JOURNAL OF PHYSICAL ORGANIC CHEMISTRY, VOL. 10, 777–780 (1997)

TANDEM ENERGY TRANSFER–ELECTRON TRANSFER IN THE PHOTOSENSITIZED ALKYLATION OF α,β-UNSATURATED KETONES

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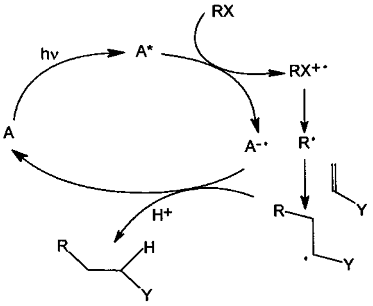
α,β-Unsaturated ketones are not conveniently alkylated by radicals generated from tetraalkylstannanes via photoinduced electron transfer (PET), either by direct irradiation or when a singlet sensitizer (an aromatic nitrile, a pyrilium salt) is used. However, the procedure is successful with tetramethyl pyromellitate (TMPM) as the sensitizer. TMPM is promoted to the triplet state by energy transfer from the unsaturated ketones and then sensitizes the cleavage of alkylstannanes by electron transfer. The alkyl radicals thus formed finally add to the unsaturated ketones, giving the β-alkyl derivatives. © 1997 John Wiley & Sons, Ltd.

J. Phys. Org. Chem. **10**, 777–780 (1997) No. of Figures: 3 No. of Tables: 2 No. of References: 14
Keywords: tandem energy transfer–electron transfer; photosensitized alkylation; α,β-unsaturated ketones
Received 27 January 1997; revised 15 March 1997; accepted 8 April 1997

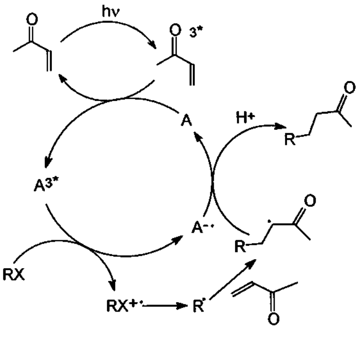
INTRODUCTION

New methods for the generation of radicals are instrumental in broadening the scope of carbon–carbon bond-forming radical reactions in organic synthesis.[1] Photosensitized electron transfer (PET)[2] and fragmentation of the radical cation add a new alternative to traditional methods for the generation of radicals,[3] and have the advantage of using unconventional substrates (since excited state are very good acceptors and oxidize even weak donors) and of operating under mild conditions.

As an example, we found that α,β-unsaturated esters and nitriles are conveniently alkylated when irradiated in the presence of an aromatic nitrile, A, as the sensitizer and of various donors RX (such as acetals and tetraalkylstannanes and -silanes; see Scheme 1).[4] On the other hand, Hasegawa *et al.*[5] found that α,β-unsaturated ketones are aminoalkylated when irradiated in the presence of α-aminosilanes. In both cases the mechanism involves PET (in the latter instance to the ketone triplet) and following fragmentation of the radical cation (this is why an aminosilane is required, since α-deprotonation of amines is slow). The thus produced radical adds to the alkene and the radical adduct is reduced by $A^{-\cdot}$ and protonated (see Scheme 1). Alkylation of unsaturated ketones can be predicted *not* to occur in this way, since the triplet states of such substrates are not sufficiently oxidizing even for the better donors among precursors of unsubstituted aliphatic



Scheme 1.



Scheme 2.

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Contract grant sponsor: CNR.

CCC 0894–3230/97/100777–04 $17.50

radicals, such as tetraalkylstannanes. In this paper, we report that whereas direct irradiation and singlet sensitization fail, tandem (triplet) energy transfer–electron transfer (Scheme 2) is successful.

