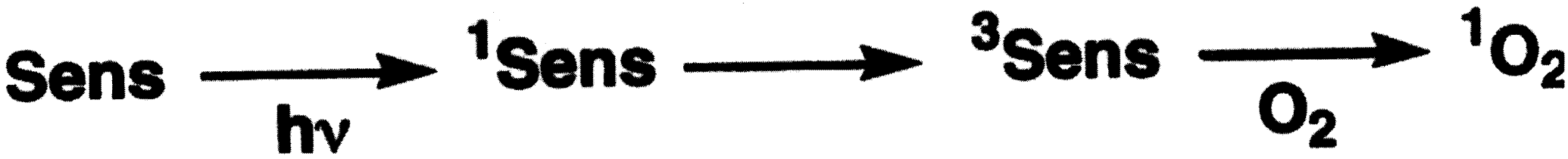
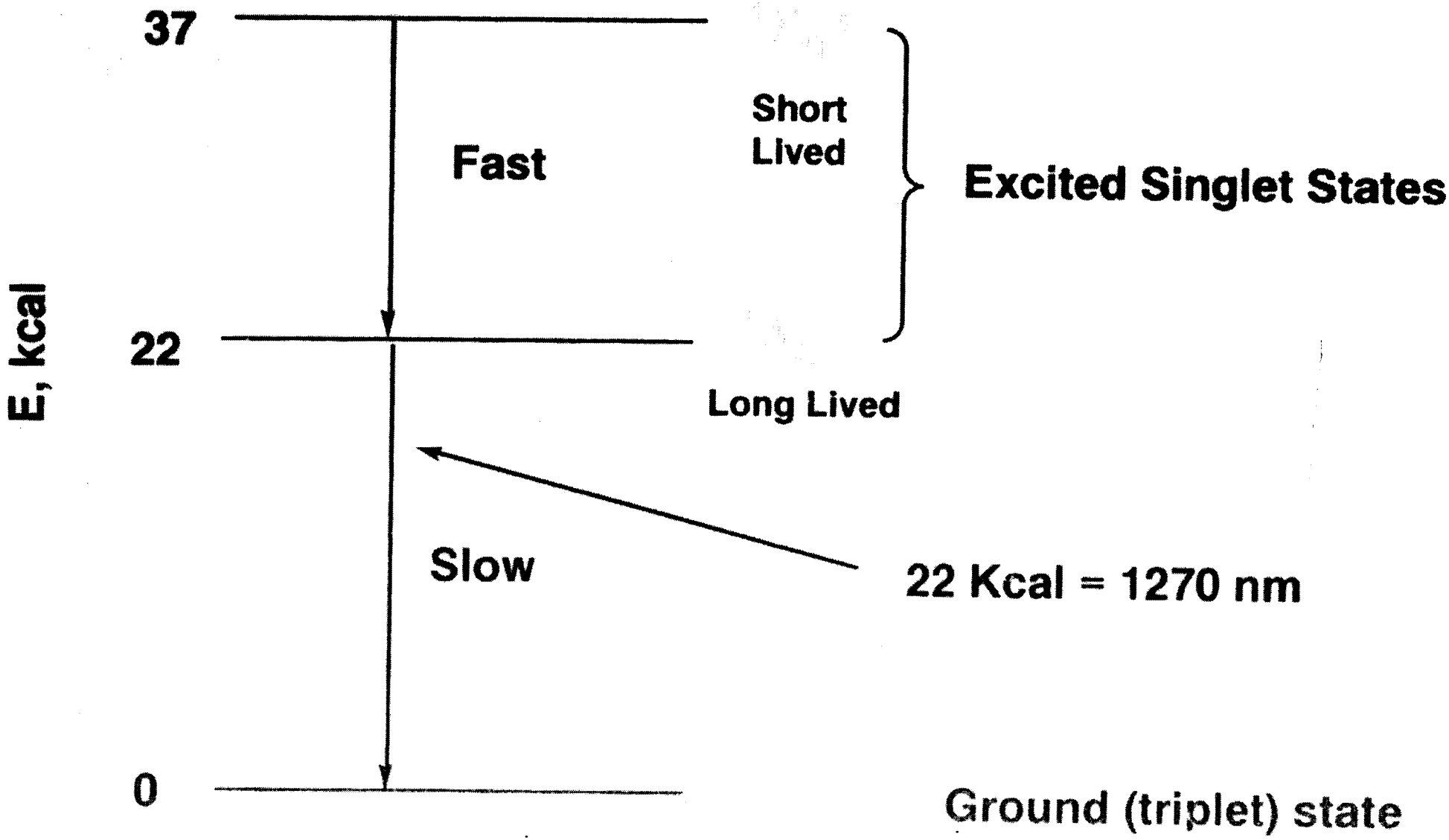
Photooxidation as a Preparative Reaction

Singlet Oxygen Formation

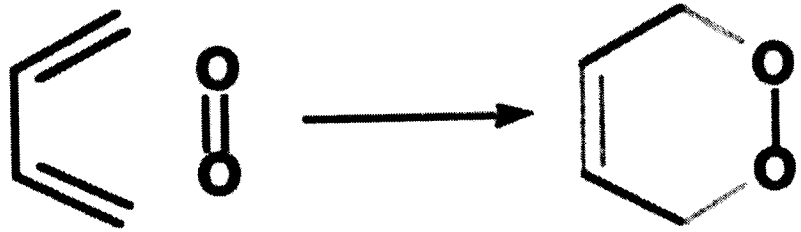


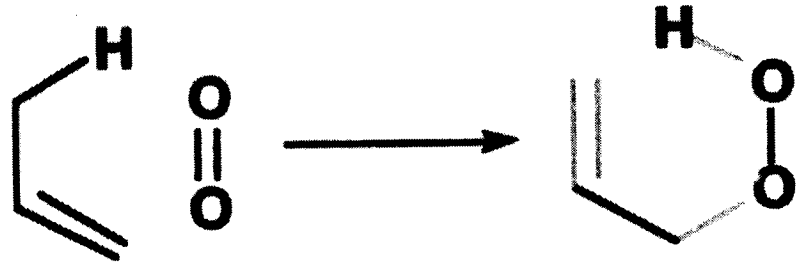
Typically, only 10^{-5} - 10^{-4} M Sensitizer

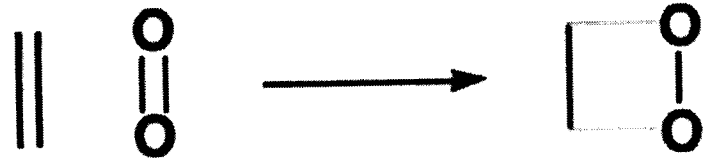
What is Singlet Oxygen?



