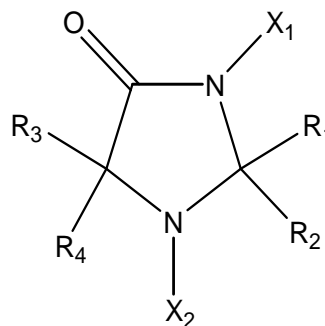
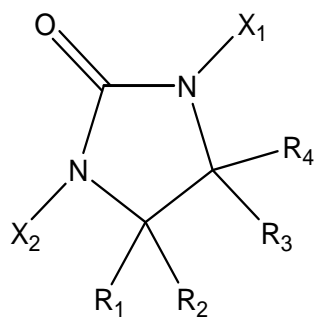
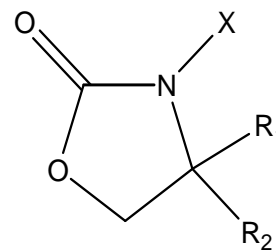
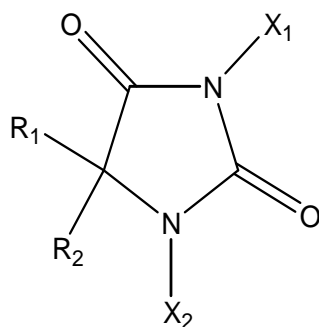
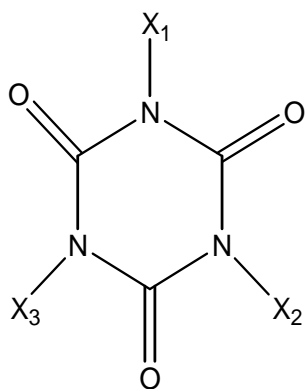


Effect of Phenyl Derivatization on N-halamine Antimicrobial Siloxane Coatings

S. D. Worley,* H. B. Kocer, A. Akdag, R. M. Broughton,
O. Acevedo, and T. S. Huang

Department of Chemistry and Biochemistry
Auburn University

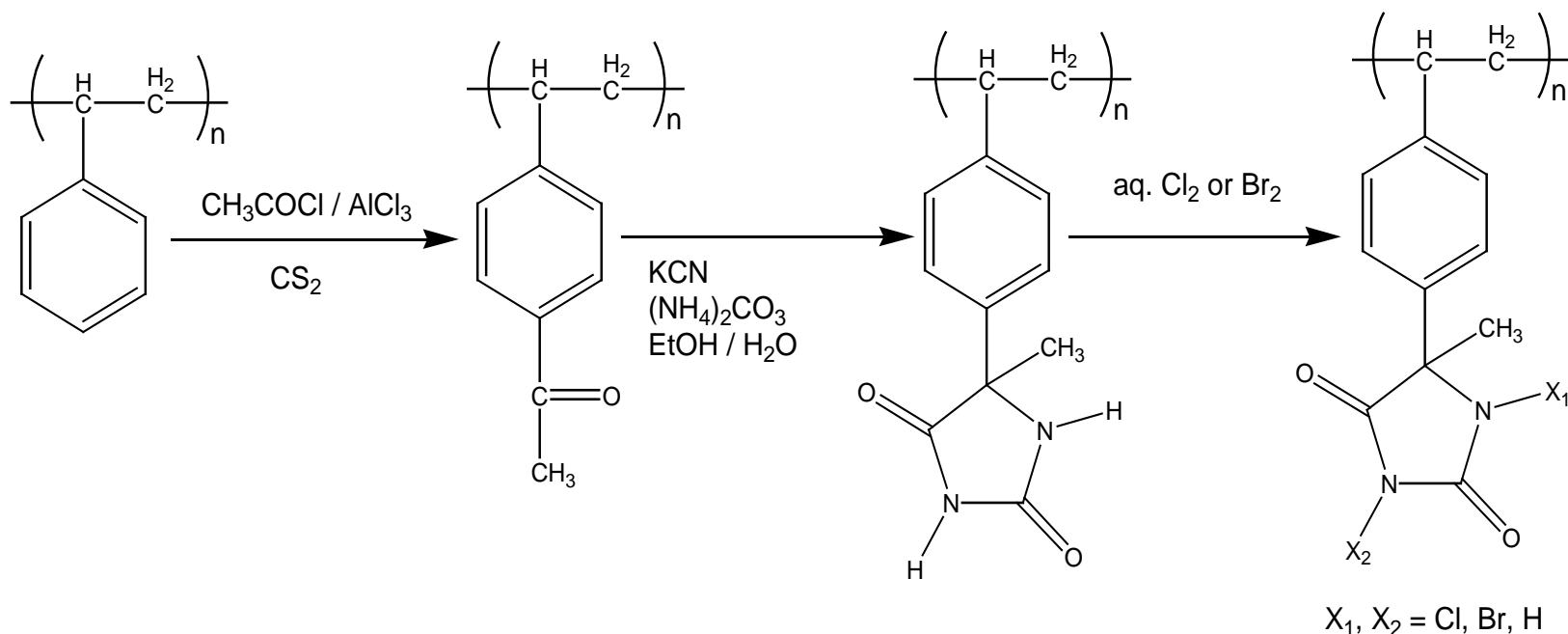
N-Halamine Structures



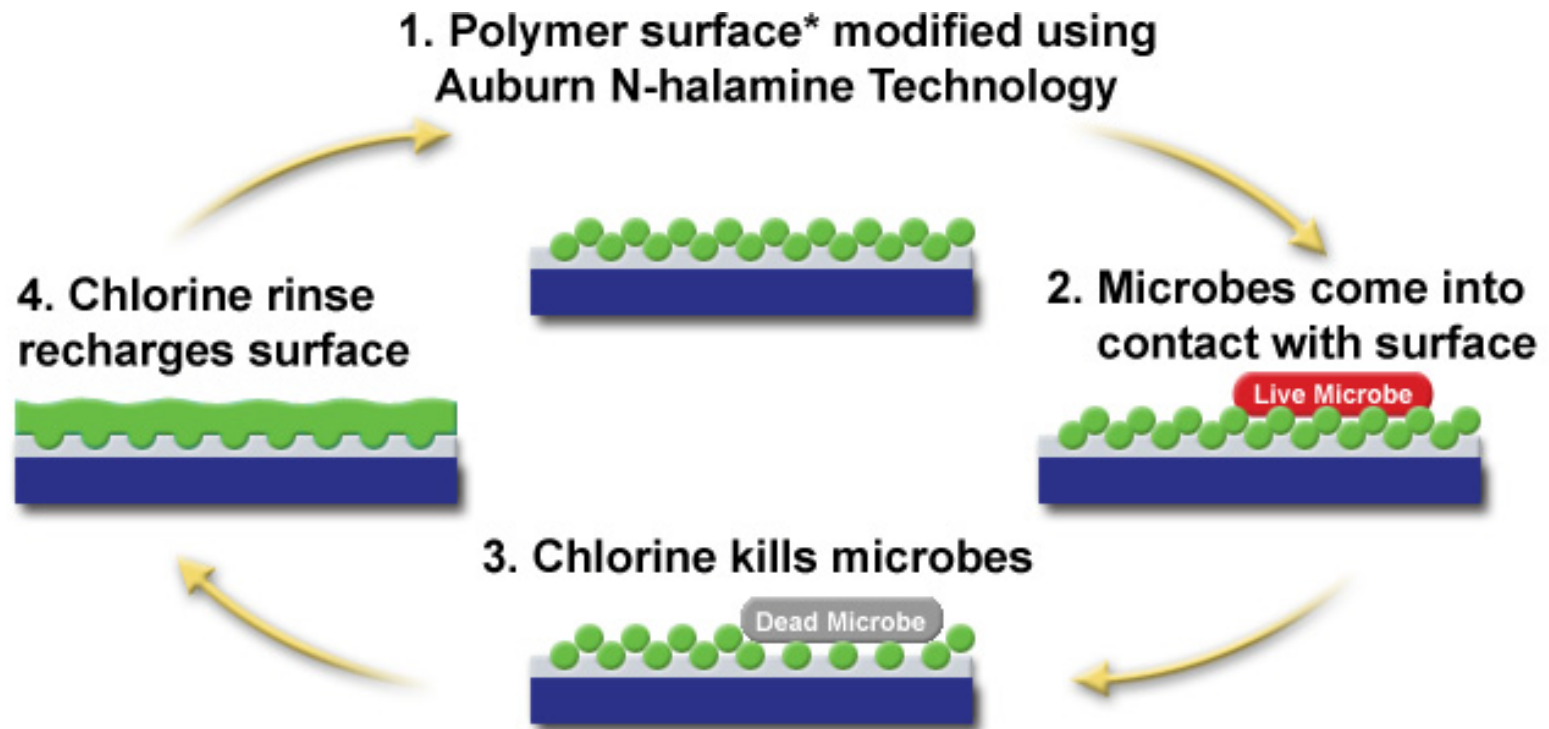
Methods of Producing Contact Biocidal Polymers

- Physical blends of active biocides and polymeric moieties
- Polymerization or copolymerization of a biocidal monomer
- Functionalization of a commercial polymer
e.g., Bond hydantoin group onto polystyrene as shown in the next figure

