A Facile Multi Component Synthesis of Some Functionalized Chromenes and Spiroindole Derivatives using DABCO as an Efficient Catalyst

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Summary: Chromene and spirocyclic 2-oxindole derivatives were readily synthesized in good yields via a one-pot three-component reaction involving Knoevenagel condensation of aromatic aldehyde or isatin with an active methylene reagent then the intermediate was reacted with another different active methylene reagent via a DABCO-catalysed Michael addition to yield the main products. Some advantages of this protocol are good yields, use of available catalysts, simple workup procedure and short reaction times. All synthesized products were characterized by FT-IR, ^{1}H- and ^{13}C-NMR spectroscopy.

Key words: Multicomponent, DABCO, Tetrahydrochromene, Dihydropyran, Spirocyclic 2-oxindole, Catalyst.

Introduction

Isatin and spirooxindole frameworks are attractive synthetic targets for their various biological activities and some their derivatives are present in a number of key intermediates in pharmaceuticals and natural products. Spirocyclic systems are widely distributed structural framework, which are structurally interesting due to having one sp^3 stereogenic center that share to two rings [1]. The heterocyclic spiro-2-oxindole systems form the basis of cytostatic alkaloids such as spirotryprostatins A and B, alstonisine and macroxin and bisindole spirocyclic alkaloids from the group of gardmultine having an antimalarial and ganglioblocking action [2].

It is well known that multifunctionalized 5-oxo-4,5-dihydropyrano-[3,2-c]-chromene and tetrahydro 4*H*-chromene are of special interest due to their wide range of biological and pharmacological properties such as anti-coagulant, anticancer, anti-microbial, antioxidant, diuretic, spasmolytic, and anti-anaphylactic activities. 4-Phenyl-4*H*-pyrans are known as potent and specific IK_{Ca} channel (Ca^{2+}-activated potassium ion channel) blockers [3], inhibiting tyrosinase [4] and acting as anti-influenza virus agents [5] and photoactive materials [6]. Furthermore, these compounds may be used as cognitive enhancer drugs for treatment of several neurological diseases such as Parkinson, Alzheimer, amyotrophic lateral sclerosis (ALS), Huntington and also treatment of schizophrenia and myoclonus [7].

Among the heterocyclic spirooxindole ring system, substituted 4*H*-chromenes have received considerable attention due to their wide range of biological properties including spasmolytic, diuretic, anticoagulant, antiflammatory, antibacterial, antiprotozoal, anticancer and and antianaphylactin activities [8].

Several reagents or catalysts including tetrabutylammonium bromide [9], tetra-methyl ammonium hydroxide [10], (S)-proline, [11] rare earth perfluorooctanoates [12], hexadecyltrimethyl ammonium bromide [13], heterogeneous strong basic Mg/La mixed oxide [14], DBU [15], TEBA (triethyl benzylammonium chloride) [16] and $InCl_3$ [17] have been used for the preparation of these compounds. 4*H*-pyrans have also been synthesized under microwave and ultrasonic irradiations [18, 19]. Although these methods worked nicely in many cases, however, some of them suffer from one or more limitations such as low yields, non available catalysts or reagents and tedious workup.

Recently, the use of non-metallic reagents and catalysts has attracted special interests in organic synthesis due to environmental regulations. Among them, DABCO (1,4-diazabicyclo [2,2,2] octane) is generally employed as an efficient nucleophilic catalyst, which can be used as a organic base in various organic reactions such as deprotection of peptides [20], Baylis–Hillman reaction [21], isoxazoles preparation [22], o-alkylations of phenols [23], deprotection of benzylic trimethylsilyl ethers [24].

Multicomponent reactions have known as an effective protocol for preparation of these bioactive compounds. Most of the protocols based on acid catalyzed condensation reaction that anyway claimed to use newer reagents with more efficiency,

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inexpensive practical procedure, simplify reaction condition and higher yield of products.

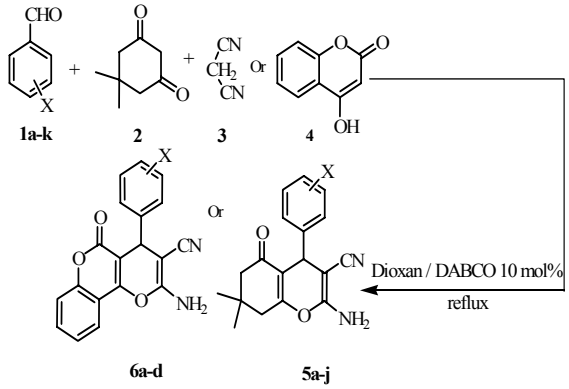
In view of this report and also as a continuation of our work on one-pot multicomponent reactions (MCRs) for the synthesis of heterocyclic compounds [25] we wish to report a highly efficient procedure for preparation of 4*H*-pyran and spiro-2-oxindole derivatives via a multicomponent in the presence of DABCO.

