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Synthesis and Antituberculosis Activity of substituted 3,4-(di-coumarin-3-yl)-2,5-diphenyl furans and pyrroles†

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Abstract: Increasing rates of multi-drug resistant (MDR) and extremely-drug resistant (XDR) cases of tuberculosis (TB) strains are alarming, which eventually hampered an effective control of the pathogenic disease. In present study, **9** derivatives of 2,3-bis(2-oxochromen-3-yl)-1,4-diphenyl-butane-1,4-dione (**11a-c**) and 3,4-(dicoumarin-3-yl)-2,5-diphenyl furans and pyrroles (**12a-f**) have been synthesized successfully. The experimental data for the Anti-tuberculosis activity (using MABA assay) of 2,3-bis(2-oxochromen-3-yl)-1,4-diphenyl-butane-1,4-dione (11a-c) revealed that in this series compound 11a showed better minimum inhibitory concentration of 1.6 µg/ml against *Mycobacterium tuberculosis* (H37 RV strain) ATCC No- 27294 which was better than the MIC value of Pyrazinamide-3.125 µg/ml, Streptomycin-6.25 µg/ml and Ciprofloxacin- 3.125 µg/ml. Our synthesis and in-vitro studies thus pointed out the moderate to good anti-TB profiles of substituted furans and pyrroles.

Keywords: tuberculosis; *Mycobacterium*; furans; pyrroles.

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1. Introduction

Coumarins are naturally occurring compounds known for their low toxicity and varied biological activity. The biological spectrum of coumarin has intrigued medicinal researchers to investigate coumarin scaffolds for their relevance as anti-TB drugs [1]. Akiyama K *et al.* [1] evaluated antifungal activities of the optically pure (>99%ee) (-)- and (+)-virgatusin, a tetra-substituted tetrahydrofuran lignan. Molvi KI *et al.* [2] synthesized various tetrasubstituted thiophene compounds and evaluated them for their anti-inflammatory activity. The same group has also developed synthesis of tetrasubstituted thiophene esters and evaluated them for anti-inflammatory, analgesic and antioxidant activities [3]. Padron JM *et al.* [4] synthesized various tetrasubstituted pyrrole derivatives and evaluated for their in vitro anti-proliferative activities using the human promyelocytic leukemia cell line HL60.

Pagadala LR *et al.* [5] developed the synthesis of 1,2,3,5-tetrasubstituted pyrrolyl-N-acetic acid derivatives and evaluated for anti-mycobacterial activity. Jose M. Padron *et al.* [6] developed the synthesis of tetrasubstituted pyrrole derivatives and evaluated for anti-breast cancer activity. W. M. Basyouni *et al.* [7] synthesized a series of 3,4,5-trisubstituted 2(5H)-furanone derivatives through one-pot reaction of amines, aldehydes and diethyl acetylenedicarboxylate. The synthesized compounds were tested against HEPG-2, MCF-7 and CACO tumor cell lines. Babu S. P. *et al.* [8] synthesized 2,4-disubstituted furan derivatives and evaluate them for anti-diabetic activity. Molvi K. I. *et al* [9] synthesized

various trisubstituted thiophene compounds and evaluated them for their anti-inflammatory activity. Weiqin Jiang *et al* [10] synthesized various trisubstituted thiophene compounds and evaluated them for their progesterone receptor modulator activity. Gonul Velicelebi *et al.* [11] synthesized various trisubstituted thiophine analogs and evaluated them as compounds, which modulate the activity of store-operated calcium (SOC) channels. Raquel Pereiraet *et al.* [12] synthesized various trisubstituted heterocyclic scaffolds mostly thiophenes of PPAR ligands, which displayed PPAR agonist activity as revealed by reporter assay in living cells.

Dhruv Panchal *et al* [13] synthesized and evaluated the activity of a trisubstituted Pyrrole in inhibiting Sporozoite invasion and blocking malaria infection. Giuseppe Vecchi [14] synthesized various trisubstituted Pyrrole and evaluated their activity against pathogenic microorganisms, and particularly against mycetes and Gram-positive and Gram-negative bacteria.