Using Polystyrene as the Commercial Polymer: Derivatization to Hydantoinyl PS

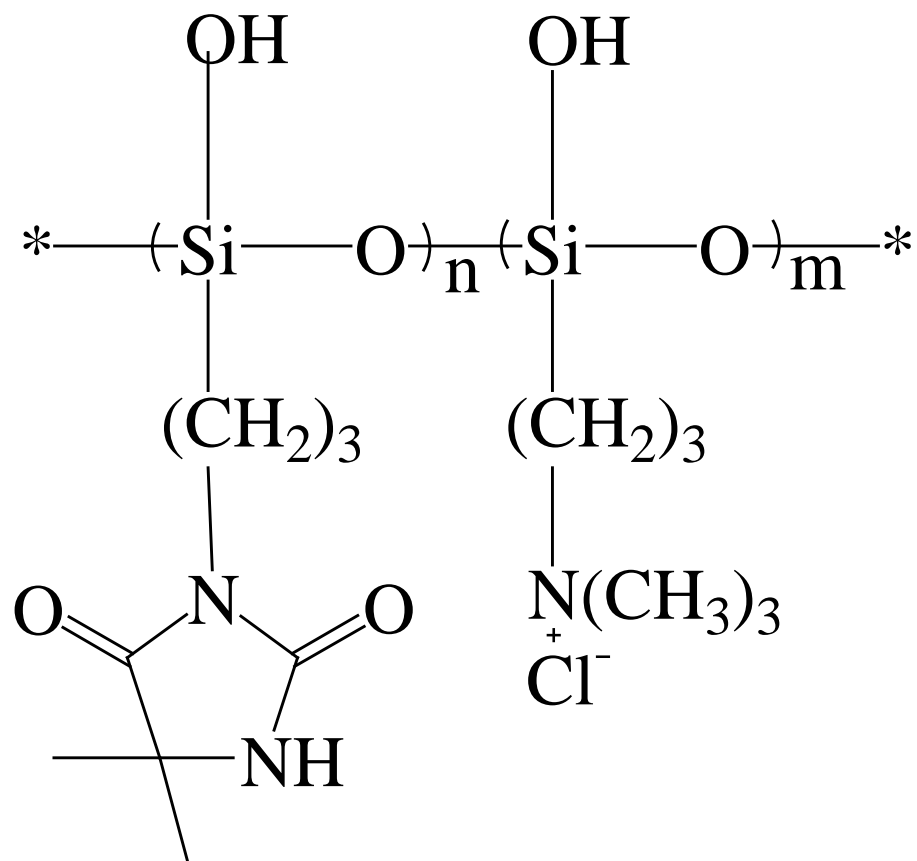


Polymers Functionalized with N-halamine Moieties at Auburn University

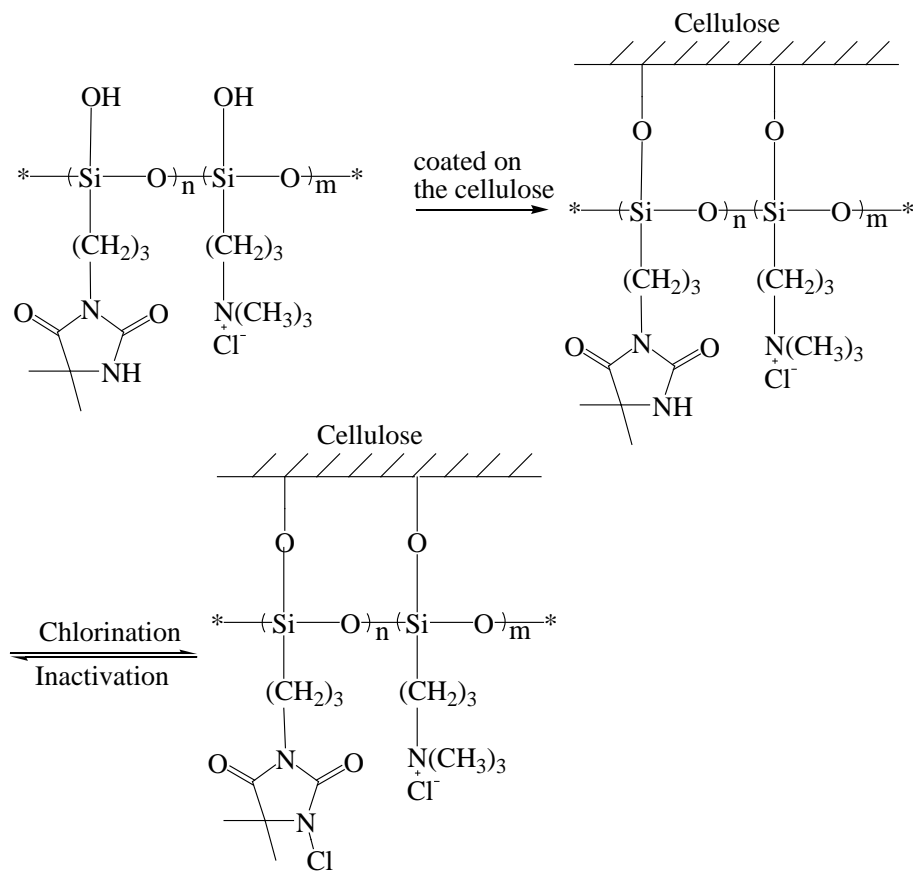


* Polystyrene, Cellulose, PET, Nylon, Polyurethanes, Polysiloxanes, Rubber

Structure of a Quat/hydantoinyl Siloxane Copolymer

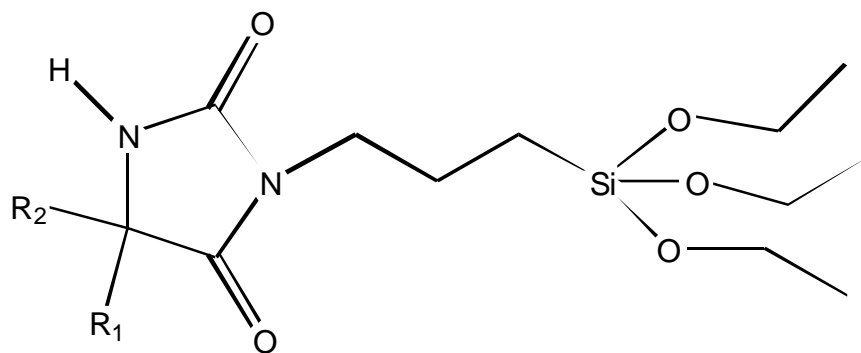


Deposition of the hydantoinyl/quat copolymer onto cellulose and inactivation after chlorination



