

Task ID: 425.013

Task Title: Non-PFOS/non-PFAS Photoacid Generators: Environmentally Friendly Candidates for Next Generation Lithography

Deliverable: Report on the assessment of the environmental compatibility of new PFOS-free photoacid generators.

PIs:

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Summary Abstract:

Perfluorooctyl sulfonate (PFOS) and related long-chain perfluorinated compounds (PFAS) are under increased scrutiny as priority environmental contaminants due to recent reports of their detection in environmental and biological matrices as well as concerns regarding their persistence and toxicity. Nevertheless, PFOS and other long chain perfluorinated materials are vital to many industrial processes, including semiconductor manufacturing where they are utilized in photoacid generators (PAGs), anti-reflective coatings (ARCs) and certain surfactants.

This project aims to develop new PFOS-free (and PFAS-free) PAGs and investigate their environmental behavior. Our strategy is to create PAGs that have acidity equivalent to that of PFOS based materials by incorporating short (1, 2 or 3) CF₂ units next to the sulfonic acid. Our hypothesis is that these materials are environmentally friendly because the additional functions on the PAG lack fluorination.

This research task considers the investigation of the environmental compatibility of new PFOS-free PGAs developed by the Ober Lab. The performance characteristics of such materials have been demonstrated [1], but the ESH attributes are virtually unknown. Key environmental properties of the novel PAGs, *i.e.*, 1) susceptibility to biodegradation by microorganisms commonly found in wastewater treatment systems; 2) toxic effects, and 3) their bioaccumulation potential were investigated in this study. The chemical structures of the PAGs and PAG counterions evaluated are shown in Figure 1a (nonionic PAGs), 1b (ionic PAGs) and 2 (counterions).

Method of Approach

Toxicity: The toxicity of the various PAG compounds and typical PAG counterions (diphenyliodonium and triphenylsulfonium) was evaluated in assays employing common indicator organisms (e.g., Microtox assay, methanogenic microorganisms in anaerobic wastewater treatment sludge). In addition, the cytotoxicity was also monitored using the

mitochondrial toxicity test (MTT). Perfluorobutane sulfonate (PFBS), a commercial compound that has been proposed as a more environmentally benign alternative to PFOS, has also been included as a reference compound in these assays. The inhibitory effect of the chemicals towards the various targets was calculated based on the activity of the control sample lacking the toxicant. The initial concentrations causing 20%, 50% and 80% reduction in activity compared to an uninhibited control were referred to as IC₂₀, IC₅₀ and IC₈₀, respectively.

Microtox is a standardized toxicity bioassay which is rapid and sensitive. There exist a larger body of published data comparing the Microtox system with toxicity values for fish and other aquatic organisms for a wide range of chemicals. The MTT assay is widely used in the testing of drug action, cytotoxic agents and screening other biologically active compounds. The assay is based on the cleavage of the yellow tetrazolium salt MTT (3-(4,5-dimethylthiazol-2-yl)-2,5-diphenyltetrazolium bromide) to purple formazan crystal by a mitochondrial dehydrogenase enzyme of metabolic active cells. The number of surviving cells is directly proportional to the level of the formazan product formed, which can be quantified using a simple colorimetric assay.

Microbial degradation: Experiments were set up to evaluate the susceptibility of the various PAG compounds to microbial degradation. Biodegradation was investigated under different redox conditions, namely, aerobic degradation as sole carbon source, aerobic cometabolism, and anaerobic reductive dehalogenation. Bioassays were designed to simulate typical conditions in municipal wastewater treatment plants. Test solutions containing the various PAG compounds were supplied at a concentration of 1 mM. Control assays (e.g. abiotic treatments; killed-cell controls) were run in parallel to account for the loss of the compounds by mechanisms other than degradation. Methane was utilized as cosubstrate in assays evaluating aerobic cometabolic degradation. To promote reductive dehalogenation, hydrogen gas (H₂) was supplied as the electron donor. Fluoride concentration using an ion selective electrode and analysis of fluorinated compounds by high-performance liquid chromatography with suppressed conductivity detection or by HPLC with ultraviolet detection were performed periodically to determine if the PAGs were susceptible to microbial defluorination.

