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NEW REACTIONS OF INDOLINE-2-THIONES AND ARYL ALDEHYDES: MICROWAVE-INDUCED ONE STEP SYNTHESIS OF STRUCTURALLY DIVERSE THIOPYRANO-DIINDOLES

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Abstract – A general and efficient synthesis of 7-aryl-5*H*-thiopyrano[2,3-*b*:4,5-*b*']diindoles and 12-aryl-7,12-dihydro-5*H*-thiopyrano[2,3-*b*:6,5-*b*']diindoles described from easily available, common starting materials in simple, microwave assisted reactions. The selectivity was controlled simply by the choice of base. The explored new reactions with the isolated by-products and intermediates give an interesting, new insight into the chemistry of the indoline-2-thiones.

INTRODUCTION

The 3-(het)arylidene-1,3-dihydroindolin-2-one derivatives are important chemical building blocks and in addition a large number of molecules containing this skeleton display a wide range of biological activity.[1] A few of them already reached the clinic, the most important ones are the known kinase inhibitors with a 3-(1*H*-pyrrol-2-ylmethylidene)indolin-2-one scaffold, including such molecules as sunitinib,[2] vorolanib[3] or S 49076[4] and others (Figure 1).

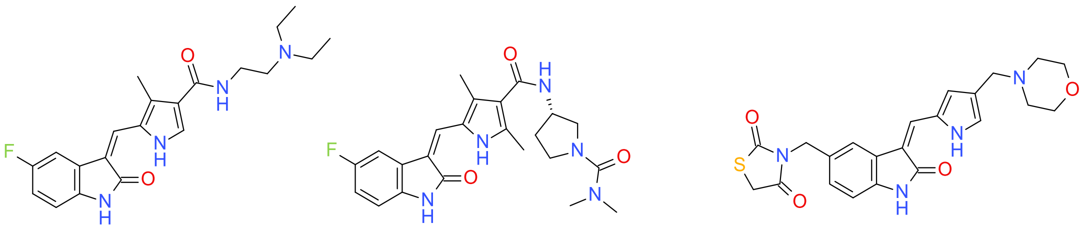


Figure 1. Kinase inhibitors with a 3-(1*H*-pyrrol-2-ylmethylidene)indolin-2-one scaffold

There are much less reports regarding the synthesis, application and pharmacology of the analogous 3-(het)arylidene-1,3-dihydroindoline-2-thione derivatives **2**, only a few of them was identified as a novel potent inhibitors of α-melanocyte stimulating hormone inducing melanogenesis[5] and others were described as tyrosine kinase inhibitors.[6] The first synthesis of **2** was described in 1935 by Oddo and Mingoia,[7] but a later study[8] found out, very likely they have isolated only a stereoselectively formed dimer **6** as the original Knoevenagel adduct was shown to be stable only for a short period of time at room temperature in solution. The conjugated (het)arylidene-indoline-2-thione system easily reacts as a diene with itself or with any other added dienophiles via a facile normal electron demand Diels-Alder cycloaddition giving rise the formation of dihydrothiopyrano[2,3-*b*]indole derivatives (**3** and **4**).[9] The facile formation of spiro[4,9-dihydro-2*H*-thiopyrano[2,3-*b*]indole-3,3'-indoline]-2'-thione **6** later was rediscovered by others.[10] Based on these results an elegant intramolecular version of this Diels-Alder reaction was described without the isolation of the initial Knoevenagel adduct for **7**.[11] On standing in solution oxidative dimerization of **2** was also observed resulting in **5**.[6a] In the light of these results, summarized in Figure 2, and accordingly to our own observations, some of the experimental procedures for the preparation of **2** described recently (base, ethanol, piperidine, 90 °C, 3 hours reaction time)[5,6,9] were not reproducible.

