Int. Ed. Engl. **1997**, *36*, 486–488; K. Himmel, M. Jansen, *Chem. Commun.* **1998**, 1205–1206; K. Himmel, M. Jansen, *Eur. J. Inorg. Chem.* **1998**, 1183–1186; b) K. Himmel, M. Jansen, *Inorg. Chem.* **1998**, *37*, 3437–3439.

[8] X-ray structural analysis of **1**: black needles, crystal dimensions $0.4 \times 0.1 \times 0.1\,mm^3$, orthorhombic, space group $Pna2_1$ (no. 33), $a = 20.289(4)$, $b = 20.357(4)$, $c = 12.870(3)$ Å, $V = 5315(2)$ Å^3, $\rho_{calcd} = 1.563\,g\,cm^{-3}$, $Z = 4$, $F(000) = 2544$, $\lambda = 71.073$ pm, $T = 143$ K, SMART-CCD (Bruker-AXS), 26738 measured reflections, 6954 symmetry independent reflections, empirical absorption correction (SADABS[10]), $R_{int} = 0.2677$. The R_{int} value given includes all data measured up to an angle of $2\theta = 45.4°$. This large value is caused by a high proportion of reflections of very low intensity in the high-angle range. If, for example, only the reflections up to an angle of $2\theta = 30°$are taken into consideration, then R_{int} decreases to a value of 0.1606. The determination and refinement of the position of all the atoms is, however, only possible when all the measured reflections are taken into consideration. The determination of the positions of the heavy atoms was carried out by direct methods,[11] the positions of the light atoms were determined with difference Fourier transformation.[12] The best fit with anisotropic temperature factors was obtained with the assumption of a noncrystallographic twofold rotation axis for the C_{70}^{2-} unit, as shown in Figure 4, in combination with the correlating bond lengths. The anisotropic temperature factors were positively defined, although in some cases they led to deflection parameters which were not physically meaningful. No indication of twinning was found during the refinement. The absolute configuration found is validated with a Flack parameter of 0.052. Refined parameters = 750, $R_1 = 0.1188$, wR_2(all data) = 0.2846, GOF = 0.894. Crystallographic data (excluding structure factors) for the structure reported in this paper have been deposited with the Cambridge Crystallographic Data Centre as supplementary publication no. CCDC-157752. Copies of the data can be obtained free of charge on application to CCDC, 12 Union Road, Cambridge CB21EZ (fax: (+44)1223-336-033; e-mail: deposit@ccdc.cam.ac.uk).

[9] J. Daniels, N. Korber, *Z. Anorg. Allg. Chem.* **1996**, *622*, 1833–1838.

[10] G. M. Sheldrick, SADABS, Göttingen, **1998**.

[11] G. M. Sheldrick, SHELXS97, Programs for Crystal Structure Determination and Refinement of Structures, Göttingen, **1997**.

[12] G. M. Sheldrick, SHELXL97, Programs for Refinement of Crystal Structures, Göttingen, **1997**.

Orthogonal Photolysis of Protecting Groups**

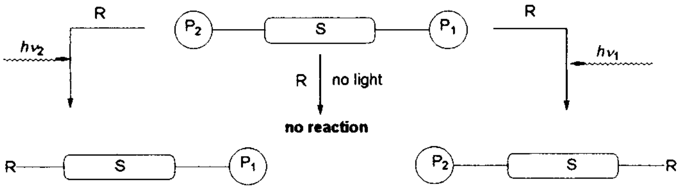
Christian G. Bochet*

Dedicated to Professor Barry M. Trost
on the occasion of his 60th birthday

One of the major challenges in the chemistry of protecting groups is orthogonality, that is, the possibility of selectively removing one group in the presence of others in any chronological sequence.[1] Photolabile protecting groups form an attractive subclass of these groups, since they are essentially cleaved without the need for any reagent, which thus increases compatibility with other functionalities.[2, 3] However, orthogonality between such protecting groups has never been observed. We recently published our preliminary results on the possible use of monochromatic light to differentiate photolabile groups,[4] and we wish to disclose here the first orthogonal photochemical protection/deprotection of polyfunctional molecules.

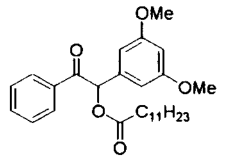
Before considering applying a strategy such as that shown in Scheme 1, several critical issues have to be addressed:

a) The intrinsic stability of each protecting group should be very different at various wavelengths.
b) The energy transfer between an excited chromophore and its ground-state neighbor should be suppressed.
c) The cleavage at high energy (for example, at 254 nm) should be very fast, to avoid photodegradation of otherwise sensitive groups.