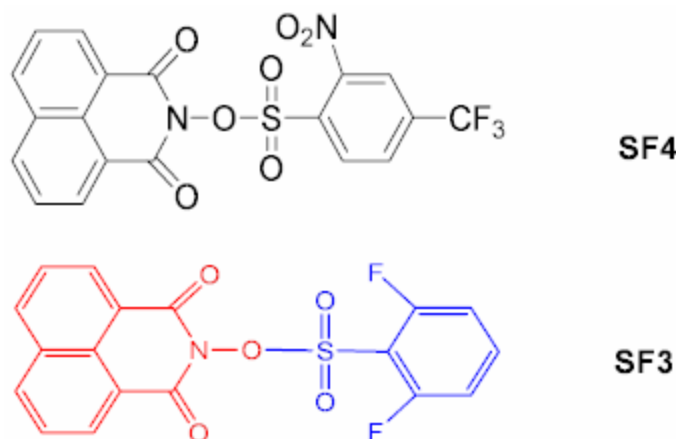


Figure 1a. Chemical structures of the two nonionic PAGs, SF3 and SF4, tested in this study.

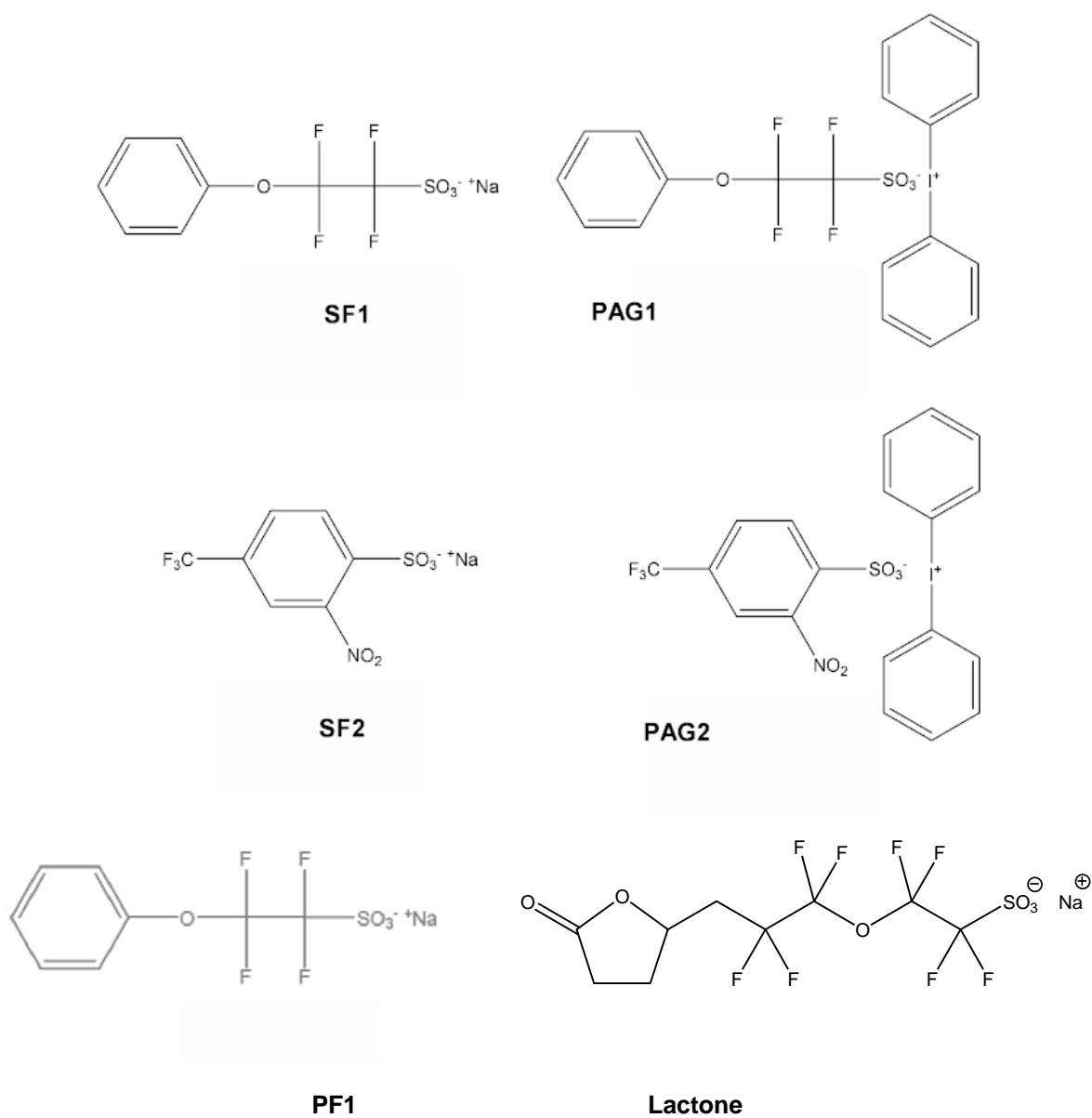
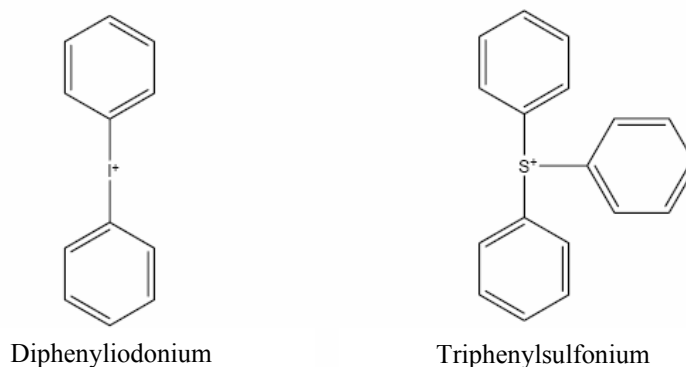


