.1×10^8	1.9×10^8
$BP^{\bullet+}$	7.5×10^9	7.5×10^9

intense transient in the range 300−340 nm. The spectrum and the lifetime (τ 5−8 μs) were similar in MeCN and cyclohexane (see Figure 1a). This transient was quenched by oxygen and accordingly was attributed to the triplet−triplet absorption. Addition of the stannanes caused no measurable effect in cyclohexane, while it led to quenching of this absorption with concurrent formation of a much longer lived (200 μs) transient in acetonitrile (Figure 1b). Rate constants for the quenching are reported in Table 5.

Discussion

The present reactions are PET-initiated radical conjugate alkylation on activated alkenes and alkynes. This method differs from the well-known thermal oxidative initiation[5] of radical addition in two main respects. The first one is that the choice of radical precursors is much larger than in the thermal case. This is due to the much higher oxidation potential of the excited states or organic molecules (A*, eq 1) with respect to ground-state (usually inorganic) oxidants (M^{n+}, eq 2).

$$A^* + RX \rightarrow A^{\bullet-} + RX^{\bullet+} \qquad (1)$$

$$M^{n+} + RX \rightarrow M^{(n-1)+} + RX^{\bullet+} \qquad (2)$$

As an example, the singlet excited state of DCN [$E_{red}(DCN^{1*}) = E_{red}(DCN) + E_{exc}(DCN^{1*}) = -1.28 + 3.45 = 2.17$ V vs SCE in MeCN] is more powerful than typical ground-state oxidants, such as Mn(III) or Ce(IV), e.g., $E_{red.}$(Ce(IV)/Ce(III)) 1.28 V vs SCE. Thus, weak donors such as the presently used aliphatic derivatives are susceptible to photochemical activation, whereas thermal oxidative initiation is limited to good donors, most often (tautomeric) enols.[5]

The latter difference concerns the final step of the reaction, since, as shown in Scheme 1, path b, in the present method the radical adduct is reduced by the sensitizer radical anion, whereas this is oxidized when a ground-state oxidant is used. This is due to the fact that in the photochemical oxidation the active species is an excited state present at a very low steady-state reaction. This makes the oxidation of a second short-lived species such as the adduct radical an unlikely process, while this is the normal occurrence when a ground-state oxidant (obviously present at a much higher concentration) is used. As a result, the end products by the two methods are different.

These additions occur with no significant concurrent polymerization of the unsaturated substrates and in moderate to good yield. The scope of the reaction is rather broad and differs from that of “conventional” radical addition; e.g., dimethyl acetylenedicarboxylate (**7**) is expediently alkylated under this condition, indeed more efficiently than maleate or fumarate, while alkynes are usually less reactive than alkenes (vide infra). The unsaturated esters obtained from **7** are not further alkylated and are obtained as a mixture of *E* and *Z* isomers (secondary *E*/*Z* isomerization may obviously occur under irradiation).

In the following text, the scope and the application of the present alkylation with regard both to the substrates and to the sensitizers used will be discussed in detail to distinguish the different steps of the mechanism.

Generation of the Radicals. The generation of radicals and ions via photoinduced electron transfer and fragmentation of the thus-formed radical ions has been previously well documented.[1,2] Initially, we used in these studies singlet excited aromatic nitriles as convenient PET oxidants, in view of their largely positive $E_{red.}$ and the stability of the radical anion. As indicated in Scheme 1, this can lead either to radicalic aromatic substitution of an alkyl for a cyano group,[1c,6] or, as in the present case, to radicalic addition to a suitable additive, in particular to an electron-withdrawing substituted multiple C−C bond.

A condition for the sensitization is that electron transfer in the excited state (eq 1) has a negative ΔG. When a moderately good donor such as a stannane is used as the radical precursor [$E_{ox.}$(**2**) = 1.75 V vs SCE, $E_{ox.}$(**4**) = 1.60 V], various nitriles can be used as the sensitizer, e.g., DCN or DCA [$E_{red.}(DCA^{1*}) = 1.97$ V] (see Table 3). When the substrate has a more positive oxidation potential, as it is the case with ketals such as **8** and **12** ($E_{ox.}$ ca. 2.2 V) or with carboxylic acids such as **9** and **13** ($E_{ox.}$ >3 V) the choice is limited to the strongest photochemical oxidants, with the last substrates only to TCB [$E_{red.(TCB^{1*})} = 3.15$ V].

