Effect of Phenyl Derivatization on N-halamine Antimicrobial Siloxane Coatings

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

1. Polymer surface* modified using Auburn N-halamine Technology

4. Chlorine rinse recharges surface

2. Microbes come into contact with surface

3. Chlorine kills microbes

* 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

B

R₁ / R₂
Methyl / Methyl  MM
Methyl / Phenyl  MP
Phenyl / Phenyl  PP

X=H
MMm
MPm
PPm

X=Cl
MMm-Cl
MPm-Cl
PPm-Cl
Antimicrobial efficacies of 5-substituted hydantoinysiloxanes against E. coli O157:H7; total bacteria: $2.10 \times 10^8$ (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)

<table>
<thead>
<tr>
<th>Machine washes</th>
<th>MM</th>
<th>MP</th>
<th>PP</th>
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</thead>
<tbody>
<tr>
<td></td>
<td>Xᵦ</td>
<td>Yᵦ</td>
<td>Zᵦ</td>
</tr>
<tr>
<td>0</td>
<td>0.39</td>
<td>0.39</td>
<td>0.38</td>
</tr>
<tr>
<td>5</td>
<td>0.21</td>
<td>0.24</td>
<td>0.07</td>
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<td>10</td>
<td>0.16</td>
<td>0.21</td>
<td>0.05</td>
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<td>0.11</td>
<td>0.13</td>
<td>0.03</td>
</tr>
<tr>
<td>50</td>
<td>0.08</td>
<td>0.09</td>
<td>0.03</td>
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<tr>
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<td>X</td>
<td>Y</td>
<td>Z</td>
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<tr>
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<td>0.38</td>
<td>0.38</td>
<td>0.41</td>
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<td>0.12</td>
<td>0.17</td>
<td>0.10</td>
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<tr>
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<td>0.06</td>
<td>0.12</td>
<td>0.07</td>
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<tr>
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<td>0.03</td>
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<td>0.14</td>
<td>0.14</td>
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<tr>
<td>50</td>
<td>0.01</td>
<td>0.07</td>
<td>0.06</td>
</tr>
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</table>

ᵦ 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

<table>
<thead>
<tr>
<th>R_1</th>
<th>MMm</th>
<th>MPm</th>
<th>PPm</th>
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<tr>
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<td>phenyl</td>
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<td>phenyl</td>
<td>phenyl</td>
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FTIR spectra of the model compounds in the N-H and C-H stretching region
$^1$H NMR spectra of the model compounds before and after chlorination (the aromatic region; the solvent was acetone-d$_6$)
5,5-Diphenyl-3-butylhydantoin with Cl bonded at the N$_1$ 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

\[ \text{hv} \]

\[ R_1 = R_2 = \text{alkyl} \]
Possible photolytic rearrangements for 3-butyl-1-chlorohydantoin

(A) + (B)
FTIR Spectra of (a) MMm, (b) MMm-Cl, and (c) UV irradiated MMm-Cl
The $^1$H NMR spectra of (a) MMMm and (b) UVA light-irradiated MMMm-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) MMMm and (b) UVA-irradiated MMMm-Cl

Calculated Mass: 182.106

Calculated Mass: 218.082
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.
Calculated bond dissociation enthalpy (BDE) for the N$_1$-Cl bond in MMMm-Cl and activation enthalpies, $\Delta H^\ddagger$, for the 1,5- and 1,6-proton transfers in MMMm radical$^a$

<table>
<thead>
<tr>
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<th>BDE (N$_1$-Cl)</th>
<th>$\Delta H^\ddagger$ (1,5-H)</th>
<th>$\Delta H^\ddagger$ (1,6-H)</th>
</tr>
</thead>
<tbody>
<tr>
<td>MMMm</td>
<td>50.5</td>
<td>52.9</td>
<td>38.2</td>
</tr>
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</table>

$^a$ Enthalpies (in kcal/mol) computed at the UB3LYP/6-311++G(2d,p) theory level. 1,5-proton transfer between atoms C$_7$ and N$_1$ and 1,6-proton transfer between atoms C$_8$ and N$_1$. 
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.