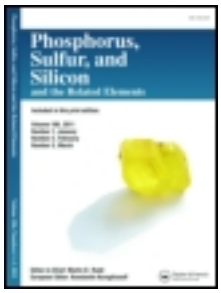

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Synthesis and Reactions of Some 2-Methyl-4-oxo-4 H -1-benzopyrans and 2-Methyl-4-oxo-4 H -1-benzo[b]-thiopheno[3,2- b]pyrans

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SYNTHESIS AND REACTIONS OF SOME 2-METHYL-4-OXO-4*H*-1-BENZOPYRANS AND 2-METHYL-4-OXO-4*H*-1-BENZO[*b*]-THIOPHENO[3,2-*b*]PYRANS

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(Received May 6 2001.)

*2-Methyl-4-oxo-4*H-*1-benzothiophenopyran (**3**) was prepared together with its thio analoge **4**. A facial conversion of **3** and some 2-methyl-4-oxo-4*H-*1-benzopyrans (**5**) to 2-oxo-2*H-*1-pyrans and 2(1*H)-pyridones was achieved under the influence of some carbon nucleophiles (NCCH$_2$R). The behavior of the active methyl group of **3** or **5** toward benzaldehyde, ethyl oxalate, and phthalic anhydride was discussed, where the styryl derivatives **12, 16**, the pyruvates **20, 24**, and phthalide **33** were obtained, respectively. Bromination of **12, 16**, followed by reaction with phenylenediamine and 2-aminothiophenol, led to the formation of quinoxalinyl and benzothiazinyl derivatives. Treatment of the pyruvic acids derived from **20, 24** with phenylenediamine gave quinoxalinyl derivatives, but with benzaldehyde and aniline, atophan analogues were formed. In addition, compound **33** was isomerized to the corresponding phthalone derivative. Compound **3** was allowed to react with amines, hydrazine, hydroxylamine, thiourea, and guanidine, where opening of the pyrone ring was observed and alkylaminobutene, pyrazole, isoxazole, aminopyrimidine, thioxopyrimidine derivatives were obtained, respectively.*

Keywords: Benzopyrans; benzothiophene; IR; NMR spectrum

INTRODUCTION

4-Oxo-4*H*-1-benzopyrans (trivial name chromones) and their derivatives have been receiving great attention as some of them proved to be of special importance in medicine and other applications.[1–3] Some other 4-oxo-4*H*-1-pyrans fused to heterocyclic rings have been

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synthesized, for example 4-oxo-4*H*-1-pyridobenzopyrans.[4] Herein we tried to prepare other derivatives containing a pyran ring fused to the benzo[*b*]thiophene moiety and describe their reactions together with some other benzopyrans.

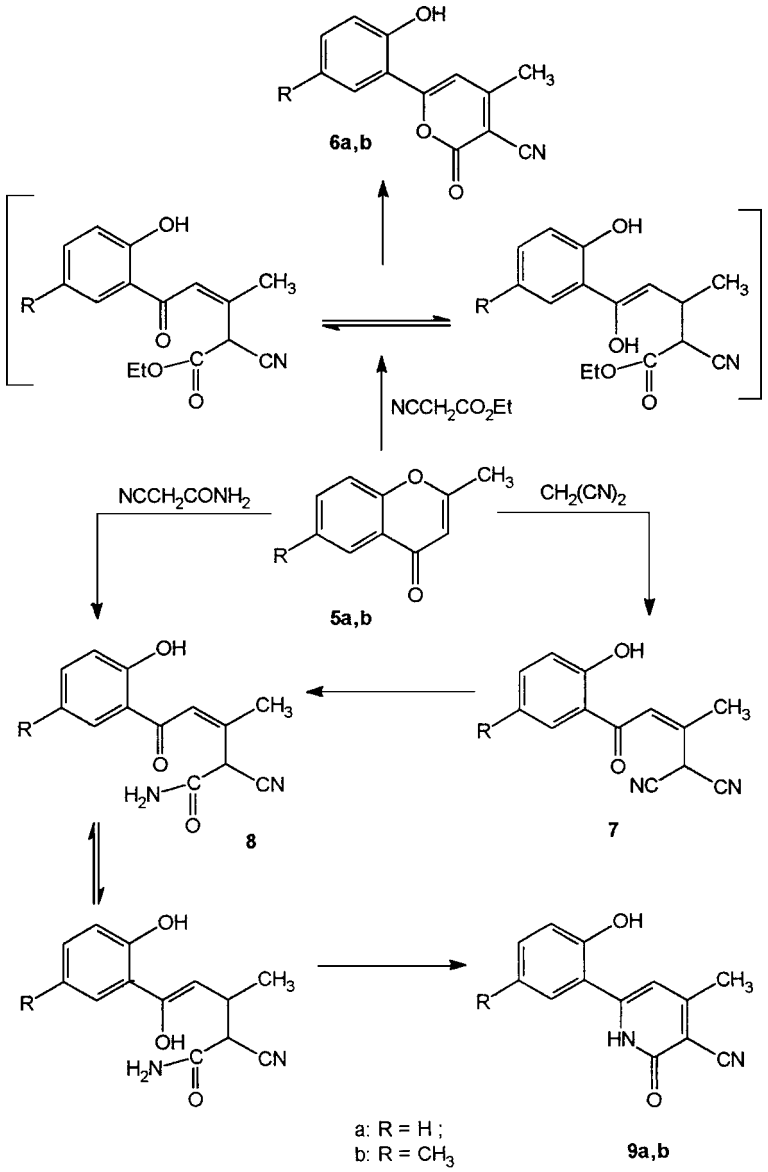
RESULTS AND DISCUSSION

2-Methyl-4-oxo-4*H*-1-benzo[*b*]thiopheno[3,2-*b*]pyran (**3**) was prepared *via* the reaction of 2-acetyl-3-hydroxybenzo[*b*]thiophene (**1**) with ethyl acetate in the presence of sodium metal under Claisen condensation conditions to give the diketone **2**. Cyclization of **2** with concentrated sulphuric acid gave the target compound **3** (Scheme 3), which was insoluble in 5% aqueous sodium hydroxide solution and gave no colour with ferric chloride, indicating the absence of free OH group. The structure of compounds **2** and **3** was inferred from their elemental analysis and IR spectra. The ^{1}H NMR spectrum of **3** showed no signal for O—H but showed the characteristic bands of the fused pyrone ring.

2-Methyl-4-thio-4*H*-1-benzo[*b*]thiopheno[3,2-*b*]pyran (**4**) was obtained by heating **3** with phosphorus pentasulphide in boiling benzene (Scheme 3).

