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Synthesis, Anti-microbial, Flameretardance and Anti-corrosive Activity of Some New Heterocycles Incorporating Coumarin moiety

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Authors' contributions

This work was carried out in collaboration among all authors. Author SMM designed the study, performed the statistical analysis, wrote the protocol and wrote the first draft of the manuscript. Authors NTAD and NAEK managed the analyses of the study. Author WMM managed the literature searches. All authors read and approved the final manuscript.

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ABSTRACT

In the present study a series of novel heterocyclic compounds (**2-16**) incorporating coumarin moiety was synthesized. The newly synthesized compounds were elucidated on the basis of elemental analysis, spectral data, were tested for *in-vitro* antibacterial activity against *Staphylococcus aureus*, *Bacillus subtilis* (Gram-positive bacteria), *Salmonella typhimurium*, *Escherichia coli* (Gram-negative bacteria) and *Candida albicans*, *Aspergillus fumigatus* (fungi).
Coumarin derivatives **(1,6,16)** were chosen to evaluate the anti-corrosion, flame retardant properties. The results clearly showed that, the incorporation of coumarin derivatives into epoxy coating have led to improve the flame residency, corrosion resistance, and mechanical properties of investigated coating and confirmed that these new developed varnishes have an excellent properties as flame resistance and anticorrosive for mild steel.

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Keywords: 3-acetyl-7-hydroxy-2-oxo-2H-chromen-2-one; multicomponentreactions, anti-microbial, anti–corrosion; flame retardance.

1. INTRODUCTION

A number of natural and synthetic coumarin derivatives have been reported to exert notable antimicrobial [1,2], antifungal [3,4] and cytotoxic [5] activity. Furthermore it has been reported by different scientists that coumarin derivatives incorporating, pyrazole, thiazole, oxazole, traizole, pyridineand pyrimidine derivatives have also attracted increasing attention due to their numerous pharmacological applications and biological activities, such as anti-inflammatory, analgesic, antimicrobial, anti-HIV, anti-hypertensive and herbicidal activity. Chalcone derivatives have received a great deal of attention due to their relatively simple structure and wide variety of pharmacological activities [6] reported for these compounds including antifungal [7,8], antibacterial [9] and antitumor activities [10,11]. MCRs comply with the principles of green chemistry in terms of economy of steps as well as many of the stringent criteria of an ideal organic synthesis. Coumarins and their derivatives have attracted considerable attention from organic and medicinal chemists for many years as a large number of natural and synthetic products contain this heterocyclic nucleus [12,13].

Corrosion is the deterioration of metal by chemical attack or reaction with its environment. It is a constant and continuous problem, often difficult to eliminate completely. Corrosion processes develop fast after disruption of the protective barrier and are accompanied by a number of reactions that change the composition and properties of both the metal surface and the local environment, for example, formation of oxides, and diffusion of metal cations into the coating matrix, local pH changes, and electrochemical potential. Corrosion can lead to failure of metal structures which have serious consequences for humans and the environment. Thus, the study of mild steel corrosion and the inhibition of mild steel corrosion of have invited the attention of scientists and technocrats to devise ways to control the corrosion [14-16].

The use of a green corrosion inhibitor as well as flame retardant is nowadays very common because they are eco-friendly environmental.

Recently, several chemical compounds were tested as an inhibitor of corrosionofmetals and alloys, most of the reported corrosion inhibitors are organic compounds containing heterocyclic atoms (nitrogen, oxygen, sulfur and phosphorous), incorporated in an aromatic system or triple bond used to reduce the corrosion.

Organic corrosion inhibitors are widely used in industry because of effectiveness at wide range of temperatures, compatibility with protected materials, and good solubility in water, low costs and relatively low toxicity.

Organic corrosion inhibitors adsorb on the surface forming protective film which displace water and protect it against deteriorating. The adsorption of organic inhibitors takes place via charged molecules and metal attract electrostatically, or by the interaction between unpaired electrons and the metal surface, which forming a metallic insoluble complex. The free electrons on the oxygen and nitrogen atoms form chemical bonds with the metal surface as shown in the Fig. 1 [17].

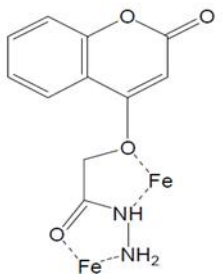


Fig. 1. Suggested mechanism of corrosion inhibitor

In view of these observations and in continuation of our previous work on the synthesis of heterocyclic systems and biological evaluation [12,13]. Herein, we report a facile route to synthesize various heterocycles incorporating coumarin moiety to use as new green corrosion inhibitors, and flame retardant additives by incorporating into epoxy resin to form a new modified epoxy varnishes.

2. EXPERIMENTAL

2.1 Instruments

All melting points were measured on a Gallenkamp melting point apparatus. IR spectra

(KBr) were acquired with a Perkin–Elmer model 157 infrared spectrophotometer. 1H-NMR spectra were recorded on a Bruker spectrophotometer at 400 MHz using tetramethylsilane (TMS) as internal standard. 13C-NMR spectra were recorded on the same spectrometer at 100 MHz in DMSO-d6 as solvent. Electron Ionization (EI)-MS were measured on a ShimadzuGC-MS-QP-1000 EX mass spectrometer instrument operating at 70 eV.

2.2 Synthesis

Synthesis of 3-acetyl-7-hydroxy-2- oxo -2H-chromen-2-one (1)

A mixture of 2,4- dihydroxybenzaldhyde (0.01 mol) and ethyl acetoacetate (0.01 mol) in the presence of few drops of piperdine was heated on hot plate and stirring for 15 min , cooled to room-temp, ice cold water was added. The solid that separated was filtered off, dried and recrystallized from ethanol to give (1).

1: $C_{11}H_8O_4$ (MW 204), yellowish color, m. p. 185-187ºC, 85% yield. FT-IR (KBr cm^{-1}), umax: 3481(OH), 3063(CH-Aromatic), 2990, 2886(CH-Aliphatic), 1711(δ-Lactone). 1664 (CO), 1595(C=C), 1377 cm^{-1}(CH3), ^{13}C-NMR (100 MHz, DMSO-d6): δ/ppm =30.51(CH_3), 102.65, 109.09, 115.65, 130.92, 132.91, 133.36, 158.25 (aromatic >C=C<), 191.51(C=O ketone), 159.53-165.64 (hetero aromatic > C=O lactone, C-OH). ; Anal. Calcd: C, 64.70; H, 3.92: Found; C, 64.68; H, 3.90.

Synthesis of 3-(3-(2-chlorophenyl)acryloyl)-7-hydroxy-2H-chromen-2-one (2)

A mixture of 3-acetyl-7-hydroxy-2- oxo -2H-chromen-2-one (1) (0.01 mol) and o-chlorobenzaldhyde (0.01 mol) in ethanolic solution of NaOH(0.5 gm in 30 ml ethanol) was heated under reflux for 8 hrs. , cooled to room-temp, poured onto ice cold water contatining drops of 10% HCl. The solid obtained was filtered off, washed well with hot water, dried and recrystallized from toluene to give (2).

