Thermally Stable Antimicrobial Polyvinylchloride/Maleimido Aromatic Hydrazide Composites

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Antimicrobial novel substituted maleimido aromatic hydrazides were synthesized from N-[4-(chlorocarbonyl) phenyl] maleimide with salicylhydrazide, *p*-aminobenzohydrazide, or *p*-aminosalicylhydrazide. They were characterized by Fourier transform infrared (FTIR), hydrogen-1 nuclear magnetic resonance (^{1}H-NMR), mass spectra, elemental analyses, and antimicrobial activities. These derivatives were investigated as thermal stabilizers for rigid polyvinylchloride (PVC) at 180°C in air by measuring the rate of dehydrochlorination, the extent of discoloration, and the changes that occurred in the molecular masses of the degraded PVC samples. The previously reported stabilizing efficiency data of a nonsubstituted derivative, which was synthesized from N-[4-(chlorocarbonyl) phenyl] maleimide with benzohydrazide, is also given for comparison. The results reveal the greater stabilizing efficiency of the investigated derivatives as shown by their longer thermal stability (Ts) periods and lower dehydrochlorination rates in relation to dibasic lead carbonate, cadmium-barium-zinc stearate, and n-octyltin mercaptide industrial stabilizers. The stabilizing efficiency increases with the introduction of electron donating substituent groups in the aromatic ring of the stabilizer molecules. Moreover, the investigated stabilizers impart better color stability for the degraded samples as compared with the reference stabilizers. A synergistic effect is achieved when the materials under investigation were mixed in various weight ratios with any of the reference stabilizers, reaching its maximum at equivalent weight ratio of the investigated stabilizer to the reference one. J. VINYL ADDIT. TECHNOL., 00:000–000, 2014.

INTRODUCTION

Polyvinylchloride (PVC) has been widely used in the fields of construction materials, food package, decoration, medicine (e.g., for the fabrication of indwelling catheters in the hospital care), and commodities, such as construction tubing, films, toys, wallpaper, etc. These materials and products cannot avoid smirching with bacteria or microbes during their daily usage so that it is important to develop antibacterial PVC composites for such applications. Some attempts have been performed to prepare antibacterial PVC composites using different antibacterial nanoparticles. Zirconium phosphate containing nano-sized silver particles [1] and TiO_2/Ag^+ nanoparticles [2] were used for these studies. Further, isothiocyanate nucleophilically substituted PVC could also be used as antibacterial PVC [3].

On the other hand, PVC is known to undergo extensive degradation, especially during its molding and applications at high temperatures. Its thermal degradation occurs by an autocatalytic dehydrochlorination reaction with subsequent formation of conjugated double bonds [4]. This results in an unacceptable discoloration of the polymer and a loss of its physical and mechanical properties together with a decrease or an increase in molecular weight as a result of chain-scission or cross-linking of the polymer molecules, respectively [5–7]. It is assumed that various defect sites in the polymer chains are responsible for this instability. Possible defect structures in PVC are branching, chloroallyl groups, end groups, oxygen containing groups, head-to-head structures, and the stereo order of the monomer units (tacticity) [8–13]. Various kinds of stabilizers have been used to inhibit the thermal degradation of PVC either by reacting with the evolved hydrogen chloride gas produced as a result of the degradation process, such as basic salts [14], or by displacing the labile chlorine in PVC chains by more stable ester or mercaptide groups, such as with metallic soaps [15], esters, or mercaptides of dialkyltin [16]. Most of the mentioned stabilizers lead to the formation of heavy metal chlorides as byproducts, which will act as strong catalysts for the subsequent dehydrochlorination of PVC and may present a serious environmental problem [17, 18]. Various organic ligands have been proposed as co-stabilizers so as to react with these metal chlorides and provide more protection to the polymer [19, 20]. Recently, metal-free and environmentally acceptable fully organic stabilizers have been established for the thermal stabilization of PVC [21–23]. Because the time of fabrication of PVC is relatively short, and determination of the amount of stabilizer consumed after various processing times indicates that most of the stabilizer remains unreacted, the final product contains large amounts of heat stabilizer. For this, a new

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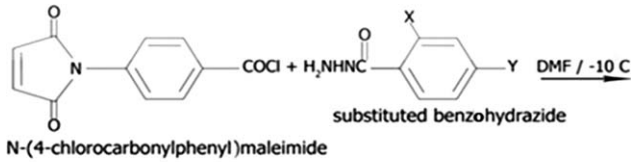

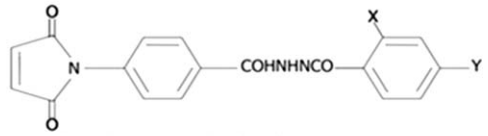

Derivative No.	1	2	3	4
X	H	OH	H	OH
Y	H	H	NH_2	NH_2

SCH. 1. Typical synthetic scheme for maleimido aromatic hydrazide derivatives.

trend has been established based on the use of thermal stabilizers of an antimicrobial nature to obtain thermally stable antimicrobial PVC composites [22, 23].

The hydrazide-hydrazone derivatives represent a class of compounds possessing a wide range of biological activities, such as antimicrobial [24], antimycobacterial [25], antitumor [26], anti-inflammatory [27], trypanocidal [28], antimalarial [29], and anti-human immunodeficiency virus (HIV) activities [30]. Important biological properties concerning bactericidal, fungicidal, and anticancer properties were also reported for N-substituted maleimides [31–36]. It is known that maleimides are inhibitors of cysteine proteinase or other proteins with an essential cysteine. Maleimides interact preferably with the hydrophobic domains of enzymes through the inactivation of sulfhydryl groups. They are usually considered as nonspecific toxic and inexpensive family of products and could be interesting candidates for the formation of new antimicrobial activity [37].

N-substituted maleimides [38] and aromatic hydrazides [39] have been proven to be effective stabilizers for PVC against thermal degradation. The stabilizing efficiency of the N-substituted maleimides are strongly affected both by the nature and position of the substituents in the aryl ring being greater for substituents of the electron donating nature and lower for those having electron withdrawing effect; with the nonsubstituted derivative being in the middle [38]. In addition, the maleimides act as powerful radical traps and can exchange the labile chlorine in the PVC chains for a more stable maleimide moiety. On the other hand, the aromatic hydrazides act mainly as hydrogen chloride gas absorbers, in addition to their ability to form metal complexes. This property enables them to react with various metal chlorides, which result as byproducts from the soap or basic salt stabilizers, thus preventing or at least minimizing their catalytic degradation effect.