It is known that the pyrone ring of 2-methyl-4-oxo-4*H*-1-benzopyrans are susceptible to ring opening under the influence of nitrogen nucleophiles such as, amines,[5] thiourea,[6] guanidine,[6] hydrazine,[7] and hydroxylamine,[8] but the effect of carbon nucleophiles has not been discussed. In the present work, 2-methyl-4-oxo-4*H*-1-benzopyrans (**5a**,**b**) were allowed to react with some carbon nucleophiles, namely, ethyl cyanoacetate, cyanoacetamide, and malononitrile in ethanolic EtONa, where cleavage of the pyrone ring was observed, followed by cyclization to give different heterocyclic products (Scheme 1). With ethyl cyanoacetate, compounds **5a**,**b** gave 2-oxo-2*H*-1-pyran derivatives **6a**,**b**, the ^{1}H NMR spectrum of compound **6a** being an example, displayed neither signals for the ethyl ester nor a signal for the H-3 of the γ-pyrone ring in the starting compound. Reaction of **5a**,**b** with either cyanoacetamide or malononitrile gave the same 2(1H)-pyridone derivatives **9a**,**b**. Formation of **9a**,**b** from cyanoacetamide may be explained via opening of the pyrone ring of **5a**,**b** at C-2 to give intermediate **8**, which then cyclized. With malononitrile, the intermediate **7** so formed was subjected to hydrolysis of one of its cyano groups to give intermidiate **8**, which then cyclized.

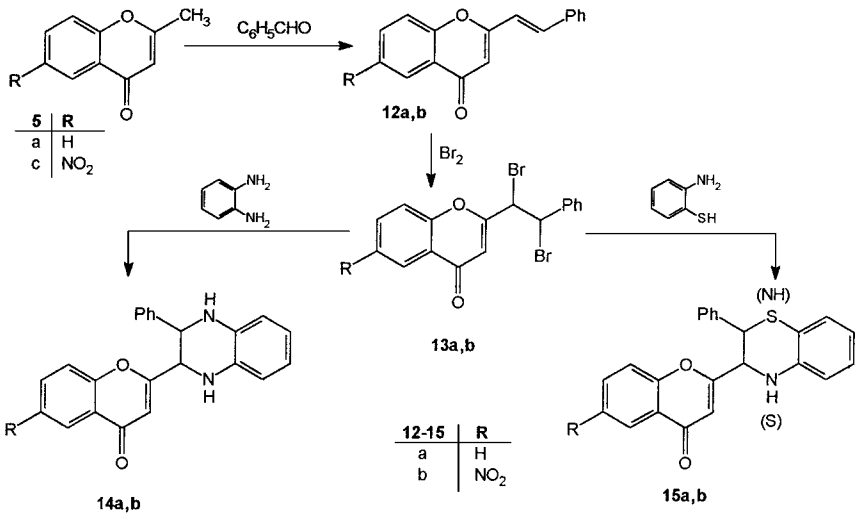
Investigation of the reactivity of the newly synthesized benzothiophenopyran derivative **3** towards the same carbon nucleophiles indicated that the susceptibility of the pyrone ring to cleavage was not



SCHEME 1

altered, and it behaved similarly to the other benzopyrans **5a**,**b**. Thus, reaction of compound **3** with ethyl cyanoacetate gave the 2-pyranone derivative **10**, while with either cyanoacetamide or malononitrile the pyridone derivative, **11** was obtained (Scheme 3).

In earlier work we found that 2-methyl-4-oxo-4*H*-1-benzopyrans condensed with aromatic aldehydes to give the corresponding 2-styryl derivatives.[7] In the present work when 2-methylbenzopyran derivative **5c** was allowed to react with benzaldehyde, the 2-styryl derivative **12b** was obtained (Scheme 2). Its structure was assigned the expected transconfiguration on the basis of its ^{1}H NMR spectrum which showed a signal for a doublet (1 H, J = 17 Hz) at δ 6.81.



SCHEME 2

2-Styryl-4-oxo-4*H*-1-benzopyrans **12a**[9] and **12b** were used successfully for the synthesis of 2-heterocyclic derivatives (flavone analogues). Thus bromination of compounds **12a**,**b** with bromine led to the formation of 1,2-dibromophenylethane derivatives **13a**,**b** (Scheme 2), the ^{1}H NMR spectrum of **13a** being an example, showed signals at δ 4.22–4.27 [m, 2 H, (CH—Br)$_2$], 6.43 (s, 1 H, H-3), and 7.31–8.25 ppm (m, 9 H, Ar-H).

On reacting compounds **13a**,**b** with 2-phenylenediamine or 2-aminothiophenol, two novel and interesting systems were formed and characterized as tetrahydroquinoxaline derivatives **14a**,**b** and benzothiazine derivatives **15a**,**b** respectively (Scheme 2). The ^{1}H NMR spectrum of compound **14a** showed signals at δ 3.82–3.87 (m, 2 H, quinoxaline H-2 + H-3), 5.61–5.72 (b, 2 H, two NH), 6.46 (s, 1 H, H-3), and 7.32–8.31 ppm (m, 13 H, Ar-H), while the ^{1}H NMR spectrum of **15a** showed signals at δ 3.72–3.77 (m, 2 H, SCH—CHN), 5.92 (b, 1 H, NH), 6.51 (s, 1 H, H-3), and 7.13–8.24 ppm (m, 13 H, Ar-H).

Testing the reactivity of the 2-methyl group of 2-methyl-4-oxo-4*H*-1-benzo[*b*]thiopheno[3,2-*b*]pyran (**3**) toward aromatic aldehydes showed

that it condensed easily with benzaldehyde in the presence of sodium ethoxide to give the trans 2-styryl derivative **16** (Scheme 3). Its ^{1}H NMR spectrum showed signals at δ 6.52 (s, 1 H, H-3), 6.91 (d, 1 H, CH, J = 16 Hz), and 7.32–8.21 ppm (m, 10 H, Ar-H and vinyl-H).

Bromination of compound **16** with bromine in acetic acid took place easily to afford the dibromophenylethyl derivative **17**. Reacting the latter compound with 2-phenylenediamine and 2-aminothiophenol led to the formation of the 2-quinoxalinyl and 2-benzothiazinyl derivatives **18** and **19** respectively (Scheme 3).

