11a′, respectively. Reductive ring opening of the benzylidene acetal with a mixture of lithium aluminum hydride and aluminum chloride efficiently produces the 2,3,4-tri-*O*-benzyl-substituted derivatives **13a** and **14a** in excellent overall yield. Further operations required to achieve a specific aim (e.g., the synthesis of any of fragments A–D of palytoxin) are obvious.[1,6d-f,12]

Acknowledgment. We are greateful to the National Institutes of Health (GM 31124) and to the National Science Foundation for financial support. We also thank Mary A. Blanchette for her assistance at a late stage in this work. High-resolution mass spectra were provided by the facility, supported by the National Institutes of Health (Grant RR 00317; principal investigator, Professor K. Biemann), from the Biotechnology Resources Branch, Division of Research Resources.

Registry No. 1a, 83416-93-7; **1b**, 83416-94-8; **2a**, 83416-95-9; **2b**, 83416-96-0; **3a**, 83461-73-8; **3b**, 83416-97-1; **4a**, 83416-98-2; **4b**, 83416-99-3; **5a**, 83417-00-9; **5b**, 83417-01-0; **6a**, 83417-02-1; **6b**, 83417-03-2; **7a**, 83461-74-9; **7b**, 83461-75-0; **8a**, 83417-04-3; **8b**, 83417-05-4; **9a**, 53461-76-1; **9b**, 83461-77-2; **10a**, 83417-06-5; **10a′**, 83417-08-7; **10b**, 83417-07-6; **11a**, 83461-78-3; **11a′**, 83461-80-7; **11b**, 83461-79-4; **12a**, 83417-09-8; **13a**, 83417-10-1; **14a**, 83461-81-8; Ti(O-*i*-Pr)$_4$, 546-68-9; Ph$_3$P=CHCO$_2$Et, 1099-45-2.

Supplementary Material Available: Listings of physical properties of new compounds, a summary of known methods for synthesis of *C*-glycopyranosides, and synthesis of **3a** and **3b** (10 pages). Ordering information is given on any current masthead page.

---

(12) **Note Added in Proof**: We (M. A. Blanchette and S. Masamune) now find that the three precautionary steps that were incorporated in the above reaction sequence are no longer necessary and thus can be eliminated. These steps are as follows: (1) protection of the free OH group of an unsaturated ester (typically **4b**), (2) liberation of the same OH group after epoxidation, and (3) pyrano-ring closure. The resulting simplified sequence (involving the Wittig reaction of **3b**, Dibal reduction, and epoxidation) directly provides **8b** or **9b** with (near-) perfect stereoselection and excellent overall yield. The ring closure is effected with titanium during the epoxidation reaction.

Photonitration of Phenols by Tetranitromethane under Visible Light[1]

Stanley Seltzer*

Chemistry Department, Brookhaven National Laboratory
Upton, New York 11973

Eric Lam

Department of Biophysics, University of California
Berkeley, California 94720

Lester Packer

Membrane Bioenergetics Group
Lawrence Berkeley Laboratory
University of California, Berkeley, California 94720

Received August 2, 1982

Tetranitromethane (TNM) is a reagent commonly used for protein modification.[2] In aqueous media at pH 8, TNM converts tyrosyl to 3-nitrotyrosyl residues. Bruice and co-workers[3] showed that the substituted phenolate anion is the kinetically active form in this reaction while the undissociated substituted phenol is unreactive toward TNM. On the basis of the ability of olefins to form complexes with TNM[4] and because irradiation of these complexes yield free radicals,[5] Bruice et al. proposed that substituted phenolate anions form charge-transfer complexes (CTC) with TNM in aqueous solution (eq 1), which then undergo electron transfer in a slow step (eq 2) to provide the substituted phenoxy radical, the NO$_2$ radical, and the nitroform anion in a solvent cage. Radical–radical addition within the solvent cage provide nitrated phenoxy anions. NO$_2$ radicals that escape, however, yield nitrite ion.

$$\text{X-PhO}^- + \text{TNM} \rightleftharpoons \text{CTC} \tag{1}$$

$$\text{CTC} \xrightarrow{e^-\ \text{transfer}} \overline{\text{X-PhO}\cdot + \text{NO}_2\cdot + \text{C(NO}_2)_3^-} \tag{2}$$