However, in order that sensitized alkylation takes place satisfactorily, it is further needed that fragmentation of the radical ion (formed in a pair with the radical anion, see eq 3) is fast enough to compete with back-electron transfer (eq 4) and that the radical is trapped

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(6) Albini, A.; Fasani, E.; Mella, M. *Top. Curr. Chem.* **1993**, *168*, 143.

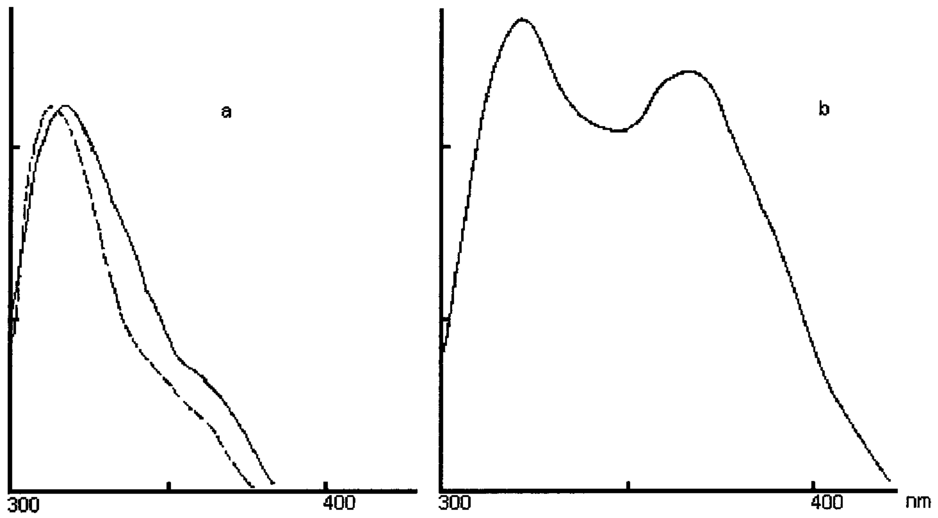
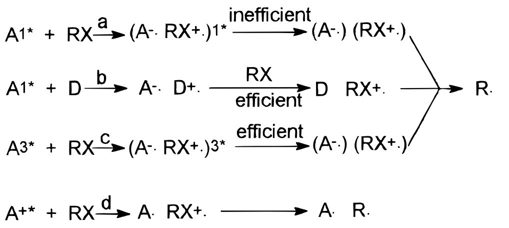


Figure 1. **a**. Absorption observed 1 μs after flashing a TMPM solution in MeCN (—) or cyclohexane (- - -). **b**. Absorption observed 10 μs after flashing a TMPM solution in MeCN containing 0.015M **2**. No effect when **2** is added to a cyclohexane solution.

Scheme 3



by the alkene rather than adding to the acceptor radical anion (which gives aromatic substitution, see Scheme 1, paths a and b).

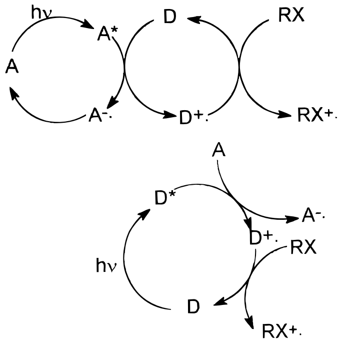
$$(A^{\bullet-}\ RX^{\bullet+}) \rightarrow A^{\bullet-} + R^{\bullet} + X^{+} \tag{3}$$

$$(A^{\bullet-}\ RX^{\bullet+}) \rightarrow A + RX \tag{4}$$

For this aim, aromatic nitriles are not necessarily the best choice. One of the reasons is that even if the radicals were formed efficiently, they would then undergo fast coupling with the nitrile radical anion (Scheme 1, path a), and this would lead to rapid loss of the sensitizer. As may be seen in Table 1, some alkylations have been carried out with TCB. As mentioned above, this is a forced choice with weak donors. Alkylation under these conditions meets with some success, although the sensitizer is rapidly consumed. Indeed, the alkyltricyanobenzenes formed from TCB are photooxidants as strong as the starting sensitizer, and this ensures that the sensitization is pursued after that the latter is consumed. As a consequence, the turnover number with TCB (see Table 2) is not as low as might be expected.

