instead, presumably by means of β-H elimination.[7] As shown also in Scheme 3, activation of EtOPh by **1** (toluene, 110 °C, 2 h) gave compound **6** (see Supporting Information). It thus appears that the very important steric demands of the Tp^x ligand (as compared with the somewhat less bulky cyclopentadienyl ligand, Cp^x) and its rigid nature, which tends to enforce six-fold coordination to the metal center, favors α-H elimination over β-H elimination in the transformations studied here.

In summary, we have shown that the Ir^I compound **1** effects the regioselective, double C–H activation of a variety of ether and amine substrates by allowing their precoordination to the metal center. The formation of Fischer-type carbenes in this cascade activation (cyclometalation-β-elimination (or vice versa)-α-elimination) is made possible by the presence of an adequate hydrogen-accepting leaving group. The Tp^x- and Cp^x-Ir systems reported herein include O and N heteroatoms. Comparative studies on the facility of these fundamental organometallic reactions (α- and β-eliminations) on closely related Tp^x- and Cp^x-Ir systems without these heteroatoms that could alter the relative energies of the transition states and intermediates,[17] are presently in progress and will be reported in due course.

Experimental Section

1: To a suspension of $[(IrCl(coe)_2)_2]$ (175 mg, 0.20 mmol) in CH_2Cl_2 (6 mL), 2-methylbutadiene (0.3 mL, excess) was added at room temperature to give a colorless solution. A solution of $TlTp^{Ph}$ (253 mg, 0.40 mmol) in CH_2Cl_2 (6 mL) was then added. Stirring the reaction mixture for 4 h at room temperature resulted in the precipitation of TlCl. After filtration, the clear solution was evaporated to dryness. The crude product (orange powder) was purified via column chromatography (neutral aluminum oxide 90% activated, eluents PE (petroleumether):Et_2O = 15:1, eluted as a pale violet band). Compound **1** was obtained upon changing the eluents to PE:Et_2O = 4:1 and it eluted as a yellow band. Removing the solvent and drying in vacuum gave pure **1**. Yield: 198 mg (71%). Elemental analysis: calcd for $C_{32}H_{30}BIrN_6$ (%): C 54.8, H 4.3, N 12.0; found: C 54.4, H 4.1, N 12.2.

Compounds **2**–**6** can be prepared similarly by treating **1** with an excess of the corresponding ether or amine. As a representative example the synthesis of **5** is given: A solution of **1** (70 mg, 0.10 mmol) in Et_2O was heated at 60 °C for 12 h. The solution was evaporated to dryness. Purification by flash chromatography (neutral aluminum oxide 90% activated, eluents PE:Et_2O = 2:1, eluted as a yellow band) resulted in pure **5**. Yield: 58 mg (82%). Elemental analysis: calcd for $C_{31}H_{30}BIrN_6O$ (%): C 52.8, H 4.3, N 11.9; found: C 53.0, H 4.6, N 11.7.

Received: January 28, 2000 [Z14616]

[1] a) S. S. Stahl, J. A. Labinger, J. E. Bercaw, *Angew. Chem.* **1998**, *110*, 2298; *Angew. Chem. Int. Ed.* **1998**, *37*, 2181; b) B. A. Arndtsen, R. G. Bergman, T. A. Mobley, T. H. Peterson, *Acc. Chem. Res.* **1995**, *28*, 154; c) J. C. W. Lohrenz, H. Jacobsen, *Angew. Chem.* **1996**, *108*, 1403; *Angew. Chem. Int. Ed. Engl.* **1996**, *35*, 1305.

[2] a) F. Zaragoza Dörwald, *Metal Carbenes in Organic Synthesis*, Wiley-VCH, Weinheim, **1999**; b) K. H. Dötz, H. Fischer, P. Hofmann, R. R. Kreissl, U. Schubert, K. Weiss, *Transition Metal Carbene Complexes*, VCH, Weinheim, **1993**.

[3] For gas phase Fe^I-mediated 1,1-elimination of H_2 from a methoxy group, see: T. Prüsse, A. Fiedler, H. Schwarz, *J. Am. Chem. Soc.* **1991**, *113*, 8335.