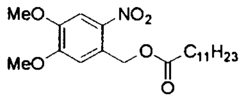


Scheme 1. General strategy for photochemical orthogonal deprotection of functional groups. S = substrate; P_1, P_2 = groups which are photoactivatable at ν_1 or ν_2; R = reacting species (for example, H).

Among the known photolabile protecting groups, the 3′,5′-dimethoxybenzoin esters attracted our attention since they were found to be equally reactive in nonabsorbent solvents and in neat piperylene (1,3-pentadiene).[5] This suggested the absence of quenching by the solvent and a very short-lived excited state. This feature, combined with the very high quantum yield ($\phi = 0.64$) makes this ester an ideal candidate for an orthogonal protecting group. On the other hand, the nitrobenzyl derivatives are known to be less reactive, but with sensitivity to much longer wavelengths (up to 420 nm).[3] These differences in wavelength sensitivity are clearly illustrated by the UV spectra of **1** and **2** (Figure 1).



1



2

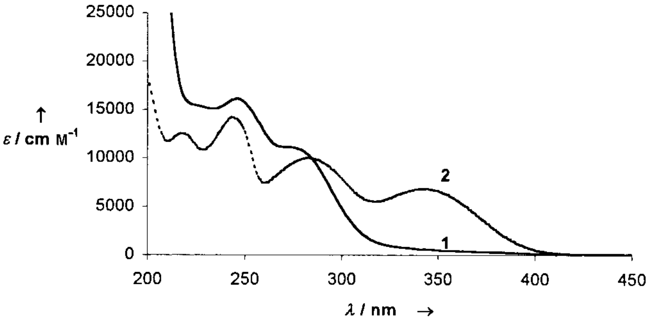


Figure 1. UV spectra of benzoin ester **1** and benzyl ester **2**.

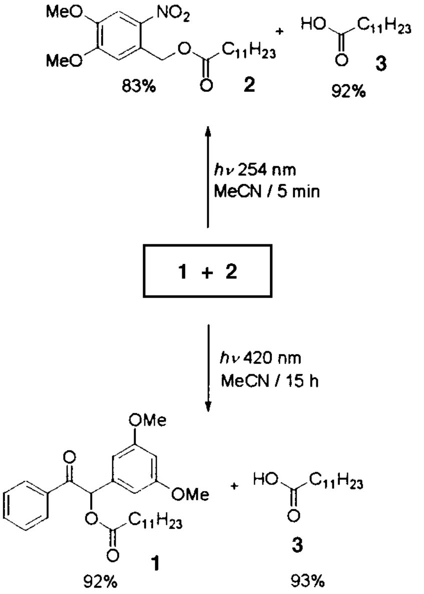
---

[*] Dr. C. G. Bochet
Department of Organic Chemistry, University of Geneva
30 quai Ernest Ansermet, 1211 Geneva 4 (Switzerland)
Fax: (+41)22-328-7396
E-mail: Christian.Bochet@chiorg.unige.ch

[**] Financial support from the Swiss National Science Foundation (grant no.: 21-57044.99) and the Fonds Frédéric Firmenich et Philippe Chuit is gratefully acknowledged.

We first exposed an acetonitrile solution of the lauryl ester **1**[6] to UV light with a wavelength of 254 nm. The half-life was determined as less than 5 minutes, which is significantly shorter than that for the nitrobenzyl ester **2** (97 minutes). On the other hand, **1** was totally unreactive at 420 nm, even for a prolonged time (24 hours), whereas **2** was quantitatively cleaved under these conditions.[7]

With these encouraging differential reactivities[8] established, we then submitted a 1:1 mixture of **1** and **2** to UV light with a wavelength of 254 nm. After irradiation for 5 minutes, 83 % of **2** was "intact" and 92 % of the acid **3** was detected (by ^{1}H NMR spectroscopy). The same experiment at 420 nm gave 93 % of **3** and 92 % of intact benzoin ester **1**, after 14 hours (Scheme 2). Figure 2 shows the ^{1}H NMR spectra of the initial 1:1 mixture of **1** and **2** and of the mixture after irradiation at different wavelengths. The signals around $\delta \approx 2.5$ arise from the methylene group adjacent to the carboxyl groups and clearly show the complementary behavior at the two wavelengths.



Scheme 2. Orthogonal stability of photolabile esters **1** and **2**.