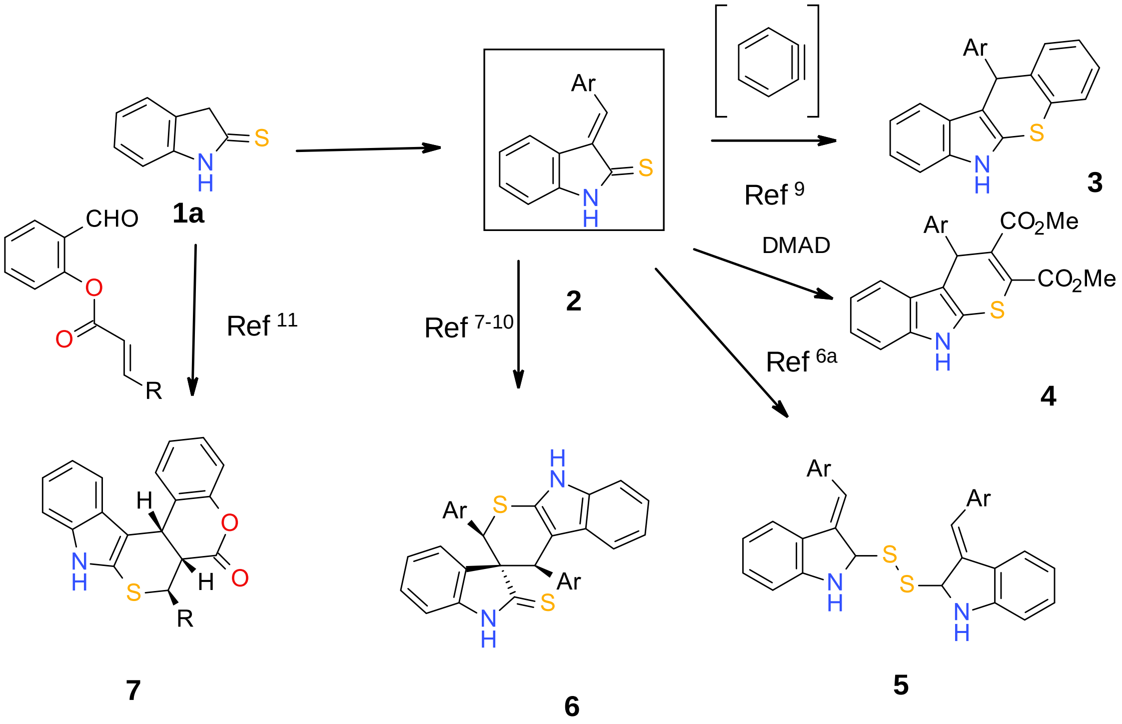
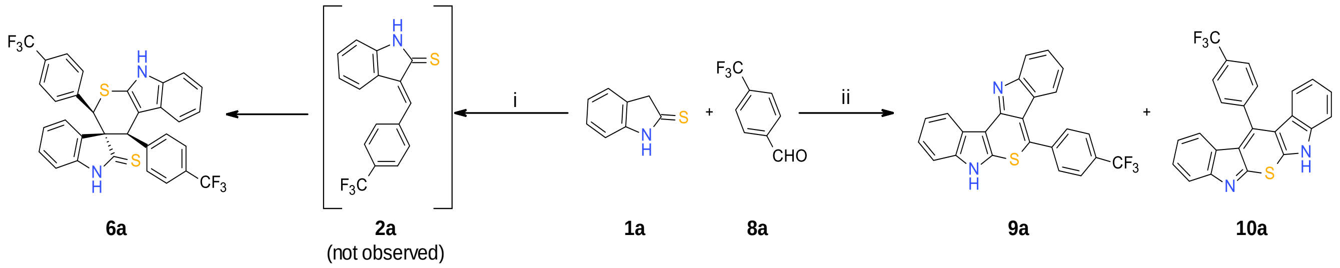


Figure 2. Chemistry of the 3-(het)arylidene-1,3-dihydroindoline-2-thiones (**2**)

In one of our recent medicinal chemistry program, based on the above cited recent reports[5,6] we decided on to synthetize some 3-arylidene-1,3-dihydroindoline-2-thiones like **2**. In order to make more simple the procedures for parallel synthesis we started to run the Knoevenagel condensation in a microwave reactor, as we have had positive experiences earlier with oxindoles in a very similar situation.[12] From the initial reaction (Scheme 1 and Table 1, Entry 1) we were able to isolate an orange powder as it was expected, however to our surprise after the first analysis it become clear, it is not the expected product **2a,** but the known dimer **6a**. Later in parallel we have repeated the experiment at room temperature but again only this dimer was observed by HPLC. On the other hand, by increasing the temperature and/or the reaction time we have found a variable mixture of further two new products in the reaction mixture. After the separation of these, the structures of the individual compounds were determined by NMR spectroscopy and HRMS. The major product was proved to be 7-aryl-5*H*-thiopyrano[2,3-*b*:4,5-*b*']diindole **9a**, while the minor was its linear structural isomer 12-aryl-7,12-dihydro-5*H*-thiopyrano[2,3-*b*:6,5-*b*']diindole **10a**. As the pentacyclic scaffold of the major product **9a** is not described in the literature, and the minor heterocycle **10a** also only hardly known[13] we have decided on to have a closer look of this microwave initiated transformation, in order to develop a new and simple, one-pot entry for these otherwise not easily accessible heterocycles.

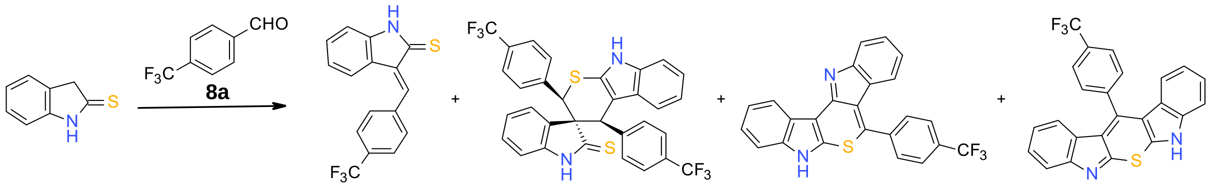


Scheme 1. *Reagents and conditions*: i. piperidine, EtOH, MW, 80 °C; ii. piperidine, EtOH, MW, 145 °C

RESULTS AND DISCUSSION

First, we have investigated the effect of applied reagents and conditions on formation of these new heterocyclic compounds using indoline-2-thione **1a** and 4-(trifluoromethyl)benzaldehyde **8a** as a starting materials. As it can be seen from Table 1, with the increase of temperature the formation of **9a** become dominant and no more **6a** was detected in the final reaction mixture by HPLC-MS. Any switch to another base or solvent gave poor results with only one exception: when pyridine was used as a base, the predominant formation of **10a** was observed, which suggested to us to use Entry 5 and Entry 9 for the targeted synthesis of **9a** and **10a**, respectively.