2: $C_{18}H_{11}ClO_4$ (M W 326.5). Orange color, m. p. 210-212ºC, yields 85%. FT-IR (KBr cm^{-1}),umax: 3182(OH), 3061, 2933 CH (aliphatic-aromatic), 1702 (δ-lactone), 1615 (C=C). ^{1}H NMR(δppm) (DMSOd6):δ== 9.94-9.14(1H,br,OH) ,8.38 (1H, s, CH-Coumarin)], 6.30-7.95 (7H, m, Ar-H &2H α-β unsaturated carbonyl group); ^{13}C- NMR spectrum (100 MHz, DMSO-d6, δ, ppm) =100.52, 110.18, 113.87, 123.17, 128.52, 129.22, 130.55, 132.99, 133.28, 134.32, 141.92, 146.79, 157.78, 158.60, 159.26, 183.39. ((aromatic> C=C <& α-β unsaturated carbonyl), Anal. Calcd: C, 66.15; H, 3.36; Cl, 10.87: Found; C, 66.12; H, 3.33; Cl, 10.85.

Synthesis of 2-amino-4-(2-chlorophenyl)-6[-(7-hydroxy-2-oxo-2H-chromen-3-yl)] nicotinonitrile (3)

A mixture of compound (2) (0.01 mol), malononitriale (0.01 mol) in ethanolic solution containing sod ethoxide (1gm sodium metal in 20 ml ethanol), Ammonium acetate (0.03 mol) was added. The reaction mixture was heated under reflux for 8 hrs. The solid obtained after cooling was collected and recrystallized from ethanol to give (3).

3: $C_{21}H_{12}ClN_3O_3$ (M W.389.5), brown color, m.p 286-288ºC, yield 70%.; FT-IR (KBr cm^{-1}) umax: 3460 (OH), 3369-3230(NHNH2), 2925, 2853 CH (aliphatic-aromatic), 2207(C≡N), 1703(δ-Lactone), 1620(C=N). The ^{1}H NMR(δppm) (DMSOd6):δ==4.99(1H,s,OH-phenolic),8.38 (1H, s, CH-Coumarin)], 6.65-7.52 (9H, m, Ar-H ,2H NH_2).^{13}C- NMR spectrum (100 MHz, DMSO-d6, δ, ppm) 101.69, 109.36, 110.86, 111.69.17, 112.86, 127.94, 130.07, 131.10, 143.70, 145.03 ((aromatic > C=C <), 115.19 157.20, 158.53, 159.20, 161.87 ,163.37(hetero aromatic >C≡N, C=O, C=N, C-NH2,C-OH). Anal Calcd: C, 64.71; H, 3.10; Cl, 9.09;N, 10.78; Found:C,64.68; H, 3.07; Cl,9.06, N,10.75.

Synthesis of ethyl N-4-(2-chlorophenyl)-3-cyano-6-(7-hydroxy-2-oxo-2H-chromen-3-yl) pyridin -2-yl]formimidate (4)

An equimolar amount of compound (3)(0.01 mol) and triethylorthoformate (0.01 mol) in acetic anhydrides (5 mL) was heated under reflux for 6 hrs., the brownish paste, formed was washed well with ice water, filtrated off. The residual brownish solid was recrystallized from ethanol to give (4).

4: $C_{24}H_{17}ClN_3O_4$ (m.wt.446.5), brown color, m.p. 330-332ºC, yield 70%. FT-IR (KBr cm^{-1}) umax: 3457(OH), 3064(CH-Aromatic), 2930, 2853(CH-Aliphatic), 2222(C≡N), 1733(δ-Lactone), 1620(C=N), 1595(C=C). ^{1}H NMR(δ ppm) (DMSOd6):δ=7.83(1H,s,N=CH) , 6.60-7.63 (10H, m, Ar-H), 5.15(1H,s, OH) ,3.53(2H,q,CH2CH_3) and 1.88(3H,t,CH_2CH_3)**.** ;Anal Calcd**:** C,64.65

;H,3.62;Cl,7.95; N,9.42; Found: C,64.62 ;H,3.60 Cl,7.92;N,9.39.

Synthesis of 3-(3-amino-5-(2-chlorophenyl)-4-imino-3, 4-dihydropyrido[2,3-d]pyrimidin-7-yl -7-hydroxy-2H-chromen-2-one (5)

A mixture of compound (4) (0.01 mol) and hydrazine hydrate (0.01 mol) in ethanol (30 mL) was heated under reflux for 8hrs.The solvent was evaporated to dryness and residue was recrystallized from ethanol to give (5).

5: $C_{22}H_{15}ClN_5O_3$ (m.wt.432.5), brown color, m.p. 299-302ºC, yield 70%. FT-IR (KBr cm^{-1}) umax: 3444(OH), 3387, 3379($NHNH_2$), 2985, 2924, 2858 CH(aliphatic-aromatic), 1735(δ-Lactone), 1627(C=N).^{1}H NMR(δppm) (DMSOd6):δ= 8.36(1H,s, OH),8.25(1H,s,NH) ,7.20-8.08 (10H, m, Ar-H), 4.48(2H,s,br,NH_2);Anal Calcd: C,61.11;H,3.47;Cl,8.10;N,16.20; Found: C,61.08 ;H,3.44; Cl,8.07;N,16.17.

Synthesis 7- hydroxy-4-(2-chlorophenyl)-3-(2-thioxo-2,3-dihydro pyrido[3,2-e][1,2,4]triazolo [1,5-c]pyrimidin-8-yl)-2H-chromen-2-one (6)

To ethanolic solution of compound (5) (0.01 mol) in ethanol (30 mL), Carbon disulphide (0.01 mol) was added. The reaction mixture was heated under reflux for 15 hrs. or until the evaporation of H_2S complete. The reaction mixture solution was evaporated to dryness and the solid obtained was collected, recrystallized from ethanol to give (6).

6: $C_{23}H_{12}ClN_5O_3S$ (MW473.5), dark brown color, m.p. 180ºC, yield 50%. FT-IR (KBr cm^{-1}) umax: 3402.43(OH),3302.28(NH),2924.09, 2854.65 CH(aliphatic-aromatic), 1728.22(δ-Lactone), 1627.92(C=N) 1165.00(C=S).^{1}H NMR(δppm) (DMSOd6):δ=10.73(1H, s, SH),10.23(1H,s,OH),8.15 (1H, s, NH) ,6.38- 7.67 (10H, m, Ar-H). ; Anal Calcd:C,58.29 ;H,2.55;Cl,7.48 ;N,14.78; S,6.77;Found: C,58.26 ;H,2.53;Cl,7.45 ;N,14.75; S,6.74.

Synthesis of 1-(4-aminophenyl)-3-(10-(2-chlorophenyl)-2-mercaptopyrido [3,2-e][1,2,4]triazolo[1,5-c]pyrimidin-8-yl)-7-hydroxyquinolin-2(1H)-one (7)

To ethanolic solution of (6) (0.01 mol),1,4-diaminobenzene (0.01 mol) was added .The reaction mixture was heated under reflux for 10-12 hrs or until the evaporation of H2S complete. The reaction mixture solution was evaporated to dryness; the solid obtained was recrystallized from ethanol to give (7).

7: $C_{29}H_{18}ClN_7O_2S$ (MW 563.5), gray crystal color, m.p. 140ºC and yield 50%.FT-IR (KBr cm^{-1}),umax: 3561(OH), 3494,3426(NH_2), 2963, 2844 CH(aliphatic-aromatic), 2650(SH), 1651(CO-amide), 1627(C=N).^{1}H NMR(δ ppm) (DMSOd6):δ= 11.53(1H,s,SH), 9.77 (1H,s,OH), 6.75- 8.33(14H, m, Ar-H & NH2).m/z 528(1.88%) of C29H18N7O2S and base peak at m/z 41.30. ;Anal Calcd : C,61.67; H,3.22 ;Cl,6.29;N,17.38; Found: C,61.64;H,3.19 ;Cl,6.26;N,17.38.

