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Synthesis of arylated highly congested indans using a domino sequence '*

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Abstract-A novel and efficient regioselective synthesis of various arylated highly congested 7-aryl-5-methylsulfanylindan-4-carbonitriles (3a-(), methyl 7-aryl-5-methylsulfanylindan-4-carboxylates (lOa-e) and 7-aryl-5-methylsulfanylindan-4-carboxylic acids (lla-e) through base-catalyzed reaction of 6-aryl-4-methylsulfanyl-2-oxo-2H-pyran-3-carbonitriles (la-() and methyl 6-aryl-4-methylsulfanyl-2-oxo-2Hpyran-3-carboxylates (9a-e) by cyclopentanone (2) has been delineated. The synthetic potential of 2-pyranone was explored further to generate mo'iecular diversity using 6-aryl-4-sec-amino-2-oxo-2H-pyran-3-carbonitriles (7a-h), 5,6-diaryl-4-methylsulfanyl-2-oxo2H-pyran-3-carbonitriles (Sa,b) and methyl 5,6-diaryl-4-methylsulfanyl-2-oxo-2H-pyran-3-carboxylates (12a,b) as precursors for the ring transformation by cyclopentanone to assess the effects of substituents on the course of the reaction to obtain highly congested indans, 6,7diaryl-5-methylsulfanylindan-4-carbonitriles (6a,b), 7-aryl-5-(piperidin-I-yl)indan-4-carbonitriles (8a-h) and methyl 6,7-diaryl-5-methylsulfanylindan-4-carboxylates (13a,b).

1. Introduction

The indan skeleton occurs in a variety of natural products and is a substructure I of therapeutic importance.z Various indan derivatives have been reported to display aldosterone synthase3 and thrombin4 inhibitoz activities, besides respiratory stimulating,: antispasmodic and antiHIV7 properties. Through an extensive literature survey it was realized that the compounds containing this rin~ system have been synthesized generally either by anionic8. or radical-mediated to cyclization strategies. The newer approaches provide an easy access to the construction of chiral indan derivatives with substitution on the cyc10pentane ring. The cyclization of the aryl radical derived from 4-(2-bromophenyl)-I-pentene also yields II a mixture of *cis*- and trans-I,3-dimethylindans. The cyc1oisomerization of the organolithium derived from 4-(2-bromophenyl)-I-pentene is more selectivelz compared to radical cyclization for the synthesis of indans. An alternative route has been developed 13 for the construction of 1,3disubstituted indans through cyclization of styrene tethered primary radical or alkyl lithium derived from 2-(2-iodo-lmethylethyl)styrene. Cyc1otrimerization of three different acetylenes ilr the presence of titanium alkoxide is an elegant approach for the preparation of highly functionalized indans. 14 This methodology provides an avenue to introduce substituents to the aryl as well as cyclopentane rings of the indan. Recently, 4,7-disubstituted indan-2-0Is have been prepared from the aryl titanium compounds obtained from two acetylenes and ethynyl p-tolylsulfone.15.16 Arylboronic acid esters bearing a pendant Michael-acceptor add to norbornene and cyclize to give the indan ring system. 17 An intramolecular addition of an organolithium to a tethered benzyne intermediate is one of the versatile approaches for the construction of arylated indans.11I A new synthesis of indan derivatives has been recently reportedl9 by the coupling of carbene complexes with 2-alkynylstyrenes. The difficulties in obtaining various precursors in multiple steps and limitations to introduce substituents in both the aryl and cyc1opentane rings prompted us to develop an easy, viable synthetic route for the construction of in dans with multiple substituents in the aryl ring.

Here, we report an elegant synthesis of indans through a carbanion induced ring transformation of suitably functionalized 2H-pyran-2-ones by cyc1opentanone. The presence of electron-acceptor and electron-donor substituents at positions 3 and 4 of the pyran ring makes it a very valuable synthon for the construction of various mono and polycyclic arenes and heteroarenes depending upon the nature of the nuc1eophileszG-z4 used. The synthetic potential of suitably functionalized 2H-pyran-2-one is enormous and can be used for generating molecular diversity through careful maneuverings of nuc1eophiles and reaction conditions. Bases such as NaH and sodium methoxide also contribute to the regioselectivity.

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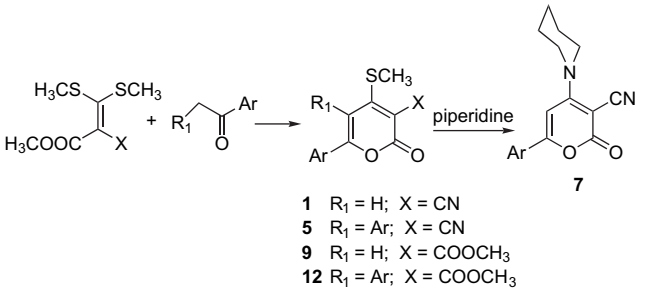
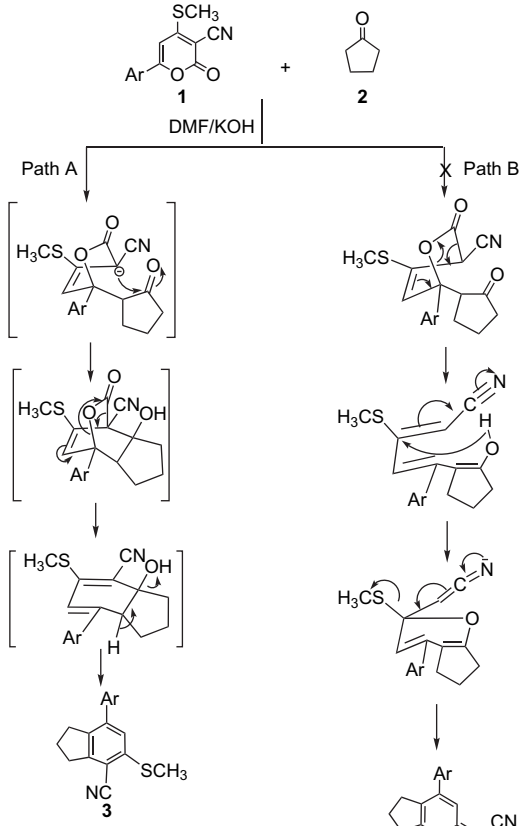
2. Results and discussion

Various 2*H*-pyran-2-ones used as precursors for the ring transformation reactions are 6-aryl-4-methylsulfanyl- (**1**), 5,6-diaryl-4-methylsulfanyl- (**5**), 6-aryl-4-(piperidin-1-yl)-2-oxo-2*H*-pyran-3-carbonitriles (**7**), methyl 6-aryl-4-methylsulfanyl- (**9**) and methyl 5,6-diaryl-4-methylsulfanyl-2-oxo-2*H*-pyran-3-carboxylates (**12**). The 2*H*-pyran-2-ones **1** and **5** have been prepared[23,25] from the reaction of an aryl methyl ketone and 1,2-diarylethanone with methyl 2-cyano-3,3-dimethylthioacrylate separately. The precursors 6-aryl-4-(piperidin-1-yl)-2-oxo-2*H*-pyran-3-carbonitriles (**7**) have been synthesized[20] by refluxing a mixture of **1** and piperidine in ethanol for 5 h, while **9** has been obtained from the reaction of an aryl methyl ketone and methyl 2-carbomethoxy-3,3-dimethylthioacrylate (Scheme 1). We had an apprehension in obtaining synthon **12** from the reaction of 1,2-diarylethanone with methyl 2-carbomethoxy-3,3-dimethylthioacrylate because of steric crowding but the reaction proceeded smoothly, possibly by acquiring non-planar conformation of both the aryl rings. Our attempts to prepare methyl 6-aryl-4-*sec*-amino-2-oxo-2*H*-pyran-3-carboxylates from the reaction of **9** with secondary amine in refluxing ethanol failed. The weaker electron-withdrawing property of $-COOCH_3$ compared to the CN substituent made the C-4 position of the pyran ring less electrophilic and resistant to amination.