[4] a) H. Werner, B. Weber, O. Nürnberg, J. Wolf, *Angew. Chem.* **1992**, *104*, 1079; *Angew. Chem. Int. Ed. Engl.* **1992**, *31*, 1025; b) O. Boutry, E. Gutiérrez, A. Monge, M. C. Nicasio, P. J. Pérez, E. Carmona, *J. Am. Chem. Soc.* **1992**, *114*, 7288; c) E. Gutiérrez-Puebla, A. Monge, M. C. Nicasio, P. J. Pérez, M. L. Poveda, E. Carmona, *Chem. Eur. J.* **1998**, *4*, 2225.

[5] a) A. Sen, M. Lin, L.-C. Kao, A. C. Hutson, *J. Am. Chem. Soc.* **1992**, *114*, 6385; b) Z.-W. Li, H. Taube, *J. Am. Chem. Soc.* **1994**, *116*, 11584.

[6] R. R. Schrock, S. W. Seidel, N. C. Mösch-Zanetti, K.-Y. Shih, M. B. O'Donoghue, W. M. Davis, W. M. Reiff, *J. Am. Chem. Soc.* **1997**, *119*, 11876.

[7] a) B. A. Arndtsen, R. G. Bergman, *Science*, **1995**, *270*, 1970; b) H. F. Luecke, B. A. Arndtsen, P. Burger, R. G. Bergman, *J. Am. Chem. Soc.* **1996**, *118*, 2517.

[8] E. Gutiérrez-Puebla, A. Monge, M. Paneque, M. L. Poveda, V. Salazar, E. Carmona, *J. Am. Chem. Soc.* **1999**, *121*, 248.

[9] C. Slugovc, K. Mereiter, S. Trofimenko, E. Carmona, *Chem. Commun.* **2000**, 121.

[10] The related compound $[Ir(\kappa^4(N,N',N'',C^{Ph})\text{-}Tp^{Ph})(Et)(\eta^2\text{-}C_2H_4)]$ activates THF to give **2** but with the other ether or amine substrates employed in this work the reaction failed due to the formation of $[Ir(\kappa^5(N,N',N'',C^{Ph},C^{Ph'})\text{-}Tp^{Ph})(\eta^2\text{-}C_2H_4)]$.[9]

[11] C. Six, B. Gabor, H. Görls, R. Mynott, P. Philipps, W. Leitner, *Organometallics*, **1999**, *18*, 3316.

[12] Crystallographic data (excluding structure factors) for the structures reported in this paper have been deposited with the Cambridge Crystallographic Data Center as supplementary publication no. CCDC- 139166. Copies of the data can be obtained free of charge on application to CCDC, 12 Union Road, Cambridge CB2 1EZ, UK (fax: (+44) 1223-336-033; e-mail: deposit@ccdc.cam.ac.uk).

[13] D. M. Heinekey, J. M. Millar, T. F. Koetzle, N. G. Payne, K. W. Zilm, *J. Am. Chem. Soc.* **1990**, *112*, 909, and references therein.

[14] U. E. Bucher, A. Currao, R. Nesper, H. Rüegger, L. M. Venanzi, E. Younger, *Inorg. Chem.* **1995**, *34*, 66.

[15] Y. Kataoka, M. Imanishi, T. Yamagata, K. Tani, *Organometallics* **1999**, *18*, 3563.

[16] M. W. Holtcamp, J. A. Labinger, J. E. Bercaw, *J. Am. Chem. Soc.* **1997**, *119*, 848.

[17] J. Jaffart, R. Mathieu, M. Etienne, J. E. McGrady, O. Eisenstein, F. Maseras, *Chem. Commun.* **1998**, 2011.

DesVI: A New Member of the Sugar *N,N*-Dimethyltransferase Family Involved in the Biosynthesis of Desosamine**