Synthesis of 11-(2-chlorophenyl)-9-(7-hydroxy-2-oxo-2H-chromen-3-yl)-3,4-dihydro-2H-pyrido[2',3':4,5]pyrimido[1,6-b][1,2,4]triazin-2-one (9)

A mixture of (5) (0.01 mol) and chloroacetyl chloride in pyridine(20 mL) was heated under reflux on water bath for 10-12 hrs., cooled to room-temp, poured onto crushed ice containing few drops of HCL. The resulting solid was dried and recrystallized from ethanol to give (9).

9: $C_{24}H_{14}ClN_5O_4$ (MW 471.5), dark brown color, m.p.317-319ºC, yield 75%; FT-IR (KBr cm^{-1}),umax : 3430(OH), 3324(NH), 3.063 , 2924, 2858, 2879 CH(aliphatic-aromatic), 1724(δ-lactone), 1691(CO-ketone), 1620 (C=N). ^{1}H NMR(δ ppm) (DMSOd6):δ= 4.48(1H,s, OH),3.87(2H,s,CH_2), 3.29(1H,s,br,NH), 7.23-7.49(10H, m, Ar-H).MS: m/z (%) 471 (M+8.97%),105 (100); Anal Calcd**:** C, 61.09;H, 2.99; Cl, 7.51 N, 14. 84; Found: C, 61.06; H,2.96; Cl, 7.48; N, 14.81.

Synthesis of ethyl 2-(10-(2-chlorophenyl)-8-(7-hydroxy-2-oxo-2H-chromen-3-yl)pyrido[3,2-e][1,2,4]triazolo[1,5-c]pyrimidin-2-yl)acetate (10)

A mixture of (5) (0.01 mol) and diethyl malonate (0.08 mol) was heated under reflux for 6 hrs. The solid obtained was filtered off, washed with hot water, dried and purified by recrystallization from ethanol to give (10).

10: $C_{27}H_{18}ClN_5O_5$ (MW 527.5), orange color, m.p308-310ºC, yield 70%. FT-IR (KBr cm^{-1}) umax : 3409(OH), 2977, 2813 CH(aliphatic-aromatic), 1723(δ- lactone), 1616(C=N),754(C-Cl).^{1}H NMR(δppm) (DMSOd6):δ= 10.64(1H,s,br, OH), 6.99-7.45(9H, m, Ar-H), 3.26(2H,s,br,$COCH_2$),4.63(2H,q,CH_2CH_3), 1.61 (3H, t, CH_2CH_3). MS: m/z (%)528(M+5.56%), 43.34(100); Anal Calcd:C,61.43; H,3.44;

Cl,6.72;N,13.27; Found: C,61.40; H,3.41; Cl,6.69;N,13.24.

Synthesis of 3-(10-(2-chlorophenyl)-2-(2-oxopropyl) pyrido [3, 2-e][1, 2, 4] triazolo[1, 5-c] pyrimidin-8-yl)-7-hydroxy-2H-chromen-2-one (11)

A mixture of (5) (0.01 mol) and ethyl acetoacetate (0.02 mol) and (0.01mol) sodium ethoxide (which is prepared by reaction of (1gm) sodium metal with 10 ml ethanol) in 30 ml ethanol was stirred on heating for 1 hrs,refluxed for another 10 hrs. The solid obtained was filtered off, washed with diethylether,dried and purified by recrystallization from ethanol to give (11).

11: $C_{26}H_{16}ClN_5O_4$ (MW 497.5), brown color , m.p. 110ºC , yield 55% .FT-IR (KBr cm^{-1}) umax: 3435(OH), 3098, 2927 CH(aliphatic-aromatic), 1727(δ- lactone),1672(CO), 776 (C-Cl). ^{1}H NMR(δ ppm) (DMSOd6):δ= 10.71(1H,s,br, OH), 6.99-9.18(10H, m, Ar-H)3.48(2H,s, CH_2),2.95(2H,s, CH_3). MS: m/z (%)495(1%M-2), 164(100); Anal Calcd :C,62.72; H,3.24; Cl,7.12;N,14.07; Found: C,62.69; H,3.21; Cl,7.09;N,14.04.

Synthesis of 2-(10-(2-chloro phenyl) -8-(7-hydroxy-2-oxo-2H-chromen-3-yl)pyrido[3,2-e][1,2,4] triazolo[1,5-c]pyrimidin-2-yl)acetonitrile (12)

A mixture of (5) (0.01 mol) and ethyl cyanoacetate (0.02 mol) and catalytic amount of pyridine was fused for 6 hrs., The solid obtained was filtered off, washed with diethylether, dried and purified by recrystallization from ethanol to give (12).

12: $C_{25}H_{13}ClN_6O_3$ (MW 480.5) brown color, m.p340-343ºC, yield 55%. FT-IR (KBr cm^{1}), umax: 3333(OH), 3073, 2927, 2934 CH(aliphatic-aromatic),2208(C≡N) 1703(δ- lactone), 1619(C=N),755(C-Cl). ^{1}H NMR(δ ppm) (DMSOd6):δ=8.73(1H,s,br, CH=N), 8.57(1H, s, NH)6.35-8.03(10H,m,H-Ar),5.29 OR 10.17 (1H,s,OH),3.83(2H,s, CH_2). ; Anal calcd.: C,62.44; H,2.73; Cl,7.37;N,17.48; Found: C,62.41; H,2.70; Cl,7.34;N,17.45.

Synthesis of (4-(2-chlorophenyl)-3-cyano-6-(7-hydroxy-2-oxo-2H-chromen-3-yl)pyridin-2-yl)carbamodithioic acid (13)

To ethanolic solution of compound (3) (0.01 mol) in ethanol (30 mL), (5 ml) 10%KOH and Carbone disulphide (0.01 mol) was added. The reaction mixture was heated under reflux for 15 hrs. or until the evaporation of H_2S complete. The reaction mixture solution was evaporated to dryness and the solid obtained was collected, filtered off and recrystallized from ethanol to give (13).

13: $C_{22}H_{12}ClN_3O_3S_2$ (MW 465.5), pale brown color, m.p327-329ºC, yield 50%.FT-IR (KBr cm^{-1}) umax: 3352(OH), 3226(NH), 2924, 2925, 2952, 2815 CH(aliphatic-aromatic), 2612(SH), 2211(C≡N)1715(δ-lactone), 1621(C=N), 1081(C=S).^{1}H NMR(δ ppm) (DMSOd6):δ= 8.65(1H,s,OH), 8.08(1H,s,NH), 4.5(1H,s,SH), 6.63-7.56 (9H, m, Ar-H) ; Anal calcd.:C,56.71; H,2.60; Cl,7.61;N,9.02;S,13.76 Found: C,56.68; H,2.57; Cl,7.58;N,9.00;S,13.73.

