Spontaneous Phase Transfer of Nanoparticulate Metals from Organic to Aqueous Media**

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The synthesis and use of nanoparticles constitute a major research area that attracts both academic and industrial interest.[1] Many applications require these particles to be water-dispersible and to remain suspended in water with no loss of physical or chemical properties over extended periods of time.[2–4] However, water-based syntheses of nanoparticles are fraught with problems as a result of ionic interactions, which are typically overcome by using low reactant concentrations (about 5×10^{-4} M),[5] or because the synthesis is carried out in the presence of stabilizers that are subsequently difficult to remove.[6] In contrast, particles synthesized in organic solvents can be made at relatively high concentrations (up to 1M of reactant)[7] with predefined size and shape,[8, 9] and with improved monodispersity compared to those prepared in aqueous solutions. Such particles are, however, water-immiscible, which limits their range of applicability.

A range of methods for the phase transfer of particles has been reported, with most studies focusing on the transfer of particles from aqueous to organic media.[10–16] Previous research into the phase transfer of nanoparticulate material from organic to aqueous solutions has involved irreversible covalent capping of the nanoparticles with amphiphilic molecules. This process permanently changes the chemistry of the particle surface,[17] and results in only a small proportion of transferred material.[18–21] Herein we report a facile, rapid, one-step method for the direct and complete transfer of nanoparticles across the phase boundary (organic to aqueous) by use of a readily available organic compound, 4-dimethylaminopyridine (DMAP). The transferred particles displayed no signs of degradation or aggregation after six months, and are expected to be indefinitely stable. Unlike previous attempts,[18–21] no precipitation steps or solvent exchanges are required, and the particles transferred by this method are not stabilized by a strong, covalently attached ligand: this is vitally different to thiol-stabilized particles when considering future applications. The availability of such concentrated nanoparticle solutions opens up new avenues for cyto-labeling,[22] hetero- and homogenous catalysis,[2, 3, 7] solid-state physics,[23] and colloidal crystal applications.[24]

Gold and palladium nanoparticles were synthesized in toluene by using tetraalkyl ammonium salts as the stabilizing agent.[25] Such particles are commonly used in catalysis, while the more commonly studied thiol-passivated nanoparticles possess a surface monolayer of metal sulfide which makes them less efficient catalysts.[7] To effect phase transfer an aqueous 0.1M DMAP solution was added to aliquots of the as-prepared nanoparticle mixtures. Phase transfer of both the gold and palladium nanoparticles was initiated instantaneously upon the addition of the DMAP solution, with direct transfer across the phase boundary completed within one hour (no stirring or agitation was required, see the Supporting Information). The synthetic procedure produces high concentrations of nanoparticles, and so samples were diluted with solvent by a factor of approximately 1000 for subsequent analysis and photography.

The complete phase transfer of metallic nanoparticles was achieved (Figure 1). The UV/Vis spectra of the gold nanoparticles in solution before and after phase transfer were also

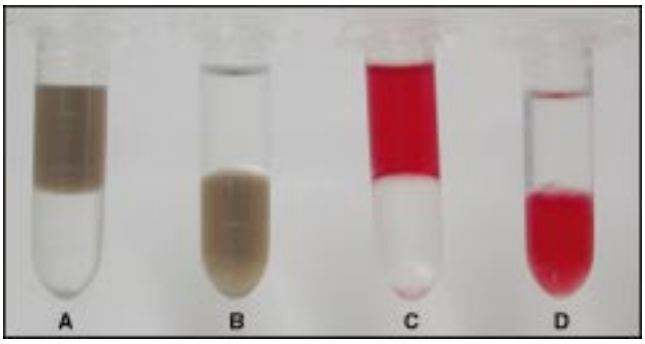

Figure 1. Photograph of a diluted aliquot of palladium nanoparticles in toluene above water (A), and a similar aliquot subsequently transferred into water by the addition of DMAP (0.1M, pH 10.5; B); a diluted aliquot of gold nanoparticles in toluene above water (C), and a similar aliquot subsequently transferred into water by the addition of DMAP (0.1M, pH 10.5; D).