A second, and more general, reason is that back-electron transfer is often the main path from the *singlet* radical ion pair (Scheme 3, path a). This is clearly exemplified by the fact that DCN and DCA are inefficiently alkylated by alkylstannanes (see Table 2) even under conditions where the fluorescence is almost completely quenched and do not act as sensitizers for the alkylation of the unsaturated derivatives.

Scheme 4



A way to ameliorate the competition between fragmentation and back-electron transfer would be to favor ion separation, eq 5 and Scheme 3, path a.

$$(A^{\bullet-}\ RX^{\bullet+})_{\text{solv}} \rightarrow (A^{\bullet-})_{\text{solv}} + (RX^{\bullet+})_{\text{solv}} \tag{5}$$

We attempted to reach this result through an increase of ionic strength (adding Et_4NClO_4). This did not help, however. A positive result was obtained through the use of a sensitizer/cosensitizer pair. In this case, initial PET leads to the radical cation of an aromatic molecule such as BP. This in turn generates the radical cation of the aliphatic radical precursor (a stannane or a ketal) via secondary electron transfer (Scheme 3, path b). This step occurs with reasonable efficiency even when slightly endothermic, due to the fact that the primary radical cation, $BP^{\bullet+}$, is relatively long lived, having no unimolecular reaction path available.

Previous examples of such use of a "cosensitizer" have been reported in the literature.[7] One can use either a light-absorbing acceptor and a nonabsorbing primary donor (indicated in Scheme 4 as A and D, respectively; these labels are preferred in this context to the sensitizer-cosensitizer terminology, which would be ambiguous) or vice versa (Scheme 4, lower part). Examples of the first choice are the DCN or TCB/BP pairs, of the latter the PH/DMP or DNB pairs. It is apparent that it is the

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[7] (a) Schaap, A. P.; Lopez, L.; Gagnon, S. D. *J. Am. Chem. Soc.* **1983**, *105*, 663. (b) Borg, R. M.; Arnold, D. R.; Cameron, T. S. *Can. J. Chem.* **1984**, *62*, 1785.

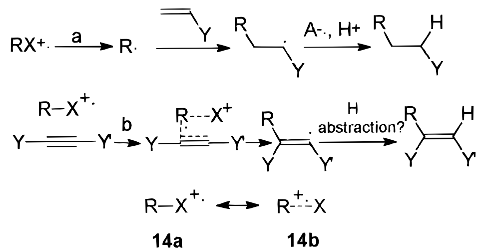
radical-cation-cleavage step that is facilitated under such conditions, since both alkylation of the alkene and, in the absence of the latter, radicalic substitution on the aromatic nitrile are efficient only in the presence of BP (see Table 2; the increase is by at least a factor of 20). That this difference is due to inefficient out-of-cage diffusion of the radical ions (eq 5) is demonstrated by the flash experiments where no $DCA^{\bullet-}$ is detected by irradiation of the DCA−stannane system, whereas both solvated radical ions, $DCA^{\bullet-}$ and $BP^{\bullet+}$, are apparent when the DCA−BP pair is irradiated and, furthermore, by the selective quenching of $BP^{\bullet+}$ at a rate close to diffusion controlled when a stannane is added (Table 5).

From the preparative point of view, the DCN−BP combination is quite effective. In the presence of 0.1 BP, the alkylation quantum yields reach values in the range 0.25−0.5, with minimal alkylation of the sensitizer. DCA is well suited for mechanistic studies, but not for synthesis because it has low solubility and is rapidly consumed, even if its alkylation is only a side path.