In view of the above, it would be expected that maleimido aromatic hydrazide derivatives combine the characteristics of both of the maleimides and the aromatic hydrazides could greatly improve the thermal stability of PVC and could effectively inhibit the growth of bacteria and fungi. In the present study, we hereby report the synthesis, characterization, and evaluation of antibacterial and antifungal activities of some new maleimido aromatic hydrazides containing substituent groups at their aromatic rings of the hydrazide part. It is of great interest to investigate these derivatives as new types of antimicrobial agents for the stabilization of rigid PVC against thermal degradation and to obtain thermally stable antimicrobial PVC composites. The effect of the substituent group on the inhibition of the thermal degradation of rigid PVC is also investigated. Our preliminary investigation on a maleimido aromatic hydrazide derivative without a substituent group has shown its greater stabilizing efficiency of PVC against thermal degradation relative to those of the industrially known stabilizers [23].

EXPERIMENTAL

Materials

The commercial PVC (suspension) used in this study had a K-value of 70 and was supplied by Hüls Co. (Frankfurt, Germany). The cadmium-barium-zinc (Cd-Ba-Zn) stearate complex was obtained from G. Siegle and Co. (Stuttgart, Germany), the n-octyltin mercaptide (n-OTM) was obtained from America Company for PVC manufacturing (Alexandria, Egypt), the dibasic lead carbonate (DBLC) was obtained from the National Lead Co. (Darmstadt, Germany), and the *p*-aminobenzohydrazide was obtained from Nacalai Tesque (Japan) were also used in this study. N-[4-(chlorocarbonyl)phenyl] maleimide was synthesized according to the method described by Oishi and Fujimoto [40]. Benzohydrazide, salicylhydrazide, and *p*-aminosalicylhydrazide were prepared from the corresponding acids by the two-step procedure in which the acid was esterified to its methyl ester followed by reaction of the produced ester with hydrazine hydrate [41].

Preparation of the Stabilizers

Maleimido aromatic hydrazide derivatives 1–4 were synthesized by dissolving 1 mol of benzohydrazide, salicylhydrazide, *p*-aminobenzohydrazide, or *p*-aminosalicylhydrazide in 100 mL of anhydrous N,N-dimethyl formamide (DMF), and allowed to cool at $-10^{\circ}C$ using an ice-salt bath for 15 min. Then, 1 mol of solid N-(4-chlorocarbonyl phenyl) maleimide was added slowly and then stirred for 1 h. The ice-salt bath was removed to let the temperature of condensation reaction rise gradually to room temperature and maintained for an additional 2 h with stirring. The reaction mixtures were precipitated in methanol-water mixture (1:2), washed with a solution of sodium carbonate to remove any residual acid, which

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TABLE 1. Inhibition indices of maleimido aromatic hydrazide Derivatives 1–4 against *B. subtilis*, *S. pneumoniae*, and *E. coli*.

Samples	Tested microorganisms		
	B. subtilis (RCMB 010069)	*S. pneumoniae* (RCMB 010019)	*E. coli* (RCMB 010055)
	Inhibition zone diameter (mm)		
1	17.4 ± 0.25	15.2 ± 0.44	11.2 ± 0.33
2	25.1 ± 0.25	24.8 ± 0.34	18.3 ± 0.58
3	19.2 ± 0.53	17.5 ± 0.43	13.9 ± 0.25
4	21.2 ± 0.58	19.3 ± 0.44	16.6 ± 0.19
Ampicillin	29.8 ± 0.15	21.6 ± 0.21	-
Gentamicin	-	-	22.8 ± 0.22

may be formed as a result of decomposition of the acid chloride, washed repeatedly with distilled water, methanol, and finally dried in a vacuum oven at 80°C overnight.

Because the reaction rate of the hydrazide group with the acid chloride group is seven times faster than that of the amino group [42], the synthesis of the amino derivatives (3 and 4) is based on the selective reactivity of the acid chloride with the hydrazide group of aminobenzohydrazide and aminosalicylhydrazide, respectively.

Measurements

The Fourier transform infrared (FTIR) spectra were recorded on a Shimadzu FTIR 8201 PC spectrophotometer using KBr pellets.

The hydrogen-1 nuclear magnetic resonance (^{1}H-NMR) spectra were recorded with a Jeol 270 MHz (Tokyo, Japan) spectrophotometer in dimethyl sulfoxide (DMSO)-d_6 as a solvent and the chemical shifts were recorded in ppm relative to tetramethylsilane (TMS) as an internal standard.

Mass spectra were recorded on a GCMS-QP 1000 ex spectra Mass spectrometer (Shimadzu, Tokyo, Japan) operating at 70 eV.

Elemental analyses were carried out in Perkin-Elmer (Model 2410 series II) C, H, N Analyzer (USA) at the Micro-Analytical Center at Cairo University, Giza, Egypt.

TABLE 2. MIC values of some selective maleimido aromatic hydrazide derivatives *against B. subtilis*, *S. pneumoniae*, and *E. coli*.

Samples	Tested microorganisms		
	B. subtilis (RCMB 010069)	*S. pneumonia* (RCMB 010019)	*E. coli* (RCMB 010055)
	MIC (μg/mL)		
1	31.250	62.50	250.00
2	0.480	0.48	7.81
Ampicillin	0.015	0.98	-
Gentamicin	-	-	.98

TABLE 3. Inhibition indices of maleimido aromatic hydrazide Derivatives 1–4 against *A. fumigatus, S. racemosum* and *G. candidum.*

Samples	Tested microorganisms		
	A. fumigatus (RCMB 02569)	*S. racemosum* (RCMB 05925)	*G. candidum* (RCMB 05098)
	Inhibition zone diameter (mm)		
1	11.5 ± 0.35	13.7 ± 0.25	12.8 ± 0.38
2	24.3 ± 0.63	19.9 ± 0.27	26.7 ± 0.35
3	12.3 ± 0.25	15.6 ± 0.25	15.8 ± 0.38
4	17.2 ± 0.58	16.5 ± 0.25	18.6 ± 0.58
Amphotericin B	22.8 ± 0.11	20.3 ± 0.19	26.7 ± 0.15

Antibacterial activities of the tested samples against *B. subtilis* (RCMB 010069) and *S. pneumoniae* (RCMB 010019) as gram-positive bacteria and against *E. coli* (RCMB 010055) as gram-negative bacteria were investigated by measuring the diameter of the inhibition zone (in mm) using the agar well diffusion method [43]. Ampicillin and gentamicin were used as antibacterial standard drugs.