recorded since particle aggregation (reversible or irreversible; flocculation or coagulation) and changes in the dielectric surroundings of the nanoparticles can be detected optically.[26, 27] The as-synthesized gold nanoparticles (in toluene) displayed a maximum in the surface plasmon band (λ_{max}) at 518 nm (Figure 2). A 6-nm (± 0.2 nm) blue-shift ($\lambda_{max} =$ 512 nm) in the wavelength of the surface plasmon band peak maximum was observed after the phase transfer (toluene to water) of the gold nanoparticles. The observed shift could arise from the combined effect of the change in refractive index of the medium on transfer (1.47 to 1.33)[26] and exchange of the adsorbed molecules on transfer. Any particle aggregation would lead to a red-shift and broadening of the plasmon band absorption.[28] The UV/Vis spectra obtained clearly indicate that the DMAP-induced phase transfer of the gold nanoparticles yields well-dispersed nanoparticles in aqueous solution. UV/Vis experiments on the palladium nanoparticles were not undertaken as they do not display a strong surface plasmon band absorbance.[29]

Transmission electron microscopy (TEM) analysis also showed that there were no discernable differences in the

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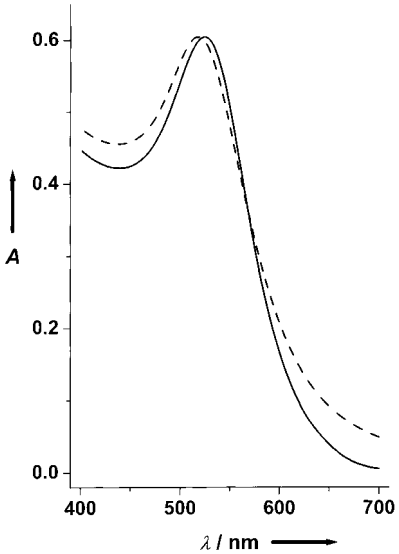

Figure 2. UV/Vis spectra of a diluted solution of gold nanoparticles in toluene (solid line) and the same sample transferred into an equal volume of 0.1M DMAP solution at pH 10.5 (dashed line).

morphology of both the gold and palladium nanoparticles after phase-transfer (Figure 3 and see the Supporting Information). Analysis of the gold nanoparticle samples yielded

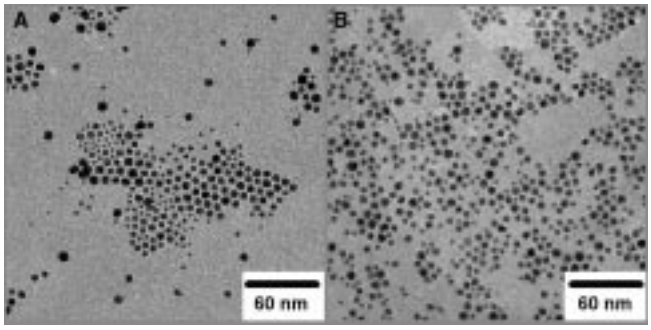

Figure 3. Transmission electron micrographs of gold nanoparticles synthesized in toluene (A) and the same sample one month after being transferred into water by the addition of DMAP (B).

average diameters of 5.5 nm (standard distribution (SD) = 0.7, 153 particles counted) and 5.5 nm (SD = 0.8, 115 particles counted) for the nanoparticles in toluene and aqueous media, respectively. Analysis of the palladium nanoparticle samples gave average diameters of 4.5 nm (SD = 0.9, 145 particles counted) and 4.8 nm (SD = 1.2, 122 particles counted) for the nanoparticles in toluene and aqueous media, respectively. In addition, energy-dispersive X-ray fluorescence analysis (EDAX) spectra of the particles transferred to the aqueous solution and dried on a TEM grid showed there were no bromide ions present (the tetraalkylammonium counterion; see the Supporting Information); however, traces of the organic salt may still remain adsorbed to the particle surface.

As TEM provides information on the morphology of the nanoparticles in the dry state, analytical ultracentrifugation (AU) measurements were conducted to determine the size distributions of the nanoparticles in solution (see the Experimental Section).[30–32] Analysis of the two samples shown in Figure 3 by AU resulted in average diameters of 5.1 (SD = 1.1), and 5.2 nm (SD = 1.1) for the nanoparticles in toluene and aqueous media, respectively. The average diameters of the palladium nanoparticles in toluene and water were found by AU to be 2.8 (SD = 1.5) and 3.1 nm (SD = 1.6), respectively. These data are in good agreement with the TEM values and further confirm that no significant aggregation of the transferred nanoparticles occurred.