Siloxanes and model compounds studied in this work

A



R₁ / R₂

Methyl / Methyl

Methyl / Phenyl

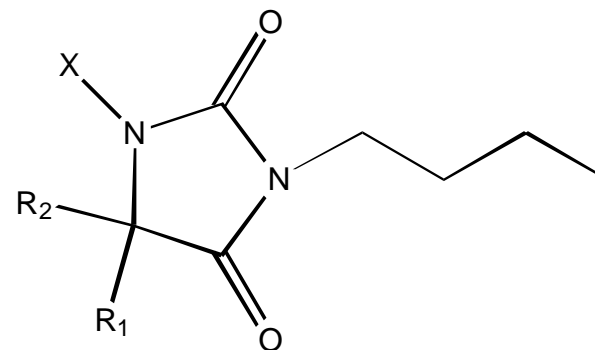
Phenyl / Phenyl

MM

MP

PP

B



X=H

MMm

MPm

PPm

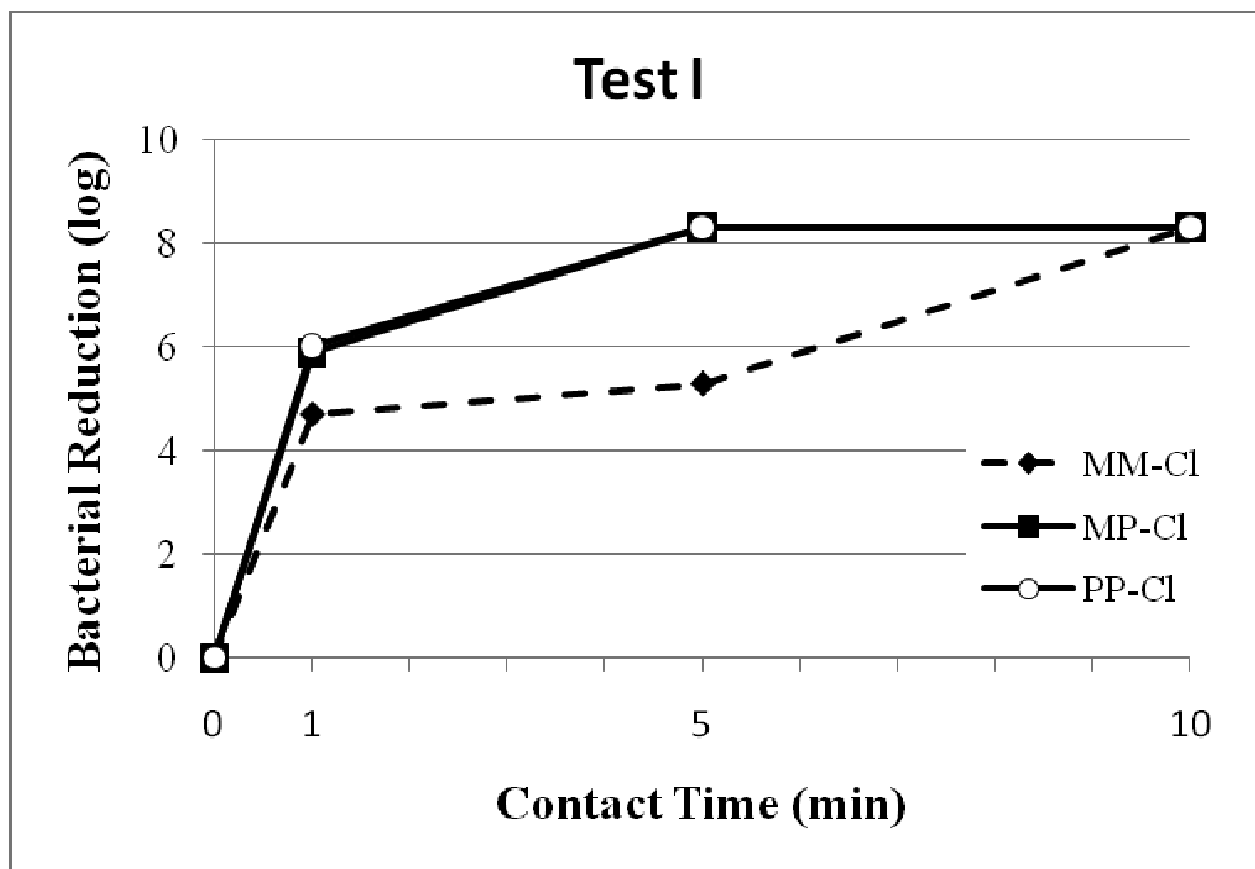
X=Cl

MMm-Cl

MPm-Cl

PPm-Cl

Antimicrobial efficacies of 5-substituted hydantoinylsiloxanes against *E. coli* O157:H7; total bacteria: 2.10×10^8 (8.32 logs); chlorine loadings on the coated swatches (MM-Cl, MP-Cl, PP-Cl) were 0.31, 0.32, and 0.29 %.



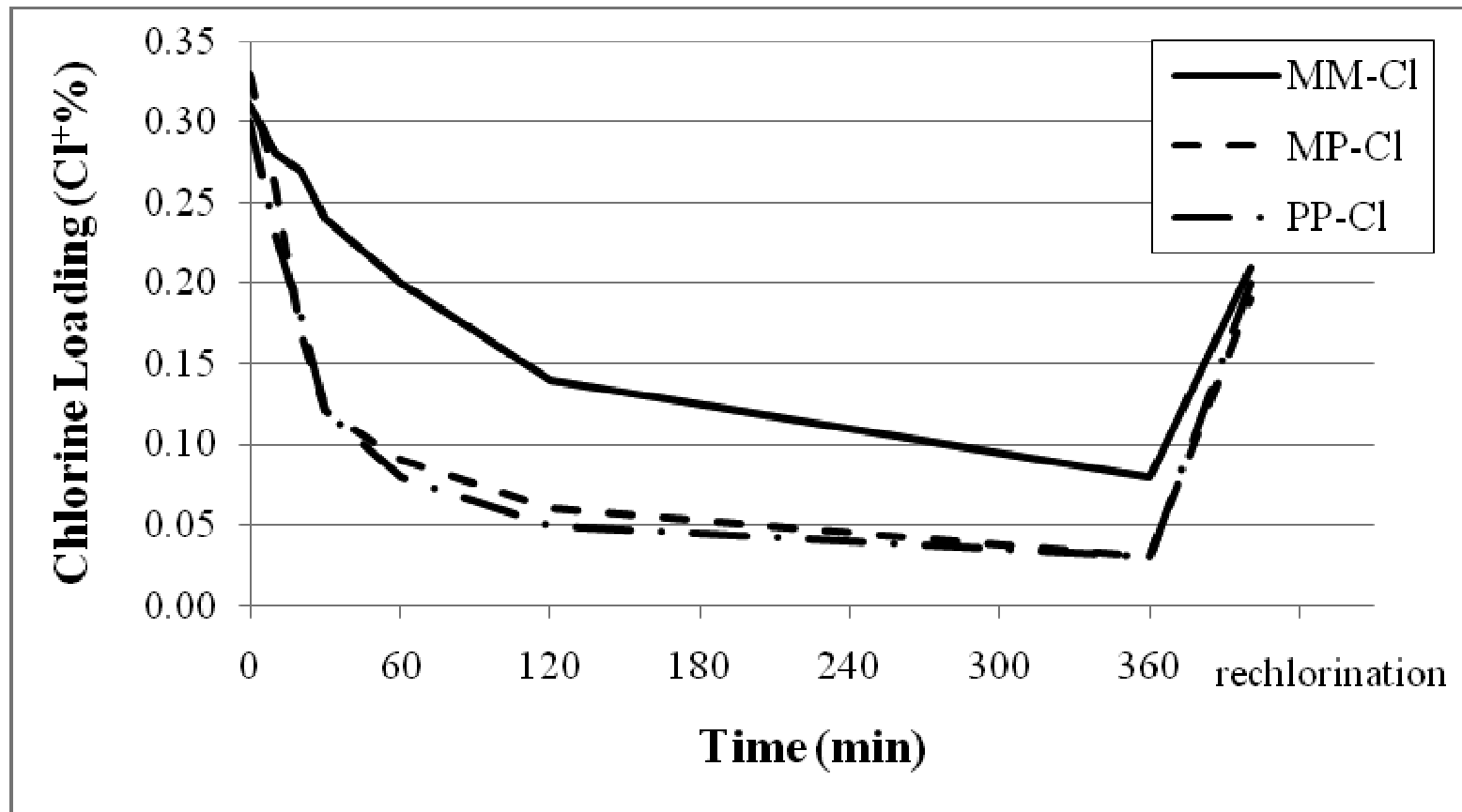
Stability toward washing of cotton coated with derivatized hydantoinyl siloxanes (Cl⁺% remaining)

	MM			MP			PP		
Machine washes	X ^a	Y ^a	Z ^a	X	Y	Z	X	Y	Z
0	0.39	0.39		0.38	0.38		0.41	0.41	
5	0.21	0.24	0.07	0.12	0.17	0.10	0.12	0.19	0.17
10	0.16	0.21	0.05	0.06	0.12	0.07	0.09	0.18	0.16
25	0.11	0.13	0.03	0.03	0.08	0.05	0.06	0.14	0.14
50	0.08	0.09	0.03	0.01	0.05	0.04	0.01	0.07	0.06

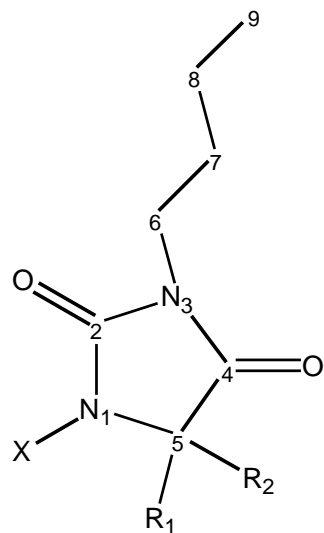
^a X: Chlorinated before washing, Y: Chlorinated before washing and rechlorinated after washing, Z: Unchlorinated before washing, but chlorinated after washing.

^b The error in the measured Cl⁺ weight percentage values was ± 0.01 .

Stability toward UVA light exposure of cotton coated with derivatized hydantoinyl siloxanes (Cl⁺% remaining).