Antifungal activities were investigated by screening the tested samples separately in vitro against *A. fumigatus* (RCMB 02569), *S. racemosum* (RCMB 05925), and *G. candidum* (RCMB 05098) fungi. The antifungal activities were investigated by measuring the diameter of the inhibition zone (in mm) using the agar well diffusion method [44]. Amphotericin B was used as an antifungal standard drug.

The minimum inhibition concentration (MIC) was determined by counting the colonies using two-fold serial dilutions of each sample. The MIC was considered to be the lowest concentration that completely inhibits against inoculums compared with the control, disregarding a single colony or a faint haze caused by the inoculums.

Samples of PVC for thermal degradation were prepared by thoroughly mixing 1 g of PVC powder with 2 mass% of the stabilizer in a mortar and 0.2 g of the resulting fine powder were used in the investigation. Evaluation of the stabilizing efficiency was carried out by measuring the rate of dehydrochlorination using a continuous potentiometric determination of the evolved hydrogen chloride gas at 180°C in air. Briefly, a reference calomel electrode and silver rode as a working electrode were used in a silver nitrate solution of known concentration. The evolved hydrogen chloride gas is absorbed in the silver nitrate solution. The change in potential during

TABLE 4. MIC values of some selective maleimido aromatic hydrazide derivatives *against A. fumigatus*, *S. racemosum*, and *G. candidum.*

Samples	Tested microorganisms		
	A. fumigatus (RCMB 02569)	*S. racemosum* (RCMB 05925)	*G. candidum* (RCMB 05098)
	MIC (μg/mL)		
1	250.00	62.50	125.00
2	0.48	3.90	0.12
Amphotericin B	0.98	1.95	0.12

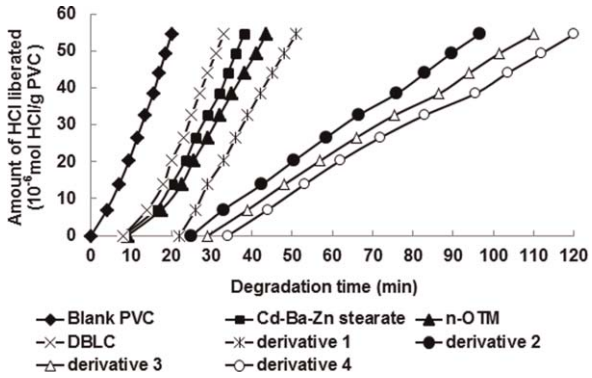

FIG. 1. Rate of dehydrochlorination of rigid PVC at 180°C, in air, in the presence of various maleimido aromatic hydrazide derivatives and reference stabilizers. All the stabilizers were used in a concentration of 2 mass% of PVC.

the assay corresponds to the change in concentration of the Ag^{+} ions in the absorbent solution as a result of its reaction with the evolved gas. The amount of the hydrogen chloride absorbed is then determined by applying the Nernst equation. A detailed description of this method was given elsewhere [45]. The extent of discoloration of the degraded PVC samples was evaluated visually by subjecting the PVC in the absence and in the presence of various stabilizers for different degradation time intervals.

Average molecular mass of PVC was determined using GPC-HPLC, Waters 600 system controller, 717 plus autosampler. Columns: phenomenex phenogel 5 μm 50 A, 300 × 7.8 mm. Detection: Waters model 2410 refractive index; ATTN = 16x eluent: THF (100% by vol.); flow rate: 0.7 ml min^{-1}; temperature: 50°C; injection volume: 25 μL; standards: polystyrene (PS) 25,000; 13,000; 4000; 2500; and 500 g mol^{-1} (1.0% m v^{-1}). Cubic foot calibration curve by Waters Millennium 32 GPC system software. Samples: dissolved in THF at an approximate 1.0% m v^{-1} concentration.

Solubility tests were carried out by stirring 0.1 g of the degraded PVC samples in 10 mL of tetrahydrofuran at 35°C overnight.

RESULTS AND DISCUSSION

Synthesis and Characterization of the Stabilizers

Four maleimido aromatic hydrazide derivatives 1–4 (Scheme 1) were synthesized via a low temperature (−10°C) solution (in anhydrous DMF) condensation reaction between N-[4-(chlorocarbonyl) phenyl] maleimide (1 mol) and benzohydrazide, salicylhydrazide, *p*-aminobenzohydrazide, or *p*-aminosalicylhydrazide (1 mol). The condensation reaction proceeded through the addition of the solid acid chloride into the cooling DMF solution of the hydrazide. The resulting condensation reaction mixtures were precipitated into methanol-water mixture, filtered, and dried in a vacuum oven at 80°C overnight.

All the derivatives are novel except derivative 1, which has been reported in our previous work [23]. All the derivatives were obtained in a quantitative yield. The structures of the synthesized derivatives 1–4 were ascertained on the basis of their consistent elemental analyses, FTIR, ^{1}H-NMR, and mass spectral characteristics. The functional groups (X, Y) were chosen based on their electron donor potency, being o and p directing, which increase the electron density on the conjugated structure of the maleimido aromatic hydrazide, and consequently increase its potency to interact with the degradative products of the PVC chains.

Analytical Data of Derivative 1

White in color; M.p. (°C) 165; ^{1}H-NMR (270 MHz, DMSO-d_6) δ (ppm): 7.0 (s, 2H, =CH), 7.50–8.11 (m, 9H, ArH), 7.43 (s, 2H, 2NH disappearing on deuteration); FTIR (KBr pellets) ν cm^{-1}: 3239 (NH), 1650 (C=O), 1603, 1509 (Ph), 1714 (C=O, imide), 830 (maleimide-moiety); MS m/z: 335 (M+); Anal. Calcd for $C_{18}H_{13}N_3O_4$: C, 64.48; H, 3.88; N, 12.54. Found: C, 64.22; H, 3.89; N, 12.50 [23].