Results and Discussion

In the course of our study on the multicomponent reaction, we carried out the one-pot, three-component reaction of substituted benzaldehyde **1**, dimedone **2** and malononitrile **3** in the presence of a catalytic amount of DABCO (10 mol%) in dioxan to give corresponding 4*H*-pyans **5** (Scheme-1).

In order to optimize the reaction conditions, some polar and non polar solvents such as methanol, ethanol, dimethyl sulfoxide, acetonitrile and chloroform were used in a model reaction of benzaldehyde **1**, dimedone **2** and malononitrile **3** in the presence of catalytic amount of DABCO to investigate the effects of solvent for preparation of 4*H*-pyans **5**. It was found that ethanol was the most effective solvent in term of safety and the yield of the product (90%) while other solvents formed the product with yields of 60-80%. An amount of catalyst less than 10 mol% could catalyze the reaction, but it needed a longer reaction time. On the other hand, increasing the amount of catalyst over 10 mol% gave no improvement in the yield of product.

Under the same condition, the replacement of dimedone by 4-hydroxy coumarin **4**, exerted higher yields and shorter reaction time. It can be concluded that these results are due to more acidic CH of 4-hydroxy coumarin. Under the above mentioned conditions, a variety of the desired chromene products **6a-d** were obtained in good yields (Scheme-1 and Table-1).



Scheme-1: Synthetic pathway for synthesis of **5a-j** and **6a-d**

Aromatic aldehydes with substitutes carrying either electron donating or electron withdrawing groups reacted successfully and gave the products in good to high yields. The results are summarized in Table-1. The structure of compounds **5a-j** and **6a-d** was confirmed by ^{1}H-NMR, ^{13}C-NMR, and IR spectral data. These products exhibited a singlet in ^{1}H-NMR spectra at about δ = 4.5 ppm for H_4 and also a distinguishing peak at δ = 55.90-58.86 ppm for C_4 in the ^{13}C-NMR spectra. The characteristic peaks for NH_2 revealed one broad peak at about δ =5 ppm.

Table-1: DABCO catalyzed synthesis of 5-oxo- 5,6,7,8- tetrahydro-4*H*- chromene **5a-j** and 5- oxo-4,5-dihydropyrano- [3,2-c]- chromene derivatives, **6a-d**

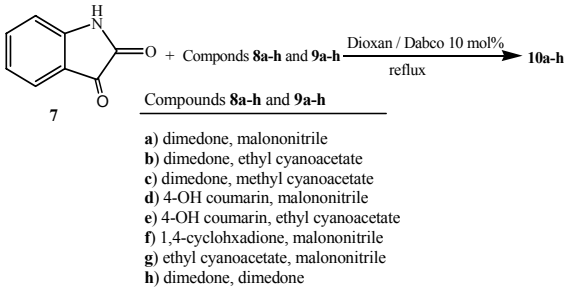
Entry	Product	X	Time[a] (min)	Time[b] (min)	Yield (%)	Melting point (°C)	
						Found	Reported
1	5a	H	15	45	90	226-228	228-230[12]
2	5b	4-NMe_2	20	40	94	218-220	230[26]
3	5c	3-Br	5	30	90	221-223	------
4	5d	2-OMe	15	50	68	197-199	------
5	5e	4-Cl	40	90	83	204-206	206[26]
6	5f	4- NO_2	45	90	50	179-180	177-179[12]
7	5g	3-OPh	60	100	79	187-189	-----
8	5h	4-OCH_2Ph	60	95	63	227-229	-----
9	5i	3,4-OH	45	90	97	208-209	-----
10	5j	4-Me	5	20	98	211-213	210-213[12]
11	6a	H	5	20	97	266-268	256-258[27]
12	6b	3-Br	3	15	98	273-275	-----
13	6c	4-Me	2	15	91	265-267	-----
14	6d	2-Cl	3	15	90	282-284	-----

[a] The products started appearing as solid mass
[b] The reaction completed

In the next step, we replaced aromatic aldehydes with isatin, and spirooxindoles obtained as the products of the reaction after a short refluxing time in dioxan in the presence of DABCO as a catalyst.

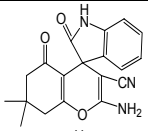
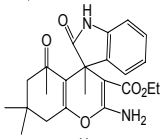
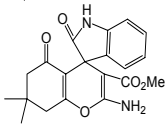
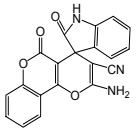
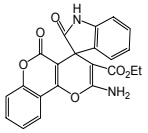
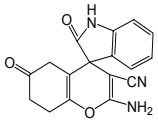
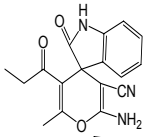
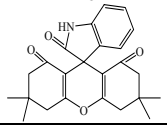
We commenced the project by a mixture of isatin **7** and a series of different compounds (**8**,**9**) with suitable acidic CH such as methyl cyanoacetat, ethyl cyanoacetat, ethyl acetoacetate, as well as using 1,3-cyclohexanedione and 4-OH coumarin. Under these conditions, the compounds, **10a-h**, with a wide range of functionalized groups such as CN, CO_2Me, CO_2Et, NH_2 and methyl groups were synthesized (Scheme-2 and Table-2).