A second approach for ameliorating the sensitizing efficiency is the use of triplet aromatic sensitizers (Scheme 3, path c). Aromatic esters are not as strong oxidants as the corresponding nitriles, but they offer two advantages. The first one is that the relevant excited state is the triplet (the singlet is too short-lived for being involved in a bimolecular reaction), and it is expected that in a triplet radical ion pair diffusion (and then fragmentation) may compete better with back-electron transfer.[8] Indeed, flash photolysis (Figure 1) shows that the triplet of TMPM (unambiguously identified by quenching by oxygen) is quenched by the stannanes. Such quenching must involve SET, since it occurs efficiently in a polar solvent (2×10^{8} M^{-1} s^{-1}) and is below detection limits ($\ll 1 \times 10^{6}$ M^{-1} s^{-1}) in cyclohexane. This evidence allows us to identify the second transient appearing after the quenching in MeCN (Figure 1b) as the TMPM radical anion. In accordance with this attribution is the long lifetime (200 μs) of such species, which has no channel for unimolecular decay and decays only through bimolecular back-electron transfer. This is an inefficient process since, as it has been shown above, the stannane radical cation diffuses and cleaves efficiently under this condition. The second advantage is the fact that the radical−radical anion coupling appears to be less important in this case, since no aromatic substitution has been observed with these esters, contrary to the case of nitriles. As a result, TMPM is a satisfactory sensitizer for the present alkylation, even if the quantum yield is lower than with the DCN/BP system. Apparently, ion separation in the triplet manifold is more effective than in the singlet, but less effective than secondary electron transfer from the singlet.

A third approach we attempted is based upon cationic sensitizers (Scheme 3, path d). In this case, there are no opposite charges in the pair after the initial PET step, and suppressing Coulombic attraction is expected to facilitate diffusion of the radical ions and thus to enhance the probability of their independent reaction. Indeed, heterocyclic salts such as TPPT have been found to be convenient for various PET-induced reactions, including fragmentations.[2,9] This is certainly true also in the present case as far as the efficiency of radical cation fragmentation is concerned. However, fast coupling between the pyranyl radical and the alkyl radical then consumes the sensitizer and gives, as already reported, 2- and 4-alkylpyranes.[10] Therefore, this approach is not appropriate for the present case.

Scheme 5



In conclusion, the best sensitizers for PET-induced conjugated alkylation are those that ensure a better chance of charge separation, viz. aromatic esters (via the triplet state) and the aromatic nitrile/aromatic hydrocarbon combination (via secondary electron transfer).

Radical Addition to Multiple Bonds. The addition of a nucleophilic alkyl radical to multiple bonds has been studied in depth, and steric and electronic effects have been well characterized.[11−13] Typical generalizations are that the alkyl substitution on the radical center makes its reaction somewhat faster and more selective and that the rate of addition is affected by a substituent in β in the alkene (or alkyne). As an example, the addition of alkyl radicals onto ester **1d** is moderately accelerated (three to five times) with respect to that onto monosubstituted **1a**.[11] Therefore, if the present reactions involve free radicals, the reactivity with various alkenes should follow the above pattern. One should notice, however, that the data reported in Table 3 are relative quantum efficiencies of the overall alkylation process and thus need not to be proportional to the rate of the radical addition step. For example, the efficiency of fragmentation must be also taken into account. Thermochemical calculation have shown that the fragmentation of a σ bond in a radical cation of this type (the C−Sn bond in stannanes, the C−C bond in ketals) has a negative ΔG and thus is fast.[2c] However, the *efficiency* of such processes depends on competition with another very fast process, back-electron transfer.

Table 3 shows that the relative efficiencies in the TMPM-sensitized alkylation of alkenes follow the same order as the relative rates in the classical chain alkylation. Diagnostic is the fact that **1d** is more reactive than **1a**, since the activation induced by the second carboxyl group overcomes the additional sterical hindering. Thus, when a triplet sensitizer is used, the radical ions diffuse out of cage and the cation cleaves as the free solvated species, the free radical then being trapped by the alkene (Scheme 5, path a). Therefore, the rate of radical addition determines the overall efficiency of alkylation.

The DCN/BP-sensitized reactions roughly follow the same order, but the steric effect (**1b** is less reactive than **1a**) is more apparent than the electronic effect (**1d** is more reactive than **1a** with *n*-butyl, but somewhat less

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[8] Mauzerall, D. C. In ref 1a, Vol. A, p 228.