Table 1. Screening of reaction conditions in microwave reactor

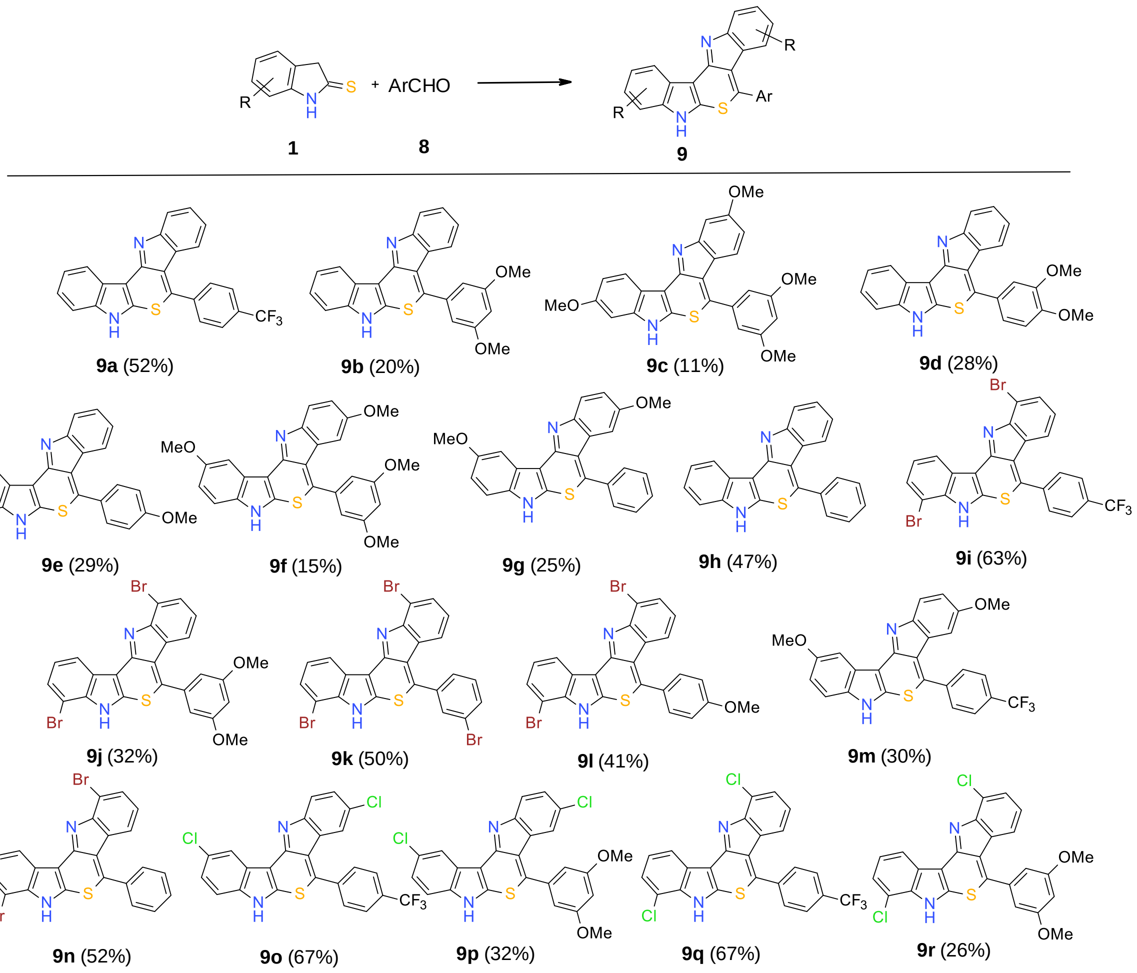


1a **2a** **6a** **9a** **10a**

Entry	base	solvent	temperature	reaction time	2a (%)	6a (%)	9a (%)	10a (%)
1	piperidine	EtOH	80 °C	5 min	0	68	0	0
2	piperidine	EtOH	80 °C	45 min	0	70	0	0
3	piperidine	EtOH	120 °C	45 min	0	22	15	8
4	piperidine	EtOH	140 °C	20 min	0	0	48	18
5	piperidine	EtOH	145 °C	45 min	0	0	52	20
6	TEA	EtOH	145 °C	45 min	0	0	9	4
7	DBU	EtOH	145 °C	45 min	0	0	14	13
8	DABCO	EtOH	145 °C	45 min	0	45	11	2
9	pyridine	EtOH	145 °C	45 min	0	0	6	42
10	butylamine	EtOH	145 °C	45 min	0	21	6	5
11	piperidine	AcOH	145 °C	45 min	0	0	18	1
12	piperidine	toluene	145 °C	45 min	0	15	3	6
13	piperidine	DMF	145 °C	45 min	0	13	6	12
14	piperidine	DCE	145 °C	45 min	0	8	20	7
15	piperidine	H_2O	145 °C	45 min	0	0	0	10