After successfully synthesizing hydrazone-hydrazides and evaluating their biological or antituberculosis activity, we diverted our research interest towards the synthesis of tetra-substituted furans and pyrroles which carried two units of such ortho substitution. The general structure shown below (**Figure 1**) shows two such units in a five-member heterocyclic ring with expected activity on the higher side. Here R1 and R2 along with C=C linkage forms the first ortho-substituted unit where as R3 and R4 along with C=C linkage forms the second ortho-substituted unit where in each of the pair one of the substituents is phenyl while the other substituent is coumarin. Based on above observation we concluded that it was worth trying the synthesis of such substituted 3,4-(dicoumarin-3-yl)-2,5-diphenyl furans and pyrroles and evaluate them for Antituberculosis Activity. In present study, all synthesized compounds were tested for their anti-tubercular activity using the microplate Alamar Blue Assay method (MABA) [15-39]. Moreover, our research group is also currently focusing biological activities of various natural as well as synthetic molecules [40-50].

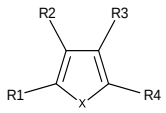


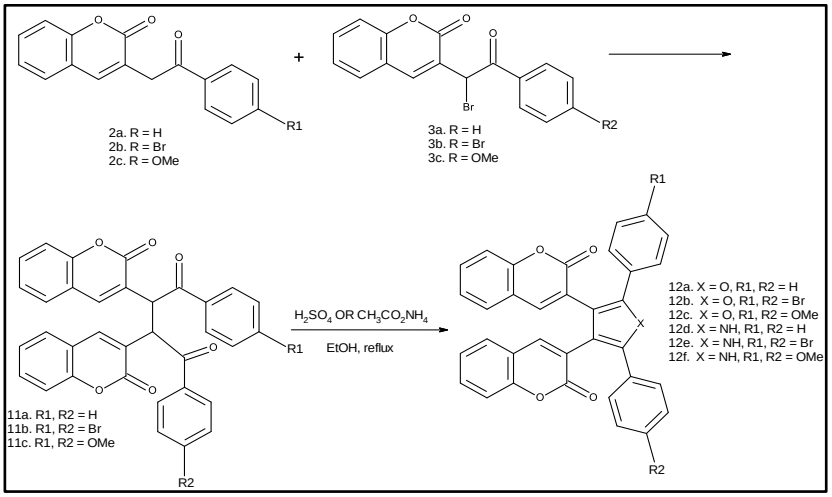
Figure 1. General chemical structures of synthesized derivatives furans and pyrroles.

2. Materials and Methods

The structures of the synthesized compounds are confirmed using modern spectroscopic techniques like ^{1}H-NMR, ^{13}C-NMR, mass spectrum and FT-IR. Purity of compounds was monitored by TLC on silica F_{254} coated aluminum plates (Merck) as adsorbent and U.V. light and Iodine chamber as a visualizing agent. Column chromatography was performed on silica gel 100–200 mesh, using ethyl acetate and hexanes mixture as eluent. Melting points were determined by using a superfit hot-stage melting point apparatus and are uncorrected.

2.1. ***Synthesis of substituted 3,4-(dicoumarin-3-yl)-2,5-diphenyl furans and pyrroles (12a-f)***

For the current study, **Scheme 1** envisages the schematic representation for the synthesis of substituted 3,4-(dicoumarin-3-yl)-2,5-diphenyl furans and pyrroles (**12a-f**). For the synthesis of the desired molecules, 3-(2-oxo-2-phenylethyl)-2H-chromen-2-ones **(2a-c)** was reacted with 3-(1-bromo-2-oxo-2-phenylethyl)-2H-chromen-2-ones **(3a-c)** in presence of strong base to give 2,3-bis(2-oxochromen-3-yl)-1,4-diphenyl-butane-1,4-dione **(11a-c)**.



