presence or absence of BSA. The initial product of the reaction is presumably 3,5-dinitronitrosobenzene (**2**) (eq 1). This is consistent with the fact that the first two-electron step in the reduction of nitrobenzene is nitrosobenzene,[8] and in this case **1** can be considered as a combination of hydride anion (a potential two-electron reducing agent) and **3**. Disproportionation of **2** (eq 2) or reduction of **2** by **1** (eq 3), followed by condensation reactions (eq 4 or 5), should lead to the final isolated products; other pathways are possible. The work of Hutchins, *et al.*, on the reduction of aromatic nitro compounds by sodium borohydride leads to a similar analysis.[9]

All our evidence to date suggests that BSA is acting as a macromolecular catalyst in this reaction (presumably catalyzing the first step, eq 1); our results indicate that the protein must be in its "native" conformation and that the reaction depends upon the binding of **1** to BSA. (1) Other molecules which bind to BSA[10] (sodium dodecyl sulfate, picrate anion, phenol red) inhibit the catalysis.[11] The nature of this inhibition must be determined. (2) BSA is able to "turnover" significant quantities of substrate. In ~20 minutes, 8×10^{-6} mol of BSA decomposed a total of 2.7×10^{-3} mol of **1** in 3 l. of solution. (3) The reaction is characterized by saturation kinetics typical of enzyme–substrate reactions (Table I). (4) A variety of samples of BSA from different companies (Schwarz/Mann, Pentex, Sigma) and of different degrees of purity (fraction V, crystallized, fatty acid free, defatted by Chen's method[12]) exhibited similar catalytic properties. (5) No catalysis is observed in 8 *M* urea, where BSA is presumably unfolded. (6) Other animal serum albumins, *e.g.*, sheep and horse, exhibit similar, though lower activities. Human serum albumin (Sigma fraction V, Schwarz/Mann) was apparently inert. This catalysis does not only depend upon binding of **1** to a protein with a hydrophobic binding site. Other proteins which bind hydrophobic molecules (β-lactoglobulin,[13] α-chymotrypsin[14]) show no catalysis at all. (7) Isolated fragments A and B[15] of BSA are ineffective alone (residual activities alone are ~0.5% or less) in catalyzing the reaction. When they are combined in aqueous solution at a concentration of about 2×10^{-6} *M* each, ~30% of full activity is restored.

Further studies on this most interesting reaction and its possible physiological implications are in progress.

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(8) N. V. Sidgwick, I. T. Millar, and H. D. Springall, "The Organic Chemistry of Nitrogen," Clarendon Press, Oxford, 1966, p 387.
(9) R. O. Hutchins, D. W. Lamson, L. Rua, C. Milewski, and B. Maryanoff, *J. Org. Chem.*, **36**, 803 (1971).
(10) J. Steinhardt and J. A. Reynolds, "Multiple Equilibria in Proteins," Academic Press, New York, N. Y., 1969.
(11) At a concentration of 1 of $\sim 7.5 \times 10^{-5}$ *M*, the following concentrations of inhibitors are needed for ~50% inhibition: sodium dodecyl sulfate, 1.5 μM; picrate anion, 13 μM; phenol red, 140 μM.
(12) (a) R. F. Chen, *J. Biol. Chem.*, **242**, 173 (1967); (b) M. Sogami and J. F. Foster, *Biochemistry*, **7** 2172 (1968).
(13) A. Wishnia and T. W. Pinder, Jr., *Biochemistry*, **5**, 1534 (1966).
(14) R. Lumry in "Enzymology in the Practice of Laboratory Medicine," P. Blume and E. Frier, Ed., Academic Press, New York, N. Y., 1973.
(15) T. P. King, *Fed. Proc., Fed. Amer. Soc. Exp. Biol.*, **32**, Abstr. 542 (1973).