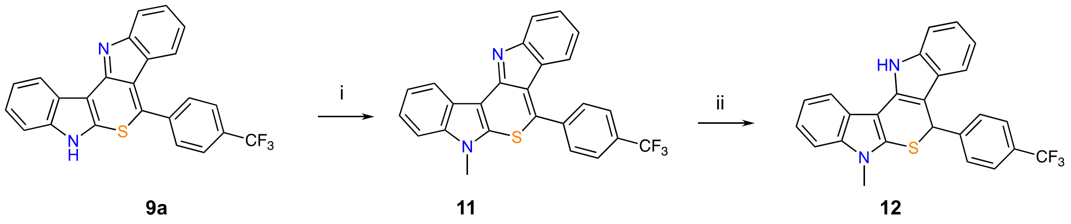
Synthesis of 7-aryl-5*H*-thiopyrano[2,3-*b*:4,5-*b*']diindoles (9)

Based on the initial results we have investigated the generality of the identified conditions and the scope and limitations using differently substituted indoline-2-thiones[14] and various aromatic aldehydes. All the reactions were run in microwave reactor at 145 °C, in ethanol in the presence of catalytic amount of piperidine. The obtained crude reaction mixtures were purified by column chromatography. The yields were varying from the low to acceptable depending on the substituents. As a general rule, the electron withdrawing substituents both on the indole or on the aldehyde gave better productivity, while compounds with methoxy substituents were isolated in lower yields, probably due to the decomposition reactions via *O*-demethylation under the applied harsh conditions (Scheme 2).



Scheme 2. Reactions of indoline-2-thiones with aromatic aldehydes in piperidine/EtOH at 145 °C in MW

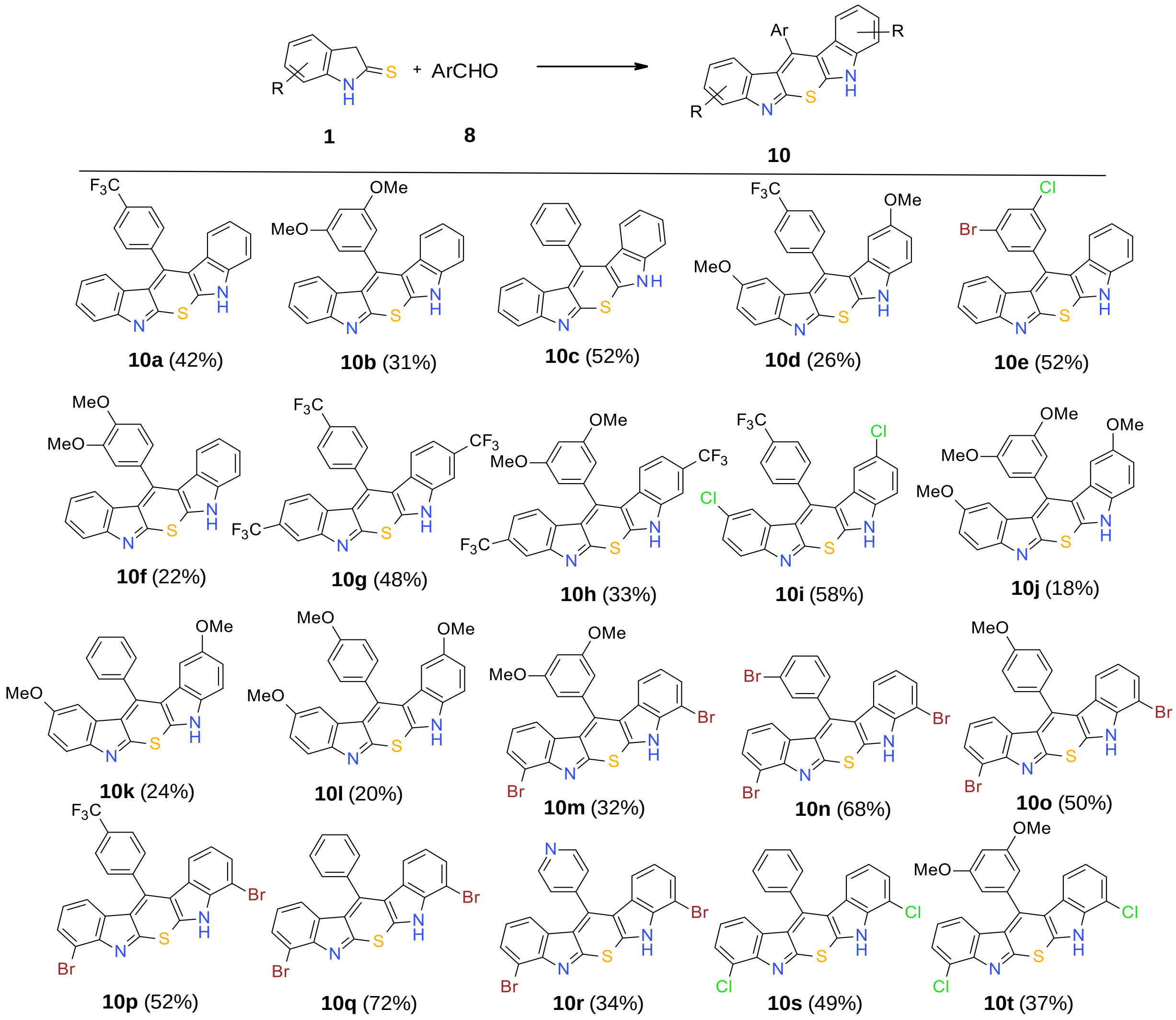
During the initial stage of the project, the structure of **9a** was confirmed by further chemical derivatization (Scheme 3). The available indole nitrogen was methylated followed by a reduction of **11** by sodium borohydride leading to **12** as a further proof for the initially suggested structure **9a**.