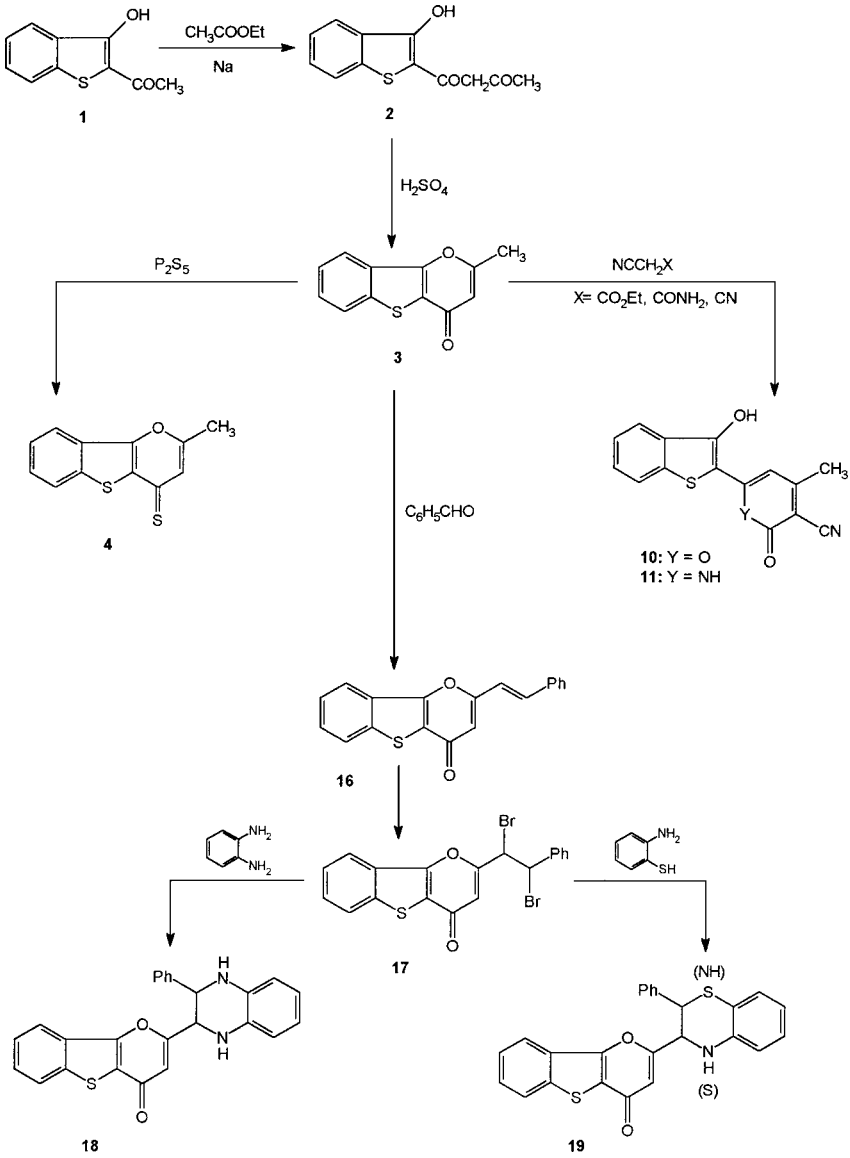
In our laboratory we previously discovered the condensation of diethyl oxalate with 2-methyl-4-oxo-4*H*-1-benzopyrans,[10] in the presence of sodium metal to give the corresponding pyruvate ester. In continuation with this work and in order to prepare 2-heterocyclic benzopyrans (flavone analogues), 2-methylbenzopyrone derivatives **5c** and **3** were allowed to react with diethyl oxalate following the same procedure (in case of **5c** sodium ethoxide was used instead of sodium metal) to give the pyruvate esters **20b** (Scheme 4) and **24** (Scheme 5), respectively.

Compound **20b** and **24** gave a color with aqueous ferric chloride, their IR spectra showed bands at 3250–2500cm^{-1} (intramolecular hydrogen bonded OH), and the ^{1}H NMR spectrum of **24** showed signals at δ 1.31 (t, 3 H, CH_3), 4.32 (q, 2 H, CH_2), 6.21 (s, 1 H, H-3), 6.77 (s, 1 H, CH=C), 7.43–7.96 (m, 4 H, Ar-H), and 11.11 ppm (s, 1 H, enol OH). This indicates that the enol form is more predominant than the keto form.

Treatment of compounds **20a**,[10] **20b**, and **24** with 10% aqueous sulphuric acid gave the corresponding pyruvic acids **21a**,**b** and **25**, which were exclusively found in the enol forms. They gave a violet color with aqueous $FeCl_3$, and their IR spectra showed broad band centered at 3140–2800 cm^{-1} for intramolecular hydrogen bonded OH and carboxylic OH.

Preparing a novel 2-heterocyclic pyrons was successfully accomplished using the previous pyruvic acids. Thus dihydroquinoxaline derivatives **22a**,**b** and **26** (Schemes 4 and 5) were prepared by reacting the former pyruvic acids **21a**,**b** and **25** with 2-phenylenediamine. In addition, when the pyruvic acids **21a**,**b** and **25** were allowed to react with benzaldehyde and aniline, the atophan[11] analogues **23a**,**b** and **27** were formed, respectively (Schemes 4 and 5). The ^{1}H NMR spectrum of compound **27** showed signals at δ 6.47 (s, 1 H, H-3), 7.28–8.06 (m, 13 H, Ar-H), and 9.35 ppm (s, 1 H, COOH).

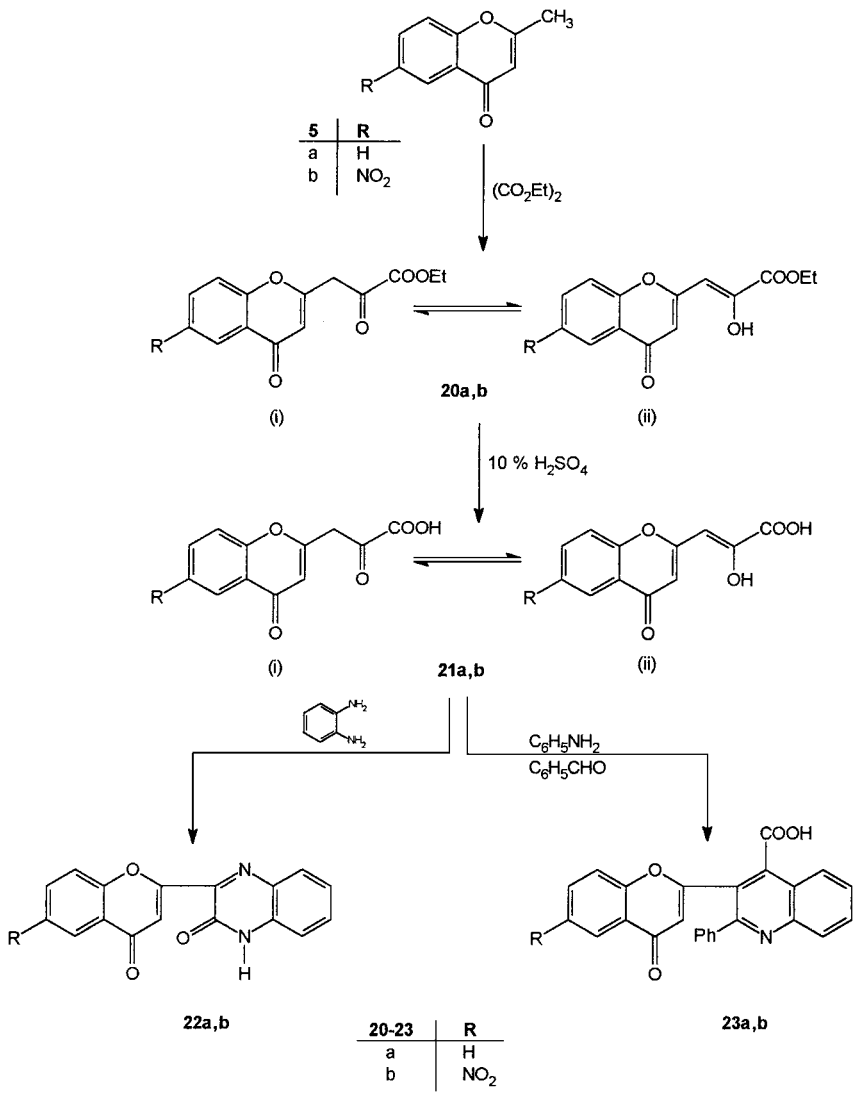
It has been reported that the pyrone ring of 2-methyl-4-oxo-4*H*-1-benzopyrans was susceptible to opening under the influence of nitrogen nucleophiles.[5–8] In the present work, the pyrone ring of compound **3** was tested toward some nitrogen nucleophiles including aliphatic amines, hydroxylamine, hydrazine hydrate, thiourea, and guanidine



SCHEME 3

hydrochloride (Scheme 6). In each case, cleavage of the pyrone ring was observed.