RESULTS AND DISCUSSION

Cyclohex-2-enone (**1a**, 0·1 M), when irradiated in oxygen-free MeCN by means of phosphor-coated lamps (centre of emission 320 nm), underwent only a slow 2 + 2 dimerization. Addition of tetrabutylstannane (**2x**, 0·05 M) did not alter the reaction, consistent with the fact that electron transfer from **2x** to $\mathbf{1a}^{3*}$ is endothermic. This can be calculated by means of the Weller equation, and shows that ΔG_{set} $(\mathbf{2x} \rightarrow \mathbf{1a}^{3*}) = +17$ kcal mol^{-1} (1 kcal = 4·184 kJ), on the basis of the following values: E_{red} (**1a**) = − 2·0 V vs SCE,[5,6] E_{ox} (**2x**) = 1·75 V (calculated from the ionization potential)[7] and E $(\mathbf{1a}^{3*}) = 70$ kcal mol^{-1}.[6]

On the other hand, the absorption of such ketones extended to the near-UV region, and thus competitive absorbance and trivial quenching precluded the use as sensitizers of the benzene or naphthalene nitriles that we had used in previous work,[4] since the singlet state of such acceptors was too high-lying. We then considered the use of a different singlet sensitizer which absorbed at a longer wavelength than the ketones. A first choice was 9,10-dicyanoanthracene (DCA). Indeed, this compound was found to sensitize the reaction so that a little 3-butylcyclohexanone (**3ax**) was formed. DCA acted catalytically (the turnover number, i.e. the ratio between the moles of alkylated ketone formed and moles of sensitizer consumed, was 3; see Table 1). However, owing to the low solubility of this sensitizer its use was impractical, since only minimal alkylation of the alkenes could be obtained before all the DCA was consumed, and the reaction stopped.

2,4,6-Triphenylpyrilium fluoborate (TPPF), also strongly absorbing in the near-UV region and much more soluble, was tested next. This was able to promote some alkylation, but the yield of the product was modest and the sensitizer turnover number low (0·2). Apparently, the pyranyl radical formed from TPPF in the sensitization process underwent different reactions (the formation of 2*H*- and 4*H*-pyrans by coupling between pyranyl and alkyl radicals is known to be fast)[8] rather than re-entering the sensitization cycle in Scheme 1.

We then turned to a different approach. This consisted in using an additive with a low enough triplet energy to be sensitized through energy transfer by the ketone, and which would be a stronger oxidant. Such conditions are fulfilled by appropriate aromatic esters. Tetralkyl pyromellitates, as an example, have practically the same triplet energy as unsaturated ketones, but are reduced to a less negative potential. Hence, it could be anticipated that they would perform the desired task. Indeed, when **1a** was irradiated in the presence of tetramethyl pyromellitate (TMPM, 0·01 M) a new reaction took place, and after the irradiation **3ax** was obtained by flash chromatography in 62% yield (Scheme 3; see Experimental for the characterization of the photoproducts).

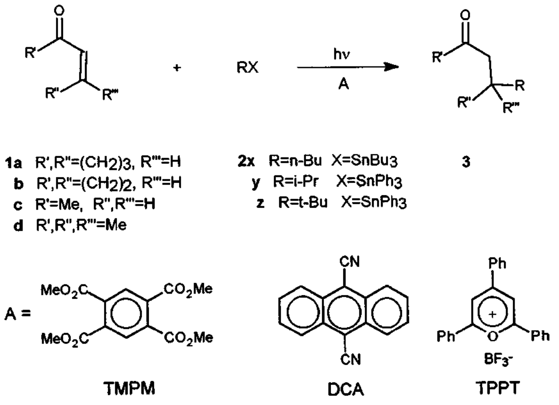
Thus, energy transfer from $\mathbf{1a}^{3*}$ leads to TMPM^{3*}, and this oxidizes the stannane. The butyl radical adds to the ketone and the adduct radical is reduced by TMPM (which has a fair turnover number of 6; see Table 1) and protonated (see Scheme 2). That this path is followed is supported by the following evidence. TMPM does not absorb significantly in the range used. TMPM quenches triplet **1a**, thus in separate experiments it was shown that TMPM quenches the photodimerization of the unsaturated ketones as well as the cycloaddition of **1a** to cyclohexene, consistent with the fact that energy transfer from $\mathbf{1a}^{3*}$ to the aromatic ester is thermoneutral, E (TMPM^{3*}) = 70 kcal mol^{-1}.[9] In turn, electron transfer from the stannane to the esters is thermoneutral, ΔG_{set} $(\mathbf{2x} \rightarrow \text{TMPM}^{3*}) = 0$ kcal mol^{-1}, since E_{red} (TMPM) = − 1·31 V,[10] whereas, as seen above, electron transfer to triplet $\mathbf{1a}^{3*}$ is largely endothermic. Furthermore, none of these alkylations occurs on omitting TMPM, and thus no homolytic cleavage of the stannane is involved. Apparently, TMPM is regenerated and functions as a non-consumed sensitizer. This is accounted for in Scheme 2 by back electron transfer from the radical anion to the radical adduct and protonation by adventitious water, although there is no specific evidence for this step. Summing up, TMPM is a convenient sensitizer for the present alkylations, since the reasonable turnover number and the good solubility allow the reaction to be carried out to completion.