Singlet Oxygen Products





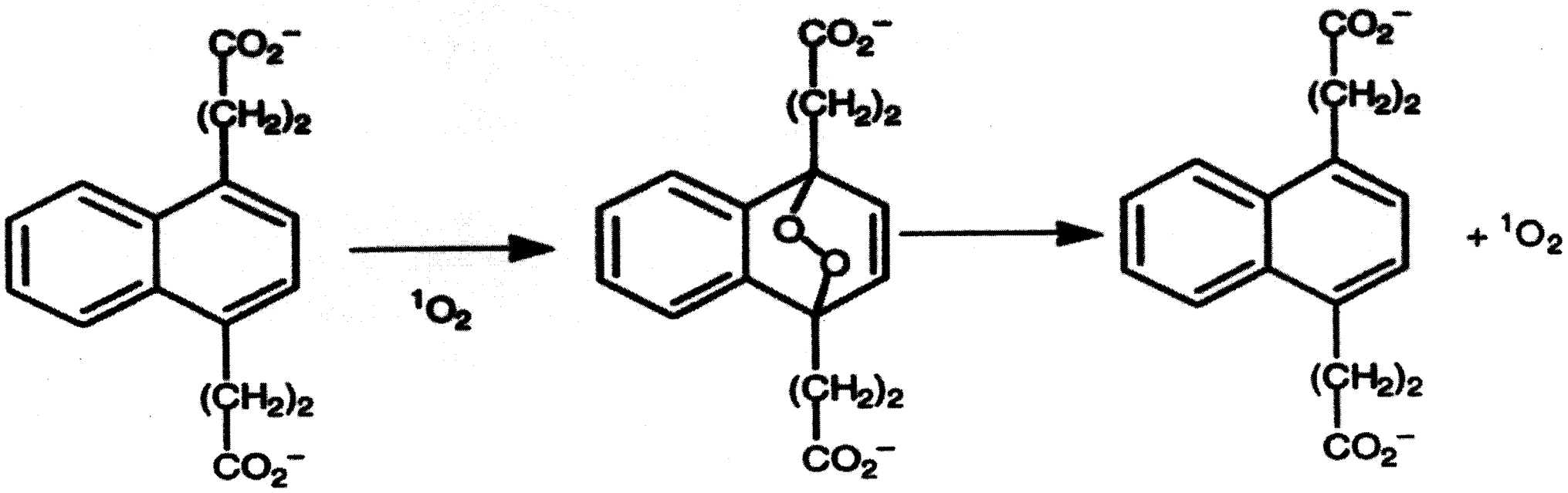


$R_2S \longrightarrow R_2S^+O^-$

Photooxidation is Green

- Reagents: light, sensitizer and O_2
- Only products, sensitizer at end
- Removal of sensitizer: adsorb or extract
- Not always possible

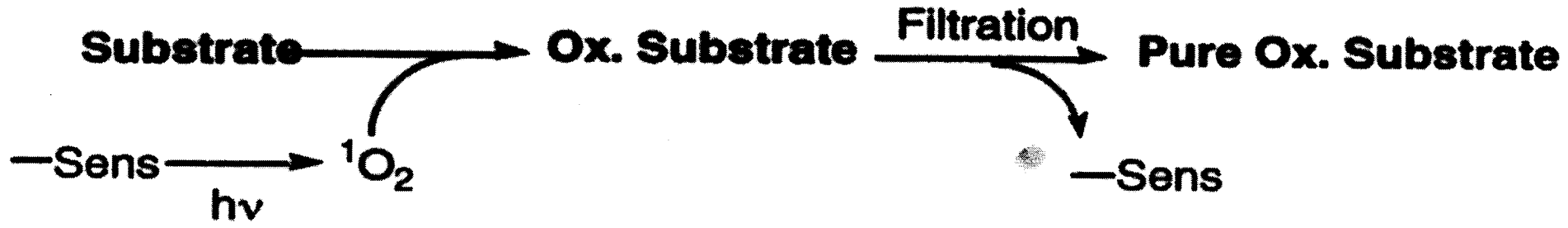
Singlet Oxygen Source



- Needed for deoxynucleotide oxidation-free of Sens

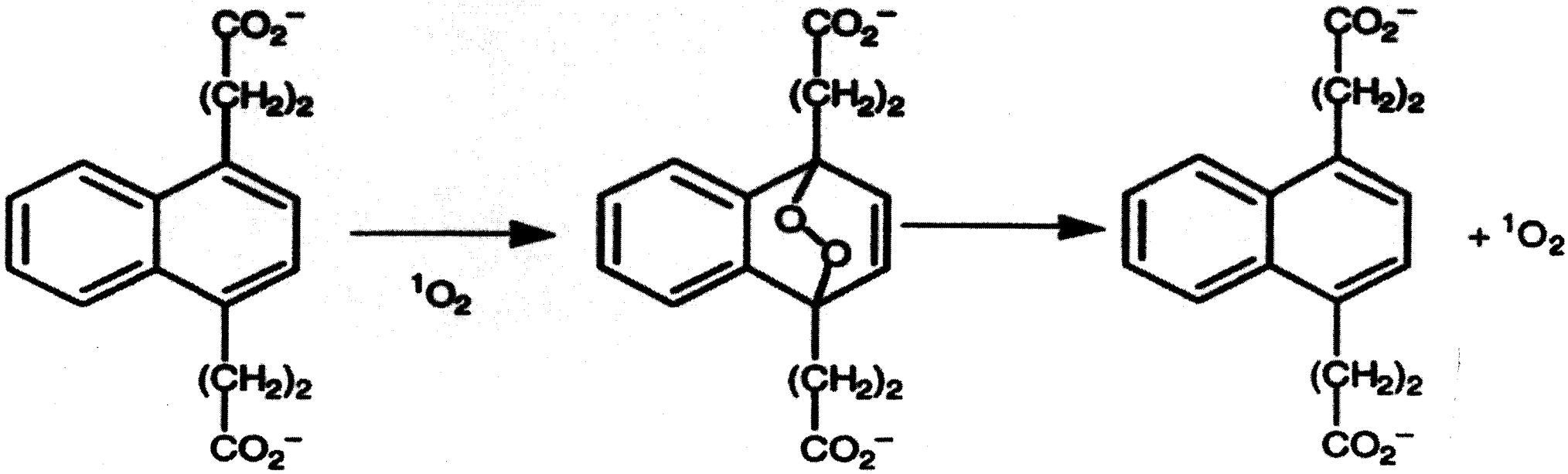
Polymer-bound Sensitizer

- Schaap: Merrifield's Resin beads (Polystyrene)
- Couple Rose Bengal
- Filter at end of reaction to remove sensitizer