Scheme 1. *Synthesis of (11a-c) and substituted 3,4-(dicoumarin-3-yl)-2,5-diphenyl furans and pyrroles (12a-f)*

These 1,4-diones were then cyclized by refluxing either with sulfuric acid or ammonium acetate using ethanol as solvent to give hydrolyzed to give substituted 3,4-(dicoumarin-3-yl)-2,5-diphenyl furans and pyrroles (12a-f). The final substituted 3,4-(dicoumarin-3-yl)-2,5-diphenyl furans and pyrroles (12a-f) isolated are shown in **Scheme 1**.

2.2 ***Experimental***

2.2.1 Synthesis of 2,3-bis(2-oxo-2H-chromen-3-yl)-1,4-diphenylbutane-1,4-dione (11a):

A mixture of 3-(2-oxo-2-phenylethyl)-2H-chromen-2-one **2a** (1.5 g, 5.68 mmol), 3-(1-bromo-2-oxo-2-phenylethyl)-2H-chromen-2-one **3a** (1.948 g, 5.68 mmol) and potassium carbonate (1.569 g, 11.35 mmol) in acetone (56.8 ml) was heated to 60 °C for 16hrs. The mixture was cooled to room temperature and then added 150 ml water solid separated out, filtered and wash with 15 ml water and dried. Crude compound was purified by column chromatography to get pure compound in 81% yield (2.42g), white solid; M.P = 160-162 ºC; **^{1}H-NMR** (400 MHz, $CDCl_3$): δ 6.14 (s, 2H), 7.24 -7.15 (m, 4H), 7.58-7.33 (m, 10H), 7.97 (s, 2H), 8.16-8.14 (d, J = 8.0 Hz, 4H); **FT-IR** (cm^{-1}): 3020 (Aromatic C-H Stretch), 1714 (Pyrano C=O group), 1666 (Aryl ketone C=O Stretch), 1608 (Aromatic C=C stretching).

2.2.2 Synthesis of 1,4-bis(4-bromophenyl)-2,3-bis(2-oxo-2H-chromen-3-yl)butane-1,4-dione (11b):

A mixture of 3-(2-oxo-2-(4-bromophenyl)ethyl)-2H-chromen-2-one **2b** (1.94 g, 5.68 mmol), 3-(1-bromo-2-oxo-2-(4-bromophenyl)ethyl)-2H-chromen-2-one **3b** (2.38 g, 5.68 mmol) and potassium carbonate (1.569 g, 11.35 mmol) in acetone (56.8 ml) was heated to 60 °C for 16hrs. The mixture was cooled to room temperature and then added 150ml water solid separated out, filtered and wash with 15 ml water and dried. Crude compound was purified by column chromatography to get pure compound in 74% yield (2.21g) white solid; M.P = 156-58 ºC; **^{1}H-NMR** (400 MHz, $CDCl_3$): δ 6.05 (s, 2H), 7.19 -7.17 (d, 2H), 7.26 (d, 1H), 7.28 (d, 1H), 7.52-7.45 (m, 4H), 7.61-7.59 (d, J = 8.0 Hz, 4H), 7.94 (s, 2H), 8.02-7.99 (d, J = 8.0 Hz, 4H); **FT-IR** (cm^{-1}): 3015 (Aromatic C-H Stretch), 1716.6 (Pyrano C=O group), 1664.5 (Aryl ketone C=O Stretch), 1608.6 (Aromatic C=C stretching).