Scheme 1. Synthesis of various 2*H*-pyran-2-ones.

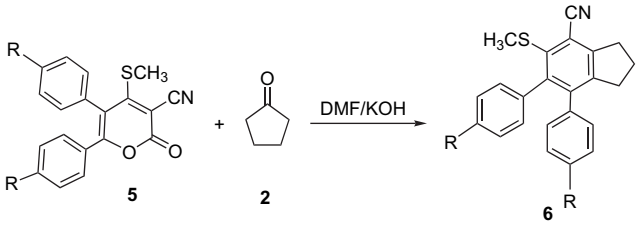
Cyclopentanone (**2**) was used as a source of carbanion for the ring transformation reactions. The position 2 of the cyclopentanone is reactive enough to form an enolate in the presence of base like KOH/DMF and NaH/THF. The C-6 position of the 2*H*-pyran-2-ones (**1a–f**) is highly electrophilic in nature due to extended conjugation and the presence of an electron-withdrawing substituent at C-3 of the pyran ring and is highly susceptible to nucleophilic attack. The first step in the formation of aryl-tethered indan **3** is the attack of an enolate generated in situ from cyclopentanone (**2**) at C-6 of the pyran ring and thereafter it may follow either path A or B. In the case of reaction following path A, the first step is the ring closure followed by elimination of carbon dioxide and water to yield indans (**3a–f**) in one step. On the other hand when reaction follows path B,[20a] enolization followed by ring closure involving attack of the enolate anion at C-4 of the pyran ring with loss of methyl mercaptan and carbon dioxide may lead to the bicyclic pyran **4**. Thus, stirring an equimolar mixture of **1**, cyclopentanone (**2**) and powdered KOH in DMF at ambient temperature afforded 7-aryl-5-methylsulfanylindan-4-carbonitriles (**3**) in more than 71% yields. However, we did not observe the formation of product **4**. The plausible mechanism of the reaction is shown in Scheme 2.



1,3	Ar	Yield (%)
a	C_6H_5	78
b	4-$CH_3C_6H_4$	81
c	2-thienyl	79
d	3-pyridyl	71
e	2,4-$(CH_3)_2C_6H_3$	75
f	2-furyl	85

Scheme 2. The proposed mechanism for the synthesis of 7-aryl-5-methylsulfanyl-indan-4-carbonitriles (**3**).

The effect of an additional aryl substituent at C-5 of the pyran ring on the course of the reaction was studied by preparing 6,7-diaryl substituted indans (**6a**,**b**) through the base-catalyzed ring transformation of 5,6-diaryl-4-methylsulfanyl-2-oxo-2*H*-pyran-3-carbonitriles (**5a**,**b**) by **2**, Scheme 3.

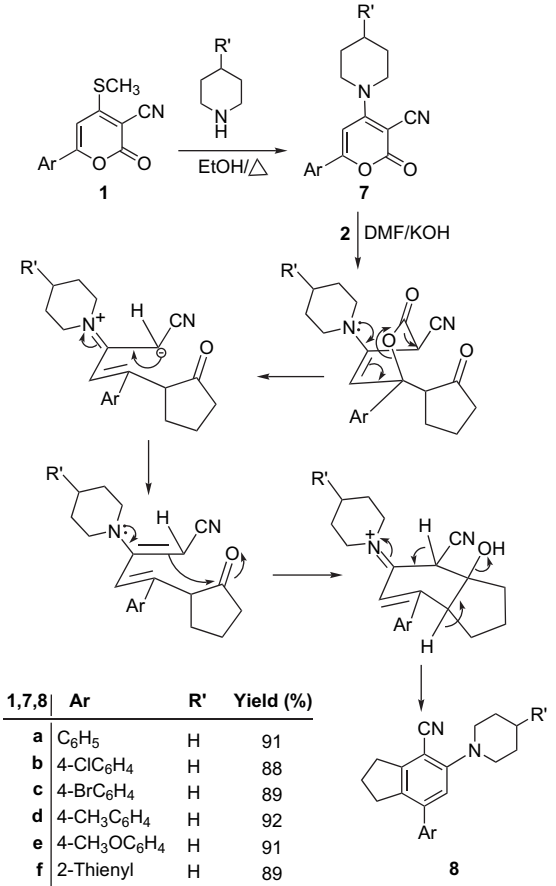


5,6	R	Yield (%)
a	H	71
b	CH_3O	65

Scheme 3. Synthesis of 6,7-diaryl-5-methylsulfanylindan-4-carbonitriles (**6**).

The presence of an aryl substituent at position 5 of the pyran ring has no significant contribution on the course of the reaction except a little variation in the yields.

The methylsulfanyl substituent at C-4 of the pyran ring, being a good leaving group gave a substitution product on reaction with piperidine/4-methylpiperidine in refluxing ethanol. However, the reaction of **5a**,**b** with piperidine failed to provide corresponding 5,6-diaryl-4-(piperidin-1-yl)-2-oxo-2*H*-pyran-3-carbonitriles, possibly due to steric hindrance. Amination in the absence of C-5 aryl substituent in **5** was facile to yield 6-aryl-4-*sec*-amino-2-oxo-2*H*-pyran-3-carbonitriles (**7a**–**h**) in good yields. The ring transformation of **7** by cyclopentanone (**2**) under analogous reaction conditions gave aminoindans (**8a**–**h**) in excellent yields. This reaction is also initiated by the attack of a carbanion generated from cyclopentanone (**2**) in situ at C-6 position of the 2*H*-pyran-2-ones (**7a**–**h**) with ring closure followed by concomitant loss of carbon dioxide and water as shown in Scheme 4. The presence of the *sec*-amino substituent at C-4 position of a pyran ring (**7**) did not influence the electrophilic character of the C-6 position and thus the reaction proceeded analogously to yield 7-aryl-5-*sec*-aminoindan-4-carbonitriles (**8a**–**h**) in more than 86% yields. The presence of a *sec*-amino group decreases the electrophilicity of C-4 position of the pyran ring and thereby reduces the possibility of side reactions by an attack of carbanion as well as enolate anion in situ from **2** (Scheme 4).

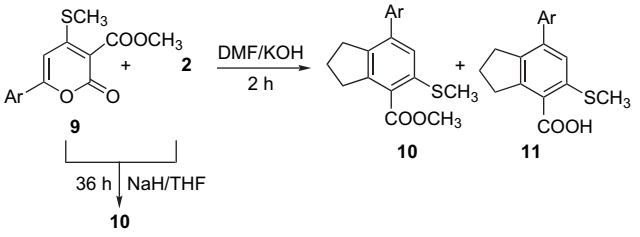


1,7,8	Ar	R'	Yield (%)
a	C_6H_5	H	91
b	4-ClC_6H_4	H	88
c	4-BrC_6H_4	H	89
d	4-$CH_3C_6H_4$	H	92
e	4-$CH_3OC_6H_4$	H	91
f	2-Thienyl	H	89
g	$C_{10}H_7$	H	87
h	C_6H_5	CH_3	86

Scheme 4. The plausible mechanism for the synthesis of 7-aryl-5-(piperidin-1-yl)indan-4-carbonitriles (**8**).

The effect of $COOCH_3$ as a weaker electron-withdrawing substituent at C-3 of the pyran ring was studied to assess its influence on the course of the reaction. Thus, a reaction of methyl 6-aryl-4-methylsulfanyl-2-oxo-2*H*-pyran-3-carboxylates (**9a**–**e**) and cyclopentanone (**2**) in the presence of powdered KOH in dry DMF under analogous reaction conditions afforded a mixture of two products in 3:2 ratio, which were separated by column chromatography. The product with higher R_f was identified as a methyl 7-aryl-5-methylsulfanylindan-4-carboxylate (**10**) while that with lower R_f was 7-aryl-5-methylsulfanylindan-4-carboxylic acid (**11**). An increase in the duration of reaction from 2 to 6 h improved the yield of acid **11** due to enhanced hydrolysis of ester **10**.