The longer reaction times and low yields of products using methyl cyanoacetate and ethyl cyanoacetate as a starting material compare to malononitrile are probably due to the lower reactivity of the cyanoacetates. The same result obtained when 1,4-cyclohexadion and ethylacetoacetate was used instead of dimedone.



Scheme-2: Synthetic pathway for synthesis of **10a-h.**

Table-2: DABCO catalyzed synthesis of spirocyclic 2-oxindole derivatives, **10a-h**

Entry	Product	Compound 8	Compound 9	Structure	Time (min)	Yield (%)	Melting point (ºC)
1	10a	dimedone	malononitrile		10	98	294-296
2	10b	dimedone	ethyl cyanoacetate		20	96	259-260
3	10c	dimedone	methyl cyanoacetate		90	69	268-269
4	10d	4-OH coumarin	malononitrile		10	98	311-312
5	10e	4-OH coumarin	ethyl cyanoacetate		20	70	273-275
6	10f	1,4-cyclohexadione	malononitrile		15	75	>340
7	10g	ethyl acetoacetate	malononitrile		80	60	>340
8	10h	dimedone	dimedone		90	65	>340

The structure of products **10a-h** was confirmed by IR and NMR spectral data. For example the IR spectrum of **10a** showed absorptions at 3374, 3314 and 2193 cm^{-1} indicating the presence of NH_2 and cyano groups. The carbonyl functionalities absorptions were appeared at 1722, 1682 and 1659 cm^{-1}. In the ^{1}H-NMR spectrum of **10a**, the aromatic signals were observed at 7.05-6.68 ppm. The appearance of two singlets at 10.13 and 7.79 is due to resonance of NH and NH_2 protons. Furthermore, full assignment of the ^{13}C-NMR data confirmed these structures, where the key signal at 195-180 ppm was assigned to the carbonyl groups and at 47 ppm assigned to the quaternary sp^3 carbon.

We have proposed a possible mechanism for this reaction [12,26,27] as shown in Scheme-3. The formation of product may be explained by the reaction of malononitrile **3** with DABCO which forms the quaternary salt of DABCO and the carboanion of malononitrile in a reversible route. Later it reacts with benzaldehyde **1,** which then subsequent dehydration of intermediate produce olefin **11** [25d]. DABCO also catalyzes the generation of dimedone or coumarin carboanion that adds to olefin to give product **5** and **6** via a Michael addition.

In conclusion, we have demonstrated an efficient one-pot multicomponent reaction for synthesis of 4*H*-pyran derivatives using DABCO as a catalyst. This method involves mild reaction conditions, easy work-up, low reaction times and clean reaction profiles.

Experimental

All reagents were commercially available without further purification. The melting points were measured by an Electrothermal WRS-1B apparatus. The NMR spectra were run on a Bruker Avance instrument operating at 300MHz using $CDCl_3$ or DMSO as a solvent and TMS as an internal standard. The spectra were acquired at room temperature (298 K) and ^{13}C spectra are broadband proton decoupled. The chemical shifts were reported in ppm with respect to the references. Infrared spectra (IR) were recorded from KBr disk on a Galaxy Series FT-IR using KBr discs.

General procedure for the preparation of 5-oxo-5,6,7,8-tetrahydro-4H-chromene **(5)**

To a mixture of aryl aldehyde **1** (0.003 mol), dimedone **2** (0.003 mol) and malononitrile **3** (0.0033 mol) in dioxan was added DABCO (10 mol%) as a catalyst under stirring at room temperature. The mixture was refluxed and continuously stirred for specified time (Table-1). The reaction mixture was cooled and the resulting solid was filtered to afford the crude product, which then recrystallized from ethanol to give pure compound.

2-Amino-5,6,7,8-tetrahydro-7,7-dimethyl-5-oxo-4-phenyl-4H-chromene-3-carbonitrile **(5a)**

Light Yellow, IR (KBr) ν_{max} 3397, 3302, 3214, 3028, 2961, 2888, 2201, 1661, 1605, 1371. cm^{-1}. ^{1}H-NMR ($CDCl_3$, ppm): δ 7.33-7.21 (m, 5H, $H_{aromatic}$), 4.55 (br, 2H, NH_2), 4.41 (s, 1H, H_4), 2.47 (s, 2H, CH_2), 2.23 (s, 2H, CH_2), 1.13 (s, 3H, CH_3), 1.05 (s, 3H, CH_3); ^{13}C-NMR ($CDCl_3$): 195.9, 161.6, 157.5, 143.2, 128.6, 127.6, 127.2, 118.7, 114.0, 63.5, 50.7, 40.7, 35.5, 32.2, 28.9, 27.7.