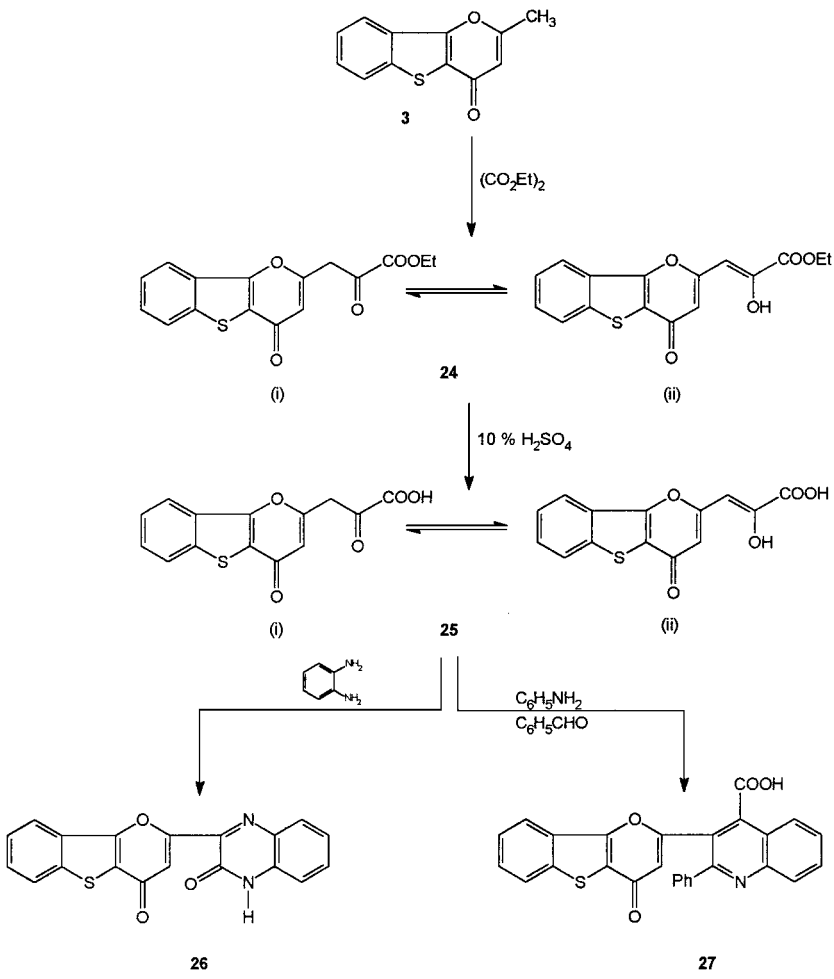
Reaction of **3** with butylamine and cyclohexylamine led to the formation of the 2-alkylaminobutenyl derivatives **28a**,**b**. Compounds **28a**,**b** regenerate the starting compound **3** upon treatment with concentrated



SCHEME 4

sulphuric acid or boiling with dilute hydrochloric acid. Refluxing the thio analogue **4** with butylamine and cyclohexylamine affected desulphurization of the thione group and formation of the former enamines **28a**,**b**.

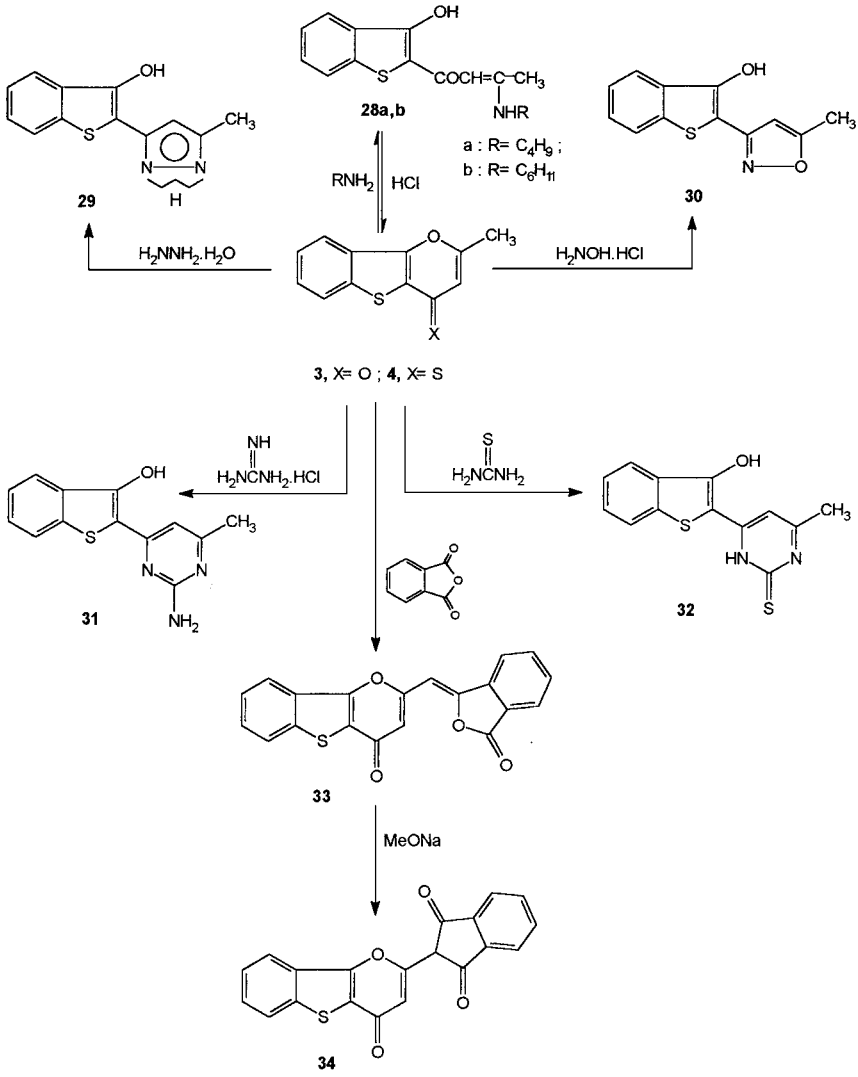
The action of hydrazine hydrate on **3** or **4** resulted in the same pyrazole derivative **29** (Scheme 6) as a result of opening of the pyrone ring and subsequent recyclization to give the product. When compound **3**



SCHEME 5

was allowed to react with hydroxylamine hydrochloride in boiling pyridine, the isoxazole derivative **30** was formed. Moreover, compound **30** was formed via the action of hydroxylamine hydrochloride on compound **4**, where desulphurization of the thione group was observed (Scheme 6).

Recently in our laboratory a novel conversion of γ-benzopyrans to pyrimidine derivatives was investigated.[6] We made use of this conversion for the synthesis of derivatives of benzo[*b*]thiophene carrying the pyrimidine moiety. Thus, when compound **3** was allowed to react with guanidine hydrochloride and thiourea in the presence of potassium hydroxide, the pyrimidine derivatives **31** and **32** were obtained, respectively (Scheme 6).