Scheme 3. *Reagents and conditions*: i. MeI, KOBu^t, THF, rt; ii. $NaBH_4$, MeOH, rt

Synthesis of 12-aryl-7,12-dihydro-5*H*-thiopyrano[2,3-*b*:6,5-*b*']diindoles (10)

As a next step we have explored the scope and limitation for the identified conditions for the selective synthesis of 12-aryl-7,12-dihydro-5*H*-thiopyrano[2,3-*b*:6,5-*b*']diindole derivatives (**10**) in a single step starting from various substituted indoline-2-thiones and aromatic aldehydes. Using the identified conditions (ethanol, pyridine, 145 °C, 45 min) twenty reaction has been devised, all of them giving the expected main product after column chromatography. In general, again the electron withdrawing substituents both on the indole or on the aldehyde part gave the better yields (Scheme 4).



1 **8** **10**

10a (42%) **10b** (31%) **10c** (52%) **10d** (26%) **10e** (52%)

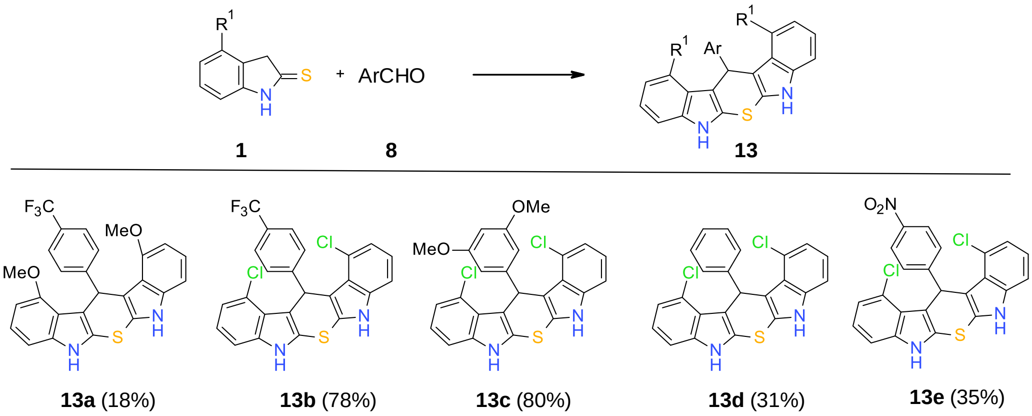
10f (22%) **10g** (48%) **10h** (33%) **10i** (58%) **10j** (18%)

10k (24%) **10l** (20%) **10m** (32%) **10n** (68%) **10o** (50%)

10p (52%) **10q** (72%) **10r** (34%) **10s** (49%) **10t** (37%)