Analytical Data of Derivative 2

Yellow in color; M.p. (°C) 251; ^{1}H-NMR (270 MHz, DMSO-d_6) δ (ppm): 7.23 (s, 2H, =CH), 7.44–8.04 (m, 7H, ArH), 10.747 (s, broad, 2H, 2NH disappearing on deuteration), 12.415 (s, broad, 1H, 1OH); FTIR (KBr pellets) ν cm^{-1}: 3320, 3270 (NH), 1639 (C=O), 1590, 1500 (Ph), 1716 (C=O, imide), 825 (maleimide- moiety); MS m/z: 351 (M+); Anal. Calcd for $C_{18}H_{13}N_3O_5$: C, 61.54; H, 3.70; N, 11.97. Found: C, 61.32; H, 3.71; N, 11.91.

Analytical Data of Derivative 3

Yellow in color; M.p. (°C) >300; ^{1}H-NMR (270 MHz, DMSO-d_6) δ (ppm): 7.22 (s, 2H, =CH), 7.471–8.099 (m, 8H, ArH), 10.466–10.577 (3s, 4H, 2NH+NH_2 disappearing on deuteration); FTIR (KBr pellets) ν cm^{-1}: 3469, 3279 (NH), 1655 (C=O), 1602, 1506 (Ph), 1713 (C=O, imide), 828 (maleimide- moiety); MS m/z: 349 (M+);

TABLE 5. Ts of rigid PVC thermally degraded at 180°C, in air, in the presence of the maleimido aromatic hydrazide stabilizers and reference stabilizers. All the stabilizers were used in concentration of 2 mass% of PVC.

Stabilizer code	Ts (min)
Blank PVC	0
DBLC	8
Cd-Ba-Zn stearate	8
n-OTM	9
1	22
2	25
3	29
4	34

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TABLE 6. Extent of discoloration of thermally degraded rigid PVC at 180°C, air, for various time intervals in the presence of different stabilizers. All the stabilizers were used in concentration of 2 mass% of PVC.

Stabilizer code	Color at 0 min	Color at 20 min	Color at 40 min	Color at 60 min
Blank PVC				
DBLC				
Cd-Ba-Zn stearate				
n-OTM				
1				
2				
3				
4				

Anal. Calcd for $C_{18}H_{14}N_4O_4$: C, 61.71; H, 4.00; N, 16.00. Found: C, 61.52; H, 4.02; N, 15.93.

Analytical Data of Derivative 4

Yellow in color; M.p. (°C) >300; ^{1}H-NMR (270 MHz, DMSO-d_6) δ (ppm): 7.21 (s, 2H, =CH), 7.377–8.078 (m, 7H, ArH), 10.232–10.728 (4s, 4H, 2NH+ NH_2 disappearing on deuteration), 12.102 (s, 1H, 1OH); FTIR (KBr pellets) ν cm^{-1}: 3351, 3245 (NH), 1650 (C=O), 1604, 1498 (Ph), 1715 (C=O, imide), 831 (maleimide- moiety); MS m/z: 366 (M+); Anal. Calcd for $C_{18}H_{14}N_4O_5$: C, 59.02; H, 3.83; N, 15.30. Found: C, 58.90; H, 3.84; N, 15.22.

Antibacterial Activity of the Stabilizers

Maleimido aromatic hydrazide derivatives 1–4 were evaluated for their in vitro antibacterial activity against gram-positive bacteria *B. subtilis* and *S. pneumoniae* and gram-negative bacteria *E. coli* by the diffusion agar technique using ampicillin and gentamicin as reference standards and the results are presented in Tables 1 and 2.

Maleimido aromatic hydrazide derivatives 1–4 showed good antibacterial activity. Their inhibitory effect against all the tested bacteria followed the sequence: 2 > 4 > 3 > 1. The presence of the hydroxy group on the aromatic ring of the hydrazide part increases the antibacterial activity as evidenced by derivative 2. Derivative 3 is less active than derivative 2, which indicates that the NH_2 group is less effective in improving the antibacterial activity than the hydroxy group. The electron donating power of the amino group is larger than that of the hydroxy group. This may increase the electron density on the amino derivative and consequently decrease its potency to interact with the negatively charged microbial cell membrane leading to lower antimicrobial activity compared to the hydroxy derivative.

The lower antibacterial activity of Derivative 4 in comparison to Derivative 2 may be attributed to the presence of an additional NH_2 group in it. The nonsubstituted Derivative 1 is the least active one among these derivatives against all the tested bacteria. The most active, Derivative 2 exhibited an inhibition zone diameter of 24.8 ± 0.34 mm (Table 1) with MIC of 0.48 μg/mL (Table 2) against *S. pneumonia*e corresponding to the inhibition zone diameter of 21.6 ± 0.21 mm (Table 1) and MIC of 0.98 μg/mL (Table 2) for the standard drug ampicillin. Thus, Derivative 2 displayed better activity against *S. pneumonia*e than that of the reference drug ampicillin. The Derivatives 1–4 have shown greater antibacterial activity against *B. subtilis* than that against *S. pneumoniae*.

Moreover, Derivatives 1–4 were more active against the gram-positive bacteria than against the gram-negative bacteria (Table 1). As the strongest, Derivative 2 caused inhibition zone diameter *of B. subtilis* and *S. pneumoniae* of 25.1 ± 0.25 and 24.8 ± 0.34 mm, respectively, corresponding to 18.3 ± 0.58 mm of *E. coli*. This may be

TABLE 7. GPC measurements of thermally degraded rigid PVC at 180°C, in air, in the presence of maleimido aromatic hydrazide stabilizers. All the stabilizers were used in concentration of 2 mass% of PVC.

Stabilizer code	Degradation time (min)	M_w (g/mol) × 10^4	M_n (g/mol) × 10^4	PD
Blank PVC	0	24.4730	9.1520	2.6741
Blank PVC	30	18.7020	4.2958	4.3536
1	30	20.5700	6.0777	3.3845
2	30	21.2915	6.8406	3.1125
3	30	22.0257	7.2651	3.0317
4	30	23.2493	8.2646	2.8131