2-Amino-5,6,7,8-tetrahydro-7,7-dimethyl-5-oxo-4-(4-dimethylaminophenyl)-4H-chromene-3-carbonitrile **(5b)**

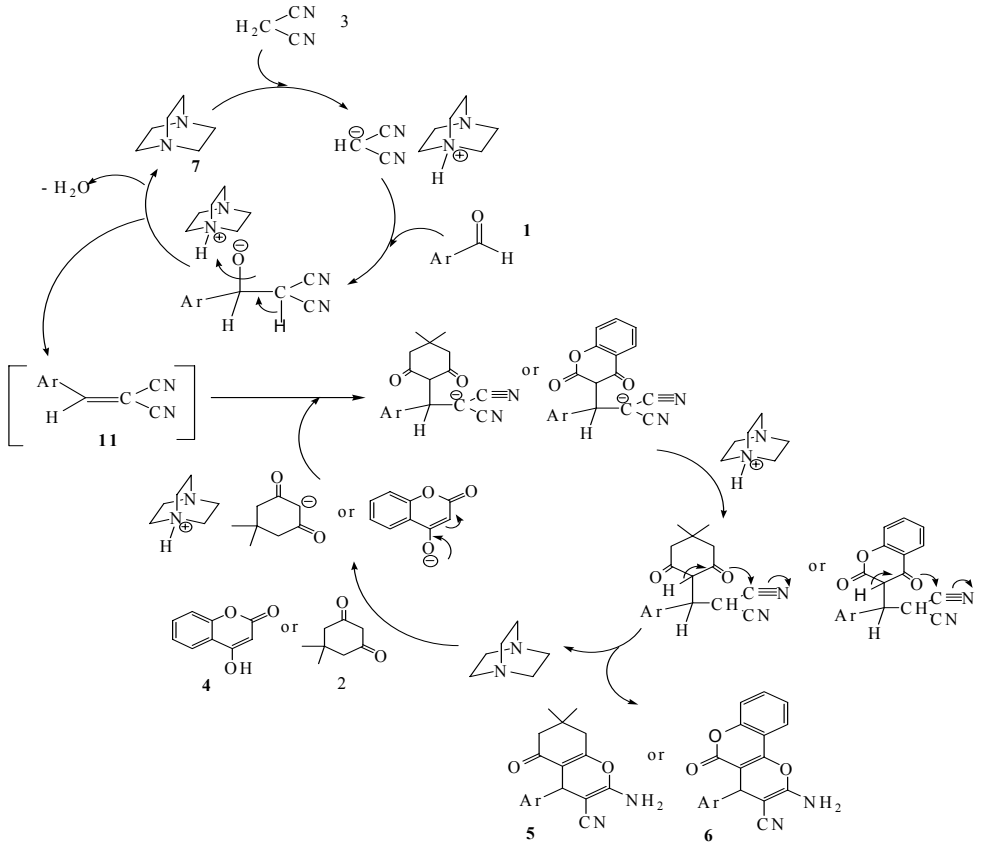
Light yellow solid, IR (KBr) ν_{max} 3381, 3318, 3210, 2963, 2897, 2191, 1682, 1657, 1368 cm^{-1}. ^{1}H-NMR (DMSO-d_6, ppm): δ 6.97 (d, 2H, $H_{aromatic}$), 6.95 (br s, 2H, NH_2), 6.66 (d, 2H, $H_{aromatic}$), 4.06 (s, 1H, H_4), 2.87 (s, 6H, $N(CH_3)_2$), 2.47-2.55 (m, 2H, CH_2), 2.27 (d, 1H, CH_2), 2.10 (d, 1H, CH_2), 1.06 (s, 3H, CH_3), 0.97 (s, 3H, CH_3); ^{13}C-NMR ($CDCl_3$): 198.9, 159.3, 155.1, 146.6, 131.7, 130.0, 117.3, 113.9, 58.1, 51.6, 44.3, 40.3, 37.3, 30.6, 28.5, 27.5.

2-Amino-5,6,7,8-tetrahydro-7,7-dimethyl-5-oxo-4-(3-bromophenyl)-4H-chromene-3-carbonitrile **(5c)**

White solid, IR (KBr) ν_{max} 3345, 3308, 3165, 2965, 2191, 1686, 1659, 1371 cm^{-1}. ^{1}H-NMR ($CDCl_3$, ppm): δ 7.36-7.16 (m, 4H, $H_{aromatic}$), 4.64 (s, 2H, NH_2), 4.39 (s, 1H, H_4), 2.49 (s, 2H, CH_2), 2.25 (s, 2H, CH_2), 1.13 (s, 3H, CH_3), 1.07 (s, 3H, CH_3); ^{13}C-NMR ($CDCl_3$): 195.8, 159.3, 155.1, 144.4, 133.8, 130.4, 130.1, 126.6, 123.0, 117.3, 113.9, 58.1, 50.6, 40.6, 35.3, 32.3, 28.8, 27.7