Blossey, E. C.; Neckers, D. C.; Thayer, A. L.; Schaap, A. P. *J. Am. Chem. Soc.* 1973, *95*, 5820-5822.
Schaap, A. P.; Thayer, A. L.; Blossey, E. C.; Neckers, D. C. *J. Am. Chem. Soc.* 1975, *97*, 3741-3745.

Singlet Oxygen Source



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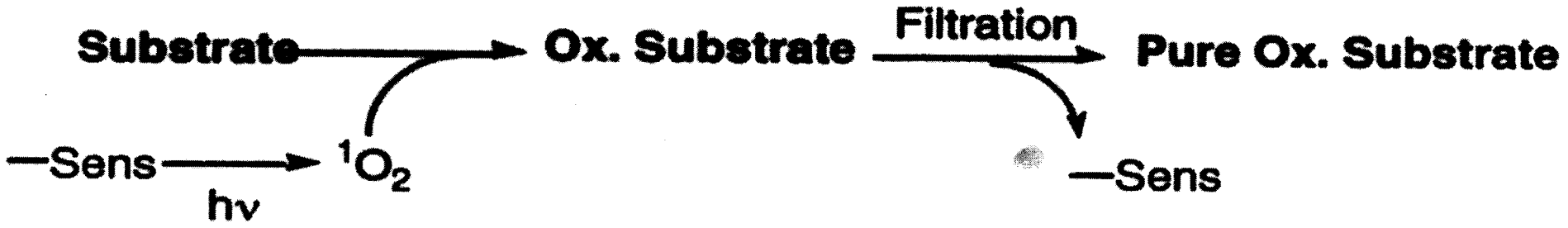

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Schaap, A. P.; Thayer, A. L.; Blossey, E. C.; Neckers, D. C. *J. Am. Chem. Soc.* 1975, *97*, 3741-3745.

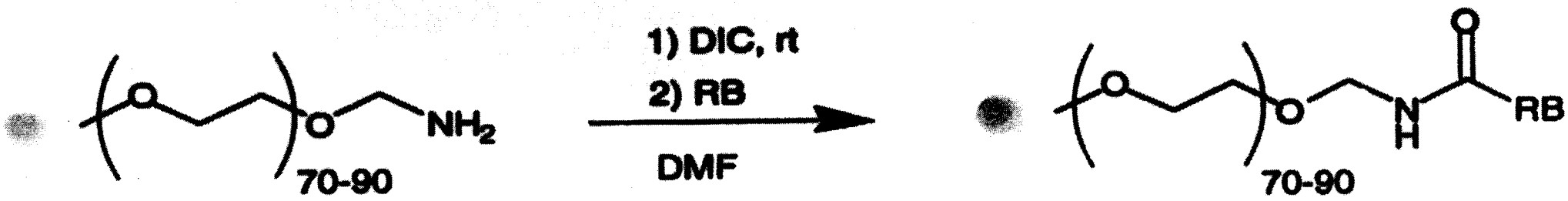
Use in Water

- Polystyrene resin is not wetted, no reaction
- Use a custom hydrophilic polymer
- Not available!

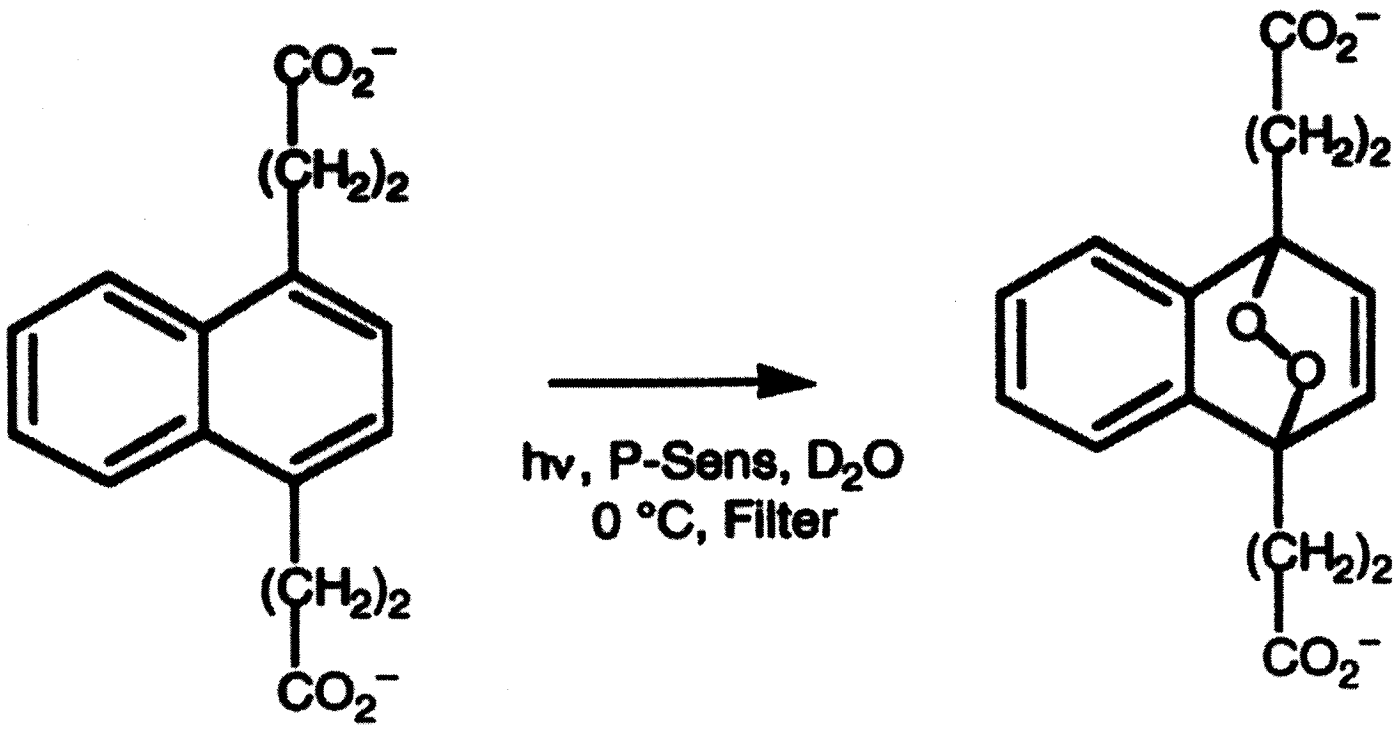
Schaap, A. P.; Thayer, A. L.; Zaklika, K. A.; Valenti, P. C. *J. Am. Chem. Soc.* 1979, *101*, 4016-4017.