2.2.3 Synthesis of 1,4-bis(4-methoxyphenyl)-2,3-bis(2-oxo-2H-chromen-3-yl)butane-1,4-dione (11c):

A mixture of 3-(2-oxo-2-(4-methoxyphenyl)ethyl)-2H-chromen-2-one **2c** (1.67 g, 5.68 mmol), 3-(1-bromo-2-oxo-2-(4-methoxyphenyl)ethyl)-2H-chromen-2-one **3c** (2.11 g, 5.68 mmol) and potassium carbonate (1.569 g, 11.35 mmol) in acetone (56.8 ml) was heated to 60 °C for 16 hrs. The mixture was cooled to room temperature and then added 150ml water solid separated out, filtered and wash with 15 ml water and dried. Crude compound was purified by column chromatography to get pure compound in 78% yield (2.33g), white solid; M.P = 145-49 ºC; **^{1}H-NMR** (400 MHz, $CDCl_3$): δ 3.83 (s, 6H), 6.08 (s, 2 H), 6.93-6.91 (d, J = 8.0 Hz, 4 H), 7.17-7.15 (d, 2H), 7.24-7.22 (m, 2H), 7.46-7.42 (m, 2H), 7.50-7.48 (dd, 2H), 8.00 (s, 2H), 8.15-8.13 (d, J = 8.0 Hz, 4 H); **FT-IR** (cm^{-1}): 3025 (Aromatic C-H Stretch), 1714.7 (Pyrano C=O group), 1662.6 (Aryl ketone C=O Stretch), 1595.1 (Aromatic C=C stretching).

2.2.4 Synthesis of 3-[4-(2-oxochromen-3-yl)-2,5-diphenyl-3-furyl]chromen-2-one (12a):

2,3-bis(2-oxo-2H-chromen-3-yl)-1,4-diphenylbutane-1,4-dione (11a) (0.5 g, 0.950 mmol) was taken in ethanol (18.99 ml) and added 17 ml of conc.H_2SO_4 drop wise, where upon the solid dissolves completely. The reaction mixture was cooled to room temperature, diluted with 100 ml ice cold water. Solid precipitates out were filtered off and recrystallized from ethanol and dried.79% yield (0.38 g) white solid; M.P = 149-51 ºC ; **^{1}H-NMR** (400 MHz, $CDCl_3$):: δ 7.37-7.24 (m, 10H), 7.46 -7.44 (dd, 2H), 7.55-7.50 (td, 2H), 7.64-7.62 (m, 4H), 7.87 (s, 2H); ^{13}C-NMR (100MHz,$CDCl_3$):δ116.3,117.8,118.7,120.8,124.2,125.7,127.8,128.0,128.4,129.5, 131.5,144.2,149.8,153.5,160.2; **FT-IR** (cm^{-1}): 3018 (Aromatic C-H Stretch), 1718.5 (Pyrano C=O group), 1595.1 (Aromatic C=C stretching).

2.2.5 Synthesis of 3-[2,5-bis(4-bromophenyl)-4-(2-oxochromen-3-yl)-3-furyl]chromen-2-one (12b):

1,4-bis(4-bromophenyl)-2,3-bis(2-oxo-2H-chromen-3-yl)butane-1,4-dione **11b** (0.65 g, 0.950 mmol) was taken in ethanol (18.99 ml) and added 17 ml of conc.H_2SO_4 drop wise, where upon the solid dissolves completely. The reaction mixture was cooled to room temperature, diluted with 100 ml ice cold water. Solid precipitates out were filtered off and recrystallized from ethanol and dried. 71% yield (0.447 gm) off white solid; M.P= 164-66 ºC; **^{1}H-NMR** (400 MHz, $CDCl_3$): δ 7.34-7.28 (m, 4H), 7.48 -7.45 (m, 9H), 7.57-7.51 (m, 3H), 7.84 (s, 2H); **FT-IR** (cm^{-1}): 3018 (Aromatic C-H Stretch), 1718.5 (Pyrano C=O group), 1595.1 (Aromatic C=C stretching)

2.2.6 Synthesis of 3-[2,5-bis(4-methoxyphenyl)-4-(2-oxochromen-3-yl)-3-furyl]chromen-2-one (12c): 1,4-bis(4-methoxyphenyl)-2,3-bis(2-oxo-2H-chromen-3-yl)butane-1,4-dione 11c (0.557 g, 0.950 mmol) was taken in ethanol (18.99 ml) and added 17 ml of conc.H_2SO_4 drop-wise, where upon the solid dissolves completely. The reaction mixture was cooled to room temperature, diluted with 100 ml ice cold water. Solid precipitates out were filtered off and recrystallized from ethanol and dried. 80% yield (0.43 g) off white solid; M.P = 136-37 ºC; **^{1}H-NMR** (400 MHz, $CDCl_3$): δ 3.80 (s, 6H), 6.88-6.86 (d, 4H), 7.27 -7.23 (t, 2H), 7.32-7.30 (d, 2H), 7.44-7.42 (d, 2H), 7.51 -7.49 (m, 2H), 7.55-7.53 (d, 4H), 7.84 (s, 2H) ; **FT-IR** (cm^{-1}): 3018 (Aromatic C-H Stretch), 1716.6 (Pyrano C=O group), 1606.7 (Aromatic C=C stretching); MS (ESI) (m/z): calcd for $C_{36}H_{24}O_7$, [M+1]+, 569.57; found, 569.1.