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[13] Curran, D. P. in *Comprehensive Organic Synthesis*; Trost, B. M., Fleming, I., Eds.; Pergamon: Oxford, 1991; Vol. 4, p 715.

with the bulky *tert*-butyl). This suggests that in the singlet manifold (ground-state species are involved after the secondary electron transfer), the radical cation and the radical formed from it remain close to the acceptor (in this case BP, see eq 6 and Scheme 3, path b).

$$\mathrm{BP}^{\bullet+}\ \mathrm{RX} \rightarrow \mathrm{BP}\ \mathrm{RX}^{\bullet+} \rightarrow \mathrm{BP}\ \mathrm{R}^{\bullet} \qquad (6)$$

This would make the rate of addition more sensitive to steric hindering than to electronic activation.

Noteworthy, in both the TMPM- and the DCN-sensitized reactions, *n*-butylation with **2** is somewhat more effective than *tert*-butylation with **4** (the *n*-Bu/*t*-Bu ratio ranges from 1.3 to 2.3; see Table 4). Since the relative rate of addition of a free radical is larger with more highly substituted radicals, this must be due to a better efficiency in ion-pair separation and/or fragmentation of $\mathbf{2}^{\bullet+}$ with respect to $\mathbf{4}^{\bullet+}$ under these conditions (see a further comment below).

Summing up, the relative reactivity with different alkenes is reasonably in accord with the intervention of "free" radicals—indeed, in excellent accord when a triplet sensitizer is used.

Addition to alkynes has a different scope: the reaction occurs only with the diester **7**, but then it is more efficient than with the alkene diester **1d** and, furthermore, the reaction works much better with tertiary than with primary radicals (*n*-Bu/*t*-Bu ratio < 0.1, see Table 4), contrary to what observed with the above alkene traps. The first characteristics does not fit with what generally observed in a free-radical reaction, where addition to alkenes is faster than to alkynes. This is rationalized as being due to the better SOMO−LUMO overlap in the first case, which leads to an early-transition-state addition.[11−13]

Thus, we assume that **7** does not efficiently trap the free radical according to Scheme 5, path a. We suggest that a different mechanism is followed here, viz. that the alkyne assists the radical cation fragmentation rather than intervening after this step. Although unusual, such a concerted radical cation fragmentation−radical addition mechanism (path b in Scheme 5) would fit with the observed characteristics. First, this reaction would have a late transition state, and this is known to favor addition to an alkyne with respect to an alkene, since in the former case orbital rearrangement is easier.[11−13] There is previous evidence that PET-induced radical-cation fragmentation may occur concertedly, e.g., through a "nucleophile-assisted" path.[14] Indeed, experiments with rearranging radicals showed that even in PET alkylation of aromatics radical cation cleavage in part occurs through a fast in cage process where radical formation is concerted with addition to the radical anion of the acceptor and, in part, via diffusion, fragmentation, and radical−radical anion recombination.[15] In the present case, an external radical trap, **7**, would exert a similar (and competing) effect. Notice also that for such a role the minimal steric hindrance and strong electronic activation make the diester **7** the ideal reagent, explaining both its enhanced reactivity with respect to the maleate **1d** and the fact that less activated alkynes do not react appreciably. Second, the above-mentioned limitation of the reaction to secondary or tertiary, not primary, radicals would be explained because more substituted σ bonds are expected to contribute more significantly to donation and thus to have a more marked single-bond character in the radical cation. Thus, such substrates are expected to participate more easily in the assisted cleavage (see mesomeric formula **14b** in Scheme 5). Electron donation from the σ bond is less important with the precursor of primary radicals, and in this case, the assisted mechanism is not sufficiently fast.