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Polymer-Based Sensitizers for Photooxidations

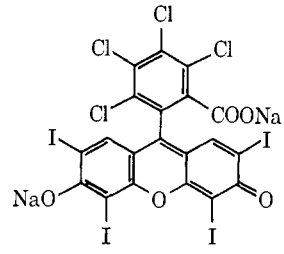
Sir:

Insoluble polymer supports were introduced several years ago by Merrifield[1] and by Letsinger[2] to facilitate polypeptide synthesis. The technique involves the use of an insoluble styrene–divinylbenzene copolymer bead to provide a foundation upon which successive chemical transformations can be carried out.

For some time we have been interested in the use of insoluble polymer supports in photochemical reactions. In this report, we describe the preparation and use of the first example of a synthetically applicable, polymer-based photosensitizer. The reagent, polymer-based Rose Bengal (Ⓟ-Rose Bengal), is utilized to sensitize the generation of singlet molecular oxygen. Rose Bengal[3] is attached to a chloromethylated polystyrene support *via* the following procedure: Rose Bengal, 2.0 g (2.1 mmol), was stirred at reflux in 60 ml of reagent grade dimethylformamide with 2.0 g of chloromethylated styrene–divinylbenzene copolymer beads (1.38 mequiv of CH_2Cl, 50–100 mesh). After 20 hr, the polymer (now dark red) was filtered and washed successively with 150-ml portions of benzene, ethanol, ethanol–water (1:1), water, methanol–water (1:1), and methanol. After these washings, the final filtrate was colorless. The polymer beads[4] were dried in a vacuum oven to a final weight of 2.17 g.

Singlet molecular oxygen exhibits three modes of reaction with alkenes:[5] 1,4-cycloaddition with con-

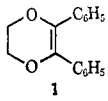
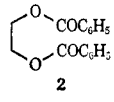
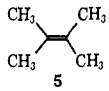
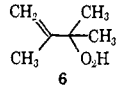
(1) R. B. Merrifield, *Science*, **150**, 178 (1965).
(2) R. L. Letsinger, M. J. Kornet, V. Mahedevon, and D. M. Jerina, *J. Amer. Chem. Soc.*, **86**, 5163 (1964).
(3) Rose Bengal



(4) The Rose Bengal is probably attached to the polymer as the carboxylate ester.
(5) (a) C. S. Foote, *Accounts Chem. Res.*, 1, 104 (1968); (b) D. R. Kearns, *Chem. Rev.*, 71, 395 (1971); (c) K. Gollnick and G. O. Schenck in "1,4-Cycloaddition Reactions," J. Hammer, Ed., Academic Press, New York, N. Y., 1967, p 255; (d) K. Gollnick, *Advan. Photochem.*, **6**, 1 (1968); (e) W. R. Adams in "Oxidation," Vol. 2, R. L. Augustine and D. J. Trecker, Ed., Marcel Dekker, New York, N. Y., 1971, p 65; (f) J. T. Hastings and T. Wilson, *Photophysiology*, **5**, 49 (1970).

jugated dienes to yield cyclic peroxides, an "ene" type reaction to form allylic hydroperoxides, and 1,2 cycloaddition[6] to give 1,2-dioxetanes which cleave thermally to carbonyl-containing products. Examples of all of these three reaction types have been carried out utilizing Ⓟ-Rose Bengal as a sensitizer (see Table I).

Table I. Photoxidations with Ⓟ-Rose Bengal

Singlet oxygen acceptor	Product	% yield (isolated)
 1	 2	95
 3	 4	69
 5	 6	82

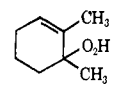
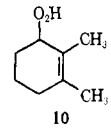
To a solution of 140 mg (0.6 mmol) of 1,2-diphenyl-*p*-dioxene (**1**) in 6 ml of CH_2Cl_2 was added 200 mg of sensitizer beads. The resultant mixture contained in a Pyrex vessel was vigorously stirred at 10° under O_2 and irradiated with a 500-W tungsten–halogen lamp through a uv-cutoff filter. Gas chromatography indicated complete oxidation of **1** after 6 hr. Removal of the sensitizer beads by filtration of the reaction mixture through a sintered glass disk[7] and removal of the solvent under vacuum gave colorless crystals of **2** in 95% yield. The photooxidation product was compared with an authentic sample of **2**.[8] Absorption spectra of the reaction solution before and after photolysis indicated that no Rose Bengal or other sensitizer is leached into the reaction solution.