Synthesis of N-(4-(2-chlorophenyl)-3-cyano-6-(7-hydroxy-2-oxo-2H-chromen-3-yl) pyridin-2-yl)benzamide (14)

A mixture of (3) (0.01 mol) and benzoylchloride (0.01 mol) in (20ml) dry benzene was heated under reflux for 6 hrs., The solid was collected after concentration, washed with diethylether, dried and purified by recrystallization from ethanol to give (14).

14: $C_{28}H_{16}ClN_3O_4$ (MW493.5), brown color, m.p 115-117ºC, yield 60%.; FT-IR (KBr cm^{-1}) umax: 3718(OH), 3431(NH), 2926, 2873 CH(aliphatic-aromatic), 1722(δ- lactone),1700(CO-amide), 1624(C=N).^{1}H NMR(δ ppm) (DMSOd6): δ=12.94(1H,s, OH), 8.83(1H,s,NHCO), 8.35(1H,s,CH-Coumarin), 6.64-8.14 (12H, m, Ar-H) ; Anal calcd. for: C,68.09; H,3.27;Cl,7.18; N,8.51; Found: C,68.06; H,3.24;Cl,7.15; N,8.48.

Synthesis of ethyl 2-(7-(4-(2-chlorophenyl)-7-hydroxy-2-oxo- 1,2-dihydroquinolin-3-yl)-4-oxo-3,4-dihydropyrido[2,3-d]pyrimidin-2-yl) acetate (15)

A Mixture of (3) (0.01 mol) and diethyl malonate (0.01 mol) in acetic acid(5ml) containing Ammonium acetate (3gm), was heated under refluxed for 8 hrs., cold to room temp, poured onto crushed ice .The solid separated was filtered off, dried and recrystallized from ethanol to give (15).

15: $C_{26}H_{19}ClN_4O_5$ (MW502.5), brown color, m.p. 330-332ºC, yield 50%. ; FT-IR (KBr cm^{-1}) υ_{max}: 3746(OH), 3427, 3226 (NH), 2924, 2925, 2952,2815 CH(aliphatic-aromatic), 1621(C=N).^{1}H NMR(δ ppm) (DMSOd6):δ=10.82, 9.32(2H,s,br,2

NHCO), 5.35(1H,s,OH), 6.10-9.32 (9H, m, Ar-H),3.9(2H,s,br,$COCH_2$) , 4.13(2H,q,CH_2CH_3) and 1.06(3H,t,CH_2CH_3).; Anal calcd.; C,62.10; H,3.81;Cl,7.05; N,11.14 Found: C,62.07; H,3.78; Cl,7.02; N,11.11.

Synthesis of 3-(2,4-diamino-5-(2-chlorophenyl)pyrido[2,3-d]pyrimidin-7-yl)-7-hydroxy-2H-chromen-2-one (16)

A mixture of guanidine hydrochloride (0.01 mol) in ethanolic solution of NaOH was stirred at room temp for 1h, compound (3) (0.01mol) was added. The reaction mixture was heated under reflux for 10 hrs. Cooled to room-temp, poured onto crushed ice. The separated solid was filtered off, dried and recrystallized from ethanol, to give (16).

16: $C_{22}H_{14}ClN_5O_3$ (MW 431.5), deep orange color, m.p180ºC, yield 65%. ; FT-IR (KBr cm^{-1}), υ_{max}: 3614(OH), 3471,3433,3279(NHNH2),2958 CH(aromatic), 1734(δ- lactone),1644(C=N).^{1}H NMR(δ ppm) (DMSOd6):δ= 11.19(2H,s,br,2 OH), 10.59 (1H,s,NH), 9.66(2H,s,br,NH2), 6.51-8.66 (9H, m, Ar-H).; Anal calcd; C,61.19; H,3.27;Cl,8.21; N,16.22 Found: C,61.16; H,3.24;Cl,8.18; N,16.19.

2.3 Coating Composition and Film Preparation

The coating compositions were prepared by means of incorporating coumarin derivatives (1, 6, and16), in the ratio of 1.0, 2.0 and 3 %, into epoxy varnish. The coating compositions were applied to steel and wood panels by means of a brush or by sweeping. All efforts were made to maintain a uniform film thickness of 50 +/- 5µm for evaluating the properties of modified films.

2.3.1 Drying time

To determine Set-To-Touch Time-lightly touch the test film at point not less than 15 mm from the film edges with the tip of a clean finger and immediately place the fingertip against a pieces of clean glass. Observe if any of the coating transferred to the glass. The film considered to set-to-touch when it still shows a tacky condition, but none of it adheres to the finger (Surface dry).

2.3.2 Hard dry time

With the end of the thumb resting on the test film and the forefinger supporting the test panel, exert a maximum downward pressure (without twisting) of the thumb on the film. Lightly polish the contacted area with a soft cloth. The film considered dry-hard when any mark left by the thumb completely removed by the polishing operation [18].

2.4 Anti-Corrosion Testing

The test pieces were 20 x 20 x 3 mm. The samples were first mechanically polished with a fine grade emery paper in order to obtain a smooth surface, followed by degreasing with acetone and then rinsed with distilled water, dried between two filter papers. A salt fog chamber was utilized for each of the resin formulations; with a set of three coated panels being placed in the salt spray chamber according to ASTM. The corrosion resistance was evaluated in terms of blistering, scribe failure and degree of rusting, in relation to ASTM standards [19-22].

2.5 Flame Retardant Testing Method

The performance of epoxy varnish, with incorporated coumarin derivatives (**1, 6 and 16**) additives, was evaluated in a limited oxygen index (LOI) chamber. LOI values were determined by standardized tests methods [23]. The test panels were prepared using a combustible material (wood specimen). It was important that the panels were free of any surface contamination, or imperfections, prior to the coating application. Hand tool cleaning (sand paper) was carefully used to treat the faces and edges of the panels. Final dry film thickness (DFT) was 50 +/- 5µm. In all cases, the film application was applied by means of brushing. Following 10 days of air drying, the panels under study were heated at 50-60°C for 2 hr. to eliminate any remaining solvent.

2.6 Screening Anti-microbial Activity

Preliminary screening for the antimicrobial activity of synthesized compounds using standardized disc-agar diffusion method [24] against the bacteria *Staphylococcus aureus*, *Bacillus subtilis* (Gram-positive bacteria) and *Salmonella typhimurium*, *Escherichia coli* (Gram-negative bacteria), in addition to the yeast *Candida albicans* and fungus *Aspergillus fumigatus* (fungi) following the filter paper disc technique. Chloramphenicol, Cephalothin and Cycloheximide were taken as standard drugs compared with standard antimicrobial agents. The synthesized compounds and reference drugs were dissolved in dimethyl formamide (DMF) at 1 mg/ml. Antimicrobial activity was

determined by measuring the diameter of the inhibition zone after an incubation for 24 h at 37°C and the activity of each compound was compared with its respective reference drug as a positive control. The results are listed in Table 1.

Antibiotic is a growing problem, some of this is due to the overuse of antibiotics in human, but some of it is probably due to the use of antibiotics as growth promoters in food of animals [25]. So, there is growing demand for new antibiotics. Coumarin derivatives were reported to exhibit interesting antimicrobial activity [26].