Hydrophilic Polymer-bound Sensitizer

- NovaSyn® TG amino resin (Novabiochem): readily available



Effective, simple



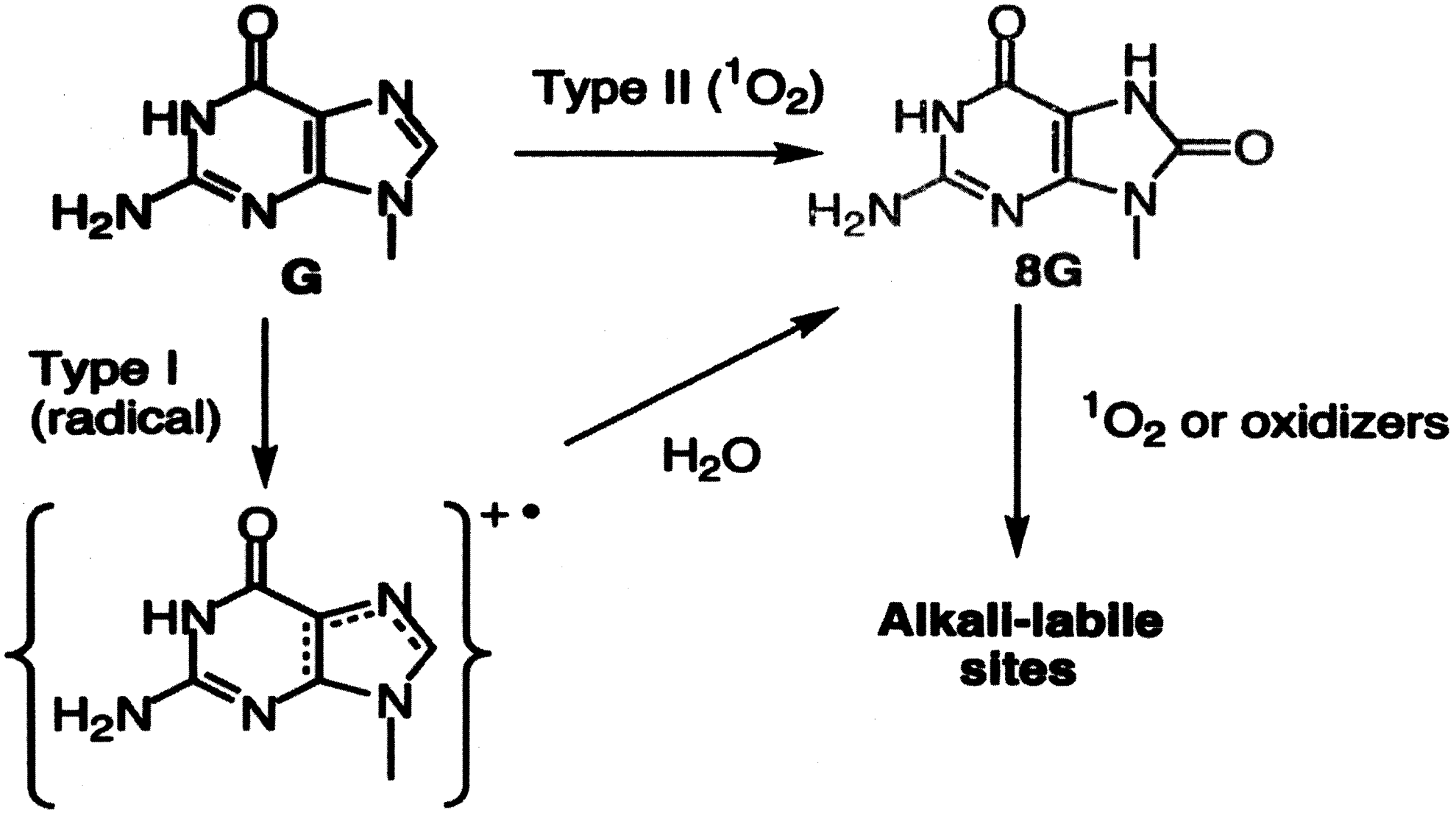
Histidine ⟶ Oxidation

hν, P-Sens, D_2O

- **Efficiency comparable to solution, excellent yield**

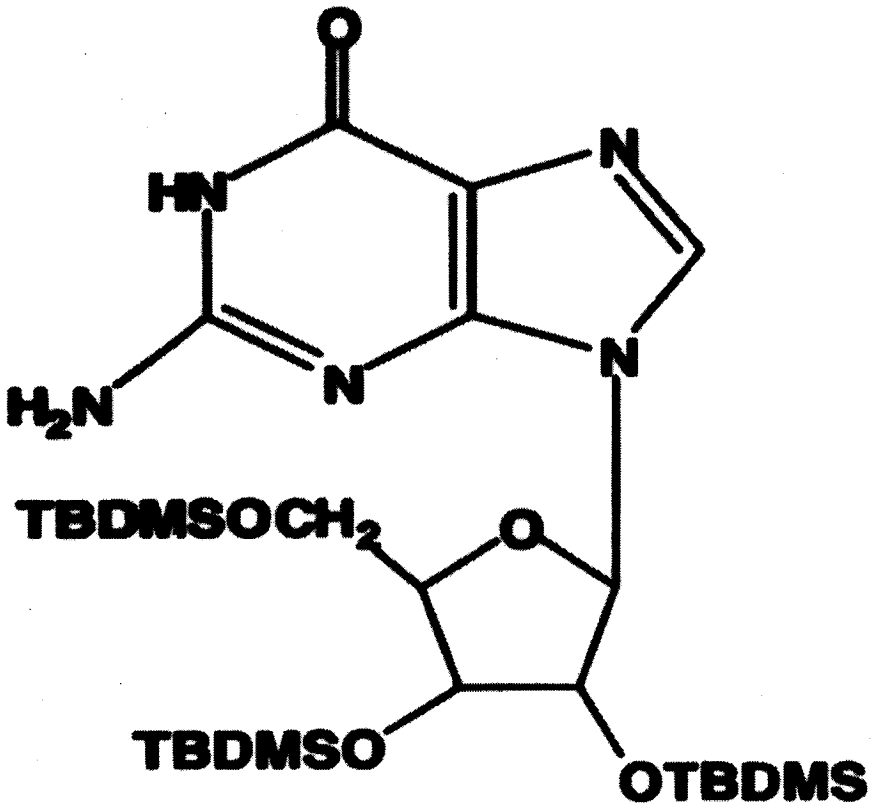