The following control experiments indicate that the conversion of **1** to **2** is a singlet oxygen-mediated reaction. The reaction is inhibited by the addition of 10 mol % (based on **1**) of 1,4-diazabicyclo[2.2.2]octane (DABCO), a singlet oxygen quencher.[9] The photooxidation of **1** can be carried out in the presence of 10 mol % of 2,6-di-*tert*-butylcresol, a free radical inhibitor. The conversion of **1** to **2** can also be effected by photooxidation with 562-nm radiation using a Bausch and Lomb grating monochromator and SP-200 mercury light source.[10] It should also be noted that a suspension of solid Rose Bengal in CH_2Cl_2 is relatively ineffective in photosensitizing the generation of singlet oxygen.

1,3-Cyclohexadiene (**3**) and tetramethylethylene (**5**) undergo the 1,4-cycloaddition and ene reactions, respectively, with singlet oxygen produced by Ⓟ-Rose Bengal sensitization. The reactions were carried out as described for the photooxidation of **1**. Products **4**[11] and **6**[12] were isolated by distillation under vacuum and compared with authentic samples.

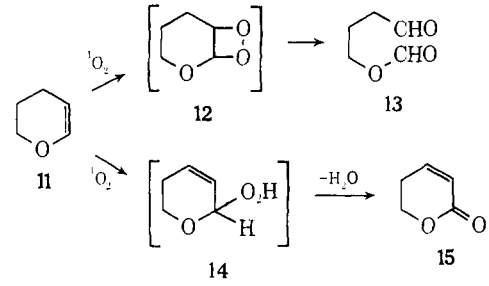
One criterion for the generation of free singlet oxygen from various sources has been the product distribution obtained from 1,2-dimethylcyclohexene (**7**). Photooxidation of **7** with polymer-based Rose Bengal yields a similar distribution of the two possible ene products **8** and **9** (see Table II).

Table II. Oxidation of 1,2-Dimethylcyclohexene (**7**) Using Various Singlet Oxygen Sources

Sources	 8	 9	 10
Ⓟ-Rose Bengal[a]	87	13	0
Photooxidation (soluble sens.)[b]	89	11	0
$OCl^- - H_2O_2$[b]	91	9	0
$(C_6H_5O)_3PO_3$[c]	96	4	0
K_3CrO_8[d]	82	18	0
Radical autoxidation[b]	6	39	54

[a] Products from this reaction were analyzed by gas chromatography as the alcohols obtained by triphenylphosphine reduction of **8** and **9**. [b] See ref 5a. [c] R. W. Murray and J. W.-P. Lin, *Ann. N. Y. Acad. Sci.*, **171**, 121 (1970). [d] J. W. Peters, J. N. Pitts, Jr., I. Rosenthal, and H. Fuhr, *J. Amer. Chem. Soc.*, **94**, 4348 (1972),

Dihydropyran (**11**) is a singlet oxygen acceptor that also yields two products: **13** is obtained by thermal cleavage of the 1,2-dioxetane **12** and **15** is formed upon dehydration under the reaction conditions of the ene product **14**. Photooxidation of **11** in CH_2Cl_2 with tetraphenylporphine gives 73% **13** and 27% **15**.[13]



With the Ⓟ-Rose Bengal sensitizer in CH_2Cl_2, the photooxidation of **11** gives an identical product distribution.

We conclude, on the basis of the experiments described in this report, that free singlet oxygen is efficiently formed by energy transfer from Ⓟ-Rose Bengal to oxygen. The possible uses for an insoluble, easily recovered sensitizer in preparative photochemical reactions are obvious. Insoluble polymer-based sensitizers may also be useful in mechanistic investigations in which the particular sensitizer is itself insoluble in the solvent of choice. Experiments with other types of Ⓟ sensitizers are in progress.

Acknowledgment. Financial support to D. C. N.

(6) (a) A. P. Schaap and G. R. Faler, *J. Amer. Chem. Soc.*, **95**, 3381 (1973); (b) N. M. Hasty and D. R. Kearns, *ibid.*, **95**, 3380 (1973).