Cheng-wei Chang, Lishan Zhao, Hiroshi Yamase, and Hung-wen Liu*

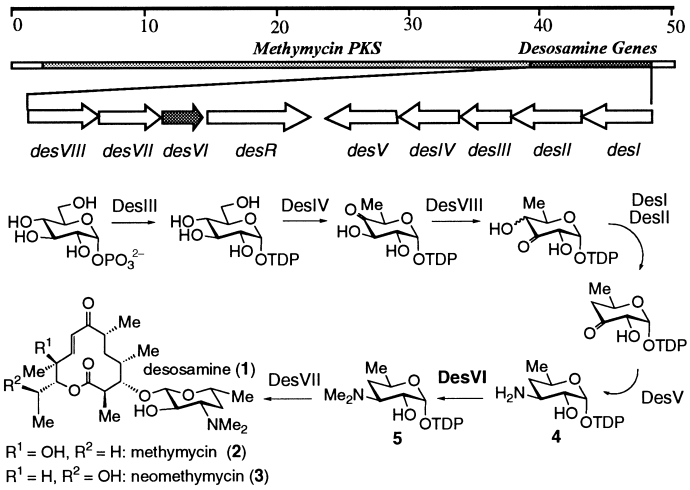
Methylation catalyzed by *S*-adenosylmethionine (AdoMet) dependent enzymes is one of the most common reactions occurring in biological systems. While a large number of methyltransferases which catalyze methylation at carbon,

[*] Prof. Dr. H.-w. Liu, C.-w. Chang,[+] L. Zhao, H. Yamase
Department of Chemistry
University of Minnesota, Minneapolis, MN 55455 (USA)
Fax: (+1) 612-626-7541
E-mail: liu@chem.umn.edu

[+] Current address:
Department of Chemistry and Biochemistry
Utah State University, Logan, UT 84322 (USA)

[**] The authors gratefully acknowledge financial support provided by the National Institutes of Health (GM 54346). H.-w.L. also thanks the National Institute of General Medical Sciences for a MERIT Award. L.Z. is the recipient of a Graduate School Dissertation Fellowship from the University of Minnesota.

oxygen, sulfur, and nitrogen atoms are known, only a few are capable of catalyzing *N*,*N*-dimethylation.[1] Our knowledge of these enzymes is scarce as most of them have never been isolated and fully characterized. Recently, genetic studies of the biosynthesis of desosamine (**1**), a structural component of the antibiotics methymycin (**2**), neomethymycin (**3**), pikromycin, and narbomycin produced by *Streptomyces venezuelae*,[2] have led to the tentative assignment of *desVI* in the methymycin/pikromycin biosynthetic gene cluster as a candidate for encoding a new *N*,*N*-dimethyltransferase.[3] The DesVI protein presumably acts on the C-3 amino group of sugar substrate **4** to give TDP-desosamine (**5**, see Scheme 1). The fact that disruption of the *desVI* gene in the genome of *S. venezuelae* resulted in the formation of a series of macrolides carrying an amino sugar devoid of *N*,*N*-dimethylation provided initial evidence to indicate that *desVI* indeed encodes an *N*,*N*-dimethyltransferase.[4]

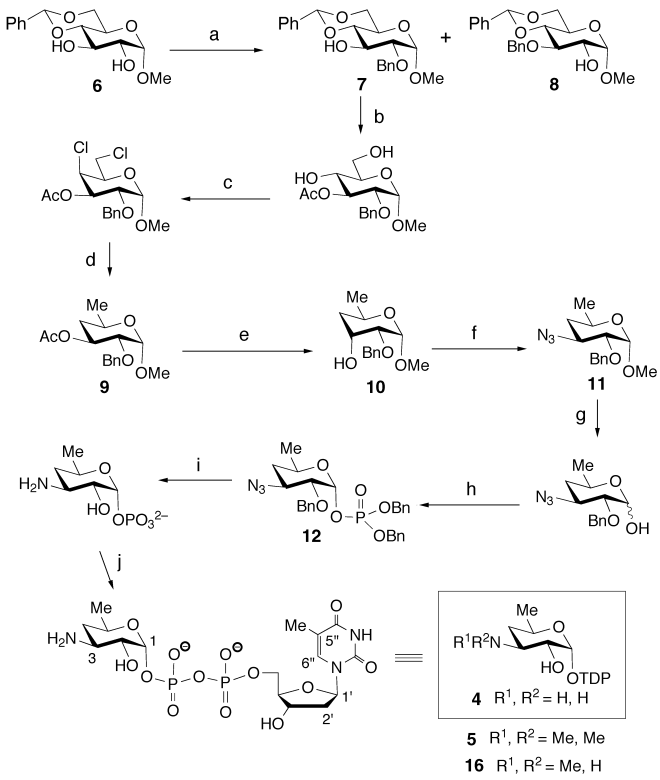


Scheme 1.