Further, an increase in the reaction time did not result in any significant change in the yields of **10** and **11**. Different solvents and bases were tried for the regioselective synthesis of **10**. Thus, a reaction of **9** with cyclopentanone (**2**) in the presence of NaH in THF produced only **10**, in 35–43% yields (Scheme 5). The yield optimization data in the presence of different bases and duration of reaction are listed in Table 1.



Scheme 5. Synthesis of methyl 7-aryl-5-methylsulfanylindan-4-carboxylates (**10**) and 7-aryl-5-methylsulfanylindan-4-carboxylic acids (**11**).

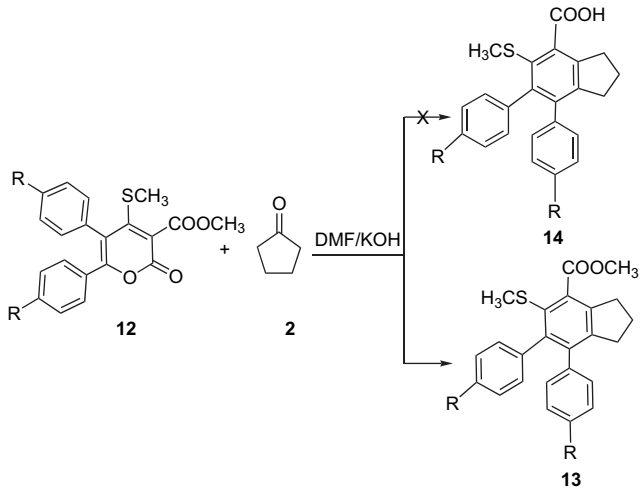
The ring transformation of methyl 4,5,6-trisubstituted-2-oxo-2*H*-pyran-3-carboxylates (**12a**,**b**) under analogous conditions led to yield only methyl 4,5-diaryl-6-methylsulfanylindan-7-carboxylates (**13a**,**b**) in good yields (Scheme 6).

Table 1. Yield optimization using bases and reaction times

10, **11**	Ar	DMF/KOH		DMF/KOH		NaH/THF
		2 h		6 h		36 h
		Yield (%)		Yield (%)		Yield (%)
		10	**11**	**10**	**11**	**10**
a	C_6H_5	32	57	5	71	42
b	4-Cl–C_6H_4	33	57	8	69	43
c	4-Br–C_6H_4	35	53	9	74	41
d	2-Thienyl	35	55	7	73	35
e	2-Naphthyl	33	57	10	67	41

3. Conclusions

We have developed a facile, economical and efficient route to the regioselective synthesis of highly congested indans that has an edge over the past literature procedures in terms of yields and option to introduce various substituents in the aryl ring. This methodology provides an opportunity to prepare such indans in which all the positions of fused aryl ring are occupied by different substituents.



12,13	R	Yield (%)
a	H	75
b	CH_3O	71

Scheme 6. Synthesis of methyl 6,7-diaryl-5-methylsulfanylindan-4-carboxylates (**13**).

4. Experimental

4.1. General

All reactions were conducted in flame-dried glassware. Precoated Merck TLC plates were used for monitoring the reaction. Column chromatographic separation was performed on neutral alumina and silica gel (60–120 mesh). IR spectra were recorded on a Shimadzu 8201 PC FTIR spectrophotometer. ^{1}H NMR spectra were recorded on Bruker DRX 200 as well as Bruker DRX 300 spectrometers in deuterated solvents with TMS as internal reference. Mass spectra were recorded on JEOL SX-102 (FAB) spectrometer. HRMS were recorded on JEOL JMS-600H (HRMS) spectrometer. Melting points were determined on Büchi-530 capillary melting point apparatus and are uncorrected.

4.2. General procedure: synthesis of 7-aryl-5-methylsulfanylindan-4-carbonitriles (3a–f)

A mixture of 6-aryl-4-methylsulfanyl-2-oxo-2*H*-pyran-3-carbonitrile (**1**, 1.0 mmol), cyclopentanone (**2**, 1.1 mmol) and KOH (1.5 mmol) in dry DMF (10 mL) was stirred for 2 h at room temperature. Thereafter, the reaction mixture was poured onto crushed ice with vigorous stirring. Neutralization with 10% HCl (10 mL) afforded a precipitate, which was filtered, dried and purified by neutral alumina column chromatography.

4.2.1. 5-Methylsulfanyl-7-phenylindan-4-carbonitrile (3a). It was prepared by following the general procedure from the reaction of **1a** (243 mg, 1.0 mmol) and **2** (0.1 mL, 1.1 mmol) using KOH (84 mg, 1.5 mmol) as a base in dry DMF (10 mL). Usual work-up and purification on neutral alumina column using 30% hexane in chloroform as eluent afforded a white solid; R_f ($CHCl_3$) 0.5; yield: 207 mg (78%); mp: 136–138 °C; IR (KBr): 2923, 2217, 1585, 1493, 1425, 1352, 1321, 1213, 1000, 861, 774, 705 cm^{-1}; δ_H (200 MHz, $CDCl_3$): 2.08–2.16 (m, 2H, CH_2), 2.56 (s, 3H, SCH_3), 2.96 (t, *J* 7.3 Hz, 2H, CH_2), 3.15 (t, *J* 7.5 Hz, 2H, CH_2), 7.14 (s, 1H, ArH), 7.39–7.46 (m, 5H, ArH); δ_C (50 MHz, $CDCl_3$): 17.20, 25.65, 33.17, 33.64, 108.05, 116.82, 126.22, 128.56, 128.67, 129.00, 139.95, 140.80, 140.86, 143.06, 151.31; MS *m/z* 266 (M^++1); HRMS (EI): M^+, found 265.0925; $C_{17}H_{15}NS$ requires 265.0920.

4.2.2. 7-(4-Methylphenyl)-5-methylsulfanylindan-4-carbonitrile (3b). It was obtained by stirring a mixture of **1b** (257 mg, 1.0 mmol), **2** (0.1 mL, 1.1 mmol) and KOH (84 mg, 1.5 mmol) in dry DMF (10 mL) as a white solid after neutral alumina column chromatography using 60:40 chloroform/hexane as eluent; R_f ($CHCl_3$) 0.5; yield: 226 mg (81%); mp: 112–114 °C; IR (KBr): 2925, 2214, 1580, 1512, 1429, 1185, 1118, 1018, 820, 723 cm^{-1}; δ_H (200 MHz, $CDCl_3$): 2.07–2.15 (m, 2H, CH_2), 2.41 (s, 3H, CH_3), 2.55 (s, 3H, SCH_3), 2.96 (t, *J* 7.3 Hz, 2H, CH_2), 3.13 (t, *J* 7.5 Hz, 2H, CH_2), 7.12 (s, 1H, ArH), 7.23–7.30 (m, 4H, ArH); MS *m/z* 280 (M^++1); HRMS (EI): M^+, found 279.1079; $C_{18}H_{17}NS$ requires 279.1077.