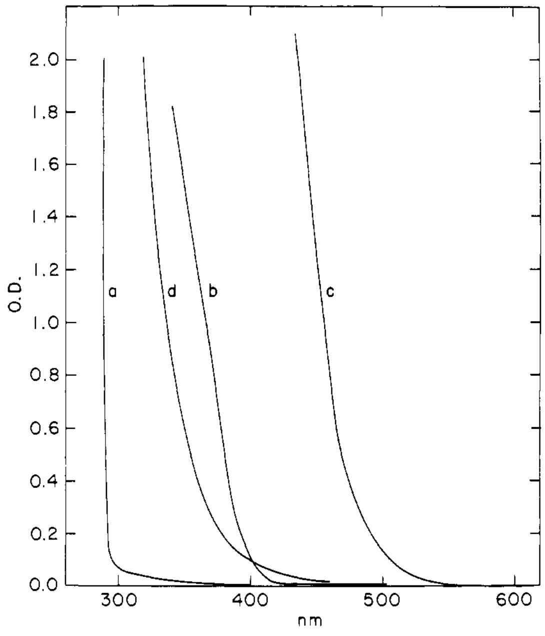


Figure 1. UV–visible spectra of tetranitromethane and phenol alone and in combination in cyclohexane: (a) 0.167 M phenol; (b) 0.167 M tetranitromethane; (c) 0.167 M phenol + 0.167 M tetranitromethane; (d) 0.0167 M phenol + 0.0167 M tetranitromethane.

Recent studies in our laboratories with bacteriorhodopsin (bR) have uncovered a different type of TNM-nitration reaction of phenols. Nitration of a tyrosine residue of bR by TNM has been found recently to be light dependent (λ ≥530 nm) at pH 5.5.[6] This observation prompted a study of model systems. We report our observations here because of the possible synthetic utility that they may have in the nitration of labile systems and because of the mechanistic information that they provide.

Since TNM photonitration of bR occurs in aqueous media, *N*-acetyl-L-tyrosine ethyl ester was subjected to the same conditions (pH 5.5, λ ≥530 nm). No apparent nitration could be detected as evidenced by the lack of nitroform anion absorption (λ_{max} 350 nm). Bacteriorhodopsin, however, is a membrane protein that is almost completely surrounded by a lipid bilayer. Hence TNM photonitration of substituted phenols in cyclohexane was attempted to mimic the nitration of a bR–tyrosine in a presumably lipophilic environment. An equimolar mixture of phenol and TNM in cyclohexane was found to absorb at considerably longer wavelength then either reactant alone at the same concentration in the same solvent (Figure 1). Upon 10-fold dilution of that solution, absorption decreases by about a factor of 100 (Figure 1), suggesting that a ground-state donor–acceptor (D–A) complex is formed by combination of TNM and phenol. Similar complexes are observed for *o*- and *p*-cresol and *o*- and *p*-chlorophenol.

In the dark these complexes in solvent cyclohexane are unreactive but react to form nitroform and ortho- and para-nitrated

---

[1] Research carried out at Brookhaven National Laboratory was supported by the Basic Energy Sciences Division of the Department of Energy. Research carried out at the Lawrence Berkeley Laboratory and the University of California was supported by the Office of Biological Energy Research of the Department of Energy. E.L. acknowledges support for an NIH Training Grant (No. T32 GMO7379).

[2] Sokolovsky, M.; Riordan, J. R.; Vallee, B. L. *Biochemistry* **1966**, *5*, 3582. Riordan, J. F.; Vallee, B. L. *Methods Enzymol.* **1972**, *25*, 515.

[3] Bruice, T. C.; Gregory, M. J.; Walters, S. L. *J. Am. Chem. Soc.* **1968**, *90*, 1612. Walters, S. L.; Bruice, T. C. *Ibid.* **1971**, *93*, 2269.

[4] Heilbronner, E. *Helv. Chem. Acta* **1953**, *36*, 1121.

[5] Lagercrantz, C.; Yhland, M. *Acta Chem. Scand.* **1962**, *16*, 1807.

[6] Katsura, T.; Lam, E.; Packer, L.; Seltzer, S. *Biochem. Int.* **1982**, *5*, 445.

[7] Beens, H.; Weller, A. In "Organic Molecular Photophysics"; Birks, J. B., Ed.; Wiley: New York, 1975; Vol. 2, p 159.