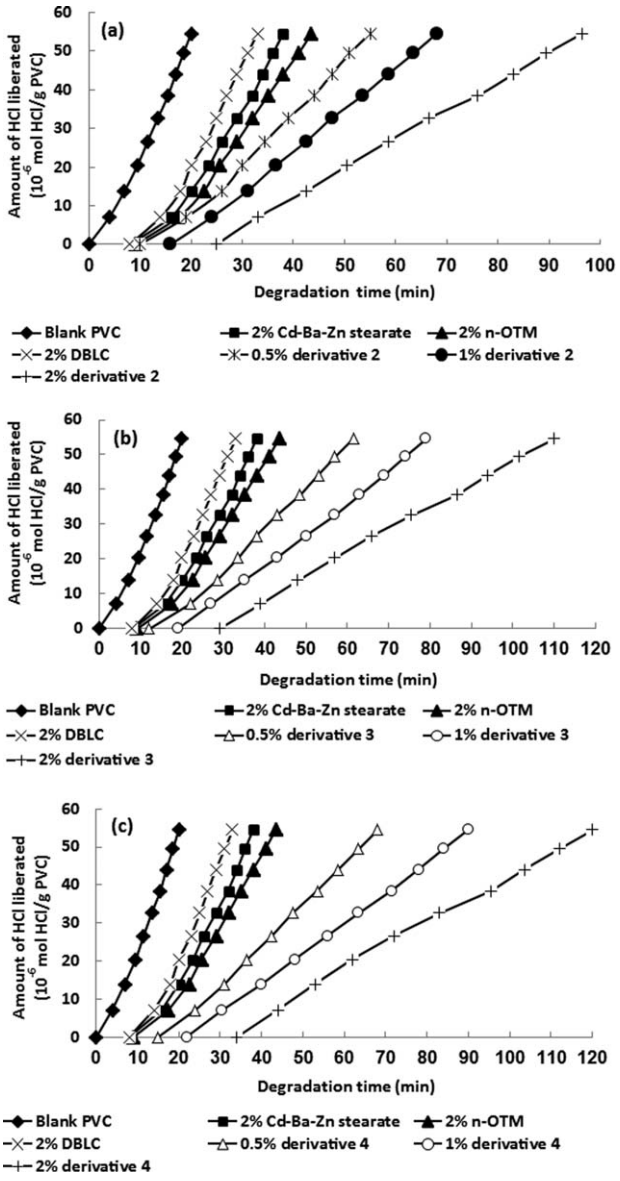

FIG. 2. Effect of the maleimido aromatic hydrazide derivatives concentration on the rate of dehydrochlorination of thermally degraded rigid PVC at 180°C, in air: (a) Derivative 2; (b) Derivative 3; and (c) Derivative 4.

attributed to their different cell wall. The cell wall of gram-positive bacteria is fully composed of peptide polyglycogen. The peptidoglycan layer is composed of networks with plenty of pores, which allow foreign molecules to come into the cell without difficulty and allow more rapid absorption of ions into the cell. However, the cell wall of the gram-negative bacteria is made up of a thin membrane of peptide polyglycogen and an outer membrane constituted of lipopolysaccharide, lipoprotein, and phospholipids. Because of the complicated bilayer cell structure, the outer membrane is a potential barrier against foreign molecules [46]. Therefore, these derivatives have different effects on the two kinds of bacteria. Additional evidence of the greater activity of these derivatives against gram-positive bacteria than that against gram-negative bacteria comes from their MIC. Because the MIC values of the Derivative 2 against *B. subtilis* and *S. pneumonia*e were 0.48 μg/mL, the MIC value against *E. coli* was 7.81 μg/mL (Table 2).

Antifungal Activity of the Stabilizers

Maleimido aromatic hydrazide Derivatives 1–4 were evaluated for their in vitro antifungal activity against *A. fumigatus*, *S. racemosum*, and *G. candidum* by the diffusion agar technique using Amphotericin B as the reference drug and the results are presented in Tables 3 and 4.

It can be noted that Derivative 2 exhibited equivalent inhibition zone diameter (26.7 ± 0.35 mm) and MIC value (0.12 μg/mL) to the reference drug Amphotericin B (26.7 ± 0.15 mm, 0.12 μg/mL) against *G. candidum*. Further, Derivative 2 emerged as the most potential candidates against *A. fumigatus* with an inhibition zone diameter of 24.3 ± 0.63 mm and MIC value of 0.48 μg/mL, which are better than those of the standard drug Amphotericin B (22.8 ± 0.11 mm, 0.98 μg/mL). The rest of the derivatives exhibited a moderate in vitro antifungal (MIC = 1.95–250 μg/mL) against the tested strains of fungi.

Stabilization Activity of the Maleimido Aromatic Hydrazide Derivatives

Results of the dehydrochlorination of rigid PVC stabilized by various maleimido aromatic hydrazide derivatives and thermally degraded at 180°C, in air, are shown in Fig. 1. Data of the nonstabilized blank PVC and those of the samples stabilized by DBLC, n-OTM, and Cd-Ba-Zn stearates reference stabilizers are also given for comparison. All the stabilizers were used in a concentration of 2 mass% of PVC and the results represent the average of three comparable experiments of each stabilizer.

The results clearly reveal the greater stabilizing efficiency of these compounds than that of the reference ones. This is indicated not only by the longer thermal stability (Ts) periods, during which no detectable amounts of hydrogen chloride gas are liberated (i.e., there is no change in potential reading from the beginning of the degradation process to the end of this period) (Table 5), but also by the lower rates of dehydrochlorination during the subsequent stages of degradation (Fig. 1). The thermal stability period of compound 4 is almost four times

TABLE 8. Effect of the maleimido aromatic hydrazide stabilizers concentration on the Ts of rigid PVC thermally degraded at 180°C, in air.

	Ts (min) Stabilizer concentration (mass% of PVC)		
Stabilizer code	0.5	1	2
2	10	16	25
3	12	19	29
4	15	22	34

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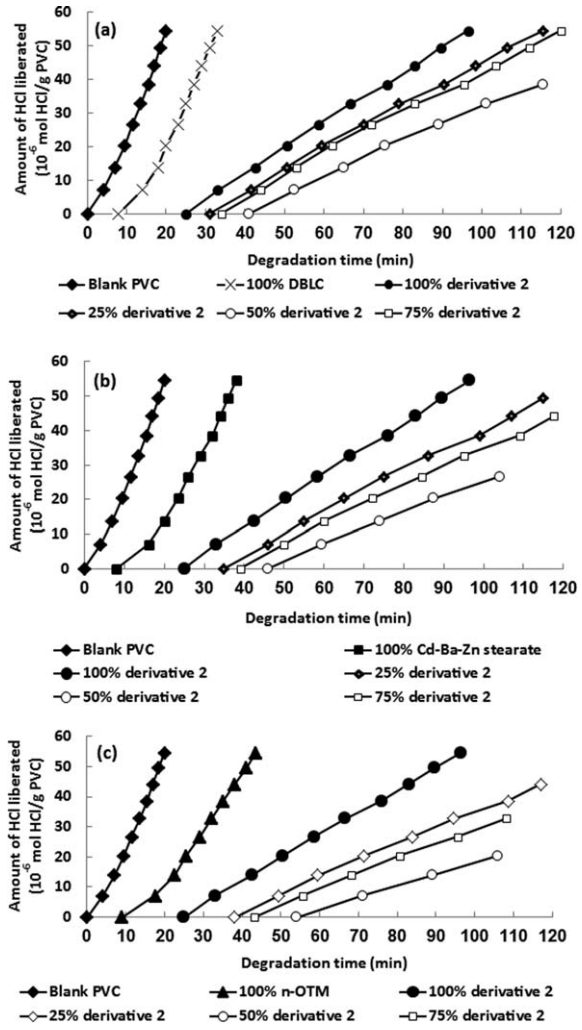