4.2.3. 5-Methylsulfanyl-7-(thiophen-2-yl)indan-4-carbonitrile (3c). It was obtained by stirring a mixture of **1c** (249 mg, 1.0 mmol), **2** (0.1 mL, 1.1 mmol) and KOH (84 mg, 1.5 mmol) in dry DMF (10 mL). Usual work-up gave a white solid after neutral alumina column chromatography using 40% hexane in chloroform as eluent; found: C, 66.11; H, 4.92; N, 5.26; $C_{15}H_{13}NS_2$ requires C, 66.38; H, 4.83; N, 5.16; R_f ($CHCl_3$) 0.55; yield: 214 mg (79%); mp: 127–129 °C; IR (KBr): 2924, 2212, 1591, 1454, 1423, 1352, 1276, 1105, 1055, 986, 701 cm^{-1}; δ_H (200 MHz, $CDCl_3$): 2.15–2.26 (m, 2H, CH_2), 2.58 (s, 3H, SCH_3), 3.14 (t, *J* 7.6 Hz, 4H, CH_2), 7.12–7.16 (m, 1H, ArH), 7.31–7.34 (m, 2H, ArH), 7.42–7.44 (m, 1H, ArH); δ_C (50 MHz, $CDCl_3$): 17.22, 25.22, 33.57, 34.09, 107.86, 116.09, 125.09, 127.29, 128.32, 135.58, 139.61, 140.88, 141.79, 151.85; MS *m/z* 272 (M^++1); HRMS (EI): M^+, found 271.0488; $C_{15}H_{13}NS_2$ requires 271.0484.

4.2.4. 5-Methylsulfanyl-7-(pyridin-3-yl)indan-4-carbonitrile (3d). It was obtained from the reaction of **1d** (244 mg, 1.0 mmol), **2** (0.1 mL, 1.1 mmol) and KOH (84 mg, 1.5 mmol) in dry DMF (10 mL) but worked up differently. After neutralization with 10% HCl the reaction mixture was extracted with $CHCl_3$ (50 mL×3) and dried over Na_2SO_4. The solvent from the extract was removed under reduced pressure and crude material obtained was purified by neutral alumina column chromatography using 30% hexane in chloroform as eluent to yield the product as a white solid; R_f ($CHCl_3$) 0.5; yield: 203 mg (71%); mp: 134–136 °C; IR (KBr): 2925, 2853, 2217, 1591, 1420, 1353, 1126, 1021, 806, 710 cm^{-1}; δ_H (200 MHz, $CDCl_3$): 2.04–2.12 (m, 2H, CH_2), 2.50 (s, 3H, SCH_3), 2.89 (t, *J* 7.3 Hz, 2H, CH_2), 3.09 (t, *J* 7.5 Hz, 2H, CH_2), 7.04 (s, 1H, ArH), 7.30–7.36 (m, 1H, ArH), 7.65–7.69 (m, 1H, ArH), 8.57–8.61 (m, 2H, ArH); MS *m/z* 267 (M^++1); HRMS (EI): M^+, found 266.0879; $C_{16}H_{14}N_2S$ requires 266.0872.

4.2.5. 7-(2,4-Dimethylphenyl)-5-methylsulfanylindan-4-carbonitrile (3e). It was prepared by following the general procedure from the reaction of **1e** (271 mg, 1.0 mmol) and **2** (0.1 mL, 1.1 mmol) using KOH (84 mg, 1.5 mmol) as

a base in dry DMF (10 mL). Usual work-up and purification on neutral alumina column using 30% hexane in chloroform as eluent afforded a white solid; R_f ($CHCl_3$) 0.55; yield: 220 mg (75%); mp: 97–99 °C; IR (KBr): 2924, 2851, 2219, 1607, 1579, 1513, 1436, 1291 cm^{-1}; δ_H (200 MHz, $CDCl_3$): 1.98–2.09 (m, 5H, CH_2 and CH_3), 2.29 (s, 3H, CH_3), 2.43 (s, 3H, SCH_3), 2.57 (t, *J* 7.3 Hz, 2H, CH_2), 3.07 (t, *J* 7.5 Hz, 2H, CH_2), 6.86–6.88 (m, 1H, ArH), 6.92 (s, 1H, ArH), 6.96 (s, 1H, ArH), 7.00–7.03 (m, 1H, ArH); MS *m/z* 294 (M^++1); HRMS (EI): M^+, found 293.1237; $C_{19}H_{19}NS$ requires 293.1232.

4.2.6. 7-(Furan-2-yl)-5-methylsulfanylindan-4-carbonitrile (3f). It was obtained from the reaction of **1f** (233 mg, 1.0 mmol), **2** (0.1 mL, 1.1 mmol) and KOH (84 mg, 1.5 mmol) in dry DMF (10 mL) under analogous reaction conditions. Usual work-up and purification on neutral alumina column using 40% hexane in chloroform as eluent afforded a light yellow solid; R_f (10% hexane in $CHCl_3$) 0.5; yield: 218 mg (85%); mp: 131–133 °C; IR (KBr): 2959, 2877, 2219, 1637, 1586, 1493, 1425, 1364, 1312, 1254, 1221, 1172, 1025, 932, 859, 807, 752 cm^{-1}; δ_H (200 MHz, $CDCl_3$): 2.17–2.30 (m, 2H, CH_2), 2.60 (s, 3H, SCH_3), 3.06–3.15 (m, 4H, CH_2), 6.53–6.56 (m, 1H, ArH), 6.71–6.73 (m, 1H, ArH), 7.55–7.56 (m, 2H, ArH); MS *m/z* 256 (M^++1); HRMS (EI): M^+, found 255.0716; $C_{15}H_{13}NOS$ requires 255.0712.

4.3. General procedure: synthesis of 6,7-diaryl-5-methylsulfanylindan-4-carbonitriles (6a,b)

A solution of 5,6-disubstituted-4-methylsulfanyl-2-oxo-2*H*-pyran-3-carbonitrile (**5**, 1.0 mmol) and cyclopentanone (**2**, 0.1 mL, 1.1 mmol) in dry DMF (10 mL) was stirred for 2 h under dry condition at room temperature in the presence of KOH (84 mg, 1.5 mmol). Thereafter, the solution was poured onto crushed ice with vigorous stirring and neutralized with 10% HCl (10 mL). The resulting precipitate was filtered, dried and purified by neutral alumina column chromatography.

4.3.1. 6,7-Diphenyl-5-methylsulfanylindan-4-carbonitrile (6a). It was prepared by following the general procedure from the reaction of **5a** (319 mg, 1.0 mmol) and **2** (0.1 mL, 1.1 mmol) using KOH (84 mg, 1.5 mmol) as a base in dry DMF. Usual work-up and purification on neutral alumina column chromatography using 40% hexane in chloroform as eluent produced a white solid; R_f ($CHCl_3$) 0.44; yield: 243 mg (71%); mp: 145–147 °C; IR (KBr): 2939, 2853, 2363, 2186, 1585, 1444, 1383, 1351, 1257, 1212, 1125, 1076, 1019, 996, 925, 905, 851, 750, 687 cm^{-1}; δ_H (200 MHz, $CDCl_3$): 2.08–2.16 (m, 2H, CH_2), 2.21 (s, 3H, SCH_3), 2.75 (t, *J* 7.4 Hz, 2H, CH_2), 3.23 (t, *J* 7.5 Hz, 2H, CH_2), 6.89–7.03 (m, 4H, ArH), 7.12–7.25 (m, 6H, ArH); MS *m/z* 342 (M^++1); HRMS (EI): M^+, found 341.1239; $C_{23}H_{19}NS$ requires 341.1233.