0002-7863/82/1504-6470$01.25/0 © 1982 American Chemical Society

Table I. Photonitration of Phenols by Tetranitromethane in Cyclohexane[a]

reactant	product	quantum yield
phenol	4-nitrophenol	0.12
	2-nitrophenol	0.17
	3-nitrophenol	1.2×10^{-3}
p-chlorophenol	4-chloro-2-nitrophenol	0.27
o-chlorophenol	2-chloro-4-nitrophenol	0.15
	2-chloro-6-nitrophenol	0.12
p-cresol	4-methyl-2-nitrophenol	0.15
o-cresol	2-methyl-6-nitrophenol	0.31
	2-methyl-4-nitrophenol	0.19
o-nitrophenol	none	*c*

[a] At 20 °C; solutions of TNM (0.167 M) and the phenol (0.167) were stirred magnetically during photolysis. See footnote 9 and the text. [b] None detected; upper limit to quantum yield. [c] None detected after 24 h of irradiation under the conditions given in the text.

phenols when irradiated at wavelengths where neither free TNM nor the free phenol absorb in cyclohexane. Irradiation was carried out with light from 500-W tungsten–halogen lamp filtered through either a Corning 3-69 or 3-71 filter.[8] All nitrated phenols were identified by comparison of their HPLC elution volumes (2 × 250 mm silica gel, 10 μm/CH_2Cl_2, detection at 280 nm) with those measured for authentic materials and additionally, in some cases, by the NMR and UV spectra of the products isolated from preparative TLC. Yields were determined by integration of the peaks in the chromatographic trace and by comparison with standards. Quantum yields were determined by sampling light intensities between 440 and 500 nm in steps of about 20 nm by passing the light through narrow band-pass filters while the energy of the transmitted light was measured with a thermopile.[9] These measurements together with the absorption curves of the complexes, the transmission curves of the filters, and the yields of products lead to the result that the quantum yields for *o*- and *p*-nitrophenol are 0.17 and 0.12, respectively. *m*-Nitrophenol was not detected; $\Phi \leq 1.2 \times 10^{-3}$. One molecule of nitroform is produced per molecule of nitrophenol formed.[10] Photonitration of *o*- and *p*-cresol and *o*- and *p*-chlorophenol under the same conditions leads to similar results (Table I). Here too, meta nitration cannot be detected. It is noteworthy that a TNM-*o*-nitrophenol complex is not detected spectroscopically when the two components are present together in cyclohexane at concentrations where similar complexes of TNM with phenol and methyl- and chloro-substituted phenols are readily detected. That TNM fails to nitrate *o*-nitrophenol when a mixture of the two are present and irradiated under the conditions stated provides further evidence that prior formation of a ground-state donor–acceptor complex is necessary for reaction to occur.

Further study is required before the scope of this reaction is fully understood, but at the present time the results presented above suggest the following mechanism. TNM and the substitued phenol associate to form a donor–acceptor complex (eq 3), which can

$$C(NO_2)_4 + \text{X-PhOH} \rightleftharpoons \underset{\text{D–A complex}}{\text{X-PhOH} \cdots C(NO_2)_4} \qquad (3)$$

be observed by the new characteristic absorbance. The D–A complex upon absorption of a photon is converted to an excited-state charge-transfer complex (CTC′, eq 4) where there is greater

$$\text{D–A complex} \overset{h\nu}{\rightleftharpoons} (\text{CTC}')^* \qquad (4)$$

electron donation from the phenol to TNM than in the ground-state complex.[7] It is probable that the excited state can revert back to the ground-state D–A complex, which would account for the quantum yield of less than unity. In competition with decay is electron transfer to form the TNM radical anion and the phenol radical–cation pair (eq 5). The TNM radical anion is expected

$$(\text{CTC}')^* \rightarrow \text{X–PhOH}^{+\cdot}\ C(NO_2)_4^{-\cdot} \qquad (5)$$

to fragment rapidly to yield nitroform anion and NO_2 radical in close proximity to the phenol radical cation (eq 6). which could

$$\begin{aligned} \text{X-PhOH}^{+\cdot}C(NO_2)_4^{-\cdot} &\rightarrow [NO_2\cdot + \text{X–PhOH}^{+\cdot} + C(NO_2)_3^{-}] \\ &\rightarrow [NO_2\cdot + \text{X–PhO}\cdot + HC(NO_2)_3] \qquad (6) \end{aligned}$$

combine to yield ortho- or para-nitrated phenols. It should be noted that if nitrophenols are produced by combination of phenoxy and NO_2 radicals as suggested then the almost exclusive fonnation of *o*- and *p*-nitrophenols are to be expected since the transition states leading to these products would be expected to be at lower energy than that leading to *m*-nitrophenol.[11]

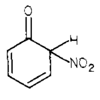
---

(8) Transmission is 1% or less for the 3-71 filter at λ ≤460 nm and for the 3-69 filter at λ ≤515 nm.