Prat, F.; Foote, C. S. *Photchem. Photobiol.* **1998**, *67*, 626-627.

8-oxoG (8G) formation



Both Type I And Type II Give Strand Breaks

TBDMS-Guanosine



TBDMS = t-butyldimethylsilyl

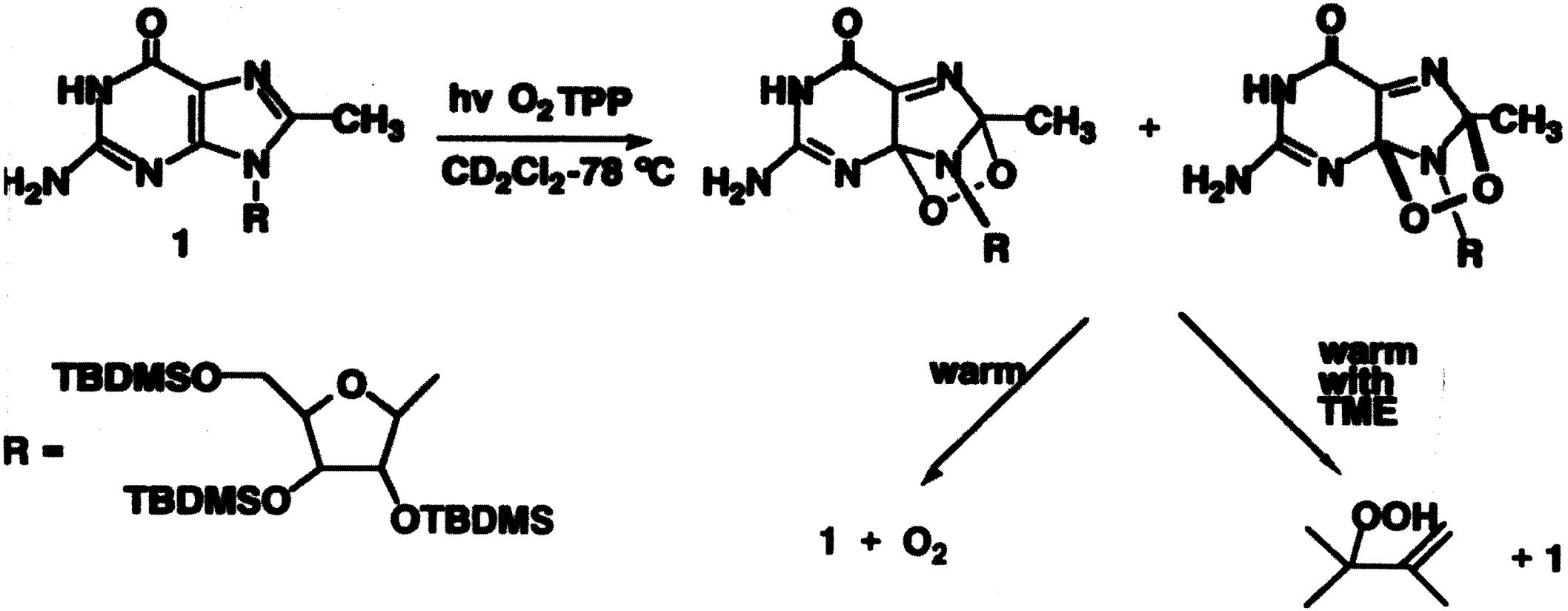
Soluble in Organic Solvents

Sheu, C.; Foote, C. S. *J. Am. Chem. Soc.* **1993**, *115*, 10446-10447.