Figure 1b. Chemical structures of the ionic non-PFOS PAGs and their corresponding sodium sulfonates evaluated in this study.

Figure 2. Chemical structures of the PAG counterions diphenyliodonium and triphenylsulfonium



Modeling of the environmental properties: The *PBT* (Persistence-Bioaccumulation-Toxicity) *Profiler* was utilized to estimate the persistence, bioaccumulation, and chronic fish toxicity potential of the various PAGs. The *PBT Profiler* (available at <http://esc.syrres.com/pbt/>) is an online screening methodology developed by the EPA which predictions are determined using structure-based estimation methods. The chemical structure of the compound to be profiled, the only input provided by the user of the *PBT Profiler*, is entered using its SMILES notation. Then, the physico-chemical properties required for *PBT* estimations (eg. water solubility, Henry's constant, water-octanol partition coefficient (K_{ow}), etc.) are estimated by the *EPI Suite*, a sub-component of the *PBT Profiler*, utilizing an atom/fragment contribution method.

Technical Results and Data:

Toxicity: The novel non-PFOS PAGs (*i.e.*, nonionic compounds and sodium salts of ionic compounds) exhibited no or only very low toxicity in the various inhibition bioassays at very high concentrations of up to 2.5 mM. In contrast, the PAG counterions, diphenyliodonium and triphenylsulfonium, were highly inhibitory in the MTT and Microtox bioassays.

The cytotoxicity of the PAG compounds (sodium salts), PFBS and the PAG counterions in the MTT assay is illustrated in Figure 3a. Only two of the PAG compounds PF1 and SF3 displayed toxicity in this assay with IC_{50} values of 333 and 238 μ M, respectively. The IC_{50} values determined for diphenyliodonium and triphenylsulfonium were one order of magnitude lower, averaging 13 and 59 μ M, respectively. The results of the Microtox assays were in good agreement with these observations and confirmed that the acute toxicity of the novel PAGs is very low compared to that of the counterions (Figure 3b). The microbial toxicity of DPI is well established in the literature. DPI and other diaryl-iodonium compounds irreversibly inactivate many redox-active proteins, primarily flavoproteins, by a mechanism involving reduction of DPI and radical recombination with the cofactor. As a result, DPI exerts cytotoxicity in mammal cells