SCHEME 6

2-Methylnaphthopyrone has been shown to condense with phthalic anhydride in the presence of zinc chloride to give phthalidene derivative.[12] In the present work, we tested the reactivity of the 2-methyl group in the benzothiophenopyran **3** toward phthalic anhydride. Performing the reaction using zinc chloride gave a tarry product from which no pure material could be isolated. However, using sodium acetate at elevated temperature gave the phthalide **33**

(60%) (Scheme 6). Compound **33** isomerized easily to the 1,3-indandione derivative **34** in the presence of sodium methoxide, similar to other phthalides.[13] The IR spectrum of compound **33** showed a sharp band at 1810 cm^{-1} corresponding to C=O of lactone, while that of **34** displayed no bands for lactones but showed a band at 1700 cm^{-1} arising from C=O of indandione. Both **33** and **34** showed bands characteristic of C=O of a γ-pyrone.

EXPERIMENTAL

Melting points were incorrected and were recorded in open capillary tubes on a Gallenkamp 595-MFB melting point apparatus. IR spectra were measured on a Perkin-Elmer 598-IR spectrophotometer using samples in KBr disks (ν, cm^{-1}). ^1H NMR spectra were determined on a Jeol FX-90 NMR spectrometer (90 MHz) using DMSO-d6 as solvent and TMS as an internal standard. Mass spectra were taken on a Hewlett Packard MS-5988, direct inlet (electron beam energy 70 eV).

2-Acetoacetyl-3-hydroxybenzo[*b*]thiophene (2)

To a mixture of 2-acetyl-3-hydroxybenzo[*b*]thiophene (**1**) (10 g, 0.05 mol) and ethyl acetate (55 ml), was added small pieces of sodium metal (4 g). The reaction mixture was heated under reflux for 4 h and left overnight at room temperature. The product was treated with crushed ice (300 g), acidified with dilute acetic acid, and aerated until a yellow solid deposited, which was collected by filtration, dried, and crystallized from petroleum ether 60–80 to give compound **2** as a white crystals. Compound **2** was soluble in 5% aqueous sodium hydroxide solution and gave a violet color with aqueous ferric chloride solution.

2-Methyl-4-oxo-4*H*-1-benzo[*b*]thiopheno[3,2-*b*]pyran (3)

2-Acetoacetyl-3-hydroxybenzo[*b*]thiophene (**2**) was dissolved in concentrated sulphuric acid, and the mixture was left for 5 min. The resulting dark brown solution was poured on ice-cold water, and the solid so obtained was filtered off and crystallized from ethanol to give the titled compound **3** in almost theoretical yield. Compound **3** was insoluble in 5% aqueous sodium hydroxide solution and gave no color with ferric chloride solution.

2-Methyl-4-thio-4*H*-1-benzo[*b*]thiopheno[3,2-*b*]pyran (4)

A mixture of compound **3** (1 g, 0.004 mol) and phosphorus pentasulphide (1 g, 0.004 mol), in dry benzene (50 ml), was refluxed for 2 h. The reaction mixture was filtered while hot. The solvent was evaporated and the product **4** crystallized from ethanol as deep orange needles.

6-(2-Hydroxy-substituted phenyl)-3-cyano-4-methyl-2-oxo-2*H*-1-pyrans 6a,b and 6-(3-Hydroxybenzo[*b*]-thiopheno)-3-cyano-4-methyl-2-oxo-2*H*-1-pyran (10)

To a mixture of **3**, **5a**, or **5b** (0.003 mol) and sodium ethoxide solution (0.003 mol sodium in 5 ml absolute ethanol) in absolute ethanol (5 ml) was added ethyl cyanoacetate (0.003 mol). The mixture was refluxed for 4 h on a boiling water bath, cooled, and acidified with 50% hydrochloric acid. The solid obtained was filtered off and crystallized from the proper solvent to give **10** and **6a**,**b** respectively.

6-(2-Hydroxy substituted phenyl)-3-cyano-4-methyl-2-(1*H*)pyridones 9a,b and 6-(3-Hydroxybenzo[*b*]thiopheno)-3-cyano-4-methyl-2(1*H*)pyridone (11)

To a solution of **3**, **5a**, or **5b** (0.003 mol) and sodium ethoxide solution (0.003 mol sodium in 5 ml absolute ethanol), in absolute ethanol (5 ml) was added malononitrile or cyanoacetamide (0.003 mol). The mixture was refluxed for 15 min on a boiling water bath. The orange reaction mixture was poured onto dilute hydrochloric acid, and the yellow solid so formed was filtered off to give compounds **11** and **9a**,**b** respectively.

2-Styryl-6-nitro-4-oxo-4*H*-1-benzopyran (12 b) and 2-Styryl-4-oxo-4*H*-1-benzo[*b*]thiopheno[3,2-*b*] pyran (16)

Compound **3** or **5c** (0.5 g, 0.002 mol) was dissolved in the least amount of absolute ethanol and treated with sodium ethoxide solution (0.002 mol sodium dissolved in 5 ml absolute ethanol). Benzaldehyde (0.24 ml, 0.002 mol) was added, and the mixture was left overnight at room temperature. The orange product formed was filtered off to give the styryl derivatives **16** and **12b** respectively. Compounds **16** and **12b** were insoluble in 5% aqueous sodium hydroxide and did not give color with ferric chloride.

2-(1,2-Dibromo-2-phenylethyl)-4-oxo-4*H*-1-benzopyrans 13a,b and 2-(1,2-Dibromo-2-phenylethyl)-4-oxo-4*H*-1-benzo[*b*]thiopheno[3,2-*b*]pyran (17)

To a stirred solution of **12a**, **12b**, or **16** (0.002 mol) in acetic acid (3 ml) was added dropwise over a period of 20 min a solution of bromine (0.003 mol) in 5 ml of acetic acid. The mixture was then stirred for 3 h, and the white precipitate formed was filtered off, washed with acetic acid (5 ml), and recrystallized from the proper solvent to give compounds **13a,b** and **17** respectively.

2-(3-Phenyl-1,2,3,4-tetrahydro-2-quinoxalinyl)-4-oxo-4*H*-1-benzopyrans 14a,b and 2-(3-Phenyl-1,2,3,4-tetrahydro-2-quinoxalinyl)-4-oxo-4*H*-1-benzo[*b*]thiopheno-[3,2-*b*]pyran (18)

To a solution of compounds **13a**, **13b** or **17** (0.0007 mol) in a mixture of ethanol (7 ml) and pyridine (3 ml) was added 1,2-phenylenediamine (0.0007 mol). The mixture was refluxed for 4 h and then left to stand overnight followed by treatment with cold dilute acetic acid. The solid deposited was collected by filtration and crystallized from the proper solvent to give compounds **14a**,**b** and **18** respectively.

2-[2(or 3)-Phenyl-2,3,4-trihydrobenzothiazin-3-(or 2)-yl]-4-oxo-4*H*-1-benzopyrans 15a,b and 2-[2(or 3)-Phenyl-2,3,4-trihydrobenzothiazin-3(or 2)-yl]-4-oxo-4*H*-1-benzo[*b*]thiopheno[3,2-*b*]pyran19

To a solution of compound **13a**, **13b**, or **17** (0.0007 mol) in a mixture of ethanol (5 ml) and pyridine (3 ml) was added *o*-aminothiophenol (0.0008 mol). The mixture was refluxed for 2 h and then left overnight. Afterward, the mixture was poured onto cold, dilute acetic acid. The solid deposited was collected by filtration and crystallized from the proper solvent to give compounds **15a**,**b** and **19** respectively.