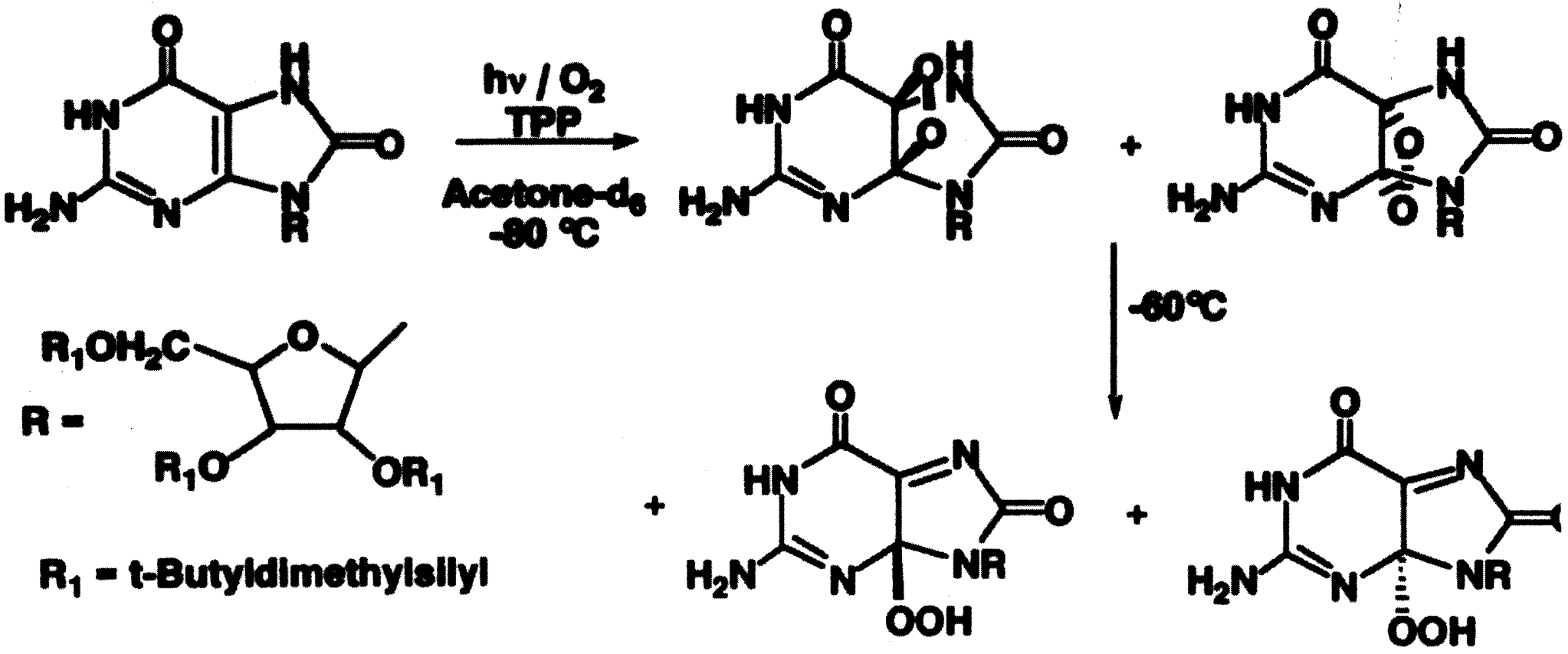
Relative Reactivity

Substrate	$(k_r + k_q)$, $M^{-1}s^{-1}$	k_r, $M^{-1}s^{-1}$	$\frac{k_r}{(k_r + k_q)}$ (%)
8-H-G (1)	6.3×10^6	1.4×10^5	2.2
8-Oxo-G (2)	5.5×10^7	1.9×10^7	35
TME	3.0×10^7		
2M2P	7.6×10^5		