The stability of the DMAP-stabilized particles was examined with respect to salt concentration and pH. All samples (Au, Pd, pH 10.5) were stable for a period of at least six months in 3M NaCl solution (for gold, $\lambda_{max} = 514$ nm). Measurements on the DMAP-stabilized nanoparticles in aqueous solution (pH 10.5) by microelectrophoresis gave an average ζ-potential of +25 mV (five measurements on three different transfer experiments), which confirmed there was a positively charged particle surface. The particles were found to be colloidally stable within the pH range 7 to 12 (ζ-potential of approximately +35 mV), although the proportion of flocculated particles increased (as seen by eye; see the Supporting Information) as the pH value was lowered (from 10.5 to 3.0) by the stepwise addition of dilute acid (1 mM HCl, pH 3).[28] This observation concurs with the postulated mechanism of phase transfer (see Scheme 1). Lowering the pH value would result in a greater proportion of the endocyclic nitrogen groups being protonated and unavailable for bonding to the nanoparticle surface (and hence stabilizing the nanoparticles). Areas of the nanoparticle surface subsequently become "deprotected", which causes reversible aggregation. A decrease in the degree of particle flocculation (detected by a blue-shift in the peak plasmon band absorption) was achieved by the addition of dilute base (1 mM NaOH) to restore the pH value back to its original value (pH 10.5). The separation of aggregated particles was not instantaneous and was only detected after several days; however, this was always repeatable. As expected from simple acid/base equilibria, raising the pH value of the solution to greater than pH 13, by the addition of dilute base, led to particle aggregation as the proportion of charged DMAP molecules decreased ($pK_a = 9.6$).

Several compounds (as 0.1M aqueous solutions) were added to aliquots of gold nanoparticle solutions to arrive at an understanding of the mechanism for the spontaneous phase transfer of metal nanoparticles from organic to aqueous phases. Pyridine and 4-aminopyridine caused immediate aggregation of the particles suspended in toluene (seen as a color change from red to blue, followed by precipitation). Only the DMAP-containing vial resulted in the transfer of the nanoparticles to the aqueous phase; in the other samples the precipitate accumulated at the toluene/water interface. These results point to the necessity of the tertiary (highly basic) amine conjugated with an electron-donating (weakly basic) group to effect the phase transfer. Evidence against the formation of a strong covalent bond between the stabilizing molecule (DMAP) and the metal nanoparticle surface was proved by repeatedly washing the aqueous phase with toluene. The toluene washings continually decreased the amount of DMAP in the aqueous phase, finally causing the particles to aggregate. This effect is indicative of the removal

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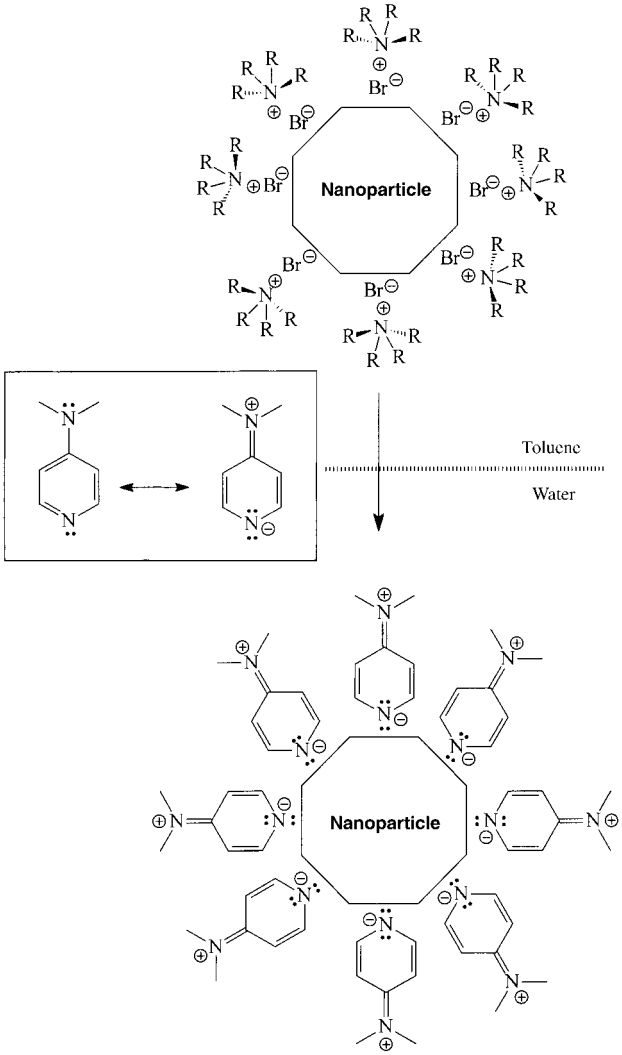
of DMAP from the particle surface. Covalently bound molecules cannot be removed by solvent washing.[18]