Summing up, addition of primary radicals occurs only via the unassisted mechanism after radical ion separation, where alkenes react faster than the alkynes. Radical cations containing primary radicals are more heteroatom-localized (and presumably better solvated) radical cations (formula **14a**), and this is consistent with the above-mentioned fact that separation from $\mathrm{A}^{\bullet-}$ and thus the ensuing fragmentation are more efficient in this case. As a result, alkenes are alkylated via path a (Scheme 5), and here, addition of primary radicals is somewhat more efficient. Alkyne **7** has available a different mechanism (path b in Scheme 5), but this requires participation of the σ bond to donation and thus the order is tertiary > secondary > primary.

Closing of the Sensitizing Cycle. In several cases, the photoexcited acceptor functions as a nonconsumed sensitizer, as shown in Table 2 for alkyne **7** and previously shown for alkenes **1c** and **1d**.[3a] Thus, the radical adduct is reduced to the alkane or, respectively, the alkene with concomitant reoxidation of the acceptor radical anion. The satisfactory closing of the sensitizing cycle is indicated both by the turnover number and by the fact that in no case does polymerization of the substrate occur to significant extent. Apparently, the adduct radical is reduced in preference to other reactions.

The mechanism of the last step does not appear to be univocal, however. Thus, in the case of **1d** with both stannane **4** and dioxolane **6**, deuteration at the α position results (for ca. 2/3) when the reaction is carried out in MeCN containing 0.1% D_2O. Thus, back-electron transfer from the acceptor radical anion to the adduct radical occurs spontaneously and the resulting anion is then protonated. In this sense, the choice of the sensitizer is again important. Indeed, such a SET step is favored when the sensitizer is relatively hard to reduce in the ground state, whereas if this has a less negative $E_{\mathrm{red.}}$, the radical anion will combine with the adduct radical rather than reducing it. As a result, DCN ($E_{\mathrm{red.}}$ −1.28 V vs SCE) and TMPM ($E_{\mathrm{red.}}$ −1.31 V) have a much better turnover number than TCB ($E_{\mathrm{red.}}$ −0.65 V); as mentioned above, the last sensitizer is in fact rapidly alkylated under this condition.

On the other hand, with alkyne **7** ≤10% deuteration results both in MeCN−0.1% D_2O and in CD_3CN, despite the fact that the turnover number is again good with DCN and TMPM. This is not surprising since the reaction with **7** follows a different mechanism (see above) and involves a more reactive (vinylic) adduct radical. Presumably, the hydrogen source is in this case the alkyl chain in the donor (Scheme 5, path b).

Conclusion

The present study confirms that photoinduced electron transfer followed by radical-cation fragmentation is an efficient method for the generation of alkyl radicals.

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These undergo conjugate addition to activated esters and nitriles, and the selectivity of such reaction parallels that found when radicals are produced by the classical atom-transfer method, particularly when a triplet sensitizer (an aromatic ester) is used. Different from the thermal redox method, which is limited to good donors—usually enols—the PET reaction can be applied to weak donors such as tetralkylstannanes or dioxolanes and further, the adduct radical is reduced and not oxidized as in the thermal method. In common with the thermal oxidative method, e.g., Mn(III), this is not a chain reaction. It has the advantage, however, that the sensitizer is used in a catalytic amount (the stoichiometric reagent is light), provided that it has a moderate to good turnover number. Furthermore, the reaction is carried out in neat organic solvent, avoiding the problems associated with the use of an inorganic oxidant. As for the alkylation of acetylenedicarboxylate, this reaction involves assisted fragmentation concerted with radical addition. Despite some limitations, these alkylations introduce a new facet to PET-sensitized reactions, a field of growing synthetic interest. From the photochemical point of view, this work supplies a quantitative evaluation of the generation of *free* radical ions, demonstrating that this is the key factor that makes advantageous the use of a triplet sensitizer or of a secondary donor with a singlet sensitizer.

Experimental Section

The aromatic compounds used as photosensitizers and the donors (stannanes, dioxolanes, and acids) were either commercial samples or were sensitized according to published procedures. HPLC-grade acetonitrile for photochemical reactions was refluxed over CaH_2 and distilled directly in the reaction vessel.