2.2.7 Synthesis of 3-[4-(2-oxochromen-3-yl)-2,5-diphenyl-1H-pyrrol-3-yl]chromen-2-one (12d):

A mixture of 2,3-bis(2-oxo-2H-chromen-3-yl)-1,4-diphenylbutane-1,4-dione **(11a)** (0.5 g, 0.950 mmol) and Ammonium acetate (0.732 g, 9.50 mmol) in ethanol (47.5 ml) were heated to reflux for 15 hrs. Ethanol was evaporated under reduced pressure. 100 ml of water was added to the reaction mixture. Solid precipitates out were filtered off and recrystallized from ethanol and dried. 77% yield (0.37 g) yellow solid; M.P = 156-59 ºC; **^{1}H-NMR** (400 MHz, $CDCl_3$): δ 7.24-7.18 (m, 2H), 7.28 -7.26 (m, 4H), 7.37-7.32 (m, 6H), 7.48-7.41 (m,6 H), 7.70 (s, 2H), 8.59 (broad s, 1H); ^{13}C-NMR (400 MHz,$CDCl_3$): δ

116.1,116.3,119.1,123.1,123.9,126.6,127.1,127.6,128.6,130.8,131.0, 131.5,143.1,153.2,161.1 ; **FT-IR** (cm^{-1}): 3015 (Aromatic C-H Stretch), 1712.6 (Pyrano C=O group), 1602.8 (Aromatic C=C stretching); MS (ESI) (m/z): calcd for $C_{34}H_{21}NO_4$, $[M^{+1}]^+$, 508.53; found, 508.

2.2.8 Synthesis of 3-[2,5-bis(4-bromophenyl)-4-(2-oxochromen-3-yl)-1H-pyrrol-3-yl]chromen-2-one (12e):

A mixture of 1,4-bis(4-bromophenyl)-2,3-bis(2-oxo-2H-chromen-3-yl)butane-1,4-dione **11b** (0.65 g, 0.950 mmol) and Ammonium acetate (0.732 g, 9.50 mmol) in ethanol (47.5 ml) were heated to reflux for 15 hrs. Ethanol was evaporated under reduced pressure. 100 ml of water was added to the reaction mixture. Solid precipitates out were filtered off and recrystallized from ethanol and dried. 72% yield (0.35g) yellow solid; M.P = 142-44 ºC; **^{1}H-NMR** (400 MHz, $CDCl_3$): δ 7.24-7.20 (m, 2H), 7.29 -7.25 (m, 6H), 7.38-7.36 (dd, 2H), 7.50-7.43 (m,6 H), 7.66 (s, 2H), 8.68 (broad s, 1H); **FT-IR** (cm^{-1}): 1712.8 (Pyrano C=O group), 1608.6 (Aromatic C=C stretching); MS (ESI) (m/z): calcd for $C_{34}H_{19}Br_2NO_4$, $[M]^+$, 663.0; found, 663.6.