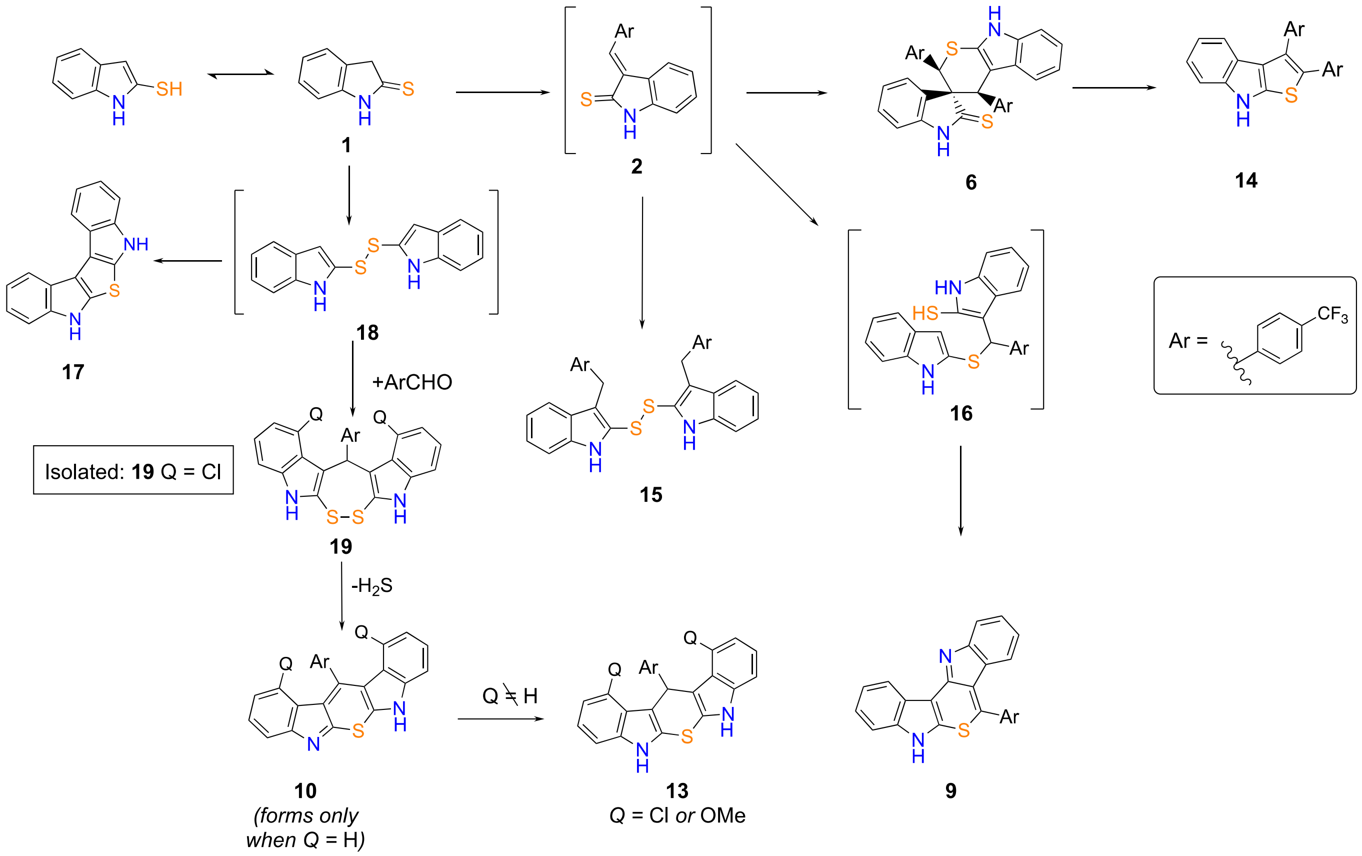
Scheme 4. Reactions of indoline-2-thiones with aromatic aldehydes in pyridine/EtOH at 145 °C in MW

Very interestingly, when 4-substituted indoline-2-thiones were used as a starting materials in all cases a reduced form of the expected products **13** were isolated from the reaction mixture, exclusively (Scheme 5).



Scheme 5. Reactions of 4-substituted indoline-2-thiones with aromatic aldehydes in pyridine/EtOH at 145 °C in MW

We cannot draw a precise mechanistic pathway for all the obtained products, however based on the occasionally isolated by-products we can suggest the following tentatively described sequence which summarize the observed intermediates and products in a rationale way (Scheme 6). Under the applied relatively harsh conditions starting from the indoline-2-thione (**1**) two major reaction pathways are in competition: in the first the Knoevenagel adduct **2** is formed which can react in various ways. The formation of **14** can be accounted for the base catalyzed decomposition of the formed Diels-Alder adduct **6** in the presence of unreacted aldehyde. This was confirmed by a control experiment starting from the isolated **6**. The formed – but very unstable - Knoevenagel adduct **2** able to form a very interesting symmetrical dimer **15** via a sulfur – sulfur bridge, but the majority of the intermediate **2** reacts with the unreacted indoline-2-thione in a nucleophilic addition of the thiol to the double bond via the non-isolable **16** intermediate to form **9** as a major product after sulfur elimination/electrophilic substitution cascade. When the piperidine base was replaced by pyridine the condensation reaction with the aldehyde is less favored and the major product in this case **10** or **13**. The first step on the way for this product is the oxidative dimerization of the indoline-2-thione. The isolated by-product **17** very probably is the remaining footprint for this intermediate, which reacts with the aromatic aldehyde to form **19** [1,2]dithiepino[3,4-*b*:7,6-*b*']diindole, which after a hydrogen sulfide elimination provides the isolated major product **10**. Interestingly, when in the formed products **10** in the position 1 and 11 any substituent larger than hydrogen is present **10** cannot be observed in the final reaction mixture, only the reduced form **13** can be isolated exclusively. This can be explained by the steric repulsion probably present in **10** with this substitution pattern, which is stabilized by the reduction of the double bond in the thiopyran ring.