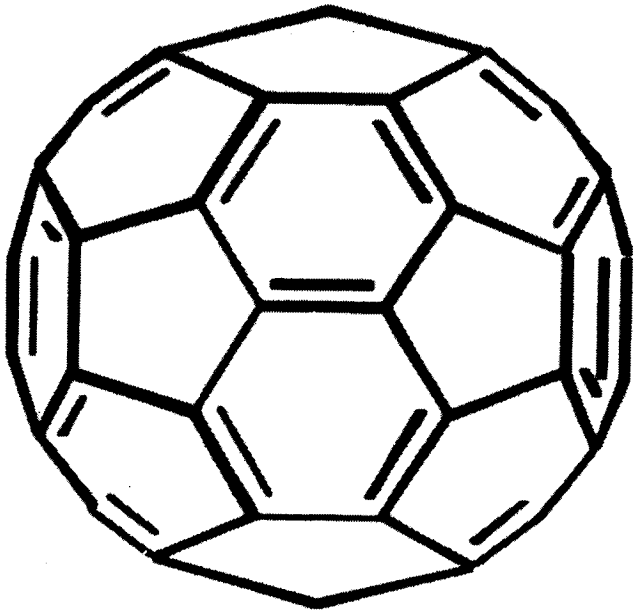
8-Methylguanosine



8-Oxoguanosine Photooxidation



C_{60} is a Quantitative $^1O_2$ Sensitizer

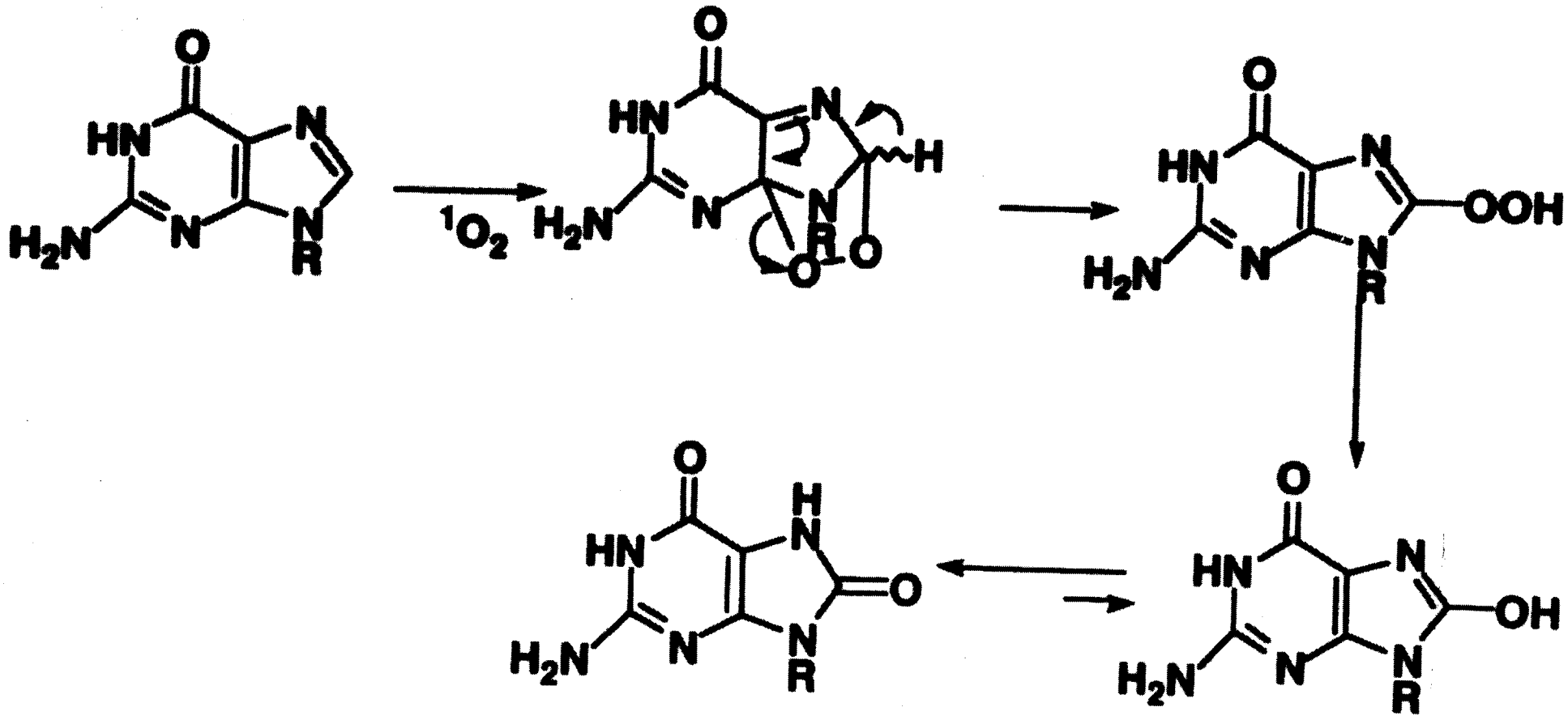


$h\nu$

$^1O_2$

But not very soluble; inert in biological systems

8-Oxo Formation



Fullerenes Neither React with or Quench $^1O_2$ Appreciably

C_{60} or C_{70} + $^1O_2$ ⟶ No Reaction

- No Products by UV/VIS Absorption or by HPLC

- Quenching Values (k_q) are Small:

C_{60}: $k_q = (5 \pm 2) \times 10^5\ M^{-1}\ s^{-1}$

C_{70}: k_q = Not Measurable

Photoelectrochemistry of C_{60}

$$\Delta E_{0,0} = 1.56 \text{ eV}$$

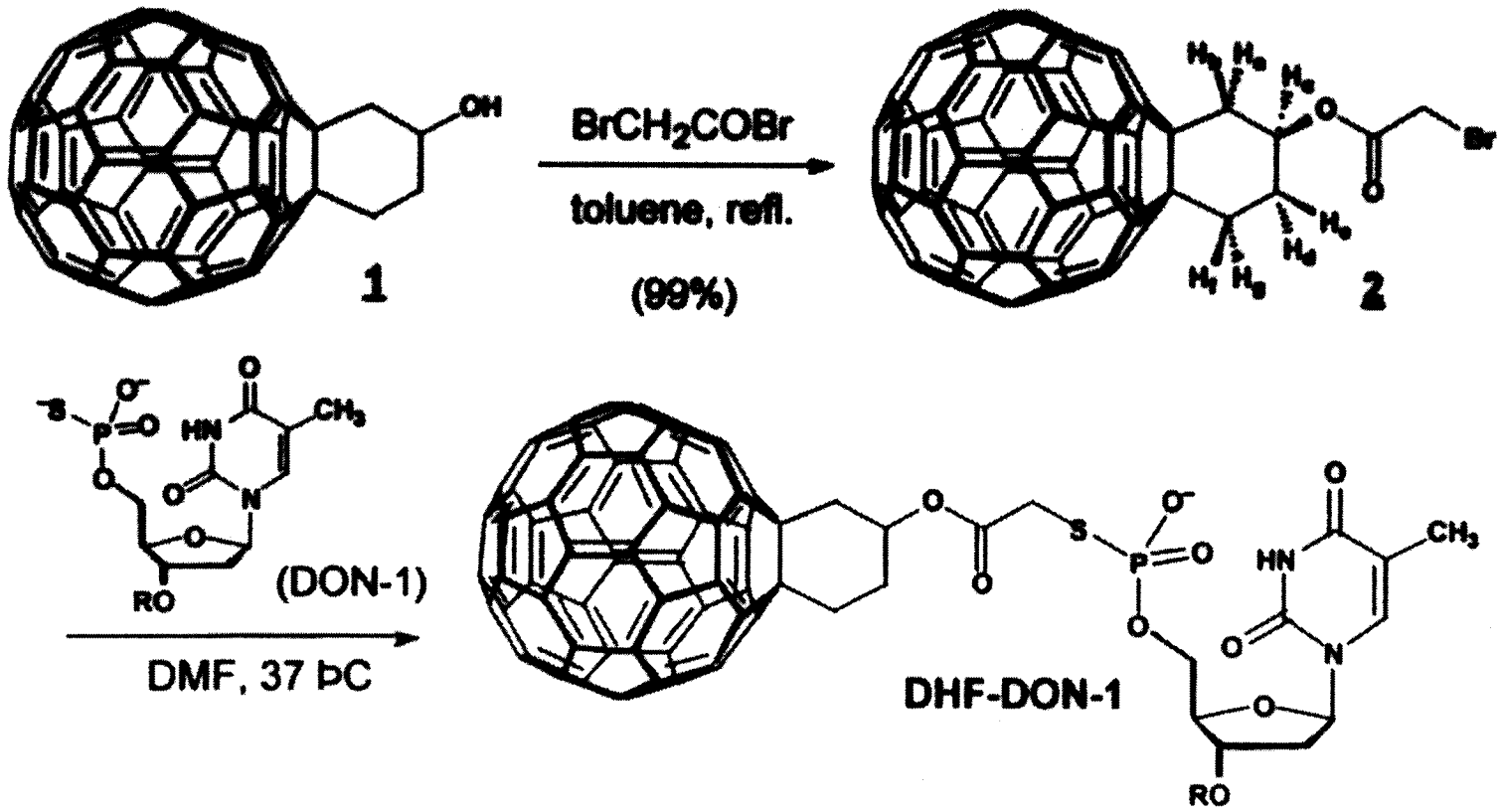
$$C_{60} \xrightarrow[h\nu]{} {}^3C_{60}$$

$E_{1/2} = -0.58$ V (benzonitrile)

$\therefore E_{1/2}({}^3C_{60}) = \sim +0.98$ V

$${}^3C_{60} + \text{Donor} \xrightarrow[\text{electron transfer}]{} {}^3C_{60}^- + \text{Donor}^+$$