A possible mechanism for the spontaneous phase transfer of nanoparticles in the presence of DMAP molecules is as follows (Scheme 1): The addition of an aqueous DMAP solution to the nanoparticle dispersion in toluene results in



Scheme 1. Proposed mechanism for the spontaneous phase transfer of gold and palladium nanoparticles from an organic reaction medium (toluene) to water by the addition of DMAP. $R = C_8H_{17}$.

the DMAP partitioning across the water/toluene phase boundary (detected by thin-layer chromatographic analysis of the organic phase), and physisorbing onto the nanoparticle surface. Simple acid-base calculations show that 98% of the DMAP is present in the free base form in a 0.1M aqueous solution. It is proposed that the DMAP molecules form a labile donor–acceptor complex with the metal surface atoms through the endocyclic nitrogen atoms, as previously reported for planar gold substrates,[33] with the surface charge arising from partial protonation of the exocyclic nitrogen atom that extends away from the nanoparticle surface being required to transfer the particles into water.[34]

In conclusion, a general method to efficiently transfer gold and palladium nanoparticles from an organic solvent (in this case, toluene) to water has been described. The benefits of such a method are threefold. Firstly, by replacing the hydrosol synthetic methods that require high dilution and lengthy dialysis purification.[22] Secondly, synthetic reactions in organic solvents produce high concentrations of nanoparticles with improved monodispersity relative to those prepared in water;[25, 35] the method reported here offers such particles to researchers requiring water-based chemistries. Thirdly, the transfer of nanoparticles out of the organic phase (*without precipitation*) permits the recycling of the relatively expensive ammonium salts. Furthermore, the method efficiently produces water-dispersible metal nanoparticles as an isolable solid, which is important when highly concentrated particle solutions are required, for example, for colloidal crystal applications.[24] The expected strong affinity of the DMAP-stabilized particles for negatively charged substrates, commonly used as supports in heterogeneous catalysis, also warrants further study.[7]

Experimental Section

Nanoparticle synthesis: A 30 mM aqueous metal chloride solution ($HAuCl_4$ or Na_2PdCl_4, 30 mL) was added to a 25 mM solution of tetraoctylammonium bromide in toluene (80 mL). The transfer of the metal salt to the toluene phase can be clearly seen visually within a few seconds. A 0.4M solution of freshly prepared $NaBH_4$ (25 mL) was added to the stirred mixture, which caused an immediate reduction to occur. After 30 min the two phases were separated and the toluene phase was subsequently washed with 0.1M H_2SO_4, 0.1M NaOH, and H_2O (three times), and then dried over anhydrous $NaSO_4$.[7, 35] Previous high-resolution TEM analysis confirmed similar nanoparticles to be crystals with a truncated octahedral morphology.[36, 37]

Phase transfer: An aqueous 0.1M 4-dimethylaminopyridine (DMAP) solution (1 mL) was added to aliquots (1 mL) of the as-prepared nanoparticle mixtures. This concentration of DMAP was found to be sufficient to effect the complete and spontaneous phase transfer of the nanoparticles. Whilst not discussed here, nanoparticles from larger volumes of the reaction solution (up to 0.5 L) have also been successfully transferred into water (1 mL), with subsequent recycling of the tetraalkylammonium salt. Direct phase transfer across the organic/aqueous boundary was completed within 1 h, with no stirring or agitation required. Solid DMAP could also be added directly to the toluene solution to precipitate the particles, which could then be resuspended in water. Phase transfer was also possible for similar particles synthesized in chloroform but not for particles obtained from synthetic reactions using different organic stabilizers, for example, sodium 5,14-diethyl-8,11-dioxo-7,12-dioxaoctadecane-2-sulfonate (Na-AOT) or didodecyldimethylammonium bromide.