4.3.2. 6,7-Bis(4-methoxyphenyl)-5-methylsulfanyl-indan-4-carbonitrile (6b). It was obtained by following the general procedure from the reaction of **5b** (379 mg, 1.0 mmol), **2** (0.1 mL, 1.1 mmol) and KOH (84 mg, 1.5 mmol) in dry DMF (10 mL) and isolated as a white solid after neutral alumina column chromatography using 30% hexane in chloroform as eluent; R_f ($CHCl_3$) 0.42; yield: 261 mg (65%); mp: 152–154 °C; IR (KBr): 2960, 2218, 1607, 1514, 1460, 1388, 1290, 1247, 1176, 1110, 1029, 837, 800, 761 cm^{-1}; δ_H (200 MHz, $CDCl_3$): 2.07–2.15 (m, 2H, CH_2), 2.20 (s, 3H, SCH_3), 2.76 (t, *J* 7.4 Hz, 2H, CH_2), 3.21 (t, *J* 7.5 Hz, 2H, CH_2), 3.74 (s, 3H, OCH_3), 3.76 (s, 3H, OCH_3), 6.67–6.74 (m, 4H, ArH), 6.81–6.92 (m, 4H, ArH); δ_C (50 MHz, $CDCl_3$): 20.25, 25.07, 33.95, 34.02, 55.46, 55.50, 113.28, 113.26, 114.09, 117.70, 130.69, 131.58, 132.09, 137.77, 143.36, 144.71, 145.26, 149.48, 158.67; MS *m/z* 402 (M^++1); HRMS (EI): M^+, found 401.1451; $C_{25}H_{23}NO_2S$ requires 401.1444.

4.4. General procedure for the synthesis of 7-aryl-5-(piperidin-1-yl)indan-4-carbonitriles (8a–h)

A mixture of 6-aryl-4-(piperidin-1-yl)-2-oxo-2*H*-pyran-3-carbonitriles (**7**, 1.0 mmol), cyclopentanone (**2**, 0.1 mL, 1.1 mmol) and KOH (84 mg, 1.5 mmol) in dry DMF (10 mL) was stirred for 2 h under dry condition at 30 °C. After completion of the reaction, DMF was removed under reduced pressure and the mixture was poured onto crushed ice with vigorous stirring and thereafter neutralized with 10% HCl. The resulting precipitate was filtered, dried and purified by neutral alumina column chromatography.

4.4.1. 7-Phenyl-5-(piperidin-1-yl)indan-4-carbonitrile (8a). It was prepared by following the general procedure from the reaction of **7a** (280 mg, 1 mmol) and **2** (0.1 mL, 1.1 mmol) using KOH (84 mg, 1.5 mmol) as a base in dry DMF. Usual work-up and purification on neutral alumina column using 30% hexane in chloroform as eluent provided a white solid; R_f (10% hexane in $CHCl_3$) 0.45; yield: 275 mg (91%); mp: 124–126 °C; IR (KBr): 2935, 2801, 2215, 1588, 1452, 1358, 1220, 1110, 1068, 996, 867, 771, 703, 666 cm^{-1}; δ_H (200 MHz, $CDCl_3$): 1.60–1.63 (m, 2H, CH_2), 1.73–1.84 (m, 4H, CH_2), 2.02–2.16 (m, 2H, CH_2), 2.92 (t, *J* 7.3 Hz, 2H, CH_2), 3.08–3.17 (m, 6H, CH_2), 6.80 (s, 1H, ArH), 7.34–7.48 (m, 5H, ArH); MS *m/z* 303 (M^++1); HRMS (EI): M^+, found 302.1783; $C_{21}H_{22}N_2$ requires 302.1778.

4.4.2. 7-(4-Chlorophenyl)-5-(piperidin-1-yl)indan-4-carbonitrile (8b). It was synthesized from the reaction of **7b** (314 mg, 1.0 mmol), **2** (0.1 mL, 1.1 mmol) and KOH (84 mg, 1.5 mmol) in dry DMF (10 mL) as a white solid after neutral alumina column chromatography using 30% hexane in chloroform as eluent; R_f ($CHCl_3$) 0.5; yield: 297 mg (88%); mp: 176–178 °C; IR (KBr): 2938, 2806, 2365, 2214, 1594, 1454, 1381, 1354, 1224, 1109, 1067, 1003, 825, 767 cm^{-1}; δ_H (200 MHz, $CDCl_3$): 1.55–1.58 (m, 2H, CH_2), 1.76–1.80 (m, 4H, CH_2), 2.02–2.17 (m, 2H, CH_2), 2.88 (t, *J* 7.0 Hz, 2H, CH_2), 3.07–3.13 (m, 6H, CH_2), 6.74–6.77 (m, 1H, ArH), 7.29–7.32 (m, 2H, ArH), 7.56 (d, *J* 8.3 Hz, 2H, ArH); MS *m/z* 337 (M^++1); HRMS (EI): M^+, found 336.1392; $C_{21}H_{21}ClN_2$ requires 336.1388.

4.4.3. 7-(4-Bromophenyl)-5-(piperidin-1-yl)indan-4-carbonitrile (8c). It was obtained from the reaction of **7c** (358 mg, 1.0 mmol), **2** (0.1 mL, 1.1 mmol) and KOH (84 mg, 1.5 mmol) in dry DMF (10 mL) as a white solid

after neutral alumina column chromatography using 30% hexane in chloroform as eluent; R_f ($CHCl_3$) 0.5; yield: 339 mg (89%); mp: 166–168 °C; IR (KBr): 2943, 2808, 2363, 2216, 1594, 1491, 1455, 1383, 1225, 1085, 878, 830, 762, 665 cm^{-1}; δ_H (200 MHz, $CDCl_3$): 1.57–1.63 (m, 2H, CH_2), 1.73–1.84 (m, 4H, CH_2), 2.02–2.17 (m, 2H, CH_2), 2.89 (t, *J* 7.3 Hz, 2H, CH_2), 3.07–3.16 (m, 6H, CH_2), 6.74 (s, 1H, ArH), 7.33 (d, *J* 8.7 Hz, 2H, ArH), 7.41 (d, *J* 8.7 Hz, 2H, ArH); MS *m/z* 380 (M^+), 382 (M^++2); HRMS (EI): M^+, found 380.0885; $C_{21}H_{21}{}^{79}BrN_2$ requires 380.0883.

4.4.4. 7-(4-Methylphenyl)-5-(piperidin-1-yl)indan-4-carbonitrile (8d). It was prepared from the reaction of **7d** (294 mg, 1.0 mmol), **2** (0.1 mL, 1.1 mmol) and KOH (84 mg, 1.5 mmol) in dry DMF (10 mL) as a white solid after neutral alumina column chromatography using 30% hexane in chloroform as eluent; R_f ($CHCl_3$) 0.54; yield: 291 mg (92%); mp: 135–137 °C; IR (KBr): 2933, 2215, 1593, 1516, 1454, 1355, 1271, 1219, 1113, 822, 764 cm^{-1}; δ_H (200 MHz, $CDCl_3$): 1.57–1.63 (m, 2H, CH_2), 1.73–1.84 (m, 4H, CH_2), 2.01–2.16 (m, 2H, CH_2), 2.40 (s, 3H, CH_3), 2.92 (t, *J* 7.3 Hz, 2H, CH_2), 3.07–3.16 (m, 6H, CH_2), 6.78 (s, 1H, ArH), 7.23 (d, *J* 7.5 Hz, 2H, ArH), 7.31 (d, *J* 8.5 Hz, 2H, ArH); MS *m/z* 317 (M^++1); HRMS (EI): M^+, found 316.1937; $C_{22}H_{24}N_2$ requires 316.1934.