The reaction was somewhat extended (Table 2), and it was shown that alkylation of cyclohexenone with secondary

Table 1. Sensitized alkylation of ketone **1a** by tetrabutylstannane in the presence of various sensitizers

Sensitizer (M)[a]	Irradiation time (h)	Product (% yield)	Sensitizer turnover number
DCA (5×10^{-4})	4	**3ax** (2·5)	3
TPPF (5×10^{-3})	2	**3ax** (2)	0·2
TMPM (1×10^{-2})	24	**3ax** (62)	6

[a] Sensitizers: 9,10-anthracenedicarbonitrile (DCA), 2,4,6-triphenylpyrylium tetrafluoborate (TPFF) and tetramethyl pyromellitate (TMPM).



Scheme 3.

Table 2. Alkylation yield on irradiation of $\alpha<\beta$-unsatured ketones in the presence of 0·01 M TMPM

Ketone	Stannane	Irradiation time (h)	Product (% yield)[a]
1a	2x	24	**3ax** (62)
1a	2y	60	**3ay** (31)
1a	2z	100	**3az** (29)
1b	2x	60	**3bx** (25)
1c	2x	10	**3cx** (67)
1d	2x	60	No reaction

[a] Isolated yield after chromatography.

and tertiary radicals to give cyclohexanones **3ay–z** was likewise possible, although in a lower yield. The faster photodimerization of cyclopentenone (**1b**) was less easily quenched under this condition, but also in this case some alkylation (to give **3bx**) was obtained by the use of the same method.

It is noteworthy that convenient (and relatively rapid) alkylation was obtained with an open-chain *α,β*-unsaturated ketone, **1c**. Presumably, autoquenching is less important with a non-rigid unsaturated ketone and gives a better chance of quenching of the triplet by TMPM. On the other hand, both cyclic and acyclic *β,β*-disubstituted analogues, such as **1d** and 9-methyl-$\Delta^{5(10)}$-octalindione, did not react appreciably under these conditions. This reasonably is not due to a change in the photochemical part of the reaction, but rather to the well known steric hindrance in the radical addition step.

No attempt to optimize the preparative conditions has been made as yet, and the long irradiation time required in the present experiments is mainly due to light loss caused by the precipitation of tin-containing by-products during irradiation. Furthermore, alkylation of unsaturated ketones obviously can more conveniently be obtained via the classical enolate and radical conjugate addition methods. However, these results demonstrate that a PET-based method can be extended to cases where the previously established strategy is ineffectual, and allow us to propose the mechanism shown in Scheme 2, based upon a tandem energy–electron transfer sequence. Since PET methods are gaining attention, in view of the mild conditions and of the fact that no sensitive or *in situ* prepared reagent is required, extending their scope may be fruitful.

EXPERIMENTAL

The stannanes **2x**, **2y** and **2z** were prepared from the corresponding Grignard reagents and purified according to published procedures.[11] TMPM was obtained by esterification of the corresponding commercial acid and purified by recrystallization. For photochemical reactions, HPLC-grade acetonitrile was refluxed over CaH_2 and distilled directly into the reaction vessel.