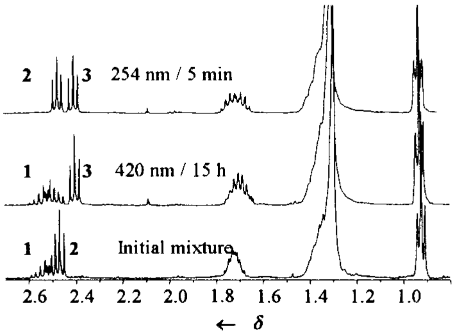
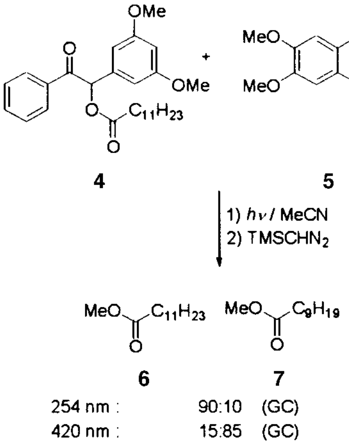


Figure 2. ^{1}H NMR spectra before and after irradiation of a mixture of esters **1** and **2**.

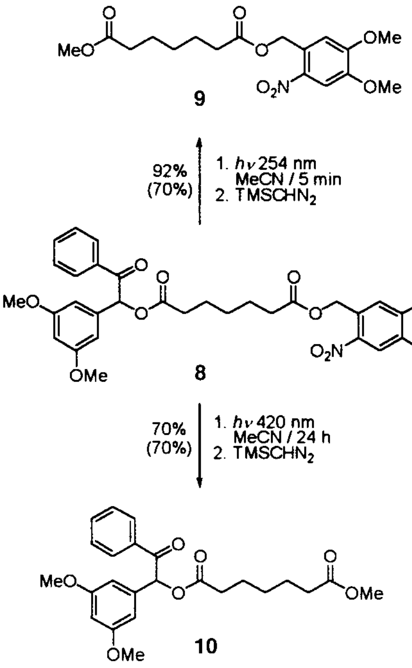
We prepared a mixture of the two esters **4** and **5**, which bear saturated aliphatic chains of different length, to check further the orthogonality. Photolysis at 254 nm for 5 minutes led to a mixture of two carboxylic acids in 82 % yield; these were converted, by esterification with trimethylsilyldiazomethane,[9] into the methyl esters **6** and **7** in a 90:10 ratio (as determined by GC analysis). A similar mixture, when irradiated at 420 nm for 24 hours, gave a 15:85 mixture in 91 % yield (Scheme 3).



Scheme 3. Photochemical cleavage of orthogonal protecting groups from different esters. TMS = trimethylsilyl.

This experiment clearly shows the absence of the intermolecular energy transfer that was observed with 3,5-dimethoxybenzyl alcohol derivatives.[4] The overall result is that is was possible to activate individual components in a mixture by using an external influence.

Intramolecular energy transfer was also found to be absent in this system (Scheme 4). The mixed diester **8** bearing a dimethoxybenzoin ester at one terminus and a nitrobenzyl derivative at the other was photolyzed at 254 nm for 5 minutes and the crude mixture was treated with trimethylsilyldiazo-



Scheme 4. Intramolecular photochemical cleavage of orthogonal protecting groups.

methane. The diester **9** was isolated in 70% yield after chromatography (92% by ^{1}H NMR spectroscopy). The same experiment at 420 nm cleanly gave the diester **10** in 70% yield (70% by ^{1}H NMR spectroscopy). In other words, it was possible to perform a photochemical orthogonal deprotection of a bifunctional substrate.

In conclusion, we have shown that chromatic orthogonality is indeed possible, in both inter- and intramolecular cases. This new strategy could be successfully applied to orthogonal deprotection of bifunctional molecules and to wavelength-selective photorelease of compounds. We are currently investigating the possibility of adding a third dimension to the set, as well as testing applications in solution- and solid-phase organic synthesis.

Received: February 9, 2001 [Z16582]

---

[1] a) T. W. Greene, P. G. M. Wuts, *Protective Groups in Organic Synthesis*, 3rd ed., Wiley, New York, **1999**; b) P. Kocienski, *Protecting Groups*, Thieme, Stuttgart, **1994**; c) M. Schelhaas, H. Waldmann, *Angew. Chem.* **1996**, *108*, 2192–2219; *Angew. Chem. Int. Ed. Engl.* **1996**, *35*, 2056–2083; d) R. B. Merrifield, G. Barany, W. L. Cosand, M. Engelhard, S. Mojsov, *Pept. Proc. Am. Pept. Symp. 5th* **1977**, 488–502.

[2] a) V. N. R. Pillai, *Org. Photochem.* **1987**, *9*, 225–323; b) V. N. R. Pillai, *Synthesis* **1980**, 1–26.