4.4.5. 7-(4-Methoxyphenyl)-5-(piperidin-1-yl)indan-4-carbonitrile (8e). It was prepared from the reaction of **7e** (310 mg, 1.0 mmol), **2** (0.1 mL, 1.1 mmol) and KOH (84 mg, 1.5 mmol) in dry DMF (10 mL) as a white solid after neutral alumina column chromatography using 30% hexane in chloroform; R_f ($CHCl_3$) 0.54; yield: 302 mg (91%); mp: 144–146 °C; IR (KBr): 2934, 2802, 2211, 1592, 1512, 1455, 1356, 1292, 1250, 1174, 1111, 1030, 835, 761 cm^{-1}; δ_H (200 MHz, $CDCl_3$): 1.57–1.62 (m, 2H, CH_2), 1.75–1.78 (m, 4H, CH_2), 2.05–2.16 (m, 2H, CH_2), 2.92 (t, *J* 7.2 Hz, 2H, CH_2), 3.06–3.16 (m, 6H, CH_2), 3.85 (s, 3H, OCH_3), 6.77 (s, 1H, ArH), 6.96 (d, *J* 8.6 Hz, 2H, ArH), 7.36 (d, *J* 8.6 Hz, 2H, ArH); δ_C (50 MHz, $CDCl_3$): 24.58, 25.74, 26.68, 33.08, 33.81, 54.06, 55.76, 101.87, 114.31, 117.21, 118.23, 129.89, 133.14, 135.57, 142.88, 151.33, 156.38, 159.79; MS *m/z* 333 (M^++1); HRMS (EI): M^+, found 332.1890; $C_{22}H_{24}N_2O$ requires 332.1883.

4.4.6. 5-(Piperidin-1-yl)-7-(thiophen-2-yl)indan-4-carbonitrile (8f). It was obtained from the reaction of **7f** (286 mg, 1.0 mmol), **2** (0.1 mL, 1.1 mmol) and KOH (84 mg, 1.5 mmol) in dry DMF (10 mL). Usual work-up and purification on neutral alumina column using 30% hexane in chloroform as eluent provided a cream coloured solid; R_f ($CHCl_3$) 0.5; yield: 274 mg (89%); mp: 106–108 °C; IR (KBr): 2933, 2814, 2213, 1590, 1436, 1353, 1224, 1117, 1059, 994, 725 cm^{-1}; δ_H (200 MHz, $CDCl_3$): 1.57–1.64 (m, 2H, CH_2), 1.73–1.89 (m, 4H, CH_2), 2.08–2.23 (m, 2H, CH_2), 3.05–3.17 (m, 8H, CH_2), 6.98 (s, 1H, ArH), 7.10–7.14 (m, 1H, ArH), 7.28–7.29 (m, 1H, ArH), 7.38–7.41 (m, 1H, ArH); MS *m/z* 309 (M^++1); HRMS (EI): M^+, found 308.1347; $C_{19}H_{20}N_2S$ requires 308.1342.

4.4.7. 7-(Naphthalen-2-yl)-5-(piperidin-1-yl)indan-4-carbonitrile (8g). It was prepared from the reaction of **7g** (330 mg, 1.0 mmol), **2** (0.1 mL, 1.1 mmol) and KOH (84 mg, 1.5 mmol) in dry DMF (10 mL) as a white solid after neutral alumina column chromatography using 30% hexane in chloroform as eluent; R_f ($CHCl_3$) 0.45; yield: 306 mg (87%); mp: 120–122 °C; IR (KBr): 3054, 2937, 2212, 1587, 1453, 1375, 1241, 1116, 821, 749 cm^{-1}; δ_H (200 MHz, $CDCl_3$): 1.55–1.58 (m, 2H, CH_2), 1.70–1.80 (m, 4H, CH_2), 2.03–2.18 (m, 2H, CH_2), 2.97 (t, *J* 7.3 Hz, 2H, CH_2), 3.06–3.20 (m, 6H, CH_2), 6.90 (s, 1H, ArH), 7.49–7.56 (m, 3H, ArH), 7.78–7.92 (m, 4H, ArH); MS *m/z* 353 (M^++1); HRMS (EI): M^+, found 352.1934; $C_{25}H_{24}N_2$ requires 352.1934.

4.4.8. 5-(4-Methylpiperidin-1-yl)-7-phenylindan-4-carbonitrile (8h). It was obtained from the reaction of **7h** (294 mg, 1.0 mmol), **2** (0.1 mL, 1.1 mmol) and KOH (84 mg, 1.5 mmol) in dry DMF (10 mL) as a white solid after neutral alumina column chromatography using 30% hexane in chloroform as eluent; R_f ($CHCl_3$) 0.47; yield: 272 mg (86%); mp: 114–116 °C; IR (KBr): 2941, 2807, 2215, 1590, 1456, 1384, 1251, 1217, 1149, 1118, 1066, 975, 869, 776, 705, 669 cm^{-1}; δ_H (200 MHz, $CDCl_3$): 0.99 (d, *J* 5.0 Hz, 3H, CH_3), 1.48–1.52 (m, 3H, CH and CH_2), 1.73–1.78 (m, 2H, CH_2), 2.02–2.16 (m, 2H, CH_2), 2.70–2.81 (m, 2H, CH_2), 2.92 (t, *J* 7.4 Hz, 2H, CH_2), 3.11 (t, *J* 7.4 Hz, 2H, CH_2), 3.52–3.58 (m, 2H, CH_2), 6.80 (s, 1H, ArH), 7.33–7.48 (m, 5H, ArH); δ_C (50 MHz, $CDCl_3$): 22.24, 25.69, 31.06, 32.92, 33.81, 34.94, 53.38, 102.29, 117.50, 118.16, 128.21, 128.67, 128.86, 135.71, 140.80, 143.21, 151.39, 156.14; MS *m/z* 317 (M^++1); HRMS (EI): M^+, found 316.1938; $C_{22}H_{24}N_2$ requires 316.1934.

4.5. General procedure for the synthesis of 7-aryl-5-methylsulfanylindan-4-carboxylic acid methyl esters (10a–e) and 7-aryl-5-methylsulfanylindan-4-carboxylic acids (11a–e)

Procedure A. These were obtained by stirring a mixture of methyl 6-aryl-4-methylsulfanyl-2-oxo-2*H*-pyran-3-carboxylates (**9**, 1.0 mmol), cyclopentanone (**2**, 0.1 mL, 1.1 mmol) and KOH (84 mg, 1.5 mmol) in dry DMF (10 mL) for 2 h under dry condition at room temperature. After completion, the reaction mixture was poured onto crushed ice and neutralized with 10% HCl (15 mL), which gave a mixture of an ester and the corresponding acid. The crude product was purified by silica gel column chromatography using 30% hexane in chloroform for ester **10** and 1% methanol in chloroform for acid **11** as eluents. Yields for **10** were in the range of 32–35% and those for **11** were in the range of 53–57%.

Procedure B. Under analogous conditions, except a change in duration of reaction from 2 to 6 h and usual work-up, the yield of **11** increased (67–74%) in the mixture possibly due to further hydrolysis of ester **10**.

Procedure C. A mixture of pyran-2-one (**9**, 1.0 mmol), cyclopentanone (**2**, 0.1 mL, 1.1 mmol) and NaH (36 mg, 1.5 mmol) in dry THF was stirred for 36 h under dry condition at room temperature. After completion of the reaction, excess THF was removed under reduced pressure and excess NaH quenched by the addition of methanol. The resulting mixture was poured onto crushed ice with vigorous stirring and neutralized with 10% HCl (15 mL). The resulting

precipitate was filtered off, dried and purified on silica gel column as 5-methylsulfanyl-7-arylindan-4-carboxylic acid methyl esters (**10a–e**).

4.5.1. 5-Methylsulfanyl-7-phenylindan-4-carboxylic acid methyl ester (10a). It was prepared by following the general procedure A from the reaction of **9a** (276 mg, 1.0 mmol) and **2** (0.1 mL, 1.1 mmol) using KOH (84 mg, 1.5 mmol) as a base in dry DMF (10 mL). Usual work-up and purification on silica column using 30% hexane in chloroform as eluent produced a white solid; R_f ($CHCl_3$) 0.54; yield: 95 mg (32%); mp: 84–86 °C; IR (KBr): 2949, 2376, 1709, 1590, 1494, 1428, 1381, 1352, 1272, 1134, 1105, 990, 770, 703 cm^{-1}; δ_H (200 MHz, $CDCl_3$): 1.99–2.07 (m, 2H, CH_2), 2.47 (s, 3H, SCH_3), 2.90 (t, *J* 7.3 Hz, 2H, CH_2), 3.09 (t, *J* 7.4 Hz, 2H, CH_2), 3.94 (s, 3H, OCH_3), 7.13 (s, 1H, ArH), 7.36–7.44 (m, 5H, ArH); MS *m/z* 299 (M^++1); HRMS (EI): M^+, found 298.1027; $C_{18}H_{18}O_2S$ requires 298.1022.