To further verify the proposed role of the *desVI* gene, we have now expressed and purified its encoded product, and characterized the catalytic function of this protein. In this paper, we report chemical evidence which establishes the role of DesVI enzyme as the methyltransferase catalyzing the *N*,*N*-dimethylation, the last step in the biosynthesis of desosamine. The *N*,*N*-dimethylation of the C-3 amino group in **4** rendered the product **5** more susceptible to protonation, a modification essential for enhancing the binding affinity of the resulting macrolide antibiotic toward its negatively charged 23S ribosomal RNA target.[5]

To study the function of DesVI, the *desVI* gene was amplified by the polymerase chain reaction (PCR) and cloned into the *Nde*I/*Eco*RI sites of the expression vector pET28b(+). The resulting plasmid was used to transform *Escherichia coli* BL21(DE3) cells, and the recombinant strain was grown at 30 °C in LB (Luria-Bertani) medium. Induction of protein expression was achieved by the addition of 0.1 mM isopropyl β-D-thiogalactoside (IPTG). The DesVI enzyme, tagged with His_6 at its N terminus, was purified to near homogeneity using Ni–nitrilotriacedic acid (Ni–NTA) resin (Qiagen), and was found to be stable in phosphate buffers containing 0.1 mM dithiothreitol (DTT) and 0.1 mM AdoMet. Further analysis using size-exclusion chromatography (Superdex 200 resin) revealed that DesVI exists as a homodimer with a subunit molecular mass of 28.1 kDa.[6] The UV/Vis spectrum of the purified enzyme is transparent above 300 nm.

The predicted substrate of DesVI, **4**, was synthesized from methyl 4,6-*O*-benzylidene-glucoside (**6**) as depicted in Scheme 2. Preparation of the first key intermediate **9** was

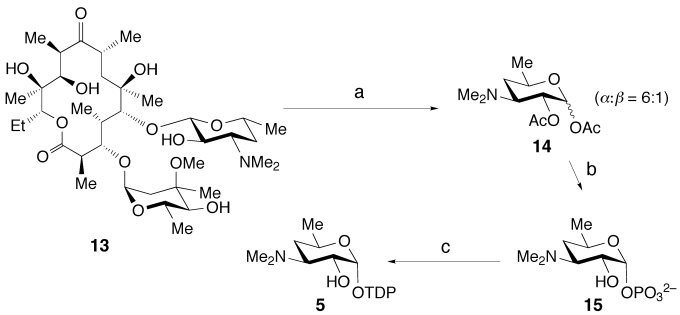


Scheme 2. a) 1. $(n\mathrm{Bu_3Sn})_2O$, toluene; 2. BnBr; b) 1. Ac_2O, pyridine; 2. HOAc, H_2O; c) SO_2Cl_2, $CHCl_3$, pyridine; d) $n\mathrm{Bu_3SnH}$, AIBN, toluene; e) 1. NaOMe, MeOH; 2. $(COCl)_2$, DMSO, DIPEA, CH_2Cl_2; 3. $NaBH_4$, MeOH; f) $(PhO)_2P(O)N_3$, Ph_3P, DEAD, THF; g) BBr_3, CH_2Cl_2; h) 1. $i\mathrm{Pr_2NP(OBn)_2}$, 1*H*-tetrazole, MeCN; 2. *m*CPBA, CH_2Cl_2; i) H_2, $Pd(OH)_2$/C, $NaHCO_3$, MeOH; j) 1*H*-tetrazole, TMP-morpholidate, pyridine. Bn = benzyl, AIBN = azobisisobutyronitrile, DIPEA = diisopropylethylamine, DEAD = diethylazodicarboxylate, *m*CPBA = *meta*-chloroperoxybenzoic acid, TMP = thymidine-5′-(trihydrogenphosphate), TDP = thymidine-5′-(dihydrogenphosphate).