3. RESULTS AND DISCUSSION

3.1 Synthesis

The synthetic strategies utilized for the synthesis of the target compounds are outlined in (Schemes 1-3) which could assemble entirely the desired coumarin derivatives (**2-16**) from the strategic starting material 3-acetyl-7-hydroxy-2-oxo -2H-chromen-2-one **(1)** which wasprepared in accordance with the method described in the literature [27] via Knoevenagel condensation reaction in the presence of piperidine without solvent. The ^{13}C- NMR spectrum of compound (**1**) revealed signals at ppm. 30.51191.51, 159.53-165.64corresponding to (CH_3), CO ketone, CO δ -lactone and C-OH.

Treatment of compound 1 with o-chlorobenzaldehyde in ethanolic solution of NaOH under Claisen Schmidt conditions afforded 3-(3-(2-chlorophenyl)acryloyl)-7-hydroxy-2H-chromen-2-one(**2**) [28-30]. Its structure was elucidated on the bases of elemental analysis and spectral data.TheIR and ^{1} H NMR spectra agreed with the assigned structure (Scheme 2).

Treatment of compound **2** with malononitrile and ammonium acetate in sodethoxide solution to afforded 2-amino-4-chloro phenyl-6[-(7-hydroxy-2-oxo-2H-chromen-3-yl)] nicotinenitrile (**3**). The IR spectrum showed absorption bands at 3369,3230, 2207 cm-1 due to NH_2 and C≡N groups. Its^1 H NMR spectrum showed signals resonated at aboutδ= 6.65-7.52 ppm in the ^{1} H NMR corresponding to NH_2 and aromatic protons.

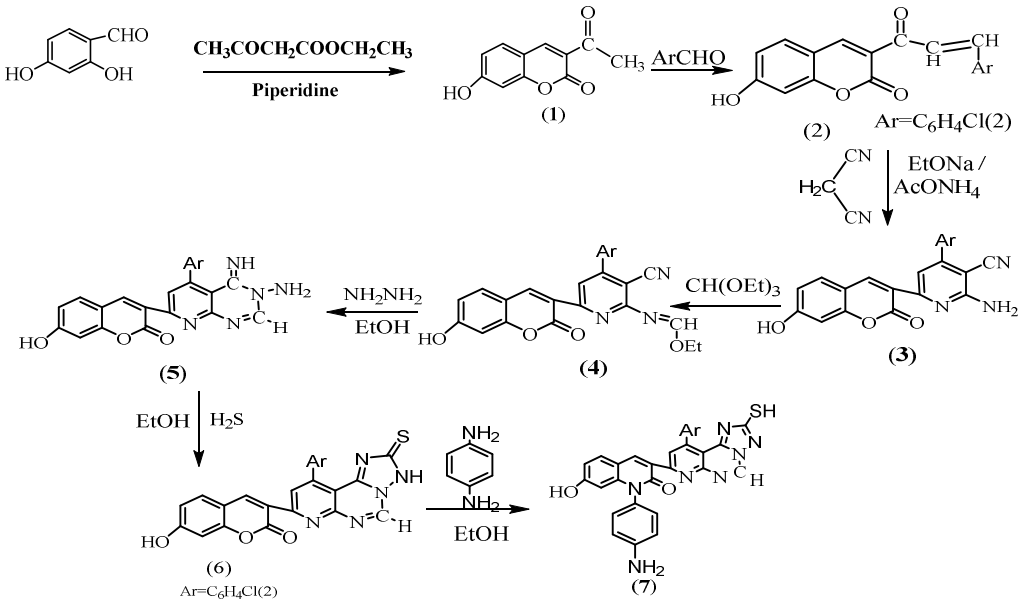
Reaction of compound **3** with triethylorthoformate in acetic anhydrideafforded the corresponding ethyl N-4-(2-chlorophenyl)-3-cyano-6-(7-hydroxy-2-oxo-2H-chromen-3-yl) pyridin -2-yl]formimidate (4). The IR spectrum showed strong absorption bands at 2222,1733 cm^{-1}, attributable to carbonitrile and carbonyl groups. Its ^{1}H-NMR spectrum revealed signalat δ= 7.83 ppm due to one proton for N=CH, a quartet signal of two protons formethylene atδ= 3.53ppmand triplet signal of three protons for methyl at δ=1.88 ppm.

Treatment of 4 with hydrazine hydrate in boiling ethanol afforded the corresponding3-(3-amino-5-(2-chlorophenyl)-4-imino-3,4-dihydropyrido[2,3d] pyrimidin- 7-yl)-7-hydroxy-2H-chromen-2-one (5). The structure of **5** have been deduced from the micro analytical and spectral data. The IR spectrum exhibited strong absorption bands at v=3444, 3387,3379 cm^{-1} attributed to OH and$NHNH_2$.

7- hydroxy-4-(2-chlorophenyl)-3-(2-thioxo-2,3-dihydro pyrido[3,2-e][1,2,4]triazolo [1,5-c]pyrimidin-8-yl)-2H-chromen-2-one(**6**) has been prepared by the interaction of **5** with carbon disulphide in boiling ethanol .The IR spectrum of **6** exhibited strong absorption bands assigning (C=S) , NH group at 3302 and 1165.00 cm-1. On the other hand, ^{1}H NMR spectrum revealed signals at δ=10.73,8.15 ppm signalof one proton for SHand signalof one proton for NH.

The structure of 6 was confirmed chemically by the interaction with 1,4-phenylenediamine in boiling ethanol to give 1-(4-aminophenyl)-3-(10-(2-chlorophenyl)-2-mercaptopyrido[3,2-e][1,2,4] triazolo[1,5-c]pyrimidin-8-yl)-7-hydroxyquinolin-2(1H)-one (**7**) not the expected3[-(2-((4-aminophenyl)amino)pyrido[3,2-e][1,2,4]triazolo [1,5-c] pyrimidin-8-yl)-]7-hydroxy-4-(2-chlorophenyl)-2H-chromen-2-one(8) .IR spectrum of (**7**) showed strong absorption bands at 3494,3426, 2650,1651 cm-1 attributed toNH_2, SH and CO-amide and devoid the presence of CO δ lactone. The ^{1}H-NMR spectrum revealed signals atδ=11.53ppm of one proton of OH ,δ= 9.77ppm of one proton of SH and one broad signal of two proton of NH_2 at δ=8.33 ppm.

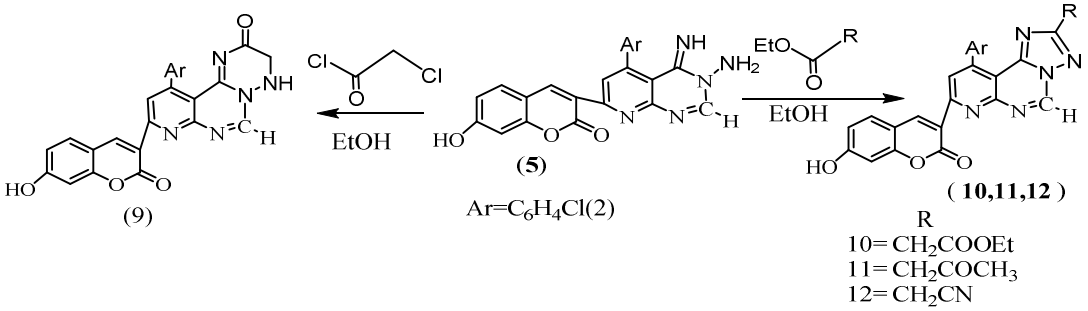
On the other hand,11-(2-chlorophenyl)-9-(7-hydroxy-2-oxo-2H-chromen-3-yl)-3,4-dihydro-2H-pyrido[2',3':4,5]pyrimido[1,6-b][1,2,4]triazin-2-one **(**9**)**was prepared bythe reaction of compound(5) with chloroacetyl chloride in boiling pyridine.IR spectrumshowed absorption bands at 3430, 3324.1691 cm^{-1} due toNH2and CO-ketone. The mass spectrum contained the molecular ion peak at m/z = 471.