All reagents were obtained from Sigma–Aldrich and used as received. UV/Vis spectra were recorded using a Cary Model 4E UV/Vis spectrophotometer (0.2 nm resolution). The ζ-potentials of the nanoparticles were determined with a Malvern Zetasizer 4 by taking the average of five measurements at the stationary level. The mobilities were converted into the electrophoretic potential by using the Smoluchowski relation. TEM measurements were performed on a Philips CM12 microscope operated at 120 kV. Particle-size distribution was estimated by analytical ultracentrifugation from sedimentation velocity experiments at 20 °C on a Beckman–Coulter Optima XL-I ultracentrifuge with absorption optics used for detection. 12-mm self-made double-sector titanium centerpieces were used. Analytical ultracentrifugation applies a constant centrifugal force to a dilute sample of nanoparticles. At the beginning of the experiment a single wavelength scan across the radius of the cell gives a constant absorbance value that is indicative of a constant colloid distribution. As the experiment continues, the time-dependent sedimentation of the particles can be detected by time-dependent radial scans of the local colloid concentration. Particle fractionation during the experiment allows the calculation of the distribution of the sedimentation coefficient from a series of radial scans over time. The particle-size distribution, together with the particle density,

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solvent density, and viscosity, can be obtained for particles with sizes even in the Ångstrom range.[31]

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[1] "Atom-Scale Research Gets Real": *Science* **2000**, *290*, 1523, special issue on nanotechnology; H. G. Craighead, *Science* **2000**, *290*, 1532; S. R. Quake, A. Scherer, *Science* **2000**, *290*, 1536; E. W. H. Jager, E. Smela, O. Inganäs, *Science* **2000**, *290*, 1540.
[2] S. C. Davis, K. J. Klabunde, *Chem. Rev.* **1982**, *82*, 153.
[3] L. N. Lewis, *Chem. Rev.* **1993**, *93*, 2693.
[4] J. H. Fendler, *Nanoparticles and Nanostructured Films*, Wiley, Weinheim, **1998**.
[5] J. Turkevich, P. C. Stevenson, J. Hillier, *Discuss. Faraday Soc.* **1951**, 55.
[6] D. V. Goia, E. Matijevic, *New J. Chem.* **1998**, *22*, 1203.
[7] H. Bönnemann, W. Brijoux in *Advanced Catalysts and Nanostructured Materials* (Ed.: W. Moser), Academic Press, New York, **1996**, p. 165.
[8] M. Green, P. O'Brien, *Chem. Commun.* **1999**, 2235.
[9] M. P. Pileni, *New J. Chem.* **1998**, *22*, 693.
[10] H. Hirai, H. Aizawa, H. Shiozaki, *Chem. Lett.* **1992**, *8*, 1527.
[11] K. V. Sarathy, G. U. Kulkarni, C. N. R. Rao, *Chem. Commun.* **1997**, 537.
[12] W. Wang, S. Efrima, O. Regev, *Langmuir* **1998**, *14*, 602.
[13] F. C. Meldrum, N. A. Kotov, J. H. Fendler, *Langmuir* **1994**, *10*, 2035.
[14] S. Underwood, P. Mulvaney, *Langmuir* **1994**, *10*, 3427.
[15] L. M. Liz-Marzan, I. Lado-Tourino, *Langmuir* **1996**, *12*, 3585.
[16] S. Chen, H. Yao, K. Kimura, *Langmuir* **2001**, *17*, 733.
[17] G. Schmid, N. Klein, L. Korste, U. Kreibig, D. Schönauer, *Polyhedron* **1988**, *7*, 605.
[18] A. C. Templeton, W. P. Wuelfing, R. W. Murray, *Acc. Chem. Res.* **2000**, *33*, 27.
[19] J. Simard, C. Briggs, A. K. Boal, V. M. Rotello, *Chem. Commun.* **2000**, 1943.
[20] W. P. Wuelfing, S. M. Gross, D. T. Miles, R. W. Murray, *J. Am. Chem. Soc.* **1998**, *120*, 12696.
[21] M. Bruchez, M. Moronne, P. Gin, S. Wiess, A. P. Alivisatos, *Science* **1998**, *281*, 2013.
[22] M. A. Hayat, *Colloidal Gold: Principles, Methods and Applications*, *Vol. 1*, Academic Press, San Diego, **1989**.
[23] R. G. Freeman, K. C. Grabar, K. J. Allison, R. M. Bright, J. A. Davis, A. P. Guthrie, M. B. Hommer, M. A. Jackson, P. C. Smith, D. G. Walter, M. J. Natan, *Science* **1995**, *267*, 1629.
[24] O. D. Velev, P. M. Tessier, A. M. Lenhoff, E. W. Kaler, *Nature* **1999**, *401*, 548.
[25] H. Bönnemann, W. Brijoux, R. Brinkmann, E. Dinjus, T. Joußen, B. Korall, *Angew. Chem.* **1991**, *103*, 1344; *Angew. Chem. Int. Ed. Engl.* **1991**, *30*, 1312.
[26] P. Mulvaney, L. M. Liz-Marzan, M. Giersig, T. Ung, *J. Mater. Chem.* **2000**, *10*, 1259.
[27] D. I. Gittins, F. Caruso, *Adv. Mater.* **2000**, *12*, 1947.
[28] P. Mulvaney, *Langmuir* **1996**, *12*, 788.
[29] M. Michaelis, A. Henglein, P. Mulvaney, *J. Phys. Chem.* **1994**, *98*, 6212.
[30] T. Svedberg, K. O. Pedersen, *The Ultracentrifuge*, Oxford University Press, Oxford, **1940**.
[31] H. Cölfen, T. Pauck, *Colloid Polym. Sci.* **1997**, *275*, 175.
[32] D. H. Rapoport, W. Vogel, H. Cölfen, R. Schlögl, *J. Phys. Chem. B* **1997**, *101*, 4175.
[33] W. Cai, L. Wan, H. Noda, Y. Hibino, K. Ataka, M. Osawa, *Langmuir* **1998**, *14*, 6992.
[34] F. A. Carey, R. J. Sundberg, *Advanced Organic Chemistry*, Plenum, New York, **1990**.
[35] M. Brust, D. Bethell, D. J. Schiffrin, C. J. Kiely, *Adv. Mater.* **1995**, *7*, 795.
[36] M. T. Reetz, W. Helbig, S. A. Quaiser, U. Stimming, N. Breuer, R. Vogel, *Science* **1995**, *267*, 367.
[37] R. L. Whetten, J. T. Khoury, M. M. Alvarez, S. Murthy, I. Vezmar, Z. L. Wang, P. W. Stephens, C. L. Cleveland, W. D. Luedtke, U. Landman, *Adv. Mater.* **1996**, *8*, 428.