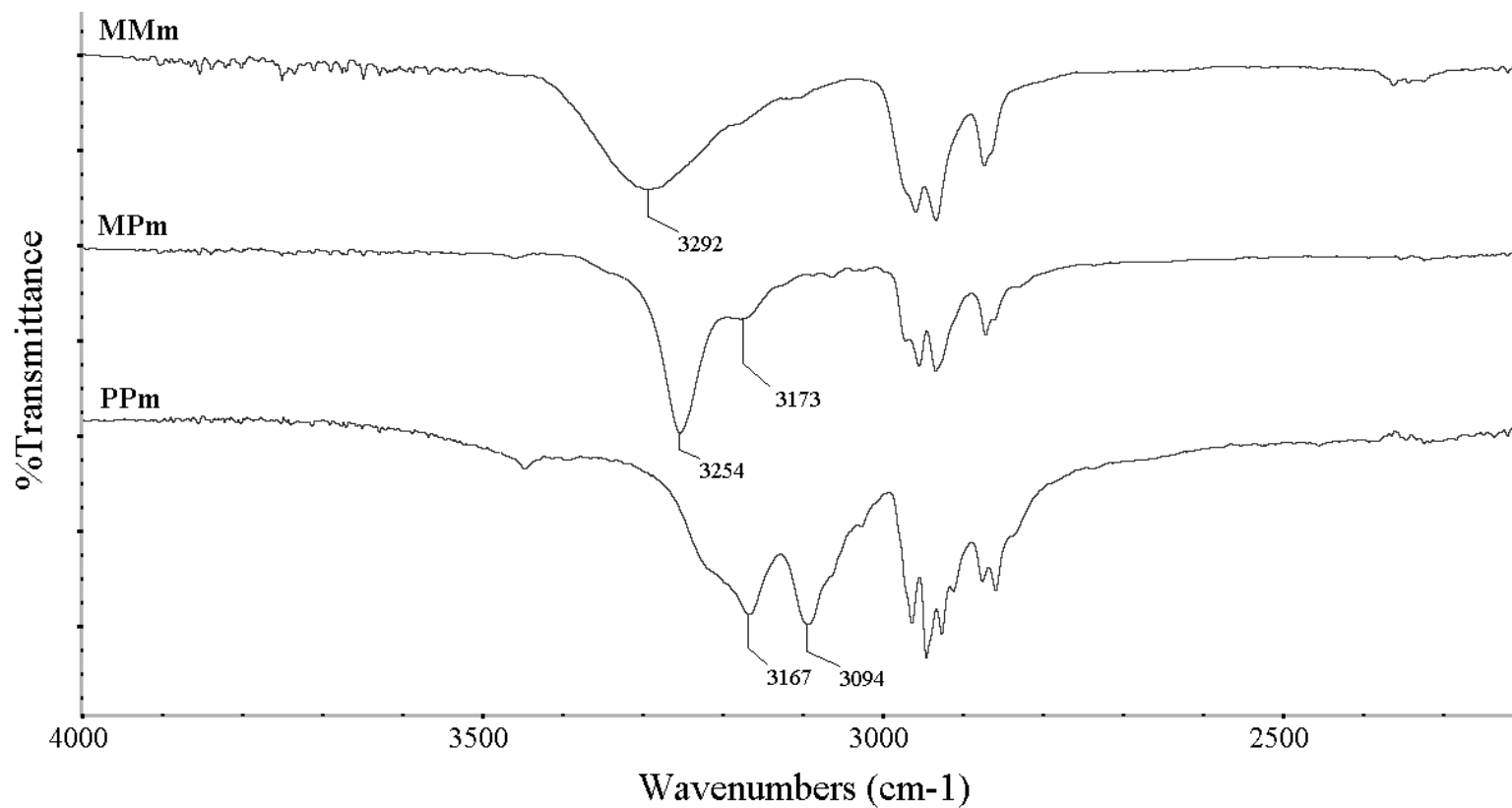
Structures of the synthesized model compounds



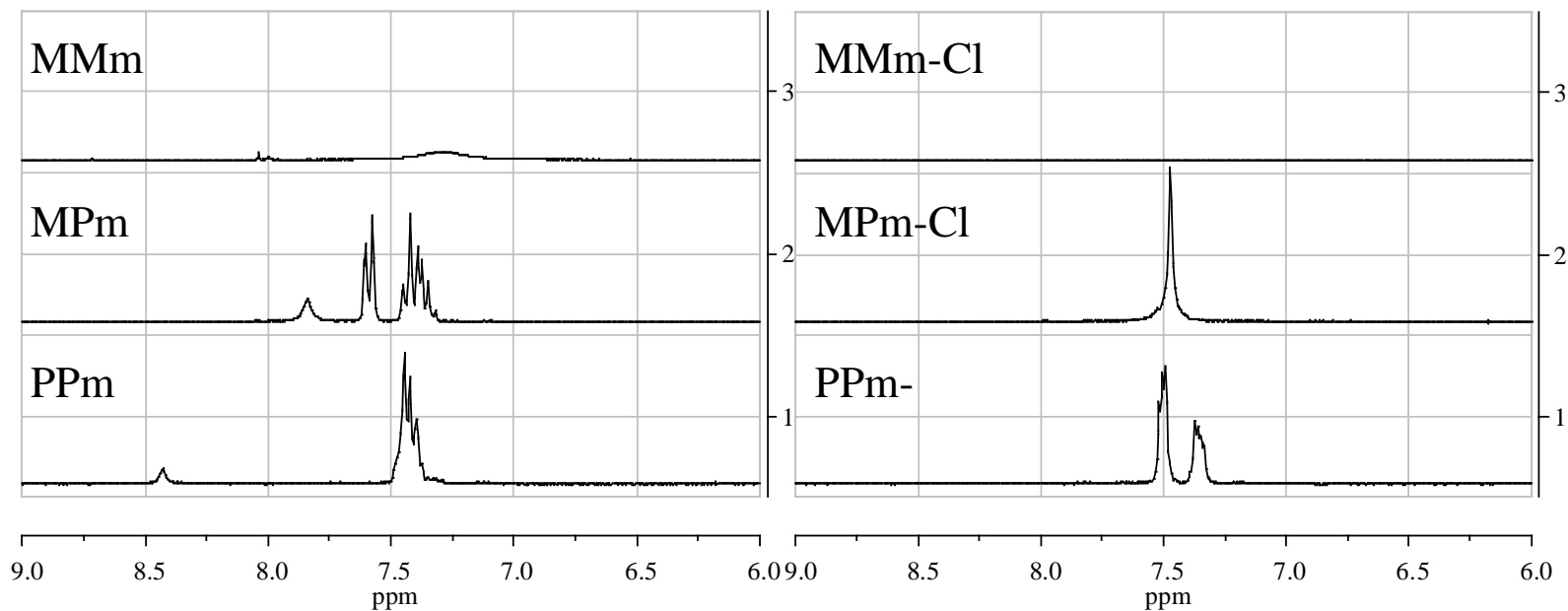
X= H, Cl

	MMm	MPm	PPm
R ₁	methyl	methyl	phenyl
R ₂	methyl	phenyl	phenyl

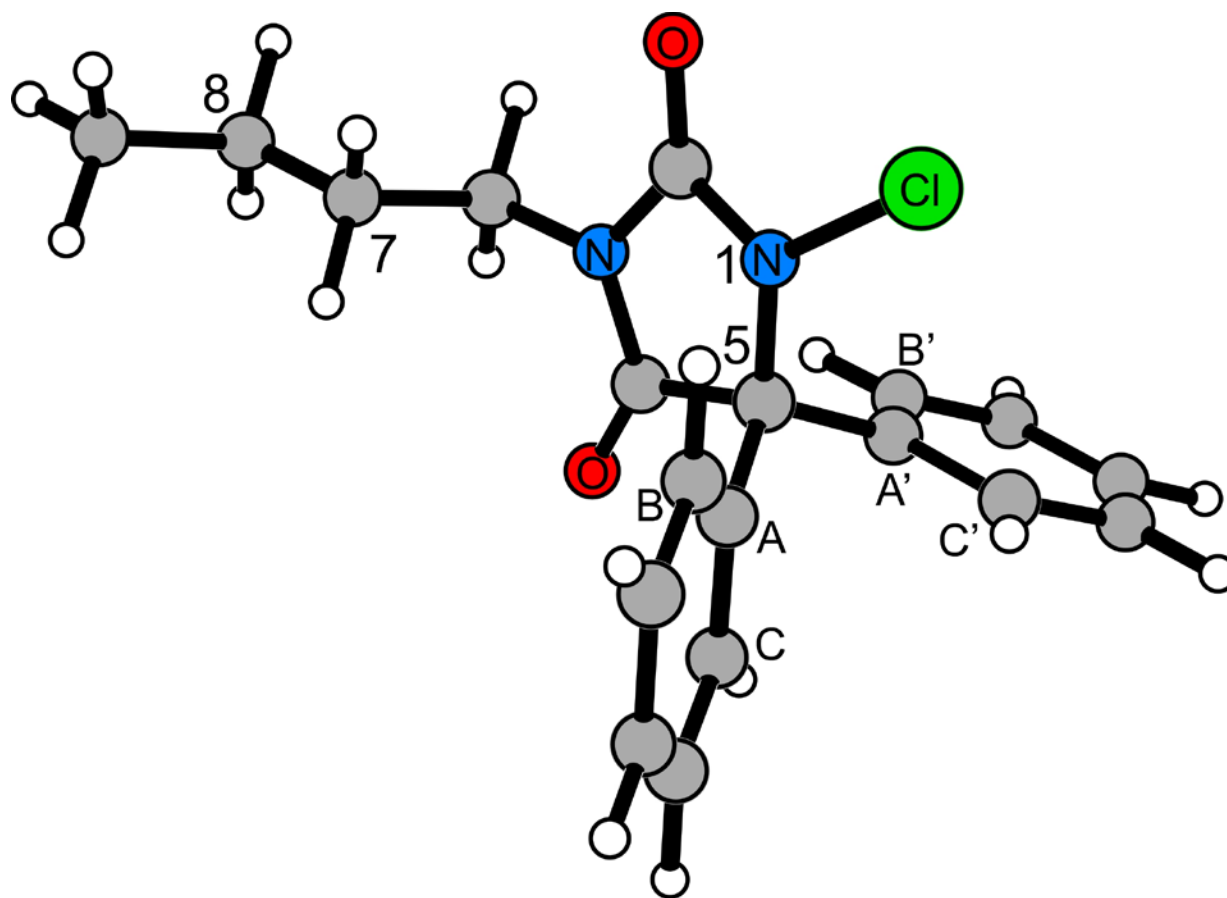
FTIR spectra of the model compounds in the N-H and C-H stretching region