2-Amino-5,6,7,8-tetrahydro-7,7-dimethyl-5-oxo-4-(2-methoxyphenyl)-4H-chromene-3-carbonitrile **(5d)**

White solid, IR (KBr) ν_{max} 3397, 3331, 3221, 2967, 2880, 2189, 1688, 1657, 1607, 1371 cm^{-1}. ^{1}H-NMR ($CDCl_3$, ppm): δ 7.22- 6.86 (m, 4H, $H_{aromatic}$), 4.73 (s, 1H, H_4), 4.20 (br, 2H, NH_2), 3.85 (s, 3H, OCH_3), 2.46 (s, 2H, CH_2), 2.24- 2.22 (d, 2H, CH_2), 1.13 (s, 3H, CH_3), 1.07 (s, 3H, CH_3); ^{13}C-NMR ($CDCl_3$): 196.1, 162.4, 158.2, 157.2, 130.8, 129.1, 128.4, 120.7, 119.3, 112.9, 111.3, 62.0, 55.6, 50.6, 40.7, 32.2, 30.8, 29.1, 27.4.



Scheme-3: The possible mechanism for preparation of chromene and spirocyclic 2-oxindole derivatives in the presence of DABCO

2-Amino-5,6,7,8-tetrahydro-7,7-dimethyl-5-oxo-4-(4-chlorophenyl)-4H-chromene-3-carbonitrile **(5e)**

White solid, IR (KBr) ν_{max} 3399, 3318, 3214, 2961, 2193, 1684, 1655, 1369 cm^{-1}. ^{1}H-NMR (DMSO-d_6, ppm): δ 7.36-7.33 (d, 2H, $H_{aromatic}$), 7.18-7.16 (d, 2H, $H_{aromatic}$), 7.04 (s, 2H, NH_2), 4.20 (s, 1H, H_4), 3.57 (s, 2H, CH_2), 2.22 (d, 1H, CH_2), 2.13 (d, 1H, CH_2), 1.03(s, 3H, CH_3), 0.95 (s, 3H, CH_3); ^{13}C-NMR (DMSO-d_6): 196.1, 163.1, 159.0, 144.2, 131.6, 129.6, 128.7, 120.0, 112.8, 66.8, 58.3, 50.4, 35.6, 32.2, 28.8, 27.3

2-Amino-5,6,7,8-tetrahydro-7,7-dimethyl-5-oxo-4-(4-nitrophenyl)-4H-chromene-3-carbonitrile **(5f)**

Light Yellow solid, IR (KBr) ν_{max} 3389, 3327, 3212, 3131, 2969, 2189, 1682, 1657, 1518, 1346 cm^{-1}. ^{1}H-NMR (DMSO-d_6, ppm): δ 8.17 (d, 2H, $H_{aromatic}$), 7.45 (s, 2H, NH_2), 7.20 (d, 2H, $H_{aromatic}$), 4.36 (s, 1H, H_4), 2.53-2.57 (m, 2H, CH_2), 2.23 (d, 1H, CH_2), 2.12 (d, 1H, CH_2), 1.04 (s, 3H, CH_3), 0.95 (s, 3H, CH_3); ^{13}C-NMR (DMSO-d_6): 196.2, 163.6, 159.0, 152.8, 146.7, 129.1, 124.1, 112.2, 57.4, 56.5, 50.3, 36.1, 32.3, 28.7, 27.4, 19.0.

2-Amino-5,6,7,8-tetrahydro-7,7-dimethyl-5-oxo-4-(3-phenoxyphenyl)-4H-chromene-3-carbonitrile **(5g)**

Milky solid, IR (KBr) ν_{max} 3377, 3329, 3212, 2959, 2191, 1686, 1655, 1369 cm^{-1}. ^{1}H-NMR ($CDCl_3$, ppm): δ 7.36-6.83 (m, 9H, $H_{aromatic}$), 4.55 (s, 2H, NH_2), 4.40 (s, 1H, H_4), 2.44 (s, 2H, CH_2), 2.30 (s, 2H, CH_2), 1.12 (s, 3H, CH_3), 1.03 (s, 3H, CH_3). ^{13}C-NMR ($CDCl_3$): 195.9, 161.8, 157.6, 157.3, 157.1, 145.3, 129.9, 129.7, 123.2, 122.7, 118.8, 118.0, 117.4, 113.7, 63.0, 50.6, 40.6, 35.4, 32.2, 28.9, 27.7.