Scheme(1)

Also, compound (**5**) was reacted with active methylene compounds, namely (diethyl-malonate, ethylacetoacetate and ethyl-cyanoacetate to afford the corresponding ethyl 2-(10-(2-chlorophenyl)-8-(7-hydroxy-2-oxo-2H-chromen-3-yl)pyrido[3,2-e][1,2,4]triazolo[1,5-c]pyrimidin-2-yl)acetate **(10)**, 3-(10-(2-chlorophenyl)-2-(2-oxopropyl)pyrido[3,2-e][1,2,4]triazolo[1,5-c]pyrimidin-8-yl)-7-hydroxy-2H-chromen-2-one **(11)**, and 2-(10-(2-chloro phenyl) -8-(7-hydroxy-2-oxo-2H-chromen-3-yl)pyrido[3,2-e][1,2,4] triazolo[1,5-c]pyrimidin-2-yl)acetonitrile **(12)**. The chemical structures of **10-12** were established based on elemental data and also on spectral data (IR, 1HNMR, mass). For example, compound **10**, IR (cm-1): 3409, 2208 cm^{-1}, attributed to OH, C≡N whereas, the ^{1}HNMR spectrum **10** displayed signals at δ=10.64,3.26, 4.63, 1.16 ppm attributed to onebroad signal of one proton for hydroxyl, one singlet of two protons for methylene, one quartet signal of two protons for methylene and one signal triplet of three protons for methyl. The mass spectrum data of each **10** and **11** exhibited a molecular ion peak at the correct molecular weight for the respective compound (see Experimental).

On the other hand, compound (**3**) was reacted with carbon disulphide in boiling ethanol to afford the corresponding (4-(2-chlorophenyl) -3-cyano-6-(7-hydroxy-2-oxo-2H-chromen-3-yl) pyridin-2-yl)carbamodithioic acid (**13**). IR spectrum showed absorption bands at 3226 , 2612,2211 and 1081 cm^{-1}, corresponding to NH , SH, C≡N and C=S . The ^{1}H-NMR spectrum showed the absence of a signal at δ=7.52 ppm of two protons for NH_2 whereas, revealed signals at δ= 8.08 ppm of one proton for NH and 4.5 ppm of one proton for SH.



Scheme(2)

Similarly, compound (**3**) was reacted with benzoyl chloride in boiling dry benzene to afford the corresponding N-(4-(2-chlorophenyl)-3-cyano-6-(7-hydroxy-2-oxo-2H-chromen-3-yl) pyridin-2-yl)benzamide (**14**). IR spectrum showed absorption bands at 3431 , 1700,1624 cm^{-1}, attributed to NH , , CO-amide. The ^{1}H-NMR spectrum revealed signals at δ=12.94 ppm of one proton for OH, δ=8.83 ppm of one proton for NH-CO.

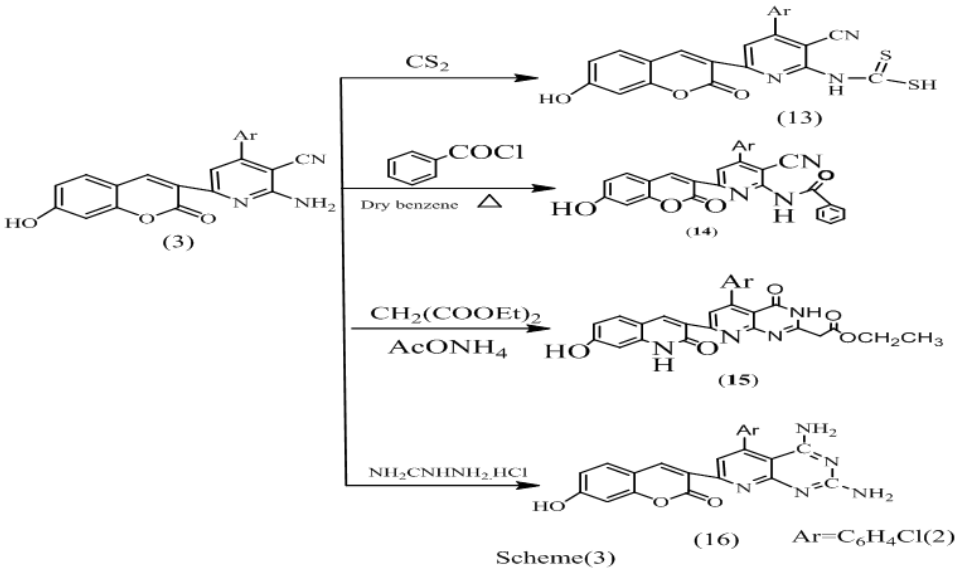
In additional, compound (**3**) was reacted with diethyl malonate in boiling acetic acid in the presence of amm-acetate to afford the corresponding ethyl 2-(7-(4-(2-chlorophenyl)-7-hydroxy-2-oxo-1,2-dihydroquinolin-3-yl)-4-oxo-3,4-dihydropyrido[2,3-d]pyrimidin-2-yl)acetate (**15**). IR showed absorption bands at 3226 cm^{-1} attributable to NH devoid the presence of CO lactone and C≡N. The ^{1}H-NMR spectrum revealed signals at δ=10.8,29.32 ppm of two protons for two NHCO,δ=5.35 ppm one proton forOH δ=3. 6ppm one broad signal of two protons for $COCH_2$, δ= 4.13 ppm one quartet signal of two protons for CH2CH3 and δ=1.06 ppm one triplet signal of three protons for CH2 CH_3.

Also, compound (**3**) was reacted with guanidine hydrochloride in ethanolic sod.hydroxide to afford the corresponding 3-(2,4-diamino-5-(2-chlorophenyl)pyrido[2,3-d]pyrimidin-7-yl)-7-hydroxy-2H-chromen-2-one (**16**). The IR spectrum devoid the presence of C≡N (Scheme 3).

3.2 Screening Anti-microbial Activity

The antimicrobial activity of the new coumarin derivatives showed that all compounds were moderate active against tested micro-organisms except compounds (**1, 2, 6**) were the most potent against *Staphylococcus aureus*, *Bacillus cereus* and Salmonella, *Escherichia coli*. In addition, compounds (**4**), (**5**), (**12**), (**15**) and (**16**) were effective in inhibiting the growth of Bacillus cereus, but less effective than (**1, 2, 6**). All synthesized compounds have high potent against Candida albicans but have not any effective against Aspergillus fumigatus. Antimicrobial activity was determined by measuring the diameter of the inhibition zone after an incubation for 24 h at 37°C.The activity of each compound was compared with its respective reference drug as a positive control and the values were listed in Table 1.

The antimicrobial screening data showed that the compounds exhibit antimicrobial activities. The increased activity of the novel coumarins can be explained by the hydroxyl group, chloro phenyl, pyridine, pyrimidine and triazolo coumarin derivatives which act as more powerful and potent bactericidal agents [31]. π-Electrons delocalization over the coumarins increases the lipophilic character and favors its permeation through the lipoid layer of the bacterial membranes. It was concluded that coumarins acting as electrophilic agents have a positive effect and inhibited bacterial growth [32,33].