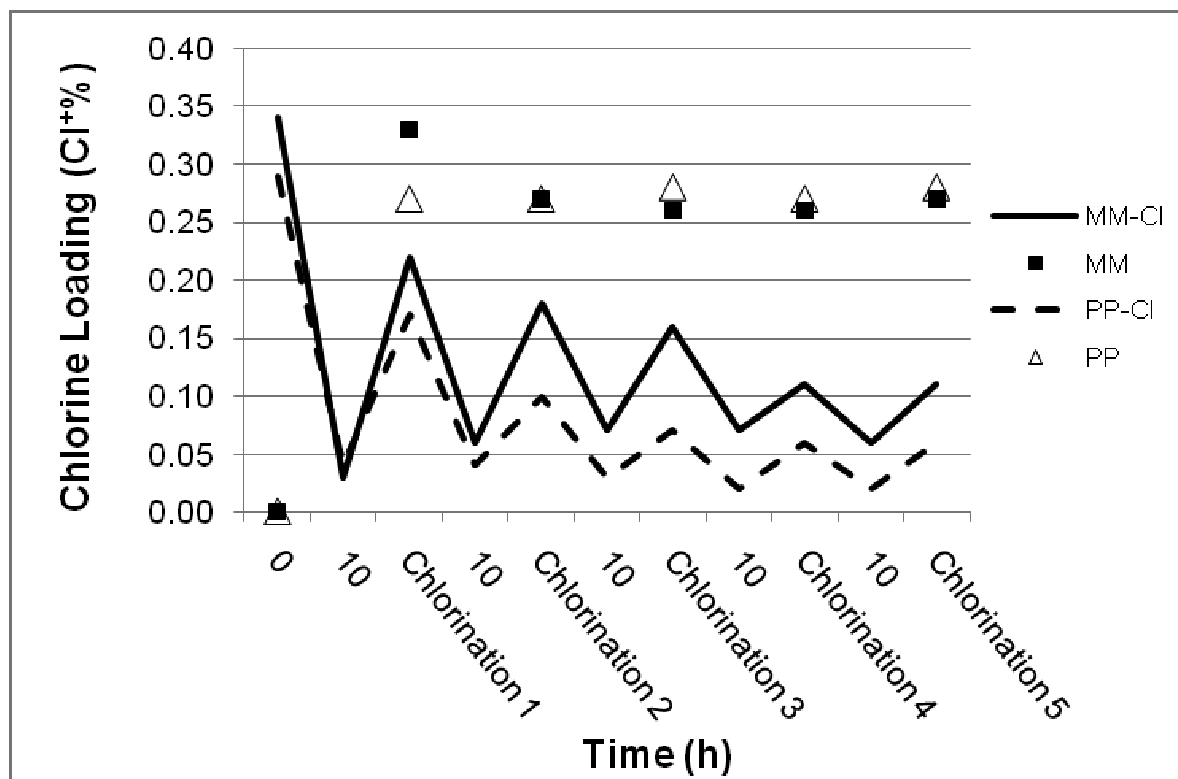
^1H NMR spectra of the model compounds before and after chlorination (the aromatic region; the solvent was acetone- d_6)



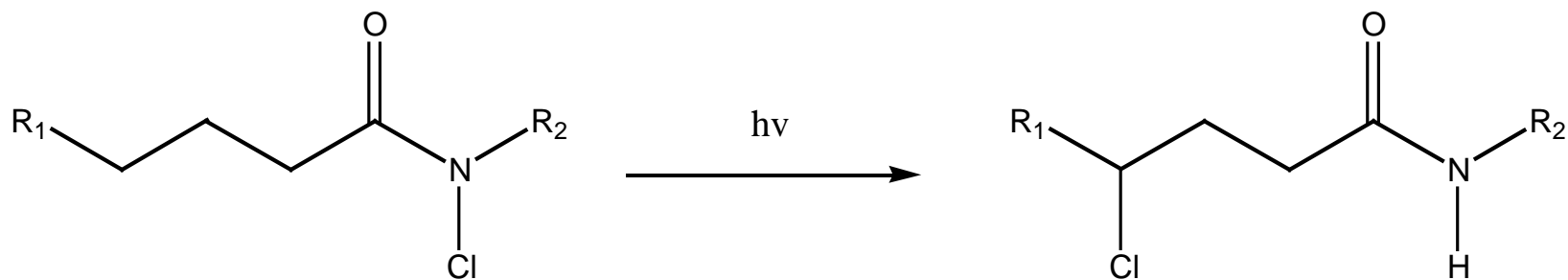
5,5-Diphenyl-3-butyldantoin with Cl bonded at the N₁ position optimized at the B3LYP/6-311+G(2d,p) level of theory



Stability toward repeated UVA light exposure of cotton coated with derivatized hydantoinyl siloxanes MM-Cl and PP-Cl (Cl⁺% remaining) following a series of rechlorinations

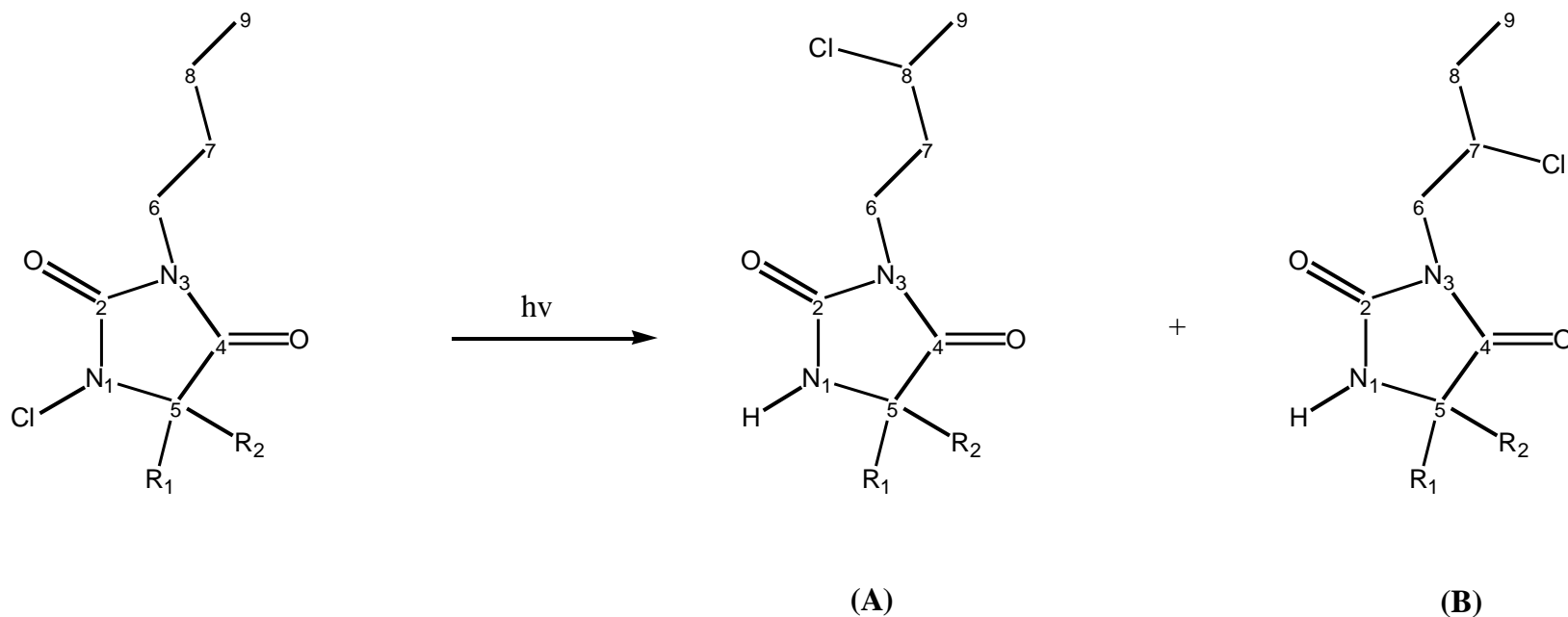


Intramolecular photorearrangement of acyclic N-halamides (1,5-hydrogen atom transfer), the Hoffmann-Loeffler rearrangement