Ethyl Pyruvates 20a,b and 24

a. To a mixture of **5c** (0.003 mol) and diethyl oxalate (2 ml) was added sodium ethoxide solution (0.2 g sodium dissolved in 10 ml absolute ethanol). The reaction mixture was left overnight and then poured onto acidified, cold water. The yellow solid deposited was collected by filtration to give compound **20b** which gave a green color

with aqueous ferric chloride and was soluble in 5% aqueous sodium hydroxide.

b. To a mixture of compound **3** or **5a** (0.005 mol), diethyl oxalate (2 ml), and dry diethyl ether (50 ml) was added sodium metal (0.4 g small pieces). After shaking and stirring, a vigorous reaction took place. The reaction was left for 0.5 h for completion and then was stoppered and left overnight at room temperature. Acidification with dilute acetic acid gave the yellow pyruvic ester derivatives **24** and **20a** respectively. Each gave a violet color with aqueous ferric chloride and were soluble in 5% aqueous sodium hydroxide. Compound **20a** was identical to an authentic sample prepared according to Jones.[9]

Pyruvic Acids 21a,b **and** 25

A suspension of compound **20a**, **20b**, or **24** (0.5 g) in dilute sulphuric acid (30 ml, 10%) was stirred on a boiling water bath for 3 h, then left to cool, and then was filtered off. The solid obtained was washed thoroughly with water to give compounds **21a**,**b** and **25** respectively, both of which gave characteristic colors with the ferric chloride test. Compound **21a** was found to be identical to an authentic sample[9] prepared by hydrolysis of ester **20a** using aqueous potassium hydroxide solution (MP and mixed MP).

2-[(2-Oxo-1,2-dihydroquinoxalin-3-yl)methyl]-4-oxo-4*H*-1-benzopyrans 22a,b **and 2-[(2-Oxo-1,2-dihydroquinoxalin-3-yl)methyl]-4-oxo-4*H*-1-benzo[*b*]thiopheno[3,2-*b*]pyran** (26)

A mixture of compound **21a**, **21b**, or **25** (0.002 mol), 1,2-phenylendiamine (0.002 mol) and ethanol (10 ml) was refluxed on a boiling water-bath for 30 min. The solid so obtained on cooling was filtered off and crystallized from the appropriate solvent to give compounds **22a**,**b** and **26**, respectively.

2-(4-Carboxy-2-phenylquinolin-3-yl)-4-oxo-4*H*-1-benzopyrans 23a,b **and 2-(4-Carboxy-2-phenylquinolin-3-yl)-4-oxo-4*H*-1-benzo[*b*]thiopheno[3,2-*b*]Pyran** (27)

A mixture of compound **21a, 21b**, or **25** (0.002 mol) and benzaldehyde (0.2 ml, 0.003 mol), in ethanol (5 ml) was boiled and then aniline (0.18 ml, 0.002 mol) in ethanol (5 ml) was added slowly with frequent shaking over 15 min. The mixture was refluxed on a boiling water bath for 3 h and allowed to stand overnight. The solid formed was filtered

off and crystallized from the suitable solvent to give compounds **23a**,**b** or **27** respectively.

2-(3-Alkylamino-2-butenyl-1-oxo)-3-hydroxybenzo[*b*]-thiophenes 28a,b

a. To a solution of compound **3** (0.002 mol) in ethanol (5 ml) was added butylamine (0.004 mol) or cyclohexylamine (0.004 mol). The mixture was then refluxed for 15 min and kept overnight at room temperature. The solid obtained was filtered off to give compounds **28a** and **28b** respectively, both of which were soluble in 5% aqueous sodium hydroxide solution and gave a violet color with aqueous ferric chloride solution.
b. Compounds **28a** and **28b** were also prepared starting from the pyranthione **4** and the appropriate alkylamines in a reaction time of 30 min using the same above method (MP and mixed MP).

3-Hydroxy-2-(3-methylpyrazol-5-yl)benzo[*b*]-thiophene (29)

a. To a solution of **3** (0.002 mol), in the least amount of ethanol was added a solution of hydrazine hydrate (2 ml) in ethanol (5 ml). The reaction mixture was refluxed for 1 h, left to cool, and then diluted with water. The solid formed was collected and crystallized from ethanol to give compound **29**, which was soluble in 5% aqueous sodium hydroxide solution and gave a green color with aqueous ferric chloride solution.
b. Compound **29** was also prepared by refluxing compound **4** and excess hydrazine hydrate following the above procedure.

3-Hydroxy-2-(3-methylisoxazol-5-yl) benzo[*b*]-thiophene (30)

a. A mixture of compound **3** (0.002 mol), pyridine (10 ml), and excess hydroxylamine hydrochloride (0.8 g), dissolved in water (5 ml), was refluxed for 1 h. The cooled mixture was acidified with dilute acetic acid, and the solid that precipitated was filtered off and crystallized from ethanol to give compound **30** which was soluble in 5% aqueous sodium hydroxide solution and gave a green color with aqueous ferric chloride solution.
b. Compound **30** was also prepared by refluxing a mixture of compound **4** and hydroxylamine hydrochloride for 2 h following the above procedure.

2-(2-Amino-4-methylpyrimidin-6-yl)-3-hydroxybenzo[*b*]-thiophene (31)

A mixture of **3** (0.5 g, 0.002 mol), guanidine hydrochloride (0.5 g, 0.005 mol), potassium hydroxide (0.25 g, 0.004 mol), dissolved in 3 ml of water, and methanol (20 ml) was refluxed for 3 h. The solution was cooled, diluted with water, and acidified with acetic acid. The solid obtained was filtered off and crystallized from ethanol to give yellow needles of compound **31**, which was soluble in 5% sodium hydroxide solution and gave a green color with ferric chloride solution.

3-Hydroxy-2-(6-methyl-2-thioxo-3-hydropyrimidin-4-yl)-benzo[*b*]thiophene (32)

A mixture of **3** (0.5 g, 0.002 mol), thiourea (0.5 g, 0.006 mol), potassium hydroxide (0.25 g, 0.004 mol), dissolved in 1 ml of water, and ethanol (20 ml) was refluxed for 3 h. The solution was then cooled and acidified with dilute HCl where upon a yellow solid was obtained, which was filtered off and crystallized from anisole to give compound **32**. The latter was soluble in 5% aqueous sodium hydroxide solution and gave a violet color with ferric chloride solution.

2-(3-Phthalidenemethylene)benzo[*b*]thiopheno[3,2-*b*]-Pyran-4-one (33)

A mixture of **3** (1 g, 0.004 mol), phthalic anhydride (3 g, 0.02 mol), and fine powdered anhydrous sodium acetate (1.5 g) was heated at 245–255°C for 30 min. After cooling the reaction mixture was triturated with dilute sodium carbonate solution, and the solid obtained was washed with hot ethanol (20 ml), filtered off, and crystallized from benzyl alcohol to give the brownish yellow product **31**.