initiated by a selective monobenzylation mediated by bis-(tributyltin) oxide (**7**:**8** = 8:1),[7] followed by acetylation, deprotection, dichlorination, and reduction with an overall yield of 14 %. After hydrolysis, the configuration of 3-OH was inverted by a Swern oxidation and $NaBH_4$ reduction (77 % yield from **9**). The amino group, masked as an azide moiety, was introduced at C-3 of **10** under Mitsunobu conditions to give **11** in 81 % yield. Subsequent demethylation was effected by BBr_3 at low temperature (−78 to 0 °C), and the product was benzylphosphorylated to give **12** (34 % yield). The final steps involved hydrogenation of **12** with $Pd(OH)_2$, Degussa type,[8] and coupling of the resulting product with TMP-morpholidate.[9] Compound **4** was purified by a Bio-P2

column (eluted with 25 mM NH_4HCO_3), and then MonoQ fast protein liquid chromatography (FPLC; linear gradient elution from 0 to 0.5 M NH_4HCO_3).[10]

To facilitate confirmation of the enzymatic product structure, a convenient protocol to make the expected product, TDP-desosamine (**5**), was also developed. As delineated in Scheme 3, the preparation began with the acid hydrolysis of



Scheme 3. a) 1. 6 N HCl, H_2O, EtOH, reflux; 2. Ac_2O, H_2SO_4; b) 1. H_3PO_4, P_2O_5; 2. 2 M LiOH; c) TMP-morpholidate, 1*H*-tetrazole, pyridine.

the commercially available erythromycin B (**13**).[11] The released desosamine was directly acetylated to give **14** in 89% yield. The crude product was relatively labile at room temperature; however, it was rendered more stable after neutralization by dissolving in dichloromethane and washing with ammonium hydroxide and water. Direct phosphorylation of **14** using crystalline phosphoric acid followed by alkaline hydrolysis with lithium hydroxide afforded desosamine 1-phosphate (**15**) as a mixture of α- and β-anomers. The crude mixture was loaded onto a Dowex-50W column (cyclohexylammonium ion form) and eluted with water. The desired α-anomer of **15** was obtained in 12% yield after further purification by a Bio-P2 column (eluted with water). The subsequent coupling with TMP-morpholidate and the purification of the desired product **5** followed a procedure which was analogous with the synthesis of **4**.[12]

To test whether DesVI is the desired methyltransferase, the purified DesVI (20 μg) was incubated with **4** (0.06 μmol), AdoMet (0.5 μmol), and DTT (2 mM) at 27 °C for 3 h in 50 mM potassium phosphate buffer (50 μL, 10% glycerol, pH 7.5). The incubation mixture was analyzed by HPLC with an Adsorbsphere SAX column (5 μ, 4.6 × 250 mm) using a linear gradient from 140 to 320 mM potassium phosphate buffer (pH 3.5) over 20 min. Detection was at 267 nm, and the flow rate was 1.0 mL min^{-1}. It was found that greater than 80% of **4**, which has a retention time of 6.5 min, was consumed and a new peak appeared at 17.0 min. A subsequent large scale incubation of 1.8 mg of DesVI, **4** (5.7 μmol), AdoMet (30 μmol), and DTT (2 mM) in 1 mL of the same buffer at 25 °C for 3 h allowed the isolation and purification of this new compound. Spectral characterization confirmed that the purified product is indeed the desired TDP-desosamine (**5**). When the reaction was quenched (boiled for 2 min) at an earlier time, an intermediate with a retention time of 9.3 min, presumably the monomethylated species **16**, could also be detected. The percentage conversions of **4** to **16** and **5** were estimated based on the integration of the corresponding HPLC peaks, and by fitting these data to the rate laws for an irreversible unimolecular consecutive reaction (**4** → **16** → **5**) led to the constants of 0.005 and 0.82 min^{-1} for the mono- and dimethylation steps, respectively. Thus, our results clearly demonstrate that DesVI is the required methyltransferase in the biosynthesis of desosamine, and it alone catalyzes the *N*,*N*-dimethylation of the 3-amino group of **4** in a stepwise manner.