Membrane-Permeant 3-OH-Phosphorylated Phosphoinositide Derivatives**

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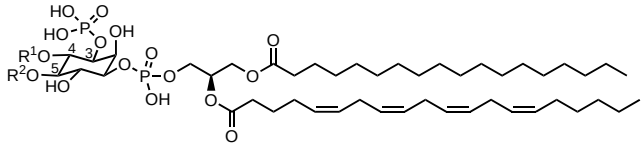
Phosphoinositides that are phosphorylated at the 3-hydroxy group (Scheme 1) are important signaling molecules in eukaryotic cells, particularly because of their participation in the receptor-mediated activation of protein kinases and in



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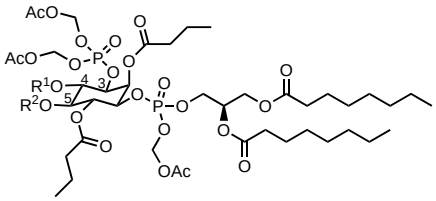

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Scheme 1. Phosphoinositides PtdIns(3,5)P_2 (**1**): $R^1 = H$, $R^2 = P(O)(OH)_2$; PtdIns(3,4,5)P_3 (**2**): $R^1 = R^2 = P(O)(OH)_2$; PtdIns(3,4)P_2 (**3**): $R^1 = P(O)(OH)_2$, $R^2 = H$ and the corresponding membrane-permeant derivatives which can be bioactivated: di-C_8-Bt_3PtdIns(3,5)P_2/AM (**4**, $R^1 = Bt$, $R^2 = P(O)(OCH_2OAc)_2$), di-C_8-Bt_2PtdIns(3,4,5)P_3/AM (**5**, $R^1 = R^2 = P(O)(OCH_2OAc)_2$), and di-$C_8$-$Bt_3$PtdIns(3,4)$P_2$/AM (**6**, $R^1 = P(O)(O\text{-}CH_2OAc)_2$, $R^2 = Bt$). $Bt = COC_3H_7$.

the control of intracellular calcium levels. The key enzyme involved in the biosynthesis is the phosphoinositide 3-kinase (PI 3-kinase), which is activated by growth factors such as epidermal growth factor (EGF) and platelet-derived growth factor (PDGF). The 3-hydroxy phosphorylated phosphoinositides formed by the enzyme have been associated with the mechanisms of oncogene transformation, cytoskeletal rearrangements, association of proteins to the plasma membrane, protein trafficking, endo- and exocytosis, the uptake of glucose by adipocytes, and the regulation of epithelial

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