[3] A. Patchornik, B. Amit, R. B. Woodward, *J. Am. Chem. Soc.* **1970**, *92*, 6333–6335.

[4] C. G. Bochet, *Tetrahedron Lett.* **2000**, *41*, 6341–6346.

[5] a) J. C. Sheehan, R. M. Wilson, *J. Am. Chem. Soc.* **1964**, *86*, 5227–5281; b) J. C. Sheehan, R. M. Wilson, A. W. Oxford, *J. Am. Chem. Soc.* **1971**, *93*, 7222–7228; c) see also: M. C. Pirrung, S. W. Shuey, *J. Org. Chem.* **1994**, *59*, 3890–3897; d) J. T. Corrie, D. R. Trentham, *J. Chem. Soc. Perkin 1* **1992**, 2409–2417; e) J. F. Cameron, C. G. Wilson, J. M. J. Fréchet, *J. Chem. Soc. Perkin 1* **1997**, 2429–2442.

[6] a) M. H. B. Stowell, R. S. Rock, D. C. Rees, S. I. Chan, *Tetrahedron Lett.* **1996**, *37*, 307–310; b) R. S. Rock, S. I. Chan, *J. Org. Chem.* **1996**, *61*, 1526–1529.

[7] The typical concentrations were between 1 and 10 mM. The irradiations were performed in a Rayonet apparatus.

[8] By reactivity, we mean the net reaction rate under specific conditions; it includes the quantum yield, the absorbance at the wavelength, and all the experimental parameters.

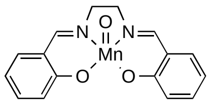
[9] a) T. Shiori, T. Aoyama, S. Mori, *Org. Synth.* **1990**, *68*, 1–7; b) N. Hashimoto, T. Aoyama, T. Shiori, *Chem. Pharm. Bull.* **1981**, *29*, 1475–1478.

Rate Enhancement and Enantioselectivity of the Jacobsen–Katsuki Epoxidation: The Significance of the Sixth Coordination Site[**]

Jaouad El-Bahraoui, Olaf Wiest,* Derek Feichtinger, and Dietmar A. Plattner*

The oxygenation of olefins by high-valent transition metal oxo complexes is one of the most useful and elegant techniques for the functionalization of organic substrates. A breakthrough was the introduction of chiral manganese–salen catalysts by Jacobsen and co-workers,[1] with a similar system developed by Katsuki and co-workers.[2] The Jacobsen–Katsuki reaction is universally recognized as one of the most useful and widely applicable methods for the epoxidation of unfunctionalized olefins.[3, 4]

Despite the synthetic utility of this catalytic transformation, the origin of its high selectivity is not well understood. The key problems that mechanistic studies of the catalytic reaction cycle need to address are: 1) the nature of the oxygen-transferring species; 2) the mechanism of oxygen transfer to the olefinic substrate; and 3) the highly efficient stereochemical communication between catalyst and substrate. By electrospray tandem mass spectrometry, we were able to show that the reaction proceeds via an oxomanganese(v) complex as catalytically active species,[5] but the remaining questions are still open despite numerous experimental[6] and computational studies.[7]



1

Herein, we report on the results of a high-level computational study[8] of oxomanganese(v)–salen complexes of type **1** bearing different axial ligands. Axial ligation of the salen catalyst is known to have a favorable influence on the asymmetric induction. This has been explained by a shortening of the Mn−O bond length and a decrease of the reactivity of the oxo species upon axial coordination.[3d] We have recently shown experimentally that axial coordination of an *N*-oxide ligand at the oxomanganese(v) complex raises the oxygen transfer reactivity of the catalyst dramatically.[5d] The question arises why it is possible in this specific case of asymmetric catalysis to raise the

---

[*] Prof. Dr. O. Wiest, Dr. J. El-Bahraoui
Department of Chemistry and Biochemistry
University of Notre Dame
Notre Dame, IN 46556-5670 (USA)
Fax: (+1) 219-631-6652
E-mail: owiest@nd.edu

Dr. D. A. Plattner, Dr. D. Feichtinger
Laboratorium für Organische Chemie der
Eidgenössischen Technischen Hochschule Zürich
ETH-Zentrum, Universitätstrasse 16, 8092 Zürich (Switzerland)
Fax: (+41) 1-632-1280
E-mail: plattner@org.chem.ethz.ch

[**] This work was made possible through generous allocation of computer resources by the OIT at Notre Dame, the National Computational Science Alliance and the Competence Center for Computational Chemistry at ETH Zürich.

Supporting information for this article is available on the WWW under http://www.angewandte.com or from the author.