In summary, the above results have clearly established DesVI as a new member of the small family of enzymes that are capable of catalyzing *N*,*N*-dimethylation.[1] It should be pointed out that the deduced sequence of DesVI reveals significant similarity to those of EryCVI from the erythromycin cluster of *Saccharopolyspora erythraea* (62% identity),[3] OleM1 from the oleandomycin cluster of *Streptomyces antibioticus* (61%),[13] TylM1 from the tylosin cluster of *Streptomyces fradiae* (60% identity),[14] SnoX from the nogalamycin cluster of *Streptomyces nogalater* (55% identity),[15] RdmD from the rhodomycin cluster of *Streptomyces purpurascens* (57% identity),[16] and SrmX from the spiramycin cluster of *Streptomyces ambofaciens* (57% identity).[17] The catalytic role of TylM1 as an AdoMet-dependent *N*,*N*-dimethyltransferase has recently been verified.[18] The fact that DesVI also acts on the amino group of a sugar substrate in a similar manner provides convincing evidence suggesting similar roles for these proteins in their respective biosynthetic pathways. The *N*,*N*-dimethylation of amino sugars could be a convenient tool to modify their chemical properties due to the changes in size, hydrogen-bonding capacity, and propensity for protonation of the amino group. Therefore, with the addition of DesVI and the expectation that other similar methyltransferases will be added in the future to the arsenal of biosynthetic genes, the ability to prepare designed glycoconjugate analogues with novel tailored biological activities should be enhanced significantly.

Received: December 16, 1999 [Z 14408]

[1] a) T. Kodaki, S. Yamashita, *Eur. J. Biochem*. **1989**, *185*, 243 – 251; b) J. D. Gary, W.-J. Lin, M. C. Yang, H. R. Herschman, S. Clarke, *J. Biol. Chem*. **1996**, *271*, 12585 – 12594; c) M. Zalacain, E. Cundliffe, *J. Bacteriol*. **1989**, *171*, 4254 – 4260.

[2] a) M. N. Donin, J. Pagano, J. D. Dutcher, C. M. McKee, *Antibiot. Annu*. **1953 – 1954**, *1*, 179 – 185; b) C. Djerassi, J. A. Zderic, *J. Am. Chem. Soc*. **1956**, *78*, 6390 – 6395.

[3] a) S. Gaisser, G. A. Bohm, J. Cortés, P. F. Leadlay, *Mol. Gen. Genet*. **1997**, *256*, 239 – 251; b) R. G. Summers, S. Donadio, M. J. Staver, E. Wendt-Pienkowski, C. R. Hutchinson, L. Katz, *Microbiology* **1997**, *143*, 3251 – 3262; c) Y. Xue, L. Zhao, H.-w. Liu, D. H. Sherman, *Proc. Natl. Acad. Sci. USA*. **1998**, *95*, 12111 – 12116.

[4] L. Zhao, D. H. Sherman, H.-w. Liu, *J. Am. Chem. Soc.* **1998**, *120*, 10256 – 10257.

[5] H. Sakakibara, S. Omura, *Macrolide Antibiotics*, Chemistry, Biology and Practice (Ed.: S. Omura), Academic Press, New York, **1984**, Chapter 3, pp. 85 – 125.

[6] The molecular mass of each subunit calculated, based on the translated DesVI sequence together with its His_6 tag, is 28,110 Da.

[7] F. Dasgupta, P. J. Garegg, *Synthesis* **1994**, 1121 – 1123.

[8] R. Wischnat, R. Martin, C.-H. Wong, *J. Org. Chem*. **1998**, *63*, 8361 – 8365.

[9] V. Wittmann, C.-H. Wong, *J. Org. Chem*. **1997**, *62*, 2144 – 2147.

[10] Spectral data for **4**: ^{1}H NMR (500 MHz, D_2O) δ = 1.24 (3H, d, J = 6.3 Hz, 5-Me), 1.50 (1H, ddd, J = 12.7, 12.3, 11.7 Hz, 4-H_{ax}), 1.93 (3H, s, 5″-Me), 2.27 (1H, ddd, J = 12.7, 4.0, 3.0 Hz, 4-H_{eq}), 2.40 (2H, m, 2′-H), 3.59 (1H, ddd, J = 12.2, 10.7, 4.0 Hz, 3-H), 3.74 (1H, dt, J = 10.7,