(7) The dried beads can be reused with no detectable decrease in efficiency.

(8) E. J. Bourne, M. Stacey, J. C. Tatlow, and J. M. Tedder, *J. Chem. Soc.*, 2976 (1949).

(9) C. Ovannès and T. Wilson, *J. Amer. Chem. Soc.*, **90**, 6527 (1968).

(10) Rose Bengal: $\lambda_{max}^{(CH_3)_2CO}$ 562 nm.

(11) G. O. Schenck and D. E. Dunlap, *Angew. Chem.*, **68**, 248 (1956).

(12) C. S. Foote and S. Wexler, *J. Amer. Chem. Soc.*, **86**, 2879 (1964).

(13) The product distribution from **11** is independent of the sensitizer used but a function of the solvent employed for the reaction: P. D. Bartlett, G. D. Mendenhall, and A. P. Schaap, *Ann. N. Y. Acad. Sci.*, **171**, 79 (1970).

from the Research Corporation (Cottrell Research Grant) and the National Science Foundation (GP-33566), to E. C. B. from the National Institutes of Health for a special post-doctoral fellowship, and to A. P. S. from the Research Corporation (Cottrell Research Grant) and the U. S. Army Research Office—Durham is gratefully acknowledged. The authors wish to thank Dow Chemical Co. for a gift of styrene–divinylbenzene copolymer beads.

(14) On leave from Rollins College, 1972–1973.
(15) Fellow of the Alfred P. Sloan Foundation, 1971–1973.

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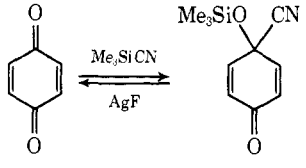
A New Selective Carbonyl Blocking Group. The Regioselective Protection of *p*-Quinones

Sir:

The quinoid nucleus embodies the potential of being a highly useful structural building block in organic synthesis. To date, the applications of quinones in complex natural products synthesis have centered around the Diels–Alder reaction.[1] The major problems associated with executing carbon–carbon bond forming reactions on either quinones or hydroquinones lie with the generally high reactivity of these species with nucleophiles and electrophiles, respectively.[2] The purpose of this communication is to disclose the first general method of reversibly protecting quinone carbonyl groups under exceedingly mild conditions, the blocking operation being effected with trimethylsilyl cyanide (TMSCN)[3,4] (eq 1). This new carbonyl derivatization

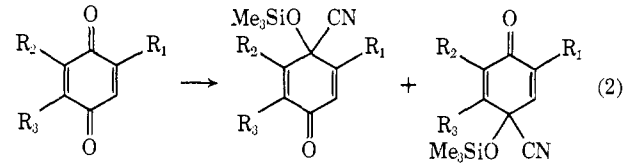


1a **2a** (1)

process should amplify the utility of quinones as electrophilic substrates in organic synthesis.

We have found that the catalyzed addition of TMSCN to both aldehydes and ketones is both mild and efficient.[3] Catalysis by both zinc iodide and cyanide ion are equally effective. In the large number of systems studied to date the addition process has been devoid of side reactions such as silyl enol ether formation[5] and, in the case of α,β-unsaturated carbonyl derivatives, 1,4 addition.[6] In the present study, we have observed the first case of catalyst specificity for cyanide ion.

In order to demonstrate the generality of this new method of carbonyl protection, we have examined the scope of the TMSCN–carbonyl insertion process with a variety of substituted *p*-benzoquinones (**1a–g**) and *p*-naphthoquinones (**1h–j**). The results are summarized in Table I.[7] It is particularly noteworthy that, with



1 **2** **3** (2)

unsymmetrical quinones, the site of cyanosilylation is dictated by relative carbonyl electrophilicity (*cf.* **1b–e**) and only in extreme cases (*e.g.*, **1g**) do steric effects become important. The position of cyanosilylation is evident from a comparison of the ^1H nmr chemical shifts of the starting quinones and the resulting adducts. The structural assignments of **2** and **3** are consistent with quinone reactivity patterns and their further transformation to *p*-quinols of known structure.[8]

The general procedure for quinone cyanosilylation involves the addition of a catalytic amount (0.01–0.02 equiv) of potassium cyanide–18-crown-6 complex[9] to a stirred mixture of quinone (1 equiv) and TMSCN (1.1 equiv) under anhydrous conditions. The reaction is exothermic and, in moderate scale reactions, cooling may be required. Solvents ($CHCl_3$, CCl_4, C_6H_6) may be used, although this was not done in the reported cases. The adducts may be purified by either molecular distillation or recrystallization; however, usually this is unnecessary.