2-Amino-5,6,7,8-tetrahydro-7,7-dimethyl-5-oxo-4-(4-benzyloxyphenyl)-4H-chromene-3-carbonitrile **(5h)**

White solid, IR (KBr) ν_{max} 3459, 3391, 3324, 3212, 2955, 2899, 2187, 1686, 1659, 1368 cm^{-1}. ^{1}H-NMR ($CDCl_3$, ppm): δ 7.45-6.90 (m, 9H, $H_{aromatic}$), 5.03 (s, 2H, OCH_2), 4.54 (s, 2H, NH_2), 4.38 (s, 1H, H_4), 2.46 (s, 2H, CH_2), 2.24 (s, 2H, CH_2), 1.12 (s, 3H, CH_3), 1.05 (s, 3H, CH_3); ^{13}C-NMR ($CDCl_3$): 196.0, 161.3, 157.9, 157.4, 137.0, 135.7, 128.6,

128.6, 127.9, 127.5, 119.0, 114.8, 114.2, 70.0, 63.7, 50.7, 40.7, 34.7, 32.2, 28.9, 27.7.

2-Amino-5,6,7,8-tetrahydro-7,7-dimethyl-5-oxo-4-(3,4-dihydroxyphenyl)-4H-chromene-3-carbonitrile **(5i)**

Yellow solid, IR (KBr) ν_{max} 3470, 3335, 3259, 2938, 2191, 1686, 1667, 1366 cm^{-1}. ^{1}H-NMR (DMSO-d_6, ppm): δ 8.50 (br s, 2H, OH), 6.93- 6.51 (m, 3H, $H_{aromatic}$), 6.50 (s, 2H, NH_2), 3.96 (s, 1H, H_4), 2.49 (s, 2H, CH_2), 2.23 (m, 2H, CH_2), 1.02 (s, 3H, CH_3), 0.95 (s, 3H, CH_3); ^{13}C-NMR (DMSO-d_6,): 196.1, 162.3, 158.8, 145.4, 144.4, 143.9, 136.2, 118.3, 115.7, 115.1, 113.7, 59.2, 50.5, 47.0, 35.3, 32.2, 28.9, 27.2.

2-Amino-5,6,7,8-tetrahydro-7,7-dimethyl-5-oxo-4-(4-methylphenyl)-4H-chromene-3-carbonitrile **(5j)**

Light Yellow solid, IR (KBr) ν_{max} 3428, 3331, 3221, 2957, 2924, 2191, 1676, 1368 cm^{-1}. ^{1}H-NMR (DMSO-d_6, ppm): δ 7.30-7.04 (m, 5H, $H_{aromatic}$), 6.05 (br s, 2H, NH_2), 3.94 (s, 1H, H_4), 2.47 (s, 2H, CH_2), 2.35 (s, 3H, CH_3), 2.23 (s, 2H, CH_2), 1.12 (s, 3H, CH_3), 1.05 (s, 3H, CH_3); ^{13}C-NMR ($CDCl_3$): 198.9, 159.3, 155.1, 139.2, 135.4, 129.0, 117.3, 112.1, 58.1, 51.6, 44.3, 37.3, 30.8, 27.5, 24.3.

General procedure for the preparation of 5-oxo-pyrano-[3,2-c]-chromenes **(6)**

To a solution of aryl aldehyde **1** (0.003 mol) in dioxan was added 4-OH-coumarin **5** (0.003 mol), malononitrile **3** (0.0033 mol) and DABCO (10 mol%) as a catalyst under stirring at room temperature. The mixture was refluxed and continuously stirred for specified time (Table-2). The crude mixture was then cooled and the resulting solid was filtered to afford the crude product. The filtrate was recrystallized from ethanol to give pure compound.

2-Amino-4,5-dihydro-4-phenyl -5-oxo-pyrano[3,2-c]chromene-3-carbonitrile **(6a)**

White solid, IR (KBr) ν_{max}: 3377, 3287, 3181, 2199, 1709, 1674, 1381 cm^{-1}. ^{1}H-NMR (DMSO-d_6, ppm): δ 7.88-7.27 (m, 11H, $H_{aromatic}$ and NH_2), 4.44 (s, 1H, H_4); ^{13}C-NMR (DMSO-d_6): 160.0, 158.4, 153.8, 152.6, 143.8, 133.4, 129.0, 128.1, 127.6, 125.1, 122.9, 119.7, 117.0, 113.4, 104.4, 58.3, 37.4.

2-Amino-4,5-dihydro-4-(3-bromophenyl)-5-oxo-pyrano[3,2-c]chromene-3-carbonitrile **(6b)**

White solid, IR (KBr) ν_{max}: 3395, 3324, 3196, 2203, 1707, 1670, 1381 cm^{-1}. ^{1}H-NMR (DMSO-d_6, ppm): δ 7.87-7.28 (m, 10H, $H_{aromatic}$ and NH_2), 4.49 (s, 1H, H_4); ^{13}C-NMR (DMSO-d_6): 160.0, 158.4, 154.2, 152.6, 146.5, 133.4, 131.2, 130.9, 130.5, 127.4, 125.1, 123.0, 122.2, 119.6, 117.0, 113.4, 103.6, 57.8, 37.1.