  0570-0833/00/3912-2162 $ 17.50+.50/0

2.9 Hz, 2-H), 4.20 (3H, m, 4′-H, 5′-H), 4.29 (1H, ddq, J = 11.7, 6.3, 3.0 Hz, 5-H), 4.62 (1H, dt, J = 5.8, 3.0 Hz, 3′-H), 5.63 (1H, dd, J = 7.3, 3.4 Hz, 1-H), 6.35 (1H, t, J = 6.8 Hz, 1′-H), 7.71 (1H, s, 6″-H); ^{13}C NMR (125 MHz, D_2O) δ = 11.6, 19.5, 35.3, 38.5, 48.9, 65.4, 69.5 (d, J = 6.6), 70.9, 84.9, 85.0, 85.3 (d, J = 10.1), 95.0 (d, J = 8.0), 111.7, 137.3, 151.7, 166.5; ^{31}P NMR (121 MHz, D_2O) δ = −12.4 (d, J = 20.9), −10.5 (d, J = 20.9); high-resolution fast atom bombardment (FAB) MS: calcd for $C_{16}H_{28}N_3O_{13}P_2$ [M^+ + 2H] 532.1097, found [M^+ + 2H] 532.1098.

[11] E. H. Flynn, M. V. Sigal, Jr., P. E. Wilex, K. Gerzon, *J. Am. Chem. Soc.* **1954**, *76*, 3121 – 3131.

[12] Spectral data for **5**: ^{1}H NMR (500 MHz, D_2O) δ = 1.24 (3H, d, J = 6.4 Hz, 5-Me), 1.62 (1H, dt, J = 12.7, 11.7 Hz, 4-H_{ax}), 1.90 (3H, s, 5″-Me), 2.12 (1H, dt, J = 12.7, 3.4 Hz, 4-H_{eq}), 2.3 – 2.4 (2H, m, 2′-H), 2.83 (6H, s, NMe_2), 3.76 (1H, dt, J = 11.7, 3.4 Hz, 3-H), 3.88 (1H, dt, J = 11.2, 2.9 Hz, 2-H), 4.1 – 4.2 (3H, m, 4′-H, 5′-H), 4.28 (1H, ddq, J = 11.7, 6.4, 3.4 Hz, 5-H), 4.59 (1H, dt, J = 5.4, 3.4 Hz, 3′-H), 5.64 (1H, dd, J = 7.1, 3.1 Hz, 1-H), 6.33 (1H, t, J = 6.8 Hz, 1′-H), 7.70 (1H, s, 6″-H); ^{13}C NMR (125 MHz, D_2O) δ = 11.6, 19.7, 29.1, 38.5, 38.6 (broad, NMe_2), 62.0, 65.5 (d, J = 5.1 Hz), 65.8, 66.7 (d, J = 8.1), 70.9, 84.9, 85.2 (d, J = 10.1), 95.2 (d, J = 6.0), 111.7, 137.3, 151.7, 166.5; ^{31}P NMR (121 MHz, D_2O) δ = −12.4 (d, J = 20.8), −10.6 (d, J = 20.8); high-resolution FAB MS: calcd for $C_{18}H_{30}N_3O_{13}P_2$ [M^+ + 2H] 560.1410, found [M^+ + 2H] 560.1400.

[13] C. Olano, A. M. Rodriguez, J. M. Michel, C. Mendez, M. C. Raynal, J. A. Salas, *Mol. Gen. Genet.* **1998**, *259*, 299 – 308.

[14] A. R. Gandecha, S. L. Large, E. Cundliffe, *Gene* **1997**, *184*, 197 – 203.

[15] K. Ylihonko, J. Tuikkanen, S. Jussila, L. Cong, P. Mäntsälä, *Mol. Gen. Genet.* **1996**, *251*, 113 – 120.

[16] J. Niemi, P. Mäntsälä, *J. Bacteriol.* **1995**, *177*, 2942 – 2945.

[17] M. Geistlich, R. Losick, J. R. Turner, R. N. Rao, *Mol. Microbiol.* **1992**, *6*, 2019 – 2029.