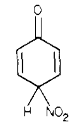
(9) Narrow band-pass filters having their maxima at 600, 580, 560, 550, 520, 500, 480, 450, and 440 nm were used. On the average these had a width of 10 nm at half-height. The thermopile was a product of the Eppley Laboratory, Newport, RI 02840. We thank Drs. N. Sutin, R. Weston, and B. Brunschwig for furnishing this apparatus.

(10) [Nitroform]/([*o*-nitrophenol] + [*p*-nitrophenol]) = 0.91. The phenol–TNM photolysate (3 mL), after a 33-fold dilution with a 50–50 mixture of CH_2Cl_2–cyclohexane, was extracted with 0.01 M H_2SO_4 (3 × 15 mL). The optical densities at 350, 400, and 415 nm of the aqueous extract, adjusted to pH 13, were measured to obtain the concentrations of nitroform and *o*- and *p*-nitrophenols. All operations were carried out in dim red light.

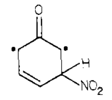
(11) Combination of phenoxy and NO_2 radicals would yield *o*- and *p*-dienone intermediates (I and II). Addition of NO_2 radical to the meta position of the phenoxy radical would yield a 1,3-diradical (e.g., III) and if the diradical is a singlet could lead to a bicyclic intermediate (e.g., IV). Both III and IV are expected to be considerably less stable than I and II. It should be emphasized that the isomer distribution produced from a radical–radical coupling reaction[12a] is expected to be clearly different from that observed from the more frequently encountered homolytic aromatic substitution.[12b]



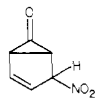
I



II



III



IV

(12) (a) Fleming, I. "Frontier Orbitals and Organic Chemical Reactions"; Wiley: New York, 1976; pp 195–200, 202–207. We thank Dr. Philip B. Shevlin for calling our attention to this reference. (b) Lowry, T. H.; Richardson, K. S. "Mechanism and Theory in Organic Chemistry"; 2nd ed.; Harper and Row: New York, 1981; pp 730–733.

β-Alkyl Transfer in a Lanthanide Model for Chain Termination

Patricia L. Watson* and D. Christopher Roe

Contribution No. 3049
Central Research and Development Department
E. I. du Pont de Nemours and Company
Experiemntal Station, Wilmington, Delaware 19898

Received April 19, 1982

The chemistry of lutetium–isobutyl complex **1**, described herein, delineates a number of reaction pathways that are energetically accessible to organolanthanide complexes. In particular, *β-alkyl elimination* has now been observed directly. We note that fundamental reactions of lanthanide–alkyl complexes are not well documented. Products obtained from attempted preparations of homoleptic alkyl complexes implicate α-hydrogen abstraction as a viable reaction,[1-3] and β-hydrogen elimination can also apparently constitute a major decomposition route.[4,5] Both β-hy-

---

(1) Vollershtein, E. L.; Yakoulev, V. A.; Tinyakova, E. I.; Dolgoplosk, B. A. *Dokl. Akad. Nauk. SSSR* **1980**, *250*, 365–366.

(2) Guzman, I. Sh.; Chigir, N. N.; Sharaev, O. V.; Bondarenko, G. N.; Tinyakova, E. I.; Dolgoplosk, B. A. *Dokl. Akad. Nauk. SSSR* **1979**, *249*, 860–862.

(3) Schumann, H.; Müller, J. *J. Organomet. Chem.* **1979**, *169*, C1–C4.

(4) Schumann, H.; Genthe, W.; Bruncks, N. *Angew. Chem., Int. Ed. Engl.* **1981**, *20*, 119–120.

(5) Evans, W. J.; Wayda, A. L.; Hunter, W. E.; Atwood, J. L. *J. Chem. Soc., Chem. Commun.* **1981**, *292*–293.

0002-7863/82/1504-6471$01.25/0