FIG. 3. Effect of mixed stabilizers on the rate of dehydrochlorination of thermally degraded rigid PVC at 180°C, in air. The overall mixed stabilizers concentration was kept constant at 2 mass% of PVC: (a) Derivative 2 and DBLC; (b) Derivative 2 and Cd-Ba-Zn stearate; and (c) Derivative 2 and n-OTM.

higher than the periods obtained for the reference stabilizers.

It has been previously suggested that N-substituted maleimides owe their stabilizing efficiency to the replacement of the labile chlorine atoms on PVC chains by a more relative thermally stable stabilizer moiety [38]. The stabilizers' efficiency is attributed to their radical potency, which interferes with the PVC radical degradation process. This most probably occurs not only through trapping the radical species in the degradation process, but also by blocking the radical sites created on PVC chains. The radical attack seems to occur first on the ethylenic carbon-carbon double bond, followed by cleavage of the imide linkages during the later stages of degradation. This mode of action has previously been published, together with experiments to prove it [38]. Furthermore, aromatic hydrazides are efficient thermal stabilizers for rigid PVC. They exhibit their stabilizing efficiency through effective absorption of the degradation products (HCl gas) by their basic groups [39]. In view of structural similarity of the investigated stabilizers to maleimides combined with aromatic hydrazides, their mechanism is outlined by assuming that their first part (maleimide) can work as a radical trapper, whereas their other part (aromatic hydrazide) acts as an HCl absorber. The data also demonstrate how the Ts and the rate of dehydrochlorination are affected by the type of the substituent group in the phenyl ring of the hydrazide part (-OH and $-NH_2$ groups) of the stabilizers. This indicates the important role played by the substituent groups in the aromatic ring in the stabilization process. The introduction of the –OH and/or $-NH_2$ group into the phenyl rings leads to an appreciable increase in the Ts (at the early stages of degradation) and slight lowering in the rate of dehydrochlorination (at the subsequent stages of degradation). This may be attributed to the nature of these substituents (electron rich substituents), which can donate electrons toward both the hydrazide and ethylenic carbon-carbon double bond, resulting in higher stabilizing efficiency relative to that of the

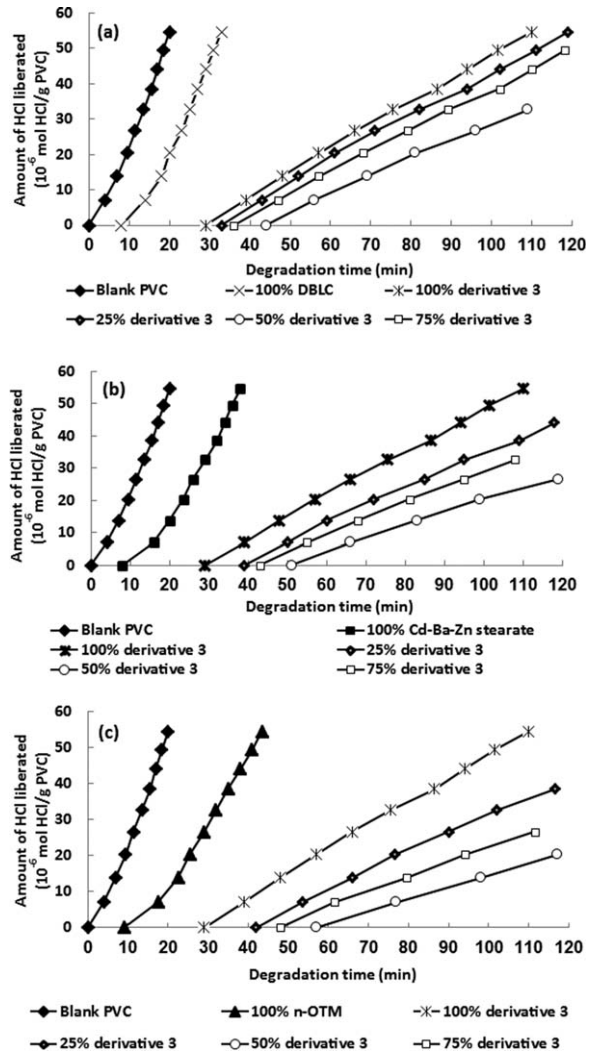

FIG. 4. Effect of mixed stabilizers on the rate of dehydrochlorination of thermally degraded rigid PVC at 180°C, in air. The overall mixed stabilizers' concentration was kept constant at 2 mass% of PVC: (a) Derivative 3 and DBLC; (b) Derivative 3 and Cd-Ba-Zn stearate; and (c) Derivative 3 and n-OTM.