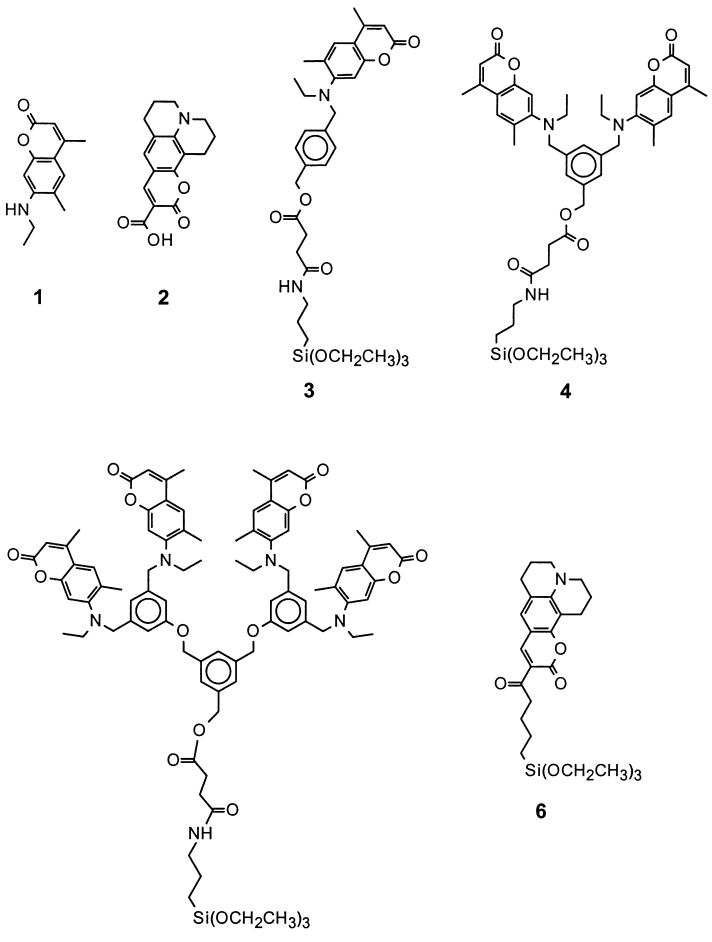
[18] H. Chen, Z. Guo, H.-w. Liu, *J. Am. Chem. Soc.* **1998**, *120*, 9951 – 9952.

Surface-Confined Light Harvesting, Energy Transfer, and Amplification of Fluorescence Emission in Chromophore-Labeled Self-Assembled Monolayers**

Lysander A. J. Chrisstoffels, Alex Adronov, and Jean M. J. Fréchet*

Light harvesting and energy transfer have received considerable attention in the literature because of their important role in natural photosynthesis. These processes involve the use of a light-absorbing antenna (donor) moiety that is capable of transferring the absorbed energy to a nearby secondary energy acceptor species. The energy-transfer process is influenced by the spatial relationship of the donor and acceptor chromophores, and recently researchers have sought to mimic the efficient arrangements found in nature. These include chromophore-functionalized polymers,[1] dendrimers,[2] supported Langmuir – Blodgett films,[3] thin films,[4] and microspheres.[5] Here, we report the use of self-assembled monolayers (SAMs) to align the donor and acceptor chromophores and facilitate intermolecular energy transfer. Intermolecular interactions between adjacent adsorbates have previously been applied to improve the chemical stability of monolayers[6] and to facilitate surface-directed polymerization[7] or surface-confined photodimerization.[8] We extend the exploration of these interactions to include long-range photo-induced Förster energy transfer[9] between donor and acceptor chromophores on SAMs. This process involves a through-space dipole – dipole interaction that does not occur by "hopping" through bonds. Energy transfer can thus be facilitated by assembly of donor and acceptor chromophores as mixed monolayers.

We have recently reported efficient light harvesting by chromophore-labeled dendrimers in which light is funneled through space by Förster energy transfer from multiple coumarin-2 (**1**) donor dyes at the dendrimer periphery to a single coumarin-343 (**2**) acceptor chromophore.[10] These dyes were also chosen for our chromophore-labeled monolayers



[*] Prof. J. M. J. Fréchet, L. A. J. Chrisstoffels, A. Adronov
Department of Chemistry, 718 Latimer Hall
University of California at Berkeley
Berkeley, CA 94720-1460 (USA)
and
Division of Material Sciences
Lawrence Berkeley National Laboratory
Berkeley, CA 94720 (USA)
Fax: (+1) 510-643-3079
E-mail: frechet@cchem.berkeley.edu

[**] This research was supported by the office of Naval Research, the AFOSR – MURI program, as well as fellowships from the Netherlands Scientific Organization (NWO), and from the Eastman Kodak Company, which are gratefully acknowledged.

Supporting information for this article is available on the WWW under http://www.wiley-vch.de/home/angewandte/ or from the author.

  0570-0833/00/3912-2163 $ 17.50+.50/0