Scheme 6. Proposed reaction pathways

In conclusion here we described an efficient and easy methodology that gives rapid access to a variety of 7-aryl-5*H*-thiopyrano[2,3-*b*:4,5-*b*']diindoles (**9**) and 12-aryl-7,12-dihydro-5*H*-thiopyrano[2,3-*b*:6,5-*b*']diindoles (**10**). The easy availability of cheap starting materials, the simple, microwave assisted reaction conditions that do not require metal catalyst or dry solvents, or inert atmosphere increase the synthetic usefulness of this protocol. The explored new reactions with the isolated by-products and intermediates give a new insight to the chemistry of the indoline-2-thiones.

EXPERIMENTAL

The starting materials were purchased from commercial sources. IR spectra were recorded with a Bruker Tensor 27 FT-IR spectrophotometer. All ^{1}H-, ^{13}C-NMR spectra were recorded in DMSO-d_6 with a Bruker Avance III. spectrometer operating at 500 MHz and 125 MHz respectively (1H-, DEPTQ-, HSQC-, HMBC-, NMR). Due to the very low solubility of some of the products not all the quaternary carbons have been successfully detected. They are not visible in the ^{13}C-NMR spectrum due to the dynamic processes taking place in the molecule. Prototropic tautomerism may also be the reason of the broadening and complete disappearance of some carbon resonance. High-resolution MS spectra were measured by Agilent 6230 TOF LC/MS spectrometer. All reagents and solvents were purchased and used without further purification.

2',4'-*Bis*[4-(trifluoromethyl)phenyl]-4',9'-dihydro-2'*H*-spiro[indole-3,3'-thiopyrano[2,3-*b*]indole]-2(1*H*)-thione (6a): To a suspension of indoline-2-thione (**1a**, 160 mg, 1.07 mmol) and 4-(trifluoromethyl)-benzaldehyde (**8a**, 370 mg, 2.14 mmol) in EtOH (4 mL) were added piperidine (6, μL, 0.53 mmol). The reaction mixture was stirred stirred at 120 °C for 30 min in an *Anton-Paar* microwave reactor. After completion of the reaction, the reaction mixture was evaporated to Celite and the residue was subjected to column chromatography over silica (eluent: heptane – EtOAc, gradient) to yield the title product (250 mg, 38%) as a yellow powder. ^{1}H-NMR (500 MHz, DMSO-*d*$_6$): δ 12.39 (s, 1H, NH-1), 11.68 (s, 1H, NH-9'), 7.76 (d, 1H, *J* = 7.8 Hz, H-4), 7.71 (d, 1H, *J* = 7.8 Hz, 4-Ph-2'H), 7.61 (d, 1H, *J* = 7.8 Hz, 4-Ph-3'H), 7.47 (d, 2H, *J* = 8.2 Hz, 2-Ph-5' and 3'H), 7.33 (d, 1H, *J* = 8.0 Hz, H-8'), 7.27 (td, 1H, *J* = 7.8 and 1.2 Hz, H-6), 7.20 (td, 1H, *J* = 7.8 and 1.2 Hz, H-5), 7.09 (d, 1H, *J* = 7.8 Hz, 4-Ph-5'H), 6.98 (td, 1H, *J* = 7.8 and 1.2 Hz, H-7'), 6.96 (d, 2H, *J* = 8.2 Hz, 2-Ph-6' and 2'H), 6.65 (t, 1H, *J* = 7.8 Hz, H-6'), 6.64 (d, 1H, *J* = 7.8 Hz, H-7), 6.47 (d, 1H, *J* = 7.8 Hz, 4-Ph-6'H), 5.85 (d, 1H, *J* = 7.8 Hz, H-5'), 5.32 (s, 1H, H-4'), 5.28 (s, 1H, H-2'); ^{13}C-NMR (125 MHz, DMSO-*d*$_6$): δ 204.3 (q), 144.6 (q), 142.6(q), 139.8 (q), 137.0 (q), 132.3 (CH), 130.8 (CH) 130.8 (q), 130.6 (2 x CH), 129.9 (CH), 129.6 (q), 128.6 (CH), 128.1 (q), 127.9 (q), 127.1 (q), 125.1 (2 x CH), 124.9 (CH), 123.7 (CH), 123.5 (CH), 121.2 (CH), 119.2 (CH), 118.2 (CH), 111.2 (CH), 110.6 (CH), 107.1 (q), 65.6 (q), 54.1 (CH), 51.0 (CH); IR (KBr, cm^{-1}): 3334, 1616, 1435, 1419, 1323, 1165, 1114, 1066, 1016, 746; HRMS [M+H]$^+$ found = 611.1035; $C_{32}H_{20}F_6N_2S_2$ required 611.1045.

Representative procedure for the synthesis of 7-aryl-5*H*-thiopyrano[2,3-*b*:4,5-*b*']diindoles (9): To a solution of indoline-2-thione (**1**, 1.0 mmol) and the corresponding aldehyde (0.4 mmol) in EtOH (2.0 mL) were added piperidine (0.4 mmol) and the reaction mixture was stirred at 145 °C for 45 min in an *Anton-Paar* microwave reactor. After completion of the reaction, the reaction mixture was evaporated to Celite and the residue was subjected to column chromatography over silica (eluent: heptane –EtOAc, gradient) to yield the title product.