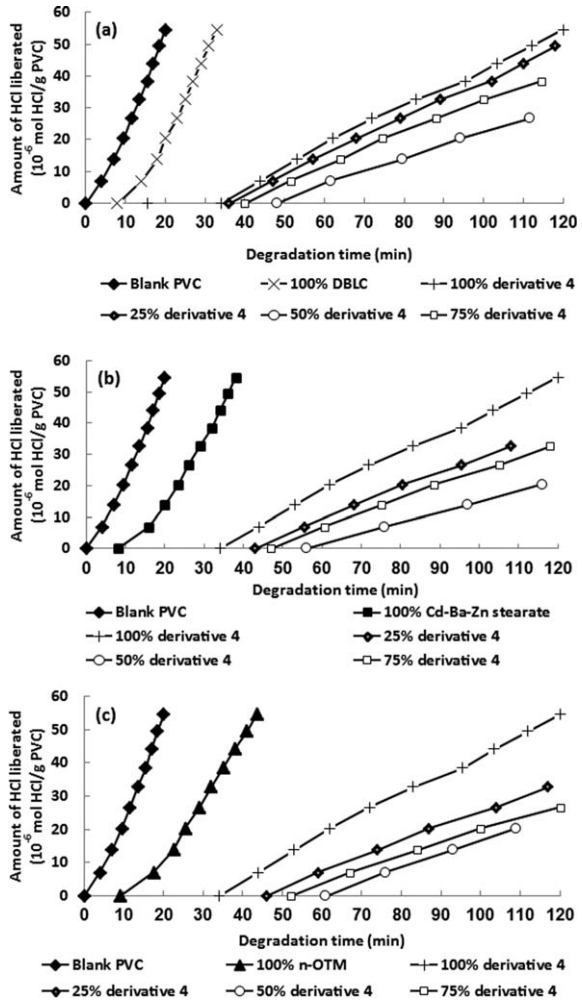

FIG. 5. Effect of mixed stabilizers on the rate of dehydrochlorination of thermally degraded rigid PVC at 180°C, in air. The overall mixed stabilizers concentration was kept constant at 2 mass% of PVC: (a) Derivative 4 and DBLC; (b) Derivative 4 and Cd-Ba-Zn stearate; and (c) Derivative 4 and n-OTM.

nonsubstituted Derivative 1, which has been reported in our previous work [23]. An experimental proof supporting this conclusion can be seen in the greater efficiency of the amino Derivatives 3 and 4 relative to that of the hydroxyl Derivative 2. This is in accordance with the greater electron donating power of the -NH_2 group relative to that of the –OH group. The enhanced efficiency of the amino derivatives can also be related to another two reasons: (1) at the early stages of degradation, the presence of the amino group in para-position in the phenyl ring may make its electron donation toward the abovementioned bonds proceed to a greater extent and be much easier; and (2) the ability of the amino group to act as a hydrogen chloride absorber at the subsequent stages of degradation, based on its basic character.

Effect of the Stabilizers on the Discoloration of the Thermally Degraded Rigid Polyvinylchloride

An additional experimental proof for the high stabilizing efficiency of the investigated stabilizers is illustrated by the improvement in the extent of discoloration of PVC samples stabilized with maleimido aromatic hydrazides and thermally degraded at 180°C, in air, for different time intervals relative to blank PVC samples and PVC samples stabilized with any of the reference stabilizers although the initial color of stabilizers 2–4 is yellow (Table 6). At early stages of degradation (during the thermal stability period), the greater stabilizing efficiency of the investigated stabilizers takes place through the replacement of the labile chlorine by a more thermally stable stabilizer moiety, which disrupts the formation of conjugated double bonds that are responsible for discoloration. The results also show that Derivative 4 resulted in a much lower degree of discoloration compared to Derivative 2. This may be attributed to the presence of the p-amino group with its higher donation power that can donate electrons toward both the hydrazide and ethylenic carbon-carbon double bond more easily and thus accelerate the replacement of the labile chlorine and increase the disruption of the formation of conjugated double bonds leading to increasing the stability of the PVC sample and consequently the degree of discoloration decreased. Moreover, the lowering of the extent of discoloration in the presence of the investigated stabilizers may be attributed to their dienophilic property, which allows them to intervene with the conjugated double bond systems formed on the PVC chains at subsequent stages of the degradation process by the Diels-Alder type of addition. The good color stability of the dibutyltin maleate stabilizer has been attributed to the same type of addition reactions [47].

Elucidation of the Molecular Mass of the Thermally Degraded Rigid Polyvinylchloride by Gel Permeation Chromatography

Gel permeation chromatography (GPC) measurements were performed on both PVC samples, before and after 30 min of thermal degradation at 180°C, in air, in the presence or absence of maleimido aromatic hydrazides. The values of M_w, M_n, and polydispersity (PD) are shown in Table 7.

The GPC measurement results indicate the small decrease in the values of molecular masses of PVC samples achieved by using the investigated stabilizers. The results of GPC measurements show the decrease in M_w value of blank PVC samples from 24.4730×10^4 to 18.7020×10^4 upon 30 min of thermal degradation with a % decrease in M_w value of 23.58. After the same time of degradation, the decrease in M_w of the PVC samples stabilized with 1, 2, 3, and 4 reached only 15.95%, 13%, 10%, and 5%, respectively. This may be due to the good stabilizing effect of the investigated derivatives that decreases the extent of chain scission of PVC. The solubility test of thermally degraded PVC indicated the absence of gel formation, which indicates the absence of cross-linking during degradation. This is evidence for the high efficiency of the investigated stabilizers, that they can decrease the chain-scission and prevent cross-linking,

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TABLE 9. Effect of mixing maleimido aromatic hydrazides with reference stabilizers on the Ts of thermally degraded rigid PVC at 180°C in air. The overall mixed stabilizers concentration was kept constant at 2 mass% of PVC.

Weight ratio	Ts (min)	Weight ratio	Ts (min)	Weight ratio	Ts (min)
2/DBLC		2/Cd-Ba-Zn stearate		2/n-OTM	
100/0	25	100/0	25	100/0	25
75/25	34	75/25	39	75/25	43
50/50	41	50/50	46	50/50	54
25/75	31	25/75	35	25/75	38
0/100	8	0/100	8	0/100	9
3/DBLC		3/Cd-Ba-Zn stearate		3/n-OTM	
100/0	29	100/0	29	100/0	29
75/25	36	75/25	43	75/25	48
50/50	44	50/50	51	50/50	57
25/75	33	25/75	39	25/75	42
0/100	8	0/100	8	0/100	9
4/DBLC		4/Cd-Ba-Zn stearate		4/n-OTM	
100/0	34	100/0	34	100/0	34
75/25	40	75/25	47	75/25	52
50/50	48	50/50	56	50/50	61
25/75	36	25/75	43	25/75	46
0/100	8	0/100	8	0/100	9

so they can preserve both the physical and mechanical properties of the polymer.