Although the silyloxynitrile protective group is inherently unstable to both nucleophiles and aqueous media,[10] the competitive reactivity of the unprotected quinone carbonyl toward hydride reagents and both lithium and magnesium alkyls is quite high.[11] Thus, by coupling cyanosilylation with selective transforma-

(1) Notable examples include (a) M. Gates and M. Tschudi, *J. Amer. Chem. Soc.*, **78**, 1380 (1950); (b) L. H. Sarett, G. I. Poos, J. M. Robinson, R. E. Beyler, J. M. Vandergrift, and G. E. Arth, *ibid.*, **74**, 1393 (1952); (c) R. B. Woodward, F. Sondheimer, D. Taub, K. Heusler, and W. M. McLamore, *ibid.*, **74**, 4223 (1952); (d) R. B. Woodward, F. E. Bader, H. Bickel, A. J. Frey, and R. W. Kierstead, *Tetrahedron*, **2**, 1 (1958).

(2) For representative reactions of quinones with organometallic reagents see W. Ried in "Newer Methods of Preparative Organic Chemistry," Vol. IV, W. Foerst, Ed., Academic Press, New York, N. Y., 1968, pp 97–110; E. Bamberger and L. Blangey, *Justus Liebigs Ann. Chem.*, **384**, 272 (1911); H. M. Crawford, *J. Amer. Chem. Soc.*, **57**, 2000 (1935); 70, 1081 (1948); H. M. Crawford and M. McDonald, *ibid.*, **71**, 2681 (1949); D. E. Worrall and S. Cohen, *ibid.*, **58**, 533 (1936); L. S. Hegedus, E. L. Waterman, and J. Catlin, *ibid.*, **94**, 7155 (1972).

(3) The reaction of TMSCN with a variety of aldehydes and ketones has been shown by us and others to be a general, high yield transformation: D. A. Evans, L. K. Truesdale, and G. L. Carroll, *J. Chem. Soc., Chem. Commun.*, 55 (1973); W. Lidy and W. Sundermeyer, *Chem. Ber.*, **106**, 587 (1973).

(4) Prepared according to the procedure of E. C. Evers, W. O. Freitag, J. N. Keith, W. A. Kriner, A. G. MacDiarmid, and S. Sujishi, *J. Amer. Chem. Soc.*, **81**, 4493 (1959). A more convenient synthesis is being developed in our laboratory.

(5) TMSCN is an efficient silicon transfer reagent; thus, alcohols and enols are smoothly silylated at room temperature.

(6) The mild conditions for this carbonyl addition process suggest that α-silyloxynitriles should be ideal protective groups for acid-labile molecules.

(7) Consistent spectral data and combustion analysis have been obtained on all new compounds reported herein.

(8) M. Lovnasmaa, *Suom. Kemistilehti A*, **41**, 91 (1968). For example, the structure of **2f** may be established by transformation to **5f** (R = CH_3) whose structure is unequivocal.

(9) The KCN·crown complex was prepared by the dissolution of equimolar amounts of KCN and crown ether [R. N. Green, *Tetrahedron Lett.*, 1793 (1972)] in anhydrous methanol. Removal of solvent *in vacuo* afforded the active catalyst. Tetra-*n*-butylammonium cyanide is equally effective.

(10) Compound **1a** appears to be stable in anhydrous methanol (37°); in aqueous methanol (37°) **1a** has a half-life of *ca.* 30 min.

(11) The addition of other carbon nucleophiles to monoprotected quinones is currently under investigation.