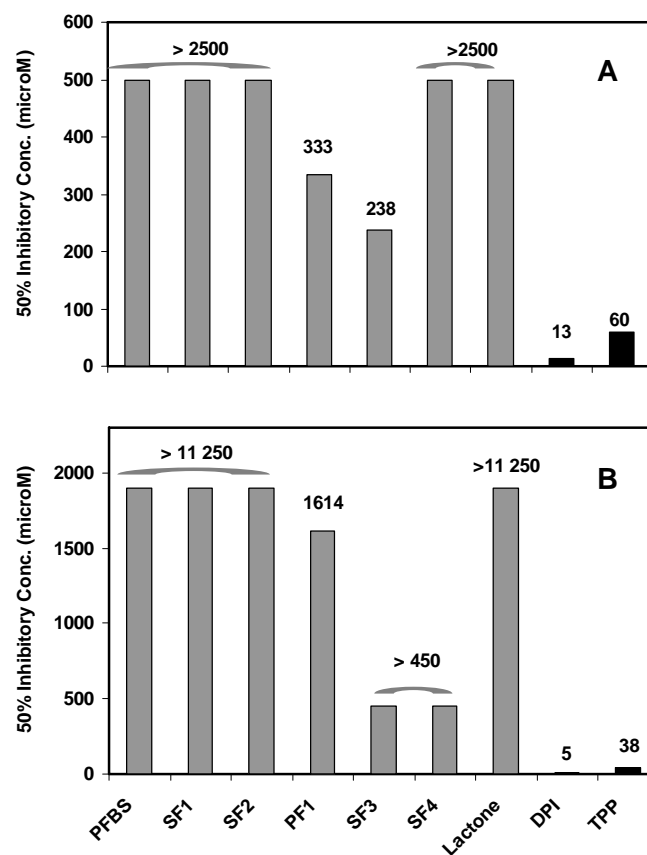


Figure 3. Toxic response of the novel PAGs (nonionic and sodium salt of the ionic compounds) in the MTT assay (A) and the Microtox assay (B). See figures 1 and 2 for compound abbreviations and chemical structures.

(Li et al., 2003; Riganti et al., 2004), and inhibits a number of microbial enzymes (Pineres et al., 1997; Shiemke et al., 2004).

PAGs were generally not inhibitory to acetate and hydrogen-utilizing methanogens in anaerobic wastewater treatment sludge at the highest concentrations tested. SF2 and the lactone displayed some methanogenic inhibition but only at very high concentrations ($IC_{50} = 1400-1500 \mu M$). The PAG counterions were also found to be moderately inhibitory to methanogens ($IC_{50} = 1500 \mu M$).

Biodegradation. The susceptibility of the novel PAG compounds (sodium salts) to microbial degradation under conditions that promote degradation of highly halogenated compounds including aerobic methylotrophic cooxidative and anaerobic reductive dehalogenation mechanisms was investigated. The new PAGs considered in this study are only partially fluorinated. Earlier reports have shown that higher halogenated compounds can undergo reductive dehalogenation, while lower halogenated hydrocarbons are generally susceptible to

attack by monooxygenases (Field & Sierra-Alvarez, 2004). Aerobic methylotrophic microorganisms are known to possess methane monooxygenases (MMO). Aerobic degradation of the PAGs as sole carbon source was also studied. Results for the lactone PAG are not presented because the compound is still under evaluation.

Activated sludge and anaerobically digested sludge, both obtained from a local municipal wastewater treatment plant, were used as inoculum in the aerobic and anaerobic degradation experiments, respectively. Both inocula are characterized by a high microbial diversity. All compounds tested were resistant to microbial attack under aerobic heterotrophic and aerobic methylotrophic cooxidative conditions. No significant fluoride release or compound removal beyond the controls has been detected in the aerobic degradation experiments after extended periods of incubation (200-400 days, depending on the assay). In contrast with the recalcitrance of other PAG compounds, SF2 was rapidly degraded under anaerobic conditions. Chromatographic analysis suggested that SF2 biotransformation involved reduction of the nitro group with formation of the corresponding aromatic amine compound. The amino derivative was poorly degradable under anaerobic conditions even after extended incubation of 343 days. Nonetheless, a small but significant release of fluoride (9.2%) was determined in the SF2 assays.

Additional experiments are planned to evaluate the cooxidation potential of the new PAGs under nitrifying conditions. Nitrifying microorganisms possess ammonia monooxygenases (AMO), which are known to attack lower halogenated hydrocarbons. The biodegradation potential of the lactone PAG and a novel PAG that is scheduled for delivery shortly is still to be tested.




