2-Amino-4,5-dihydro-4-(4-methylphenyl)-5-oxo-pyrano[3,2-c]chromene-3-carbonitrile **(6c)**

White solid, IR (KBr) ν_{max}: 3385, 3314, 3192, 2195, 1713, 1676, 1377 cm^{-1}. ^{1}H-NMR ($CDCl_3$, ppm): 7.92-7.09 (m, 10H, $H_{aromatic}$ and NH_2). 4.40 (s, 1H, H_4), 2.66 (s, 3H, CH_3), ^{13}C-NMR ($CDCl_3$): 160.0, 158.3, 153.8, 152.6, 142.8, 133.4, 129.0, 128.1, 127.5, 125.1, 122.9, 119.5, 117.0, 113.4, 104.4, 58.3, 37.4, 20.4.

2-Amino-4,5-dihydro-4-(2-chlorophenyl)-5-oxo-pyrano[3,2-c]chromene-3-carbonitrile **(6d)**

Cream solid, IR (KBr) ν_{max} 3390, 3379, 3275, 3185, 2201, 1703, 1676, 1379 cm^{-1}. ^{1}H-NMR (DMSO-d_6, ppm): δ 7.90-7.28 (m, 10H, $H_{aromatic}$ and NH_2), 4.97 (s, 1H, H_4); ^{13}C-NMR (DMSO-d_6): 159.8, 158.6, 154.5, 152.7, 140.7, 133.5, 132.9, 131.1, 130.0, 129.3, 128.1, 125.2, 123.0, 119.3, 117.0, 113.3, 103.4, 57.0, 34.8.

General Procedure for the Preparation of Spirooxindoles **(10)**

To a solution of isatin **7** (0.003 mol), **8** (0.003 mol) and **9** (0.0033) in dioxan was added 10 mol% of DABCO as a catalyst. The reaction mixture was refluxed and continuously stirred for specified time (Table-2). Then it was allowed to cool to room temperature. The resulting solid was filtered off and washed with hot ethanol to yield pure compound.

2-Amino-7,7-dimethyl-2',5-dioxo-5,6,7,8-tetrahydrospiro[chromene-4,3'-indoline]-3-carbonitrile **(10a)**

Milky, IR (KBr) ν_{max} 3374, 3314, 3146, 2961, 2928, 2193, 1722, 1682, 1659, 1605, 1472, 1348, 1223 cm^{-1}. ^{1}H-NMR (DMSO-d_6, ppm): δ 10.13 (s, 1H, NH), 7.79 (s, 2H, NH_2), 7.05-6.68 (m, 4H, $H_{aromatic}$), 2.62-2.44 (dd, 2H, CH_2), 2.19-1.98 (dd, 2H, CH_2), 1.02 (s, 3H, CH_3), 0.99 (s, 3H, CH_3); ^{13}C-NMR (DMSO-d_6): 195.4, 178.5, 164.6, 159.2, 142.5, 134.9, 128.6, 123.5, 122.2, 117.9, 111.2, 109.7, 66.8, 50.4, 47.2, 40.3, 32.4, 28.1, 27.4.

Ethyl 2-amino-7,7-dimethyl-2',5-dioxo-5,6,7,8-tetrahydrospiro[chromene-4,3'-indoline]-3-carboxylate **(10b)**

Milky, IR (KBr) ν_{max} 3372, 3235, 3181, 3115, 2961, 1715, 1690, 1670, 1649, 1614, 1526, 1472, 1348, 1223 cm^{-1}. ^{1}H-NMR (DMSO-d_6, ppm): δ 10.13 (s, 1H, NH), 7.84 (s, 2H, NH_2), 7.06-6.66 (m, 4H, $H_{aromatic}$), 3.74-3.69 (q, 2H, CH_2), 2.61-2.45 (dd, 2H, CH_2), 2.18-1.99 (dd, 2H, CH_2), 1.01 (s, 3H, CH_3), 0.95 (s, 3H, CH_3), 0.82-0.78 (t, 3H, CH_3); ^{13}C-NMR (DMSO-d_6): 195.1, 180.2, 168.1, 162.8, 159.6, 144.5, 136.4, 127.6, 122.7, 121.0, 113.6, 108.6, 76.8, 59.3, 51.1, 47.1, 40.6, 32.0, 28.2, 27.2, 13.6.

Methyl 2-amino-7,7-dimethyl-2',5-dioxo-5,6,7,8-tetrahydrospiro[chromene-4,3'-indoline]-3-carboxylate **(10c)**

Light pink, IR (KBr) ν_{max} 3478, 3385, 3281, 3188, 2960, 1721, 1694, 1614, 1489, 1354, 1281 cm^{-1}. ^{1}H-NMR (DMSO-d_6, ppm): δ 10.13 (s, 1H, NH), 7.79 (s, 2H, NH_2), 7.07-6.68 (m, 4H, $H_{aromatic}$), 2.62-2.45 (dd, 2H, CH_2), 2.19-1.99 (dd, 2H, CH_2), 1.01 (s, 3H, CH_3), 0.94 (s, 3H, CH_3), ^{13}C-NMR (DMSO-d_6): 195.1, 180.3, 168.2, 162.9, 159.5, 144.2, 136.2, 127.7, 122.7, 121.0, 113.6, 108.6, 77.1, 51.1, 50.6, 47.1, 32.0, 28.3, 27.1, 19.0.