4.5.2. 5-Methylsulfanyl-7-phenylindan-4-carboxylic acid (11a). It was isolated from the above reaction mixture after eluting the silica gel column by 1% methanol in chloroform as eluent, as a white crystalline solid; R_f (2% methanol in $CHCl_3$) 0.4; yield: 162 mg (57%); mp: 225–227 °C; IR (KBr): 3426, 2945, 2363, 1674, 1573, 1498, 1429, 1293, 1248, 1146, 1110, 1078, 1028, 934, 861, 762, 698 cm^{-1}; δ_H (200 MHz, DMSO-d_6): 1.90–2.04 (m, 2H, CH_2), 2.44 (s, 3H, SCH_3), 2.87 (t, *J* 7.3 Hz, 2H, CH_2), 3.01 (t, *J* 7.3 Hz, 2H, CH_2), 7.11 (s, 1H, ArH), 7.36–7.53 (m, 5H, ArH); MS *m/z* 285 (M^++1); HRMS (EI): M^+, found 284.0871; $C_{17}H_{16}O_2S$ requires 284.0866.

4.5.3. 7-(4-Chlorophenyl)-5-methylsulfanylindan-4-carboxylic acid methyl ester (10b). It was prepared from the reaction of **9b** (310 mg, 1.0 mmol), **2** (0.1 mL, 1.1 mmol) and KOH (84 mg, 1.5 mmol) in dry DMF (10 mL) as a white solid after silica gel column chromatography using 20% hexane in chloroform as eluent; R_f ($CHCl_3$) 0.4; yield: 110 mg (33%); mp: 91–93 °C; IR (KBr): 2948, 2640, 2359, 1720, 1588, 1490, 1434, 1364, 1252, 1137, 1105, 1013, 832, 767 cm^{-1}; δ_H (200 MHz, $CDCl_3$): 2.0–2.07 (m, 2H, CH_2), 2.46 (s, 3H, SCH_3), 2.87 (t, *J* 7.3 Hz, 2H, CH_2), 3.09 (t, *J* 7.4 Hz, 2H, CH_2), 3.94 (s, 3H, OCH_3), 7.08 (s, 1H, ArH), 7.31–7.43 (m, 4H, ArH); δ_C (50 MHz, $CDCl_3$): 24.52, 25.66, 26.62, 32.85, 33.79, 54.00, 117.15, 122.47, 126.69, 129.08, 130.30, 132.02, 135.50, 139.66, 141.92, 151.60, 156.42; MS *m/z* 333 (M^++1); HRMS (EI): M^+, found 332.0633; $C_{18}H_{17}ClO_2S$ requires 332.0632.

4.5.4. 7-(4-Chlorophenyl)-5-methylsulfanylindan-4-carboxylic acid (11b). Eluting the above silica gel column by 1% methanol in chloroform afforded a white crystalline solid; R_f (25% methanol in $CHCl_3$) 0.45; yield: 181 mg (57%); mp: 224–226 °C; IR (KBr): 3432, 2958, 2363, 1670, 1594, 1492, 1433, 1392, 1353, 1287, 1245, 1142, 1108, 1089, 1012, 975, 913, 871, 826, 780, 750, 717 cm^{-1}; δ_H (200 MHz, DMSO-d_6): 1.93–2.01 (m, 2H, CH_2), 2.45 (s, 3H, SCH_3), 2.86 (t, *J* 7.2 Hz, 2H, CH_2), 3.0 (t, *J* 7.3 Hz, 2H, CH_2), 7.11 (s, 1H, ArH), 7.51–7.55 (m, 4H, ArH); MS *m/z* 319 (M^++1); HRMS (EI): M^+, found 318.0475; $C_{17}H_{15}ClO_2S$ requires 318.0476.

4.5.5. 7-(4-Bromophenyl)-5-methylsulfanylindan-4-carboxylic acid methyl ester (10c). It was obtained by stirring a mixture of **9c** (354 mg, 1.0 mmol), **2** (0.1 mL, 1.1 mmol) and KOH (84 mg, 1.5 mmol) in dry DMF (10 mL), and the desired compound was isolated as a white solid after silica gel column chromatography using 20% hexane in chloroform as eluent; R_f ($CHCl_3$) 0.45; yield: 132 mg (35%); mp: 82–84 °C; IR (KBr): 2822, 2366, 2341, 1719, 1598, 1519, 1490, 1437, 1353, 1272, 1187, 1138, 1073, 1005, 950, 814, 773, 700 cm^{-1}; δ_H (300 MHz, $CDCl_3$): 2.02–2.11 (m, 2H, CH_2), 2.48 (s, 3H, SCH_3), 2.89 (t, *J* 7.5 Hz, 2H, CH_2), 3.11 (t, *J* 7.5 Hz, 2H, CH_2), 3.96 (s, 3H, OCH_3), 7.11 (s, 1H, ArH), 7.34–7.38 (m, 4H, ArH); MS *m/z* 378 (M^+), 380 (M^++2); HRMS (EI): M^+, found 376.0130; $C_{18}H_{17}{}^{79}BrO_2S$ requires 376.0127.

4.5.6. 7-(4-Bromophenyl)-5-methylsulfanylindan-4-carboxylic acid (11c). From the above reaction mixture it was obtained as a white solid by eluting the column using 1% methanol in chloroform as eluent; R_f (2% methanol in $CHCl_3$) 0.5; yield: 191 mg (53%); mp: 228–230 °C; IR (KBr): 3421, 2957, 2362, 1682, 1590, 1493, 1432, 1389, 1353, 1286, 1246, 1142, 1103, 1012, 914, 825, 755 cm^{-1}; δ_H (200 MHz, DMSO-d_6): 1.94–2.01 (m, 2H, CH_2), 2.44 (s, 3H, SCH_3), 2.87 (t, *J* 7.2 Hz, 2H, CH_2), 2.99 (t, *J* 7.2 Hz, 2H, CH_2), 7.10 (s, 1H, ArH), 7.48 (d, *J* 8.5 Hz, 2H, ArH), 7.66 (d, *J* 8.5 Hz, 2H, ArH); MS *m/z* 362 (M^+), 364 (M^++2); HRMS (EI): M^+, found 361.9977; $C_{17}H_{15}{}^{79}BrO_2S$ requires 361.9971.

4.5.7. 5-Methylsulfanyl-7-(thiophen-2-yl)indan-4-carboxylic acid methyl ester (10d). It was prepared from the reaction of **9d** (282 mg, 1.0 mmol), **2** (0.1 mL, 1.1 mmol) and KOH (84 mg, 1.5 mmol) in dry DMF (10 mL) as a white solid after silica gel column chromatography using 20% hexane in chloroform as eluent; R_f ($CHCl_3$) 0.45; yield: 106 mg (35%); mp: 108–110 °C; IR (KBr): 3106, 2946, 2364, 1705, 1578, 1428, 1350, 1267, 1130, 1092, 985, 919, 839, 796, 711 cm^{-1}; δ_H (200 MHz, $CDCl_3$): 2.05–2.17 (m, 2H, CH_2), 2.48 (s, 3H, SCH_3), 3.04–3.14 (m, 4H, CH_2), 3.93 (s, 3H, OCH_3), 7.09–7.14 (m, 1H, ArH), 7.25–7.28 (m, 1H, ArH), 7.31 (s, 1H, ArH), 7.36–7.39 (m, 1H, ArH); δ_C (50 MHz, $CDCl_3$): 17.76, 25.62, 33.58, 34.03, 52.27, 125.13, 126.32, 126.62, 127.20, 128.05, 133.82, 137.64, 139.61, 142.71, 146.89, 168.47; MS *m/z* 305 (M^++1); HRMS (EI): M^+, found 304.0589; $C_{16}H_{16}O_2S_2$ requires 304.0586.