Modeling of the environmental properties: The environmental persistence, bioaccumulation, and chronic fish toxicity potential estimated by the EPA *PBT Profiler* for the various PAGs (nonionic compounds and sodium salts of the ionic compounds) and for the PAG counterions are listed on Tables 1 and 2. A summary of the environmental fate estimates is presented on Table 3. The criteria utilized for compound classification are also summarized in the footnote of Table 3.

All the PAG compounds were estimated to show no bioaccumulation potential and their chronic toxicity to fish was of low concern (chronic value for SF3 and SF4 could not be calculated). However, similarly to PFBS, the ionic PAGs were estimated to be persistent chemicals. The nonionic PAGs, SF3 and SF4, were predicted to be highly persistent. The *PBT Profiler* estimated a lower environmental compatibility for PAG counterions. In particular, the screening estimates that triphenylsulfonium (TPS) may be a PBT pollutant since the compound was profiled to be persistent, bioaccumulative and highly toxic to fish. For diphenyliodonium (DPI), the screening program predicted that the compound is persistent, no bioaccumulative, and toxic. Nonetheless, the PAG counterions are very reactive and will decompose upon exposure to UV light to form radical fragments. In the environment, UV radiation in sunlight can cause these chemicals to undergo photolytic degradation.

In broad lines, these results are in agreement with the experimental results which demonstrated that the PAG compounds displayed low toxicity but were persistent to microbial degradation, and indicated the high toxic potential of the counterions. Nonetheless, the applicability of the *PBT Profiler* to surfactants, highly fluorinated compounds and reactive compounds is known to be very limited, and therefore the predictions obtained using this screening method should be used with caution. The aqueous solubility and other environmental fate parameters of surfactants cannot be accurately estimated using the methodology employed by the PBT Profiler because they form dispersions. Highly fluorinated compounds possess physical/chemical and environmental fate properties that are vastly different than their non-substituted analogs. The models used by the PBT Profiler do not accurately predict the unique characteristics of these materials, although the estimation methods are continually improving as more data become available (<http://www.pbtprofiler.net/Chemicals.asp>).

The results obtained indicate that the novel PAGs exert no or low toxicity and are not bioaccumulative. However, the compounds tested are resistant to microbial degradation. Improved PAG substitutes which are more prone to biodegradation still need to be developed. Enhanced biodegradability may require chemistries without fluorine substitutions and without stable phenyl alkyl ether groups. Furthermore, the findings of this study indicate that diphenyliodonium and triphenylsulfonium, two common PAG counterions, should be replaced by more environmentally sound alternatives. Both counterions were found to be highly toxic in assays with microbial and human cells. The EPA *PBT Profiler* estimated that triphenylsulfonium (TPS) may be a PBT pollutant since the compound was profiled to be persistent, bioaccumulative and highly toxic to fish. Future work will complete the evaluation of the environmental compatibility of the novel PAGs (two compounds still pending) and will evaluate their treatability using conventional biological and physico-chemical methods.

Table 1. Environmental fate properties predicted utilizing the EPA PBT profiler for the non-PFOS PAGs. Estimates exceed the EPA criteria (see Footnote of Table 3) as they appear in **orange** or **red** text; those that do not exceed the EPA criteria appear in **green** text.

Media	Persistence		Bioaccumulation	Toxicity
	Half-Life (days)	Percent in each medium	BCF	F_ChV* (mg/l)
SF1				
Water	60	 49%	3.2	47,000
Soil	120	 50%		
Sediment	540	0%		
Air	20	0%		
SF2				
Water	60	 49%	3.2	30,000
Soil	120	 51%		
Sediment	540	0%		
Air	110	0%		
PF1				
Water	38	 18%	3.2	140
Soil	75	 82%		
Sediment	340	0%		
Air	0.75	0%		
SF3				
Water	180	 5%	180	Not estimated
Soil	360	 94%		
Sediment	1,600	 1%		
Air	1.9	0%		
SF4				
Water	180	 5%	91	Not Estimated
Soil	360	 94%		
Sediment	1,600	 1%		
Air	0.67	0%		
PFBS				
Water	180	 18%	3.2	130
Soil	360	 79%		
Sediment	1,600	0%		
Air	120	 2%		
PFOS				
Water	180	 1%	56	0.09*
Soil	360	 51%		
Sediment	1,600	 48%		
Air	120	 1%		

* The predicted water solubility, 0.0031 mg/l, is less than the estimated ChV, 0.09 mg/l. There may be [no effect at saturation](#).