Scheme(3)

Table 1. Anti-microbial activity of Coumarin derivatives

Organism	Mean* of zone diameter, nearest whole mm.											
	Gram - positive bacteria				Gram - negative bacteria				Yeasts and Fungi**			
	Staphylococcus aureus (ATCC 25923)		*Bacillus subtilis* (ATCC 6635)		*Salmonella typhimurium* (ATCC 14028)		*Escherichia coli* (ATCC 25922)		*Candida albicans* (ATCC 10231)		*Aspergillus fumigatus*	
Conc. / Sample	1 mg/ml	0.5 mg/ml	1 mg/ml	0.5 mg/ml	1 mg/ml	0.5 mg/ml	1 mg/ml	0.5 mg/ml	1 mg/ml	0.5 mg/ml	1 mg/ml	0.5 mg/ml
1	21I	18I	23I	19I	9L	7 L	15I	13I	23I	22H	-	-
2	19I	17I	23 I	18 H	9 L	8 L	9 L	6 L	27 H	23 H	-	-
4	-	-	23 I	20 I	-	-	10L	7 L	27 H	24 H	-	-
5	-	-	16 I	14 I	10 L	6 L	-	-	29 H	23 H	-	-
6	17I	15I	20 I	17 I	14I	12I	15I	13I	33 H	28 H	-	-
12	-	-	19 I	15 I	-	-	-	-	25 H	20 H	-	-
15	-	-	10 L	8 L	8L	6 L	-	-	23 I	19 I	-	-
16			20 I	18 I	-	-	9 L	7 L	25 H	22H	-	-
Control	35	26	35	25	36	28	38	27	35	28	37	26

3.3 Coating Evaluation

After the successful preparation of the coumarin compounds, some of these compounds were selected, represented in (**1, 6 and 16**) and physically inserted into a coating formulations as modifiers, after that, the influence of these modifications on some of the properties of the epoxy coating such as the drying time of film formation, as well as the possibility of using these derivatives as anti-corrosive and as flame retardants, were studied.

These results are tabulated in Tables 2, 3 and 4 and represented in the Fig. 2 for drying time, Figs. 3, 4, 5 and 6 for anti-corrosion and Fig. 7 for flame retardant dates.

3.4 Drying Time

From Table 2 and Fig. 2 it is clear that insert coumarin modifiers leads to shortening in the drying times. As increasing the percentage of modifier the drying times decrease.

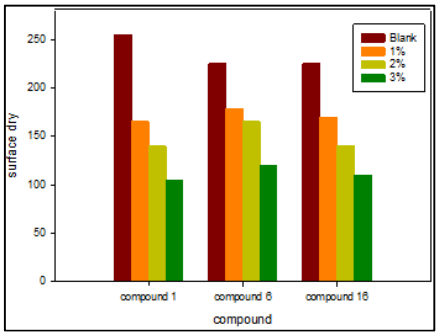
3.5 Corrosion Resistance

The epoxy paint compositions were prepared by means of incorporating coumarin derivatives (1, 6 and 16) by the ratio of 1.0, 2.0 and 3.0% by 5µm. weight into epoxy paint and film thickness 50 ± were evaluated as the anti-corrosive. The paint formulations were evaluated on coated steel panels. To ensure that the steel panels were free of all surface contamination before the coating application, pre-treatment involved wire brushing and sand paper cleaning of the surface. The coated steel panels were exposed to salt spray tests (salt fog) according to CSN ISO 9227-2017for 500 h. Photographic reference standards were used to evaluate the degree of blistering. The reference standards high light the various degrees of blistering that can potentially develop when paint systems are subjected to these specific test conditions. The blistering size is graded from 10 to 0, where 10 represents of no blistering and 0 representative of the largest blister. Blistering frequency is denoted by F, M, MD and D (few, medium, medium dense and dense). Painted, or coated, specimens subjected to a corrosive environment are also evaluated by recording the average maximum and minimum creep age from the scribe mark. Scribe failure is also rated on a scale from 10 to 0, with 10 being (zero mm) from the scribe mark and 0 is (16 mm) from the scribe mark. Finally, visual comparison of the surface with photographic reference standards, to determine the percentage of the area that has been rusted, is also used. These visual standards were developed in cooperation with the Steel Structure Painting Council (SSPC) to further standardization of test methods. The amount of rusting beneath, or through, a paint film is a significant factor in determining whether a coating system should be repaired, or replaced. The rust grade is rated on scale from 10 to 0, where10 is none rusting and 0 is severe rusting. The results of corrosion resistance of the painted films of prepared samples are given in Table 3 and Figs. 3, 4, 5 and 6 explains the photo of the painted films after salt test spray (5% of NaCl).

Concerning with the blistering test the data given in Table 3 show that all modifiers improve the blistering and as the concentration of modifier increase blistering resistance increase; except the modified varnish by modifier **(16**) [3-(2,4-diamino-5-(2-chlorophenyl)pyrido[2,3-d]pyrimidin-7-yl)-7-hydroxy-2H-chromen-2-one]did not affect blistering resistance. About the Scribe failure test from the data given in tables (**3**); it is clear that

Table 2. Surface dry and hardener dry of epoxy modifier with coumarin derivatives at 25ºC

Sample no.	Modifier %	Surface dry (minute)	Hardener dry (minute)
Blank	--	225	410
Epoxy modified with 1	1.00	165	370
	2.00	140	345
	3.00	105	300
Epoxy modified with 6	1.00	178	360
	2.00	165	300
	3.00	120	260
Epoxy modified with 16	1.00	170	370
	2.00	140	325
	3.00	110	280



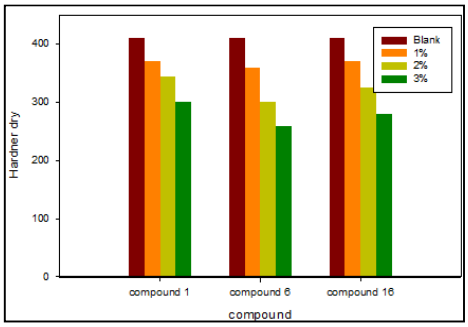


Fig. 2. Plot ofeffect modification and concentration on surface dry & hard dry - of modified Epoxy

Table 3. Evaluation the corrosion resistance of the painted films

Sample	Modifier %	Blistering size	frequency	Scribe failure (mm)	Rust grade
Blank	0	2	M	13	2
Epoxy modified	1.00	5	F	11	2
with 1	2.00	6	M	9	5
	3.00	8	M	3	8
Epoxy modified	1.00	6	MD	8	2
with 6	2.00	6	M	7	6
	3.00	8	M	2	7
Epoxy modified	1.00	7	MD	7	4
with 16	2.00	7	M	6	4
	3.00	7	M	4	6

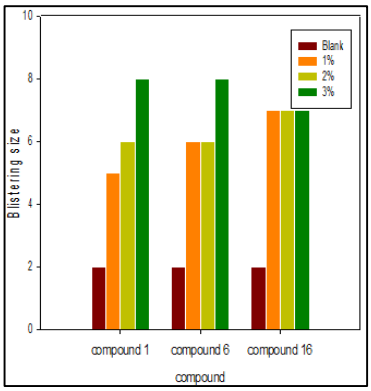


Fig. 3. Plot of effect modification and concentration on blistering of modified Epoxy