Effect of the Stabilizer Concentration on the Stabilization Efficiency of the Thermally Degraded Rigid Polyvinylchloride

The high stabilizing efficiency of the investigated stabilizers has led to the conclusion that comparable stabilizing efficiency could be observed if the investigated stabilizers are used in concentrations lower than those commonly used in the industry. For this purpose, the study was extended to determine the lowest amount of the investigated stabilizers that can provide stabilizing power comparable with the reference stabilizers. Results of the Ts values and the rates of dehydrochlorination of the PVC stabilized with the investigated stabilizers in different concentrations (0.5, 1, and 2 mass% based on PVC weight), are compared with those of the three reference stabilizers (2 mass% based on PVC weight), which are shown in Fig. 2 and Table 8. The results show the greater efficiency of the investigated stabilizers even at lower concentrations (0.5 mass% of PVC) relative to those of the reference stabilizers. This is illustrated not only from the higher Ts values, but also from the lower rates of dehydrochlorination at subsequent stages of degradation. The greater efficiency of the investigated stabilizers is most probably not only due to their possession of various centers of reactivity that can act as traps for radical species resulting during the degradation process, but also due to the ability to react with the evolved HCl gas.

Effect of Mixed Stabilizers on the Stabilizing Efficiency of Thermally Degraded Rigid Polyvinylchloride

It became of interest to study the effect of mixing the investigated stabilizers together with those used in the industry on the efficiency of stabilization in general. Mixing was effected in the ranges of 0–100% of the investigated stabilizers relative to the reference stabilizers used. The overall mixed stabilizers concentration was kept constant at 2 mass% of PVC, and the results represent the average of three comparable experiments for each stabilizer mixture. The results of the

TABLE 10. Effect of mixing maleimido aromatic hydrazide 2 with reference stabilizers on the discoloration of thermally degraded rigid PVC at 180°C, in air, for 60 min. The overall mixed stabilizers concentration was kept constant at 2 mass% of PVC.

2/DBLC		2/Cd-Ba-Zn stearate		2/n-OTM	
Weight ratio	Color	Weight ratio	Color	Weight ratio	Color
100/0		100/0		100/0	
75/25		75/25		75/25	
50/50		50/50		50/50	
25/75		25/75		25/75	
0/100		0/100		0/100	

TABLE 11. Effect of mixing maleimido aromatic hydrazide 3 with reference stabilizers on the discoloration of thermally degraded rigid PVC at 180°C, in air, for 60 min. The overall mixed stabilizers concentration was kept constant at 2 mass% of PVC.

3/DBLC		3/Cd-Ba-Zn stearate		3/n-OTM	
Weight ratio	Color	Weight ratio	Color	Weight ratio	Color
100/0		100/0		100/0	
75/25		75/25		75/25	
50/50		50/50		50/50	
25/75		25/75		25/75	
0/100		0/100		0/100	

dehydrochlorination rates of rigid PVC thermally degraded at 180°C, in air, in the presence of the mixed 2, 3, or 4 with any of the three reference stabilizers are illustrated in Figs. 3–5, respectively. The results of Ts values of such combinations are shown in Table 9. The results clearly reveal the greater stabilizing efficiency of these mixed stabilizers, and the existence of a true synergistic effect resulting from the combination of the investigated stabilizers with any of the reference ones. The maximum synergism was achieved when the investigated stabilizers and either of the reference stabilizers were mixed in equivalent weight ratios (Table 9). The results also demonstrated a slight improvement in the rate of dehydrochlorination as a result of mixing the investigated stabilizers with the reference stabilizers. It has been established that the hydrazide linkages can interact with various transition metal salts to form stable complexes [48]. For this, at subsequent stages of degradation, it would be possible for the hydrazide moiety of the investigated stabilizers to react with the accumulated metal chlorides ($PbCl_2$, $CdCl_2$, and $ZnCl_2$) formed as byproducts from reference stabilizers to form complexes with additional stabilizing power and improve the stabilizing efficiency of the mixed stabilizers. Thus, mixing the reference stabilizers with the investigated stabilizers would not only remove the deleterious effect of the metal chlorides but also give it an additional advantage from their transformation into useful new stabilizers.

Effect of Mixed Stabilizers on the Extent of Discoloration of Thermally Degraded Polyvinylchloride

The effect of mixing stabilizers 2, 3, or 4 with DBLC, Cd-Ba-Zn stearate, or n-OTM, in various weight ratios, on the degree of discoloration of thermally degraded rigid PVC is shown in Tables (10–12). It is worth mentioning that the initial color of all the PVC samples stabilized with mixed stabilizers was pale yellow. All the samples were heated at 180°C, in air, for 60 min. The results clearly reveal that all the mixed stabilizers exhibit a lower extent of discoloration than the reference stabilizer, rather than the investigated stabilizers when they are used separately. In all cases, the sample treated with 1:1 weight ratio of the investigated stabilizer and reference stabilizer showed the least degree of discoloration and consequently the better color stability.

TABLE 12. Effect of mixing maleimido aromatic hydrazide 4 with reference stabilizers on the discoloration of thermally degraded rigid PVC at 180°C, in air, for 60 min. The overall mixed stabilizers concentration was kept constant at 2 mass% of PVC.

4/DBLC		4/Cd-Ba-Zn stearate		4/n-OTM	
Weight ratio	Color	Weight ratio	Color	Weight ratio	Color
100/0		100/0		100/0	
75/25		75/25		75/25	
50/50		50/50		50/50	
25/75		25/75		25/75	
0/100		0/100		0/100	

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This result confirms the synergistic effect between their modes of action.

CONCLUSIONS

The prepared maleimido aromatic hydrazides are efficient antimicrobial agents against *B. subtilis* and *S. pneumoniae* as gram-positive bacteria and against *E. coli* as gram-negative bacteria and against *A. fumigatus*, *S. racemosum*, and *G. candidum* fungi. They are also efficient stabilizers for the thermal degradation of rigid PVC, even if they are used in lower concentrations compared with industrial stabilizers, such as DBLC, Cd-Ba-Zn stearate, and n-OTM. The investigated stabilizers lower the degree of discoloration of the degraded PVC samples. Mixing the investigated stabilizers with any of the reference stabilizers leads to a remarkable improvement both in the Ts value and in lowering the extent of discoloration, reaching its maximum at equivalent weight ratio of investigated stabilizer to the reference ones. This improvement may be attributed to the fact that the investigated stabilizers protect the polymer from the deleterious effects of the byproducts, mostly metal chlorides accumulated during the reaction of the organometallic stabilizers with the polymeric chains. This is achieved through the ability of the hydrazide linkage to coordinate with these byproducts to form stable complexes of potential stabilizing power. From the above, it is possible to recommend the use of maleimido aromatic hydrazide derivatives as antimicrobial thermal stabilizers for rigid PVC, either alone or as a co-stabilizer with various reference organometallic stabilizers to obtain thermally stable antimicrobial PVC/ maleimido aromatic hydrazide composites.

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