Table 2. Environmental fate properties predicted utilizing the EPA PBT profiler for the PAG counterions. See footnotes on Table 3.

		<u>Persistence</u>		<u>Bioaccumulation</u>	<u>Toxicity</u>
<u>Media</u>	<u>Half-Life</u> (days)	Percent in each medium		<u>BCF</u>	<u>F_ChV*</u> (mg/l)
<u>Potassium triphenylsulfonium</u>					
Water	38	□	6%	3,000	0.028
Soil	75	▬	61%		
Sediment	340	▬	33%		
Air	12	□	0%		
<u>Potassium diphenyliodonium</u>					
Water	38	□	12%	100	1.4
Soil	75	▬	87%		
Sediment	340	□	1%		
Air	5.8	□	0%		

* F ChV= Chronic Fish toxicity values

Table 3. Summary of the estimates of the persistence, bioaccumulation, and chronic fish toxicity potential of non-PFOS/PFAS PAG anions and their typical counter ions as determined using the EPA PBT Profiler. The EPA criteria are summarized in the footnote.

PBT Profiler Estimate	PBT Color code ¹	Persistence ²	Bioaccumulation ³	Fish- Chronic Toxicity ⁴
PAG anions				
SF1	PBT	+	—	—
SF2	PBT	+	—	—
PF1	PBT	+	—	—
PFBS	PBT	+	—	—
PFOS	PBT	+	—	—
SF3	PBT	++	—	Not calculated
SF4	PBT	++	—	Not calculated
Counter ions				
Diphenyliodonium (K ⁺)	PBT	+	--	+
Triphenylsulfonium (K ⁺)	PBT	+	+	++

¹ Orange or red implies that the corresponding EPA criterion has been exceeded.

² (—) No persistent; half-life in water, soil, and sediment < 60 d, and half-life in air < 2 d; (+) persistent; half-life in water, soil, and sediment ≥ 60 d, and half-life in air ≥ 2 d; (++) very persistent; half-life in water, soil, and sediment ≥ 180 d.

³ (—) No bioaccumulative; bioconcentration factor or BCF < 1000; (+) bioaccumulative; 1000 ≥ BCF > 5000; (++) very bioaccumulative; BCF ≥ 5000.

⁴ (—) Low concern; chronic value (ChV) for fish > 10 mg/l or no effect at saturation; (+) concern; fish ChV = 0.1-10 mg/l; (++) high concern; fish ChV < 0.1 mg/l. ChV is the same as the chronic no effect concentration (NEC).

References

- [1] Ayothi, R., C.K. Ober, "A Perspective on perfluorooctyl sulfonate (PFOS) and an overview of non-PFOS based photoacid generators (PAGs): Design, synthesis and performance", *Proc. 12th Annual Int. Semiconductor ESH Conf.*, June 18 - 24, 2005, Portland, OR.
- [2] Field J.A., R. Sierra-Alvarez, "Biodegradability of chlorinated solvents and related chlorinated aliphatic compounds". *Reviews Environ. Sci. Biotechnol.*. (2004) 3, 185–254.
- [3] Li, N.Y., Ragheb, K., Lawler, G., Sturgis, J., Rajwa, B., Melendez, J.A., Robinson, J.P., 2003. "DPI induces mitochondrial superoxide-mediated apoptosis." *Free Radical Biology and Medicine* 34, 465-477.
- [4] Pineres, M.A.R., Ellis, W.C., Wu, G., Ricke, S.C., 1997. "Effects of diphenyliodonium chloride on proteolysis and leucine metabolism by rumen microorganisms." *Animal Feed Science and Technology* 65, 139-149.
- [5] Riganti, C., Gazzano, E., Polimeni, M., Costamagna, C., Bosia, A., Ghigo, D., 2004. "Diphenyleneiodonium inhibits the cell redox metabolism and induces oxidative stress." *Journal of Biological Chemistry* 279, 47726-47731.
- [6] Shiemke, A.K., Arp, D.J., Sayavedra-Soto, L.A., 2004. "Inhibition of membrane-bound methane monooxygenase and ammonia monooxygenase by diphenyliodonium: Implications for electron transfer." *Journal of Bacteriology* 186, 928-937.