2-(1,3-Dioxoindan-2-yl)benzo[*b*]thiopheno[2,3-*b*] Pyran-4-one (34)

To a suspension of compound **33** in absolute methanol (10 ml) was added sodium methoxide solution (prepared from 0.5 g of sodium metal and 10 ml of methanol). The mixture was heated under reflux for 1 h. The resulting deep orange solution was cooled, diluted with water, and then acidified with cold dilute sulphuric acid. The solid product obtained was recrystallized from benzyl alcohol to afford the golden yellow compound **34**.

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APPENDIX

Characterization Data of the Newly Synthesized Compounds

Compound	Yield (%)	M.P. (°C) Solvent	Molecular formula (MW)	Elemental analysis calcd./found (%) C	H	N	S	IR (ν, cm^{-1})	^1H NMR (δ, ppm)
2	93	87 Pet. ether (60–80)	$C_{12}H_{10}O_3S$ (234)	61.5 61.3	4.3 4.4		13.7 13.6	3130 (OH), 1670–1640 (C═O)	
3	98	176 Ethanol	$C_{12}H_8O_2S$ (216)	66.7 66.5	3.7 3.8		14.8 14.8	1645 (γ-pyrone C═O)	2.41 (s, 3H, CH_3), 6.63 (s, 1H, H-3), 7.41–8.32 (m, 4H, Ar-H)
4	95	220 Ethanol	$C_{12}H_8OS_2$ (232)	62.1 62.0	3.4 3.4		27.6 27.5	1605 (C=C), 1230 (C=S)	
6a	85	>300 AcOH	$C_{13}H_9NO_3$ (227)	68.7 68.6	3.9 3.8	6.2 6.1		3130 (OH), 2220 (C≡N), 1750 (C═O)	2.46 (s, 3H, CH_3), 5.59 (s, 1H, H-3), 7.37–8.29 (m, 4H, Ar-H), 12.71 (s, 1H, OH_{PhOH})
6b	82	>300 Dioxane	$C_{14}H_{11}NO_3$ (241)	69.7 69.5	4.6 4.6	5.8 5.7		3130 (OH), 2210 (C≡N), 1740 (C═O)	
9a	79	>300 AcOH	$C_{13}H_{10}N_2O_2$ (226)	69.0 69.0	4.4 4.3	12.4 12.4		3230–3100 (OH + NH), 2218 (C≡N), 1680 (C═O)	2.41 (s, 3H, CH_3), 7.08–8.13 (m, 5H, Ar-H + Pyridone H), 11.58 (s, 1H, NH), 12.45 (s, 1H, OH)

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Characterization Data of the Newly Synthesized Compounds *(Continued)*

Compound	Yield (%)	M.P. (°C) Solvent	Molecular formula (MW)	Elemental analysis calcd./found (%) C	H	N	S	IR (ν, cm^{-1})	^1H NMR (δ, ppm)
9b	81	>300 Pyridine	$C_{14}H_{12}N_2O_2$ (240)	70.0 70.0	5.0 4.9	11.7 11.5		3210–3150 (NH), 2210 (C≡N), 1665 (C=O)	
10	75	>300 AcOH	$C_{15}H_9NO_3S$ (283)	63.6 63.5	3.2 3.1	4.9 4.8	11.3 11.3	3120 (OH), 2215 (C≡N), 1755 (C=O)	2.41 (s, 3H, CH_3), 5.68 (s, 1H, pyran H), 7.21–8.32 (m, 4H, Ar-H), 12.63 (s, 1H, OH)
11	72	>300 Pyridine	$C_{15}H_{10}N_2O_2S$ (282)	63.8 63.6	3.6 3.6	9.9 9.8	11.3 11.2	3250–3130 (NH + OH), 2220 (C≡N), 1670 (C=O)	2.48 (s, 3H, CH_3), 7.21–8.24 (m, 5H, Ar-H + $H_{pyridone}$), 11.53 (s, 1H, NH), 12.71 (s, 1H, OH)
12b	79	190 Ethanol	$C_{17}H_{11}NO_4$ (293)	69.6 69.5	3.8 3.8	4.8 4.8		1655 (C=O)	6.42 (s, 1H, H-3), 6.81 (d, 1H, CH=C, J = 17 Hz), 7.21–8.21(m, 9H, Ar-H + vinyl H)
13a	88	212 AcOH	$C_{17}H_{12}Br_2O_2$ (408)	50.0 50.0	2.9 2.8			1645 (C=O γ-pyrone), 1080 (C—Br)	4.22–4.27 (m, 2H, $(CHBr)_2$), 6.43 (s, 1H, H-3), 7.31–8.25 (m, 9H, Ar-H)
13b	89	225 AcOH	$C_{17}H_{11}Br_2NO_4$ (453)	45.0 45.0	2.4 2.3	3.1 2.9		1640 (C=O γ-pyrone), 1085 (C—Br)	

14a	79	>300	$C_{23}H_{18}N_2O_2$	77.9	5.1	7.9		3240–3180 (NH), 1650 (C═O γ-pyrone)	3.82–3.87 (m, 2H, $(NCH)_2$), 5.61–5.72 (b, 2H, two NH), 6.46 (s, 1H, H-3), 7.32–8.31 (m, 13H, Ar-H)
		Ethanol	(354)	77.7	5.2	7.9			
14b	89	>300	$C_{23}H_{17}N_3O_4$	69.2	4.3	10.5		3230–3170 (NH), 1645 (C═O γ-pyrone)	
		Acetone	(399)	69.1	4.2	10.3			
15a	82	290	$C_{23}H_{17}NO_2S$	74.4	4.6	3.8	8.6	3220–3180 (NH), 1650 (C═O γ-pyrone)	3.72–3.77 (m, 2H, SCH—CHN), 5.92 (b, 1H, NH), 6.51 (s, 1H, H-3), 7.13–8.24 (m, 13H, Ar-H)
		Ethanol	(371)	74.3	4.6	3.7	8.6		
15b	84	>300	$C_{23}H_{16}N_2O_4S$	66.3	3.9	6.7	7.7	3210–3160 (NH), 1647 (C═O γ-pyrone)	
		Butanol	(416)	66.1	3.7	6.8	7.7		
16	85	175	$C_{19}H_{12}O_2S$	75.0	4.0		10.5	1647 (C═O γ-pyrone)	6.52 (s, 1H, H-3), 6.91 (d, 1H, CH═C, $J = 16$ Hz), 7.32–8.21 (m, 10H, Ar-H + vinyl H)
		Ethanol	(304)	75.2	3.8		10.5		
17	92	200	$C_{19}H_{12}Br_2O_2S$	49.2	2.6		6.9	1640 (C═O γ-pyrone), 1075 (C—Br)	4.25–4.30 (m, 2H, $(CHBr)_2$), 6.38 (s, 1H, H-3), 7.33–8.15 (m , 9H, Ar-H)
		AcOH	(464)	49.1	2.5		6.7		
18	78	>300	$C_{25}H_{18}N_2O_2S$	73.1	4.4	6.8	7.8	1645 (C═O γ-pyrone), 3320–3240 (NH)	3.72–3.77 (m, 2H, NCH—CHN), 5.55–5.76 (b, 2H, 2 × NH), 6.51 (s, 1H, H-3), 7.31–8.24 (m, 13H, Ar-H)
		Acetone	(410)	73.1	4.5	6.7	7.7		
19	84	270	$C_{25}H_{17}NO_2S_2$	70.2	4.0	3.3	15.0	3310–3230 (NH), 1645 (C═O γ-pyrone)	3.66–3.71 (m, 2H, NCH—CHS), 5.82 (b, 1H, NH), 6.48 (s, 1H, H-3), 7.22–8.31 (m, 13H, Ar-H)
		Butanol	(427)	70.1	4.2	3.3	15.3		