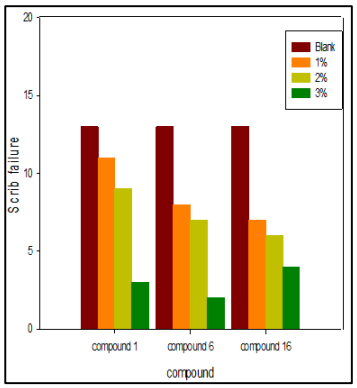


Fig. 4. Plot of effect modification and concentration on scribe failure of modified Epoxy

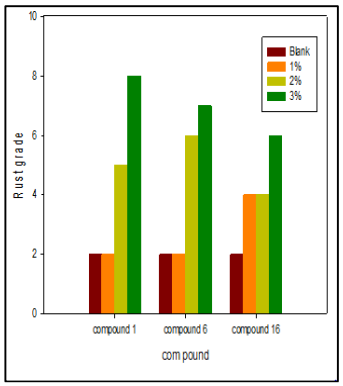


Fig. 5. Plot of effect modification and concentration Rust grade of modified Epoxy

the adding of modifiers improve the scribe value. It is clear that the compounds**(6)**[7- hydroxy-4-(2-chlorophenyl)-3-(2-thioxo-2,3-dihydro pyrido [3,2-e][1,2,4] triazolo [1,5-c]pyrimidin-8-yl)-2H-chromen-2-one] give the best results which shifts from 13 mm within epoxy varnish along to (2 mm) within epoxy varnish modified 3%. The order of inhibition can be arranged as follow: 6 > 16 > 1.

Finally rust grade of epoxy modified films the adding of modifiers in all percentage improves the rust grade inhibition especially modifier **(1)** [3-acetyl-7-hydroxy-2- oxo -2H-chromen-2-one]. From the previous study it is clear that there are satisfactory differences between the blank and modified samples, the coumarin derivatives (1, 6 and 16) are considered an corrosion inhibitor for mild steel when added to epoxy coating. The

improvement of corrosion resistance may be attributed to the introducing of a compound that containing nitrogen, sulfur and oxygen.

3.6 Evaluation of Coumarin Derivatives as a Flame Retardant

The LOI is defined as the minimum concentration oxygen, expressed as a percentage that will support combustion of a polymer. It is measured by passing a mixture of oxygen and nitrogen over a burning specimen, and reducing the oxygen level until a critical level is reached. The LOI is expressed as:

$$\mathrm{LOI} = 100\frac{02}{[02]-[N2]}$$

This method proved suitable as a semi-quantitative indicator of the effectiveness of the flame retardant during the research and development phase of the work. This was due to the fact that the equipment is relatively inexpensive and the size of the test sample that is required is reasonably small. It is clear that the incorporation of coumarin derivatives into epoxy paint, in the ratio's mentioned in the experimental section, results in enhanced flame retardancy when compared with an epoxy control sample. The results obtained from the LOI test are shown in Table 4 and Fig. 7.

The most important finding from flame retardant characteristic data given in Table 4 proved that increasing the percentage of modifier with coumarin derivative compound (1,6,and 16) lead to increasing limiting oxygen index (LOI) (**16 > 6 > 1**).

The improvement of LOI value may be attributed to the introducing of a compound that containing nitrogen, sulfur, oxygen, and chlorine atoms and aromaticrings within their structure.

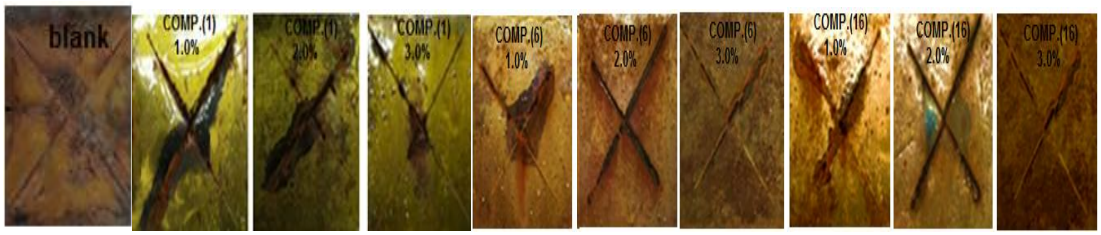


Fig. 6. The photo of the painted samples after exposed to salt spray test (5%NaCl)

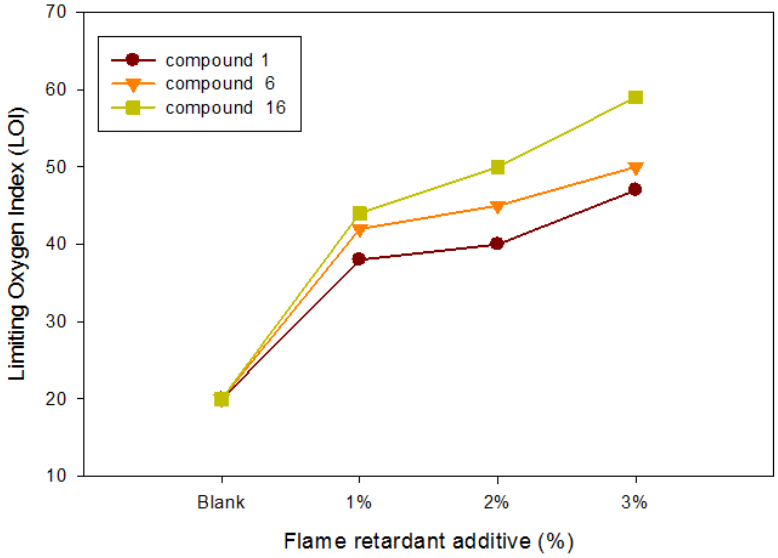


Fig. 7. Limiting oxygen index (LOI) – Flameretardant additive curve in absence and presence of different concentration of modified epoxy

Table 4. Limiting Oxygen Index (LOI) of modified epoxy coumarin

Sample	Modifier %	Limiting Oxygen Index (LOI)
Blank	-	20
Epoxy modified with 1	1.00%	38
	2.00%	40
	3.00%	47
Epoxy modified with 6	1.00%	42
	2.00%	45
	3.00%	50
Epoxy modified with 16	1.00%	44
	2.00%	50
	3.00%	59

4. CONCLUSION

In the present work, a series of some new heterocyclic compounds (**1-16**) containing coumarin moiety was synthesized, the structures of the new compounds were confirmed by suitable physical, chemical methods and were tested for their antimicrobial activities. Compounds (**1,2,6**) were the most potent coumarin derivative against Gram-positive and Gram-negative bacteria. Also a new green corrosion inhibitor as well as flame retardant additives from coumarins (**1,6,16**) are successfully synthesized and physically incorporating into epoxy resin to form a new modified epoxy varnish. Corrosion inhibitor was carried out by using salt spray technique, and flame retardant was evaluated by measuring the limiting oxygen index (LOI) of the coated films. Compounds (**1,6 and 16**)were physically mixed with epoxy resin to produce anew modified coatings as flame retardants and anti-corrosive organic coatings, the results obtained confirmed that these new developed varnishes have an excellent properties as flame resistance and anticorrosive for mild steel.

COMPETING INTERESTS

Authors have declared that no competing interests exist.

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