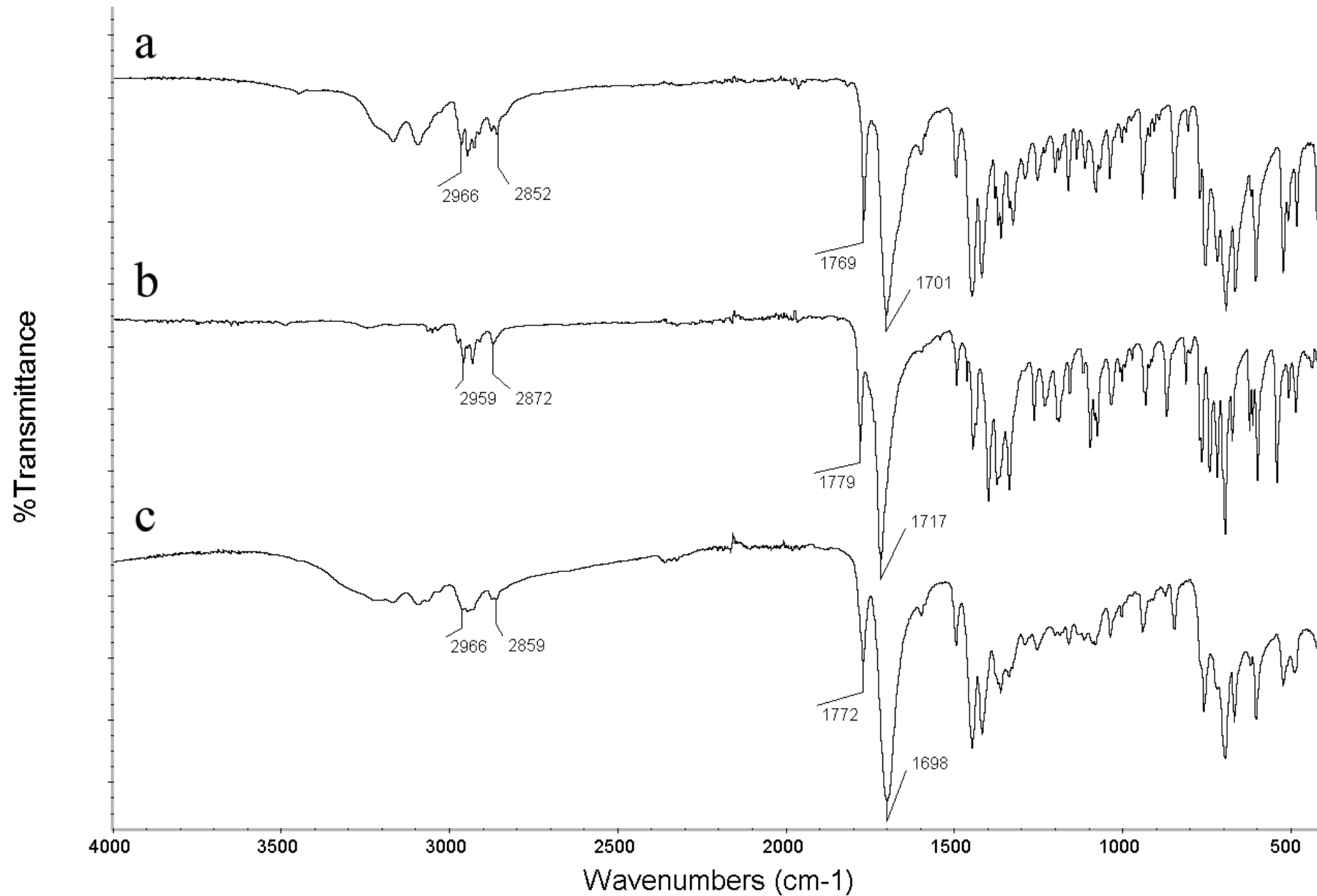


$R_1 = R_2 = \text{alkyl}$

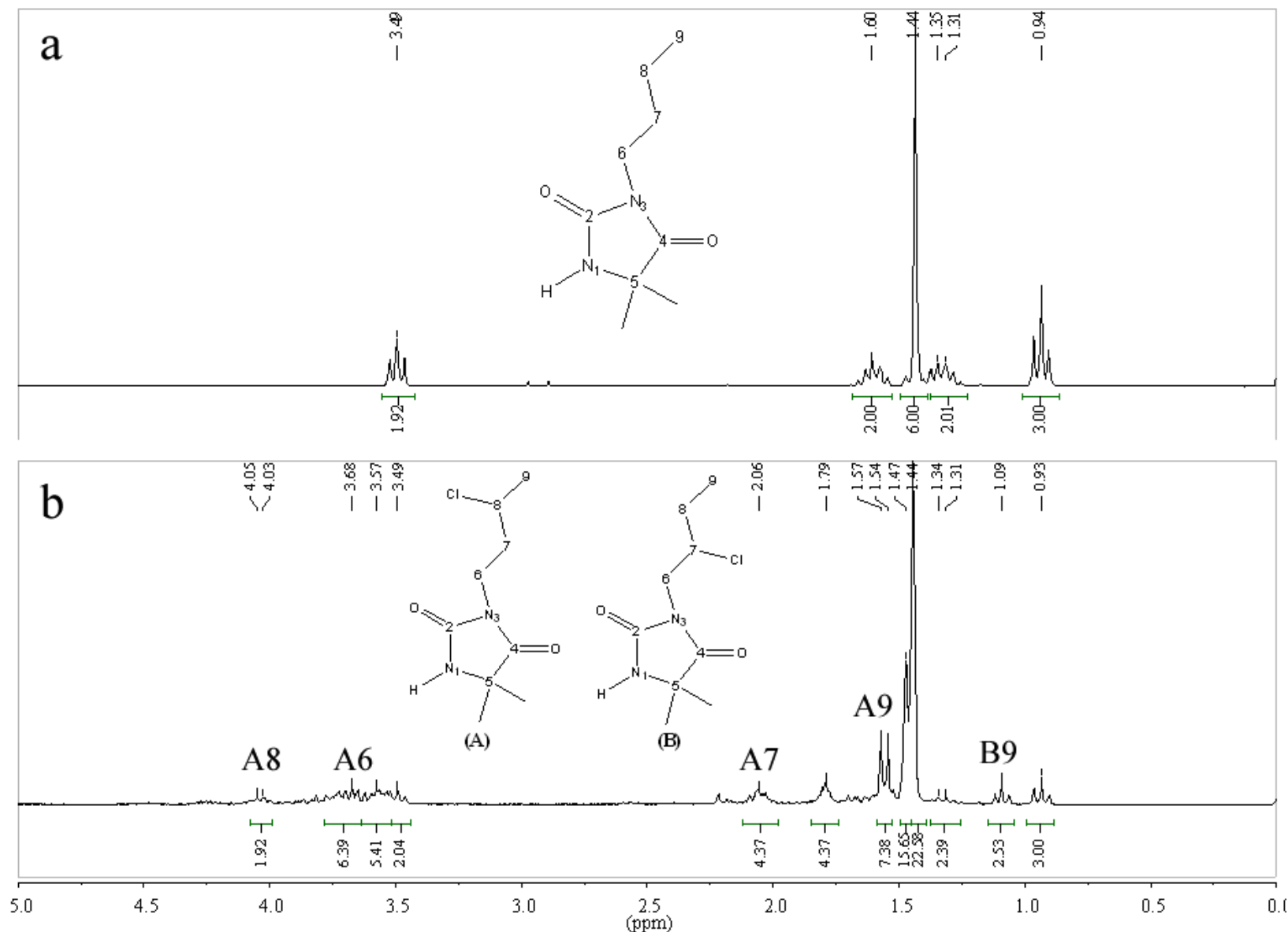
Possible photolytic rearrangements for 3-butyl-1-chlorohydantoin



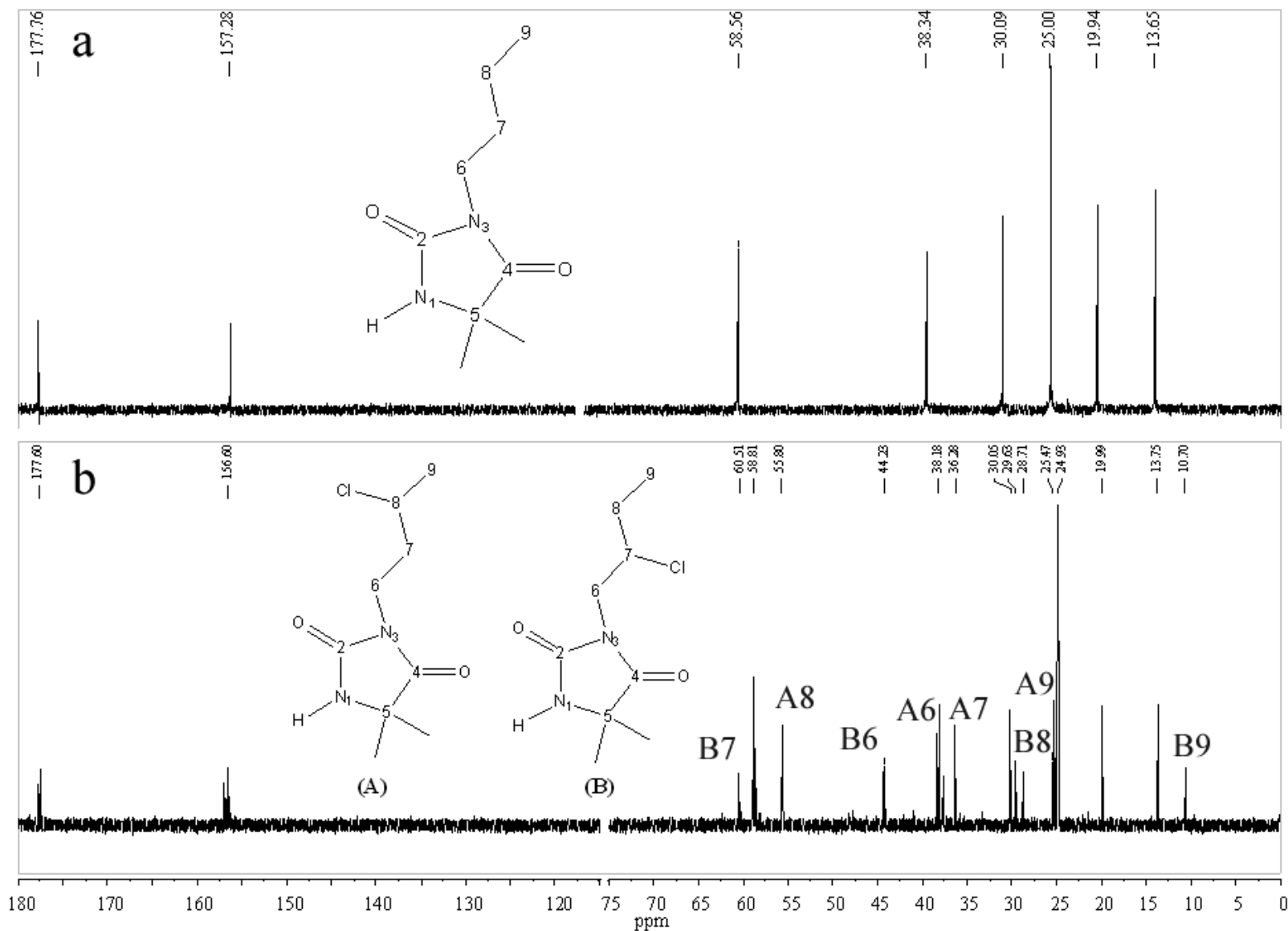
FTIR Spectra of (a) MMm, (b) MMm-Cl, and (c) UV irradiated MMm-Cl