2.2.9 Synthesis of 3-[2,5-bis(4-methoxyphenyl)-4-(2-oxochromen-3-yl)-1H-pyrrol-3-yl]chromen-2-one (12f): A mixture of 1,4-bis(4-methoxyphenyl)-2,3-bis(2-oxo-2H-chromen-3-yl)butane-1,4-dione 11c (0.557 g, 0.950 mmol) and Ammonium acetate (0.732 g, 9.50 mmol) in ethanol (47.5 ml) were heated to reflux for 15 hrs. Ethanol was evaporated under reduced pressure. 100 ml of water was added to the reaction mixture. Solid precipitates out were filtered off and recrystallized from ethanol and dried. 76% yield (0.34 g) yellow solid; M.P = 121-24 ºC; **^{1}H-NMR** (400 MHz, $CDCl_3$): δ 3.79 (s, 6H), 6.88-6.85 (d, 4H), 7.21 -7.18 (t, 2H), 7.27-7.24 (m, 3H), 7.36-7.33 (m,5H), 7.46 -7.42 (t, 2H), 7.67 (s, 2H), 8.43 (broad s, 1H); **FT-IR** (cm^{-1}): 3015 (Aromatic C-H Stretch), 3425 (pyrrolo NH group), 3020 (Aromatic C-H Stretch), 1712.8 (Pyrano C=O group), 1602.8 (Aromatic C=C stretching); MS (ESI) (m/z): calcd. for $C_{36}H_{25}NO_6$, $[M^{+1}]^+$, 568.2; found, 568.0.

3. Results and Discussion

3.1. Spectroscopic Characterizations

^{1}H-NMR spectra were acquired on Bruker (400 MHz) instrument. The $CDCl_3$ and DMSO-$_{d6}$, were used as solvents with tetramethylsilane (TMS) as the internal standard. The chemical shifts were given on the delta scale as parts per million (ppm). The 1H NMR spectra of the compounds (12a-e) were recorded majority in $CDCl_3$ solvent over the range of 0-14 ppm. For the compounds (11a-c), appearance of singlet peak integrated two protons in the range of 6.0-6.3 ppm assignable to the -CH group which has isomeric position next to carbonyl confirms the condensation of (2a-c) with (3a-c). Compounds (11a-c) also confirmed by disappearance of singlet peak integrated two protons in the range 4.0-4.5 ppm of (2a-c) and disappearance singlet peak integrated one proton in the range of 6.5-6.7 ppm of (3a-c). Disappearance of singlet peak integrated two protons in the range of 6.0-6.3 ppm assignable to the -CH group which has isomeric position next to carbonyl confirmed the formation of compounds (12a-e). In addition, a set of multiplet observed in the range 7.6-8.4 ppm were ascribed to the aromatic protons in all the synthesized compounds (12a-e). The ^{1}H-NMR spectral assignments with chemical shifts and coupling constants for the compounds (12a-e) are given in experimental section. Electron impact ionization mass spectra were recorded on Agilent Technologies 5975C MSD detector at 70 eV. The formation of desired compounds was confirmed by presence of intense molecular ion peak in the mass spectrum. Spectral evaluation predicts the molecular weights of the synthesized compounds. The FT-IR spectrum of compound (11a-c) showed strong absorption bands in the range 1714-1717 cm^{-1} region corresponds to Pyrano C=O group and bands in the range 1664-1666 cm^{-1} region corresponds to Aryl ketone C=O Stretching. Disappearance of bands in the range 1664-1666 cm^{-1} region which belogs to Aryl ketone C=O Stretching confirmed the formation of cyclized product (12a-f).