4.5.8. 5-Methylsulfanyl-7-(thiophen-2-yl)indan-4-carboxylic acid (11d). It was obtained by eluting the above silica gel column using 1% methanol in chloroform as a white crystalline solid; R_f (2% methanol in $CHCl_3$) 0.44; yield: 160 mg (55%); mp: 228–230 °C; IR (KBr): 3420, 2951, 2369, 1670, 1594, 1504, 1432, 1389, 1335, 1290, 1245, 1135, 1098, 1017, 944, 823 cm^{-1}; δ_H (200 MHz, DMSO-d_6): 1.97–2.12 (m, 2H, CH_2), 2.51 (s, 3H, SCH_3), 2.98–3.18 (m, 4H, CH_2), 7.17–7.22 (m, 1H, ArH), 7.30 (s, 1H, ArH), 7.47–7.49 (m, 1H, ArH), 7.66–7.69 (m, 1H, ArH); MS *m/z* 291 (M^++1); HRMS (EI): M^+, found 290.0434; $C_{15}H_{14}O_2S_2$ requires 290.0430.

4.5.9. 5-Methylsulfanyl-7-(naphthalen-2-yl)indan-4-carboxylic acid methyl ester (10e). It was obtained from the reaction of **9e** (326 mg, 1.0 mmol), **2** (0.1 mL, 1.1 mmol) and

KOH (84 mg, 1.5 mmol) in dry DMF (10 mL). It was isolated as a white solid by eluting the silica gel column with 20% hexane in chloroform; found C, 76.20; H, 6.02; $C_{22}H_{20}O_2S$ requires C, 75.83; H, 5.79; R_f ($CHCl_3$) 0.5; yield: 114 mg (33%); mp: 84–86 °C; IR (KBr): 2948, 2363, 1717, 1594, 1502, 1429, 1502, 1429, 1383, 1353, 1270, 1128, 1096, 989, 912, 859, 825, 796, 759 cm^{-1}; δ_H (200 MHz, $CDCl_3$): 2.0–2.08 (m, 2H, CH_2), 2.48 (s, 3H, SCH_3), 2.50 (t, *J* 7.3 Hz, 2H, CH_2), 3.12 (t, *J* 7.4 Hz, 2H, CH_2), 3.96 (s, 3H, OCH_3), 7.23 (s, 1H, ArH), 7.50–7.57 (m, 3H, ArH), 7.85–7.92 (m, 4H, ArH); δ_C (50 MHz, $CDCl_3$): 17.84, 26.04, 32.86, 34.13, 52.33, 126.18, 126.71, 126.86, 126.94, 127.76, 128.14, 128.45, 128.57, 134.31, 135.01, 138.08, 139.31, 142.21, 143.33, 146.07, 168.01; MS *m/z* 349 (M^++1); HRMS (EI): M^+, found 348.1183; $C_{22}H_{20}O_2S$ requires 348.1179.

4.5.10. 5-Methylsulfanyl-7-(naphthalen-2-yl)indan-4-carboxylic acid (11e). From the above reaction mixture the product was isolated as a white crystalline solid after eluting the silica gel column by 1% methanol in chloroform; R_f (2% methanol in $CHCl_3$) 0.44; yield: 190 mg (57%); mp: 200–202 °C; IR (KBr): 3432, 3052, 2951, 2369, 1670, 1594, 1504, 1389, 1353, 1290, 1245, 1135, 1098, 1017, 944, 855, 823, 750 cm^{-1}; δ_H (200 MHz, DMSO-d_6): 1.96–2.06 (m, 2H, CH_2), 2.49 (s, 3H, SCH_3), 2.96 (t, *J* 7.2 Hz, 2H, CH_2), 3.06 (t, *J* 7.3 Hz, 2H, CH_2), 7.26 (s, 1H, ArH), 7.54–7.63 (m, 2H, ArH), 7.66–7.73 (m, 1H, ArH), 7.93–8.12 (m, 4H, ArH); MS *m/z* 335 (M^++1); HRMS (EI): M^+, found 334.1024; $C_{21}H_{18}O_2S$ requires 334.1022.

4.5.11. 6,7-Diphenyl-5-methylsulfanylindan-4-carboxylic acid methyl ester (13a). It was obtained by following the general procedure A from the reaction of **12a** (352 mg, 1.0 mmol), **2** (0.1 mL, 1.1 mmol) and KOH (84 mg, 1.5 mmol) in dry DMF (8 mL), as a white solid after silica gel column chromatography using 30% hexane in chloroform as eluent; R_f ($CHCl_3$) 0.42; yield: 281 mg (75%); mp: 128–130 °C; IR (KBr): 2971, 2931, 2833, 2716, 2364, 1704, 1629, 1591, 1495, 1425, 1363, 1244, 1177, 1070, 1028, 971, 914, 844, 780, 747, 706 cm^{-1}; δ_H (300 MHz, $CDCl_3$): 2.02 (s, 3H, SCH_3), 2.05–2.14 (m, 2H, CH_2), 2.75 (t, *J* 7.3 Hz, 2H, CH_2), 3.5 (t, *J* 7.4 Hz, 2H, CH_2), 3.99 (s, 3H, OCH_3), 6.90–7.16 (m, 10H, ArH); MS *m/z* 375 (M^++1); HRMS (EI): M^+, found 374.1338; $C_{24}H_{22}O_2S$ requires 374.1335.

4.5.12. 6,7-Bis(4-methoxyphenyl)-5-methylsulfanyl-indan-4-carboxylic acid methyl ester (13b). It was obtained from the reaction of **12b** (294 mg, 1.0 mmol), **2** (0.1 mL, 1.1 mmol) and KOH (84 mg, 1.5 mmol) in dry DMF (8 mL) by following the general procedure A as a white solid by silica gel column chromatography using 20% hexane in chloroform as eluent; found: C, 71.52; H, 6.26; $C_{26}H_{26}O_4S$ requires C, 71.86; H, 6.03; R_f ($CHCl_3$) 0.44; yield: 308 mg (71%); mp: 152–154 °C; IR (KBr): 2956, 2838, 2363, 2054, 1725, 1601, 1512, 1456, 1386, 1345, 1288, 1248, 1172, 1114, 1031, 835, 776 cm^{-1}; δ_H (200 MHz, $CDCl_3$): 2.0 (s, 3H, SCH_3), 1.97–2.07 (m, 2H, CH_2), 2.70 (t, *J* 7.3 Hz, 2H, CH_2), 2.98 (t, *J* 7.4 Hz, 2H, CH_2), 3.72 (s, 3H, OCH_3), 3.74 (s, 3H, OCH_3), 3.96 (s, 3H, OCH_3), 6.65–6.72 (m, 4H, ArH), 6.84 (d, *J* 8.5 Hz, 2H, ArH), 6.96 (d, *J* 8.5 Hz, 2H, ArH); δ_C (50 MHz, $CDCl_3$): 20.58, 25.37, 30.43, 32.34, 33.68, 52.64, 55.40, 113.02, 113.45, 130.46, 130.93, 132.30, 132.54, 135.82, 140.58, 141.22, 144.64, 145.42, 158.29, 158.37, 169.78; MS *m/z* 435 (M^++1); HRMS (EI): M^+, found 434.1553; $C_{26}H_{26}O_4S$ requires 434.1546.

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