Dihydrofullerene Deoxynucleotide

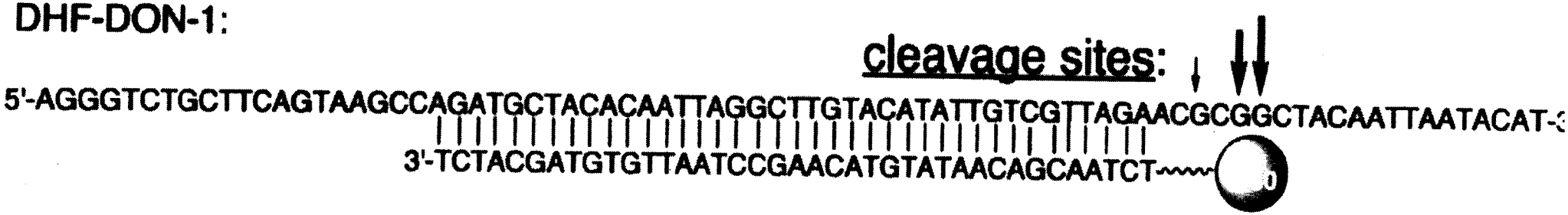


3'-TCTACGATGTGTTAATCCGAACATGTATAACAGCAATC = R

Chi-Hong B. Chen, Yi-Zhong An, David S. Sigman, Christopher S. Foote, Yves Rubin J. Am. Chem. Soc., submitted

The DHF-DON Cleaves DNA Photochemically

DHF-DON-1:



- Only at G
- Selective for G in the neighborhood of DHF

Reaction Mechanism: $^1O_2$?

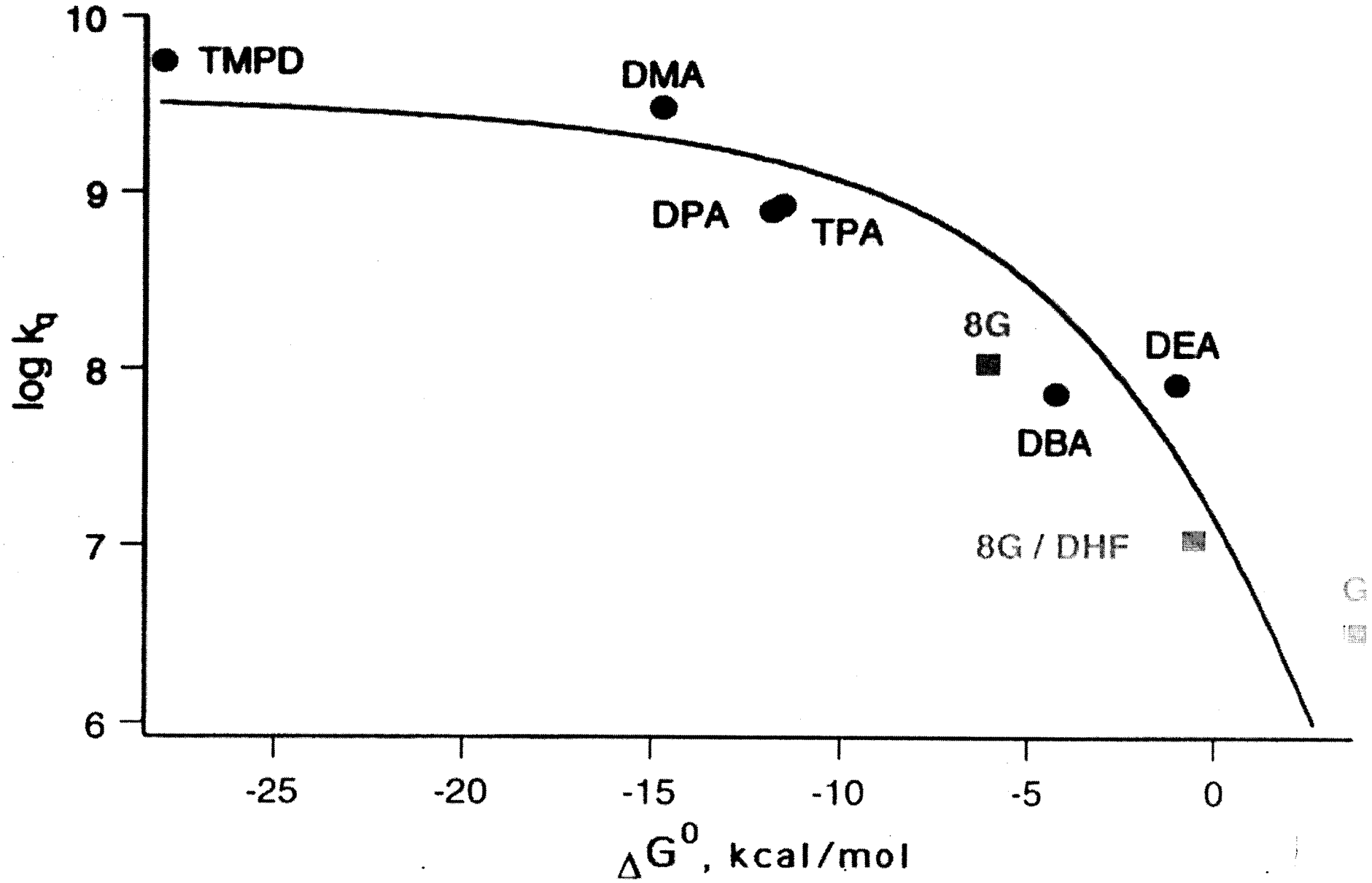
- **Eosin selectivity is different from DHF**
- **$^1O_2$ quenchers inhibit Eosin reaction, not DHF**
- **D_2O (longer $^1O_2$ lifetime) promotes Eosin reaction, not DHF**
- **NOT a $^1O_2$ reaction. Probably Type I, electron transfer**

An, Y.-Z.; Chen, C.-H. B.; Anderson, J. L.; Sigman, D. S.; Foote, C. S.;Rubin, Y. *Tetrahedron* **1996**, *52*, 5179-89.

Methods

- Use $TBDMS_3$ Guanosine
- Transient Absorption Spectroscopy (ND-YAG, 7 ns excitation)
- C_{60}^- (λ= 1070 nm) and Triplet (λ= 720 nm) detected with Ge Photodiode
- in Benzonitrile (only "polar" solvent for C_{60})

Rehm-Weller Plot



Conclusions

- C_{60} will barely take an electron from Guanosine (endothermic)
- Very efficient for 8-G
- Should be very good for G-G too (similar redox to 8G).
- DHF is a little less reactive, but enough to do electron transfer from 8G
- The high local concentration of G (actually 8G) in the DON should favor electron transfer