Photochemical reactions. A solution of **1a** (0·7 ml, 0·1 M), **2x** (1·185 ml, 0·05 M) and TMPM (223 mg, 0·01 M) in 72 ml of MeCN was subdivided in four quartz tubes, flushed with nitrogen for 10 min and irradiated for 1 day by means of six 15 W phosphor-coated lamps (centre of emission, 320 nm). The course of the reaction was monitored by vapour-phase chromatography. The solution was then rotary evaporated and the residue was separated by flash chromatography, eluting with cyclohexane–ethyl acetate (9:1) to yield 3-butylcyclohexanone (**3ax**, 345 mg, 62% yield). Analogously obtained were 3-(1-methylethyl)cyclohexanone (**3ay**), 3-(1,1-dimethylethyl)cyclohexanone (**3az**), 3-butylcyclopentanone (**3bx**) and octan-2-one (**3cx**) (see Table 2). The saturated ketones obtained were known compounds[12–14] and had IR and NMR in accordance with the assigned structures. **3ax**: ^{13}C NMR δ 13·9, 22·6, 25·2, 28·7, 31·2, 36·2, 39·0, 41·4, 48·1, 212·1**3ay**: ^{13}C NMR, δ 19·2, 19·4, 25·4, 28·2, 32·3, 41·3, 45·2, 45·3, 212·6**3az**: ^{13}C NMR, δ 25·5, 25·9, 27·0, 32·5, 41·2, 43·5, 49·2, 213·0**3cx**: ^{13}C NMR, δ 13·8, 22·3, 23·6, 28·7, 29·7, 31·4, 43·6, 209·3.

Experiments with both TPPT and DCA as the sensitizers were carried out by means of phosphor-coated lamps centred at 360 nm.

ACKNOWLEDGEMENTS

This work was supported in part by CNR, Rome, in the framework of ‘Progetto Strategico Tecnologie Chimiche Innovative.’

REFERENCES

1. B. Giese, *Radicals in Organic Synthesis. Formation of Carbon–Carbon Bonds.* Pergamon Press, Oxford (1986).
2. J. Mattay, *Angew. Chem.* **99**, 849 (1987); *Angew. Chem., Int. Ed. Engl.* **26**, 825 (1987); M. A. Fox and M. Chanon (Eds), *Photoinduced Electron Transfer.* Elsevier Amsterdam (1988).
3. A. Albini, M. Mella and M. Freccero, *Tetrahedron* **50**, 575 (1994).
4. M. Fagnoni, M. Mella and A. Albini, *J. Am. Chem. Soc.* **117**, 7877 (1995); M. Fagnoni, M. Mella and A. Albini, *Tetrahedron* **51**, 859 (1995).

5. E. Hasegawa, W. Xu, P. S. Mariano, U. C. Yoon and J. U. Kim, *J. Am. Chem. Soc.* **110**, 8099 (1988); U. C. Yoon and P. S. Mariano, *Acc. Chem. Res.* **25**, 233 (1992).
6. D. A. Dunn, D. I. Schuster and R. Bonneau, *J. Am. Chem. Soc.* **107**, 2802 (1985).
7. C. L. Wong and J. K. Kochi, *J. Am. Chem. Soc.* **101**, 5593 (1979).
8. S. Kyushin, Y. Nakadaira and M. Ohashi, *Chem. Lett* 2191 (1990).
9. D. R. Arnold, J. R. Bolton and J. A. Pedersen, *J. Am. Chem. Soc.* **94**, 2872 (1972).
10. C. De Luca, C. Giomini and L. Rampazzo, *J. Electroanal. Chem.* **207**, 161 (1986).
11. S. Bouè, M. Gielen and J. Nasielski, *J. Organomet. Chem.* **9**, 443 (1967).
12. E. J. Corey and D. J. Beames, *J. Am. Chem. Soc.* **94**, 7210 (1972).
13. J. J. Barrieux and J. Gore, *Bull. Chim. Soc. Fr.* **38**, 3978.
14. G. H. Posner, D. J. Brunell and L. Sinoway, *Synthesis* 662 (1974).