2'-Amino-2,5'-dioxo-5'H-spiro[indoline-3,4'-pyrano[3,2-c]chromene]-3'-carbonitrile **(10d)**

Milky, IR (KBr) ν_{max} 3360, 3296, 3198, 2207, 1734, 1713, 1674, 1605, 1472, 1360, 1219 cm^{-1}. ^{1}H-NMR (DMSO-d_6, ppm): δ 10.68 (s, 1H, NH), 7.96-6.85 (m, $10H_{aromatic}$, NH_2); ^{13}C-NMR (DMSO-d_6): 177.6, 158.9, 158.7, 155.5, 152.5, 142.7, 134.1, 133.5, 129.4, 125.5, 124.6, 123.1, 122.5, 117.4, 117.1, 112.9, 110.0, 101.9, 57.5, 48.1.

Ethyl 2'-amino-2,5'-dioxo-5'H-spiro[indoline-3,4'-pyrano[3,2-c]chromene]-3'-carboxylate **(10e)**

Milky, IR (KBr) ν_{max} 3385, 3316, 3281, 3196, 3138, 1721, 1692, 1653, 1614, 1472, 1354, 1281 cm^{-1}. ^{1}H-NMR (DMSO-d_6, ppm): δ 10.41 (s, 1H, NH), 8.13-6.74 (m, 10H, $H_{aromatic}$, NH_2), 3.79-3.75 (q, 2H, CH_2), 0.86-.081(t, 3H, CH_3); ^{13}C-NMR (DMSO-d_6): 179.3, 167.6, 159.0, 158.2, 154.2, 152.3, 144.6, 135.2, 133.8, 128.3, 125.2, 123.6, 123.3, 121.4, 116.7, 112.9, 108.9, 104.3, 76.1, 59.6, 47.8, 13.6.

2-Amino-2',6-dioxo-5,6,7,8-tetrahydrospiro[chromene-4,3'-indoline]-3-carbonitrile **(10f)**

Milky, IR (KBr) ν_{max} 3435, 3372, 3296, 3177, 2197, 1711, 1636, 1603, 1470, 1414, 1222 cm^{-1}. ^{1}H-NMR (DMSO-d_6, ppm): δ 10.64 (s, 1H, NH), 7.29-6.87 (m, 10H, $H_{aromatic}$, NH_2), 3.43 (m, 4H, CH_2-CH_2), 2.17-2.12 (dd, 2H, CH_2); ^{13}C-NMR (DMSO-d_6): 208.0, 178.1, 160.9, 142.0, 141.2, 131.9, 129.8, 125.1, 123.2, 118.9, 110.3, 102.5, 67.1, 54.1, 51.5, 43.5, 26.5.

2'-Amino-6'-methyl-2-oxo-5'-propionylspiro[indoline-3,4'-pyran]-3'-carbonitrile **(10g)**

Milky, IR (KBr) ν_{max} 3484, 3281, 3158, 3075, 2980, 2191, 1722, 1701, 1678, 1597, 1470, 1383, 1288 cm^{-1}. ^{1}H-NMR (DMSO-d_6, ppm): δ 10.38 (s, 1H, NH), 7.18-6.78 (m, 6H, $H_{aromatic}$, NH_2), 3.79-3.74 (q, 2H, CH_2), 2.31 (s, 3H, CH_3), 0.81-0.76 (t, 3H, CH_3); ^{13}C-NMR (DMSO-d_6): 179.0, 164.9, 159.4, 158.9, 142.6, 135.0, 129.0, 123.8, 122.3, 117.9, 109.8, 105.1, 60.7, 57.0, 49.4, 19.0, 13.4.

3',3',6',6'-Tetramethyl-3',4',6',7'-tetrahydrospiro[indoline-3,9'-xanthene]-1',2,8'(2'H,5'H)-trione **(10h)**

Milky, IR (KBr) ν_{max} 3360, 3130, 2960, 2928, 1722, 1714, 1682, 1604, 1471, 1348, 1222 cm^{-1}. ^{1}H-NMR (DMSO-d_6, ppm): δ 10.98 (s, 1H, NH), 7.40-6.68 (m, 4H, $H_{aromatic}$), 2.55-1.88 (m, 8H, $8CH_2$), 0.99 (s, 12H, $4CH_3$); ^{13}C-NMR (DMSO-d_6): 203.9, 194.7, 182.3, 168.6, 144.7, 133.5, 128.0, 122.0, 121.6, 111.7, 109.8, 101.4, 59.0, 54.2, 50.6, 47.3, 46.9, 42.6, 33.7, 32.8, 31.6, 29.2, 27.3, 26.4.

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