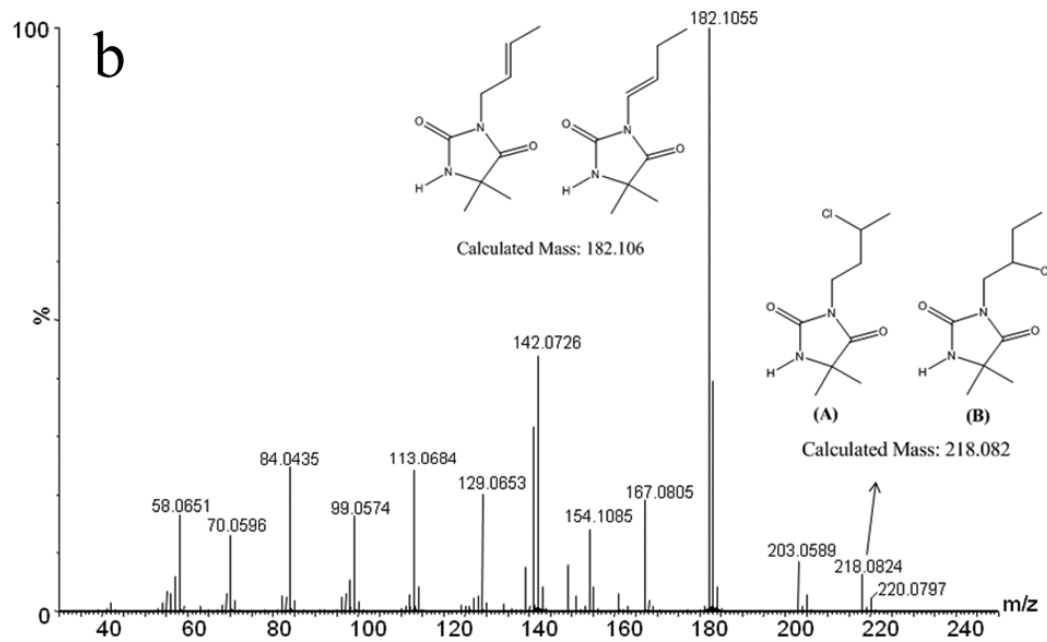
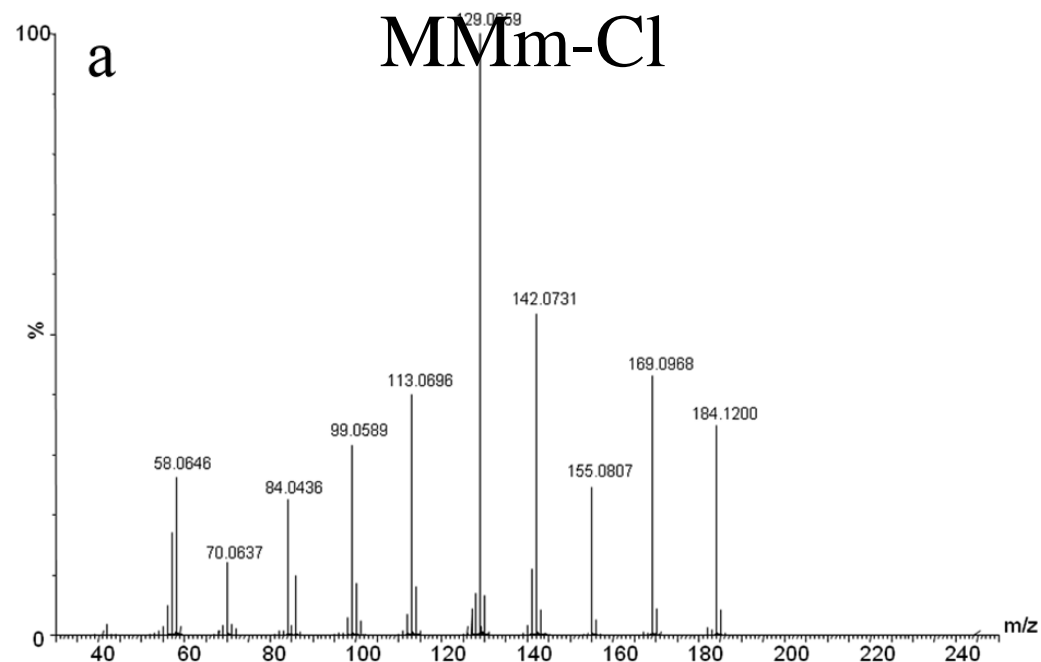
The ^1H NMR spectra of (a) MMm and (b) UVA light-irradiated MMm-Cl; the solvent was CDCl_3



The ^{13}C NMR spectra of (a), MMm and (b) UVA-light-irradiated MMm-Cl; the solvent was CDCl_3

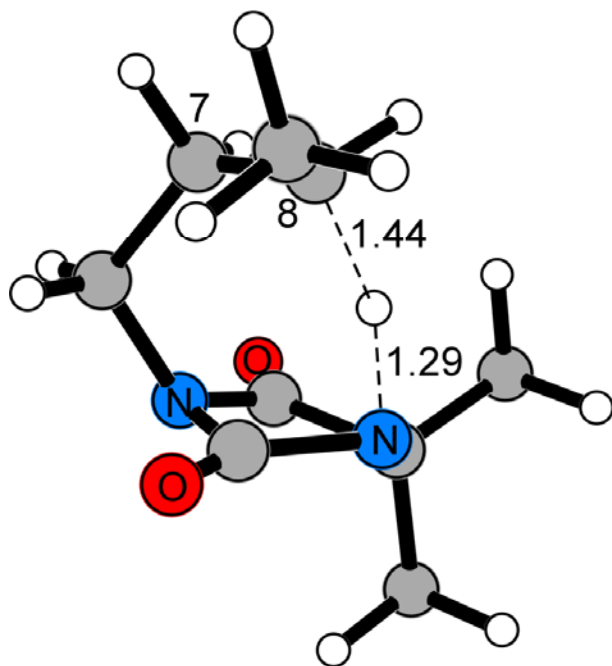


GC/MS spectra of (a) MMm and (b) UVA-irradiated

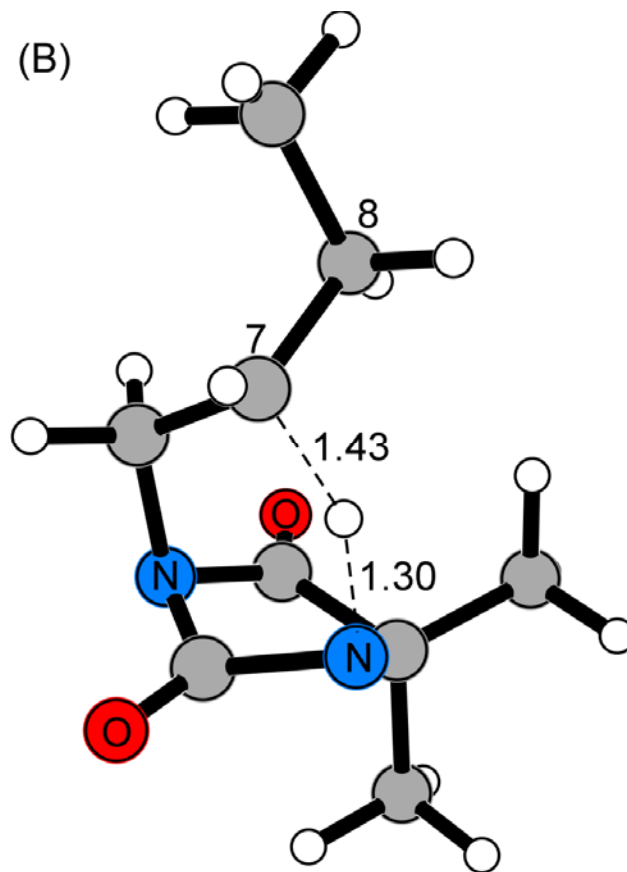


Transition structures at the UB3LYP/6-311++G(2d,p) theory level for the 1,6- and 1,5-hydrogen atom transfers between atoms (A) C₈ and N₁ and (B) C₇ and N₁ in the MMm radical; distances in angstroms