Methyl Heptanoate (3a). A solution of methyl acrylate (484 μL, 0.1 M), tetrabutylstannane (882 μL, 0.05 M), and TMPM (168 mg, 0.01 M) in 54 mL of MeCN was subdivided in three serum-capped quartz tubes, deaerated by flushing with argon, and then irradiated in a multilamp apparatus fitted with six 15 W phosphor-coated lamps (center of emission, 320 nm). After 15 h, the solvent was evaporated and the raw photolyzate chromatographed on silica gel, eluting with a cyclohexanes−ethyl acetate 9:1 mixture to yield the title compound (105 mg, 27%). The same product was obtained in 26% yield by 10 h of irradiation in the presence of DCN (48 mg, 0.005 M) and BP (921 mg, 0.1 M).

Analogously obtained were products **3b**,[16] **3c**,**d**,[3a] **5a**,[17] **5b**,[18] **5c**,**d**,[3] **7**,[19] and **10**[20] (see Table 1). The products are known but in some cases have not been fully characterized previously. Additional data are reported below.

Methyl 3-methylheptanoate (3b): ^{1}H NMR ($CDCl_3$) δ 0.9 (m, 6H), 1.1−1.6 (m, 7H), 2.15 (dd, 1H, J = 5, 14 Hz), 2.35 (dd, 1H, J = 7, 14 Hz), 3.7 (s, 3H); ^{13}C NMR ($CDCl_3$) δ 13.91, 19.60, 22.64, 28.98, 30.18, 36.26, 41.53, 51.18, 173.68.

Methyl 3,4,4-Trimethylpentanoate (5b): ^{1}H NMR ($CDCl_3$) δ 0.85 (m, 12 H), 1.8 (m, 1H), 2.0 (dd, 1H, J = 10.5, 14 Hz), 3.7 (s, 3H); ^{13}C NMR ($CDCl_3$) δ 14.86, 26.98 (3 Me), 29.30, 37.20, 39.84, 51.25, 174.83.

Dimethyl 2-*tert*-butylmaleate ((*Z*-7): ^{1}H NMR ($CDCl_3$) δ 1.2 (s, 9H), 3.7 (s, 3H), 3.85 (s, 3H), 5.85 (s, 1H); ^{13}C NMR ($CDCl_3$) δ 28.58, 35.38, 51.53, 51.80, 115.59, 160.60, 165.49, 168.82; NOE (6.9%) effect between vinylic and *tert*-butyl hydrogens.

Dimethyl 2-*tert*-butylfumarate ((*E*-7): ^{1}H NMR ($CDCl_3$) δ 1.3 (s, 9H), 3.75 (s, 6H), 6.2 (s, 1H); ^{13}C NMR ($CDCl_3$) δ 28.27, 35.20, 51.67, 51.73, 122.64, 151.63, 167.09, 169.06; no significant NOE effect between vinylic and *tert*-butyl hydrogens.

Dimethyl 2-isopropylmaleate (10): ^{1}H NMR ($CDCl_3$) δ 1.15 (d, 6H), 2.65 (m, 1H), 3.7 (s, 3H), 3.85 (s, 3H), 5.8 (s, 1H); ^{13}C NMR ($CDCl_3$) δ 20.49, 32.75, 51.70, 52.10, 116.77, 156.85, 165.55, 169.20; NOE effect (37%) between the vinylic and methine hydrogens.

Quantum Yield Measurements. Quantum yields were measured in the above multilamp apparatus, using benzophenone−benzhydrol or ferrioxalate actinometry, and the product yield was determined by GC. Conversions were limited to 25%.

Fluorescence Measurements. Fluorescence emission was measured by means of an Aminco Bowman MPF spectrofluorimeter by using argon-flushed solutions in spectrophotometric 1 cm cuvettes. Linear Stern−Volmer plots were obtained in all cases.

Flash Photolysis. A kinetic apparatus supplied by Applied Photophysics was used. In the experiments with TMPM, the fourth harmonic of a Lumonics HY200 Nd:YAG laser was used. The monitor system, arranged in a cross-beam configuration, consisted in a 275W Xe lamp, a monochromator, and a five-stage photomultiplier. The signals were captured by a Hewlett-Packard 54510A digitizing oscilloscope, and the data were processed on a computer system using a software developed by Dr. C. Long (Dublin City University). The third harmonic of the laser was used in the experiments with DCA.

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