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Characterization Data of the Newly Synthesized Compounds *(Continued)*

Compound	Yield (%)	M.P. (°C) Solvent	Molecular formula (MW)	Elemental analysis calcd./found (%) C	H	N	S	IR (ν, cm^{-1})	^1H NMR (δ, ppm)
20b	92	222	$C_{14}H_{11}NO_7$	55.1	3.6	4.6		3250–2500 (OH), 1740 (C=O),	
		Dioxane	(305)	55.0	3.5	4.5		1650 (C=O γ-pyrone)	
21a	96	219	$C_{12}H_8O_5$	62.1	3.5			3140–2800 (OH), 1730 (C=O),	
		AcOH	(232)	62.0	3.4			1660 (C=O γ-pyrone)	
21b	95	260	$C_{12}H_7NO_7$	52.0	2.5	5.0		3130–2850 (OH), 1720 (C=O),	
		AcOH	(277)	52.1	2.6	5.0		1655 (C=O γ-pyrone)	
22a	86	296	$C_{18}H_{12}N_2O_3$	71.0	4.0	9.2		3400–3364 (NH), 1680 (C=O amide),	
		Ethanol	(304)	71.0	3.8	9.1		1640 (C=O γ-pyrone)	
22b	82	>300	$C_{18}H_{11}N_3O_5$	61.9	3.2	12.0		3350–3355 (NH), 1675 (C=O amide),	
		Ethanol	(349)	61.8	3.2	12.1		1645 (C=O γ-pyrone)	
23a	95	282	$C_{25}H_{15}NO_4$	76.3	3.8	3.6		2920 ($OH_{carboxylic}$), 1730 ($C{=}O_{carboxylic}$),	
		Ethanol	(393)	76.1	3.6	3.5		1660 (C=O γ-pyrone)	
23b	95	>300	$C_{25}H_{14}N_2O_6$	68.5	3.2	6.4		2910 ($OH_{carboxylic}$), 1710 ($C{=}O_{carboxylic}$),	
		Ethanol	(438)	68.3	3.1	6.3		1640 (C=O γ-pyrone)	

24	91	237	$C_{16}H_{12}O_5S$	60.7	3.8		10.1	3200–2450 (OH), 1735 (C=O$_{ester}$),	1.31 (t, 3H, CH_3), 4.32 (q, 2H, CH_2), 6.21 (s, 1H,
		Butanol	(316)	60.5	3.6		10.0	1645 (C=O γ-pyrone)	H-3), 6.77 (s, 1H, CH=C), 7.43–7.96 (m, 4H, Ar-H), 11.11 (s, 1H, OH$_{enolic}$)
25	98	249	$C_{14}H_8O_5S$	58.3	2.8		11.1	3125–2830 (OH), 1715 (C=O),	
		AcOH	(288)	58.2	2.7		11.0	1653 (C=O γ-pyrone)	
26	90	>300	$C_{20}H_{12}N_2O_3S$	66.6	3.3	7.8	8.9	3390–3360 (NH), 1670 (C=O amide),	
		Acetone	(360)	66.5	3.3	7.7	8.8	1645 (C=O γ-pyrone)	
27	92	>300	$C_{27}H_{15}NO_4S$	72.1	3.4	3.1	7.1	2925 (OH$_{carboxylic}$), 1720(C=O$_{carboxylic}$),	6.47 (s, 1H, Pyron H), 7.28–8.06 (m, 13H, Ar-H),
		Ethanol	(449)	72.1	3.2	3.2	7.2	1650 (C=O γ-pyrone)	9.35 (s, 1H, COOH)
28a	95[a]	178	$C_{16}H_{19}NO_2S$	66.4	6.6	4.8	11.1	1637 (α,β-unsat. C=O), 1615 (C=C)	0.91 (t, 3H, butyl CH_3), 1.52 (m, 4H, two CH_2),
	92[b]	Ethanol	(289)	66.4	6.5	4.8	11.2		2.32 (s, 3H, $CH_{3\ butenyl}$), 2.65 (m, 2H, CH_2—N), 6.14 (s, 1H, CO—CH=C), 7.15–7.92 (m, 4H, Ar-H), 10.85 (s, 1H, NH), 13.81 (s, 1H, OH)
28b	93[a]	190	$C_{18}H_{21}NO_2S$	68.5	6.7	4.4	10.1	1635 (α,β-unsat. C=O), 1620 (C=C)	
	94[b]	Ethanol	(315)	68.5	6.6	4.5	10.2		
29	88[a]	218	$C_{12}H_{10}N_2OS$	62.6	4.4	12.2	13.9	3140–3125 (NH), 2900 (OH),	2.25 (s, 3H, CH_3),
	86[b]	Ethanol	(230)	62.5	4.3	12.3	13.8	1615 (C=N)	7.10 (s, 1H, H$_{pyrazole}$), 7.57–8.22 (m, 4H, Ar-H), 12.91 (s, 1H, NH), 13.48 (s, 1H, OH)

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Characterization Data of the Newly Synthesized Compounds *(Continued)*

Compound	Yield (%)	M.P. (°C) Solvent	Molecular formula (MW)	Elemental analysis calcd./found (%) C	H	N	S	IR (ν, cm^{-1})	^1H NMR (δ, ppm)
30	85[a]	270	$C_{12}H_9NO_2S$	62.3	3.9	6.0	13.9	3160 (OH), 1620 (C=N)	2.23 (s, 3H, CH_3), 6.95 (s, 1H, $H_{isoxazole}$), 7.85–8.14 (m, 4H, Ar-H), 13.84 (s, 1H, OH)
	83[b]	Ethanol	(231)	62.1	3.7	6.3	13.8		
31	82	220	$C_{13}H_{11}N_3OS$	60.7	4.3	16.3	12.5	3400, 3380 (NH_2), 3130 (OH), 1610 (C=N)	2.46 (s, 3H, CH_3), 7.72–8.61 (m, 7H, Ar-H + $H_{pyrimidine}$ + NH_2), 14.3 (s, 1H, OH)
		Ethanol	(257)	60.9	4.2	16.2	12.4		
32	79	>300	$C_{13}H_{10}N_2OS_2$	56.9	3.7	10.2	23.4	3200 (NH + OH), 1620 (C=N), 1220 (C=S)	
		Anisole	(274)	56.8	3.6	10.1	23.3		
33	60	>300	$C_{20}H_{10}O_4S$	69.4	2.9		9.2	1810 (C=O lactone), 1650 (C=O γ-pyrone)	
		$PhCH_2OH$	(346)	69.2	2.8		9.2		
34	86	>300	$C_{20}H_{10}O_4S$	69.4	2.9		9.2	1700 ($C=O_{indandione}$), 1655 (C=O γ-pyrone)	
		$PhCH_2OH$	(346)	69.0	2.9		9.1		

[a]Yield obtained by Method A.
[b]Yield obtained by Method B.