(A)



(B)

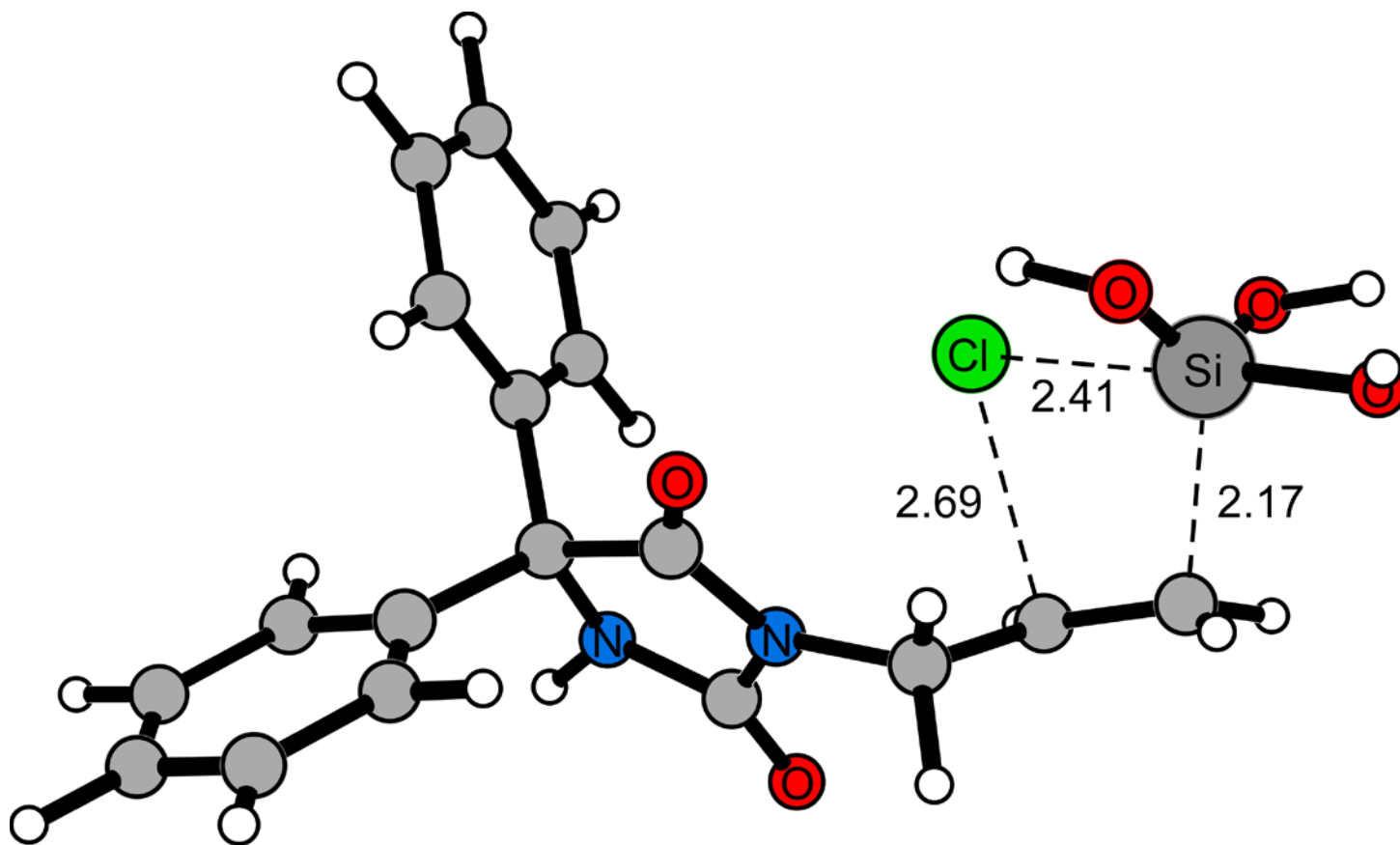


Calculated bond dissociation enthalpy (BDE) for the N₁-Cl bond in MMm-Cl and activation enthalpies, ΔH^\ddagger , for the 1,5- and 1,6-proton transfers in MMm radical^a

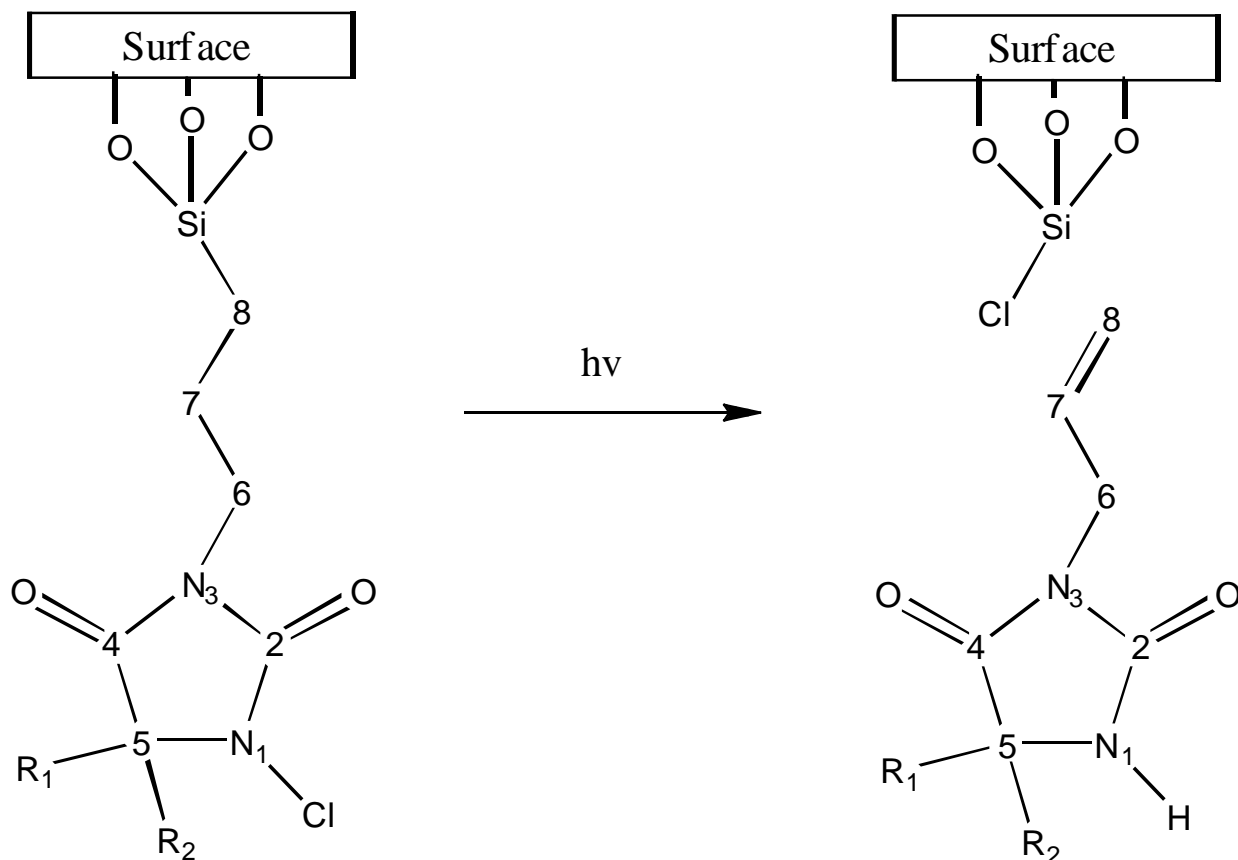
	BDE (N₁-Cl)	ΔH^\ddagger (1,5-H)	ΔH^\ddagger (1,6-H)
MMm	50.5	52.9	38.2

^a Enthalpies (in kcal/mol) computed at the UB3LYP/6-311++G(2d,p) theory level. 1,5-proton transfer between atoms C₇ and N₁ and 1,6-proton transfer between atoms C₈ and N₁.

Transition structure at the UB3LYP/6-311++(2d,p) theory level for the cleavage of the 7-chloro-5,5-diphenylhydantoin siloxane model (PPSi-Cl); distances in angstroms



Loss of antimicrobial efficacy from the siloxane surface



CONCLUSIONS

- Phenyl derivatization at the 5-position on the hydantoin ring of an N-chlorohydantoinyl silane or siloxane weakens the N-Cl bond relative to that of the 5,5-dimethyl derivative.
- The bond weakening is probably the result of a through-space interaction between the Cl atom and the pi-electron system of the aromatic rings.
- UVA degradation of the hydantoinyl siloxane is caused by homolytic rupture of the N-Cl bond, followed by hydrogen atom transfer from the alkylsilyl chain, resulting in chlorination on the chain, and subsequent cleavage of the hydantoinyl moiety from the surface.
- This process which occurs gradually renders the surface incapable of rechlorination, and hence the gradual loss of antimicrobial efficacy.

ACKNOWLEDGMENT

- This work was supported by the US Air Force.