3.2 Antimycobacterial activity

The antimycobacterial activities were evaluated according to the macro dilution protocol described by Abate et al. [15]. The antimycobacterial activities of some novel derivatives (11a-c) and (12a-f) assessed at the Department of Microbiology, Maratha Mandal's NGH Institute of Dental Sciences and Research Centre, Belgaum-590010, India against *M. tuberculosis* ATTC 27294 [15] using the micro plate Alamar Blue assay (MABA) testing method for anti-TB analysis [15-39]. This methodology is nontoxic, uses a thermally-stable reagent and shows good correlation with proportional and BACTEC radiometric methods [29d-e]. The *Mycobacterium tuberculosis* stain H37Rv (ATCC 27294) was cultured at 37 °C in Lowestein-Jensenn medium until log phase growth. Then a cell suspension was prepared at a concentration of about 2 x 10^6 UFC Ml-CM and further diluted 1:20 in Middlebrook 7H9 medium. The later was supplemented with 10% OADC (oleic acid-albumin-dextrose-catalase) and 0.001% Tween 80. One mL of bacterial suspension was added to each tube (Capped, glass) to gather with the sample solutions of various concentrations. The final concentrations of the compounds under test ranged from 0.8 to 100 μg per ml and adjusted to a final 2 ml volume. After a 7 day incubation 100 μl of 3-(4,5-dimethylthiazol-2-yl)-2,5-diphenyltetrazolium bromide (MTT) (5 mg/ml) with 20% Tween 80 was added to the glass tubes. A violet colour indicated bacterial growth. The tubes were evaluated for colour change on day 8. The colour of the dye turns from blue to pink only when the organisms are alive and viable. If a compound has anti-mycobacterial activity, then it helps to determine at what concentration it exerts its bactericidal effect (at which point the blue remains unaffected); hence useful to determine MIC. For standard tests MIC value of Pyrazinamide-3.125 μg/ml, Streptomycin-6.25 μg/ml and Ciprofloxacin- 3.125 μg/ml, were determined each time. The MIC of each sample corresponded to the lowest concentration at which the bacteria tested did not show growth. The result summarized in **Table 1**.

Table 1. The minimum inhibitory concentration values for (11a-c) and (12a-f).

Entry	The minimum inhibitory concentration							
	100 μg/ml	**50 μg/ml**	**25 μg/ml**	**12.5 μg/ml**	**6.25 μg/ml**	**3.12 μg/ml**	**1.6 μg/ml**	**0.8 μg/ml**
Pyrazinamide	S	S	S	S	S	S	R	R
Ciprofloxacin	S	S	S	S	S	S	R	R
Streptomycin	S	S	S	S	S	R	R	R
11a	S	S	S	S	S	S	S	R
11b	S	S	S	R	R	R	R	R
11c	S	S	S	R	R	R	R	R
12a	S	S	S	R	R	R	R	R
12b	S	S	S	R	R	R	R	R
12c	S	S	S	R	R	R	R	R
12d	S	S	S	R	R	R	R	R
12e	S	S	S	R	R	R	R	R
12f	S	S	R	R	R	R	R	R

(S- Sensitive, R- Resistant); MICs of compounds: 11a: 1.6 **μg**/ml; 11b: 25 **μg**/ml; 11c: 25 **μg**/ml; 12a: 25**μg**/ml; 12 b: 25**μg**/ml; 12c : 25 **μg**/ml; 12d: 25 **μg**/ml; 12e: 25 **μg**/ml; 12f: 50 **μg**/ml; Pyrazinamide: 3.12 **μg**/ml by MABA assay.

4. Conclusions

In conclusion, novel derivatives of (11a-c) and (12a-f) have been synthesized successfully. The experimental data for the Anti-tuberculosis activity of 2,3-bis(2-oxochromen-3-yl)-1,4-diphenyl-butane-1,4-dione (11a-c) revealed that in this series compound 11a showed better minimum inhibitory concentration of 1.6 μg/ml against *Mycobacterium tuberculosis (H37 RV strain)* ATCC No- 27294 which was better than the MIC value of Pyrazinamide-3.125 μg/ml, Streptomycin-6.25 μg/ml and Ciprofloxacin- 3.125. Both compounds 11b and 11c showed moderate activity i.e., MIC value 25 μg/ml. For the compounds 3,4-(dicoumarin-3-yl)-2,5-diphenyl furans and pyrroles (12a-f) all the compounds showed moderate activity with the MIC value 25 μg/ml except 12f which showed even less value of 50 μg/ml. This study would pave the way for future development of more effective 2,3-bis(2-oxochromen-3-yl)-1,4-diphenyl-butane-1,4-dione analogs for applications in biological and material science.

Supplementary Materials: Not applicable.

Author Contributions: Conceptualization, B.J and R.Y..; methodology, B.J and R.Y.; software, S.M.; writing—review and editing, B.J and R.Y.; visualization, B.J and R.Y.; supervision, B.J and R.Y.

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Conflicts of Interest: The authors declare no conflict of interest.

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