7-[4-(Trifluoromethyl)phenyl]-5*H*-thiopyrano[2,3-*b*:4,5-*b*']diindole (9a): brown powder (25 mg, 52%); ^{1}H-NMR (500 MHz, DMSO-*d*$_6$): δ 12.85 (brs, 1H, NH), 8.74 (d, 1H, *J* = 8.0 Hz, H-1), 8.10 (d, 2H, *J* = 8.1 Hz, Ar-3' and 5'H), 8.08 (d, 2H, *J* = 8.1 Hz, Ar-2' and 6'H), 7.75 (d, 1H, *J* = 8.0 Hz, H-4), 7.71 (d, 1H, *J* = 8.0 Hz, H-11), 7.54 – 7.40 (m, 3H, H-10, H-3 and H-2), 7.04 (t, 1H, *J* = 8.0 Hz, H-9), 6.88 (d, 1H, *J* = 8.0 Hz, H-8); ^{13}C-NMR (125 MHz, DMSO-*d*$_6$): δ 139.4 (2 x q), 131.6 (2 x q), 131.1 (2 x q), 131.0 (2 x CH), 129.4 (3 x CH), 126.9 (2 x CH), 125.6 (CH), 125.5 (2 x q), 123.3 (2 x q), 122.5 (CH), 122.1 (CH), 122.0 (CH), 121.1 (CH); IR (KBr, cm^{-1}): 1592, 1448, 1233, 1200, 1101, 1025. HRMS [M+H]$^+$ found = 419.0828; $C_{24}H_{13}F_3N_2S$ required 419.0830.

7-(3,5-Dimethoxyphenyl)-5*H*-thiopyrano[2,3-*b*:4,5-*b*']diindole (9b): brown powder (25 mg, 20%); ^{1}H-NMR (500 MHz, DMSO-*d*$_6$): δ 12.64 – 12.32 (brs, 1H, NH), 8.80 – 8.64 (m, 1H, H-1), 7.80 – 7.60 (m, 2H, H-11 and H-4), 7.52 – 7.35 (m, 3H, H-10, H-3 and H-2), 7.15 – 7.00 (m, 2H, H-9 and H-8), 6.91 (d, 2H, *J*

= 2.2 Hz, Ar-2' and 6'H), 6.84 (t, 1H, *J* = 2.2 Hz, Ar-4'H), 3.85 (s, 6H, 2 x *O*CH3);^{13}C-NMR (125 MHz, DMSO-*d*6): δ 161.4 (3 x q), 137.1 (2 x q), 129.0 (2 x CH), 125.4 (3 x CH), 123.3 (2 x q), 122.4 (2 x CH), 122.0 (CH), 107.7 (2 x CH), 102.6 (CH), 56.2 (2 x CH3); IR (KBr, cm^{-1}): 1595, 1452, 1363, 1230, 1205, 1149, 1055; HRMS [M+H]$^+$ found = 411.1159; $C_{25}H_{18}N_2O_2S$ required 411.1167.

7-(3,5-Dimethoxyphenyl)-3,10-dimethoxy-5*H*-thiopyrano[2,3-*b*:4,5-*b'*]diindole (9c): yellow powder (11 mg, 11%); ^{1}H-NMR (500 MHz, DMSO-*d*6): δ 12.5 (brs, 1H, NH), 8.55 (d, 1H, *J* = 8.5 Hz, H-1), 7.24 (d, 1H, *J* = 2.0 Hz, H-4), 7.18 (brs, 1H, H-11), 7.03 (dd, 1H, *J* = 8.5 and 2.3 Hz, H-2), 7.01 (d, 1H, *J* = 8.6 Hz, H-8), 6.89 (t, 2H, *J* = 2.3 Hz, Ar-2' and 6'H), 6.81 (t, 1H, *J* = 2.3 Hz, Ar-4'H), 6.68 (dd, 1H, *J* = 8.6 and 2.3 Hz, H-9), 3.89 (s, 3H, *O*CH3), 3.85 (s, 3H, *O*CH3), 3.83 (s, 6H, 2 x *O*CH3); ^{13}C-NMR (125 MHz, DMSO-*d*6): δ 161.4 (4 x q), 160.8 (3 x q), 158.7 (q), 137.3 (3 x q), 123.1 (CH), 122.9 (CH), 117.0 (3 x q), 110.5 (CH), 109.5 (CH), 107.9 (3 x CH), 102.5 (2 x CH), 56.1 (2 x CH3), 55.9 (2 x CH3); IR (KBr, cm^{-1}): 2935, 1587, 1419, 1363, 1195, 1147, 1110; HRMS [M+H]$^+$ found = 471.1375; $C_{27}H_{22}N_2O_4S$ required 471.1378.

7-(3,4-Dimethoxyphenyl)-5*H*-thiopyrano[2,3-*b*:4,5-*b'*]diindole (9d): brown powder (35 mg, 28%); ^{1}H-NMR (500 MHz, DMSO-*d*6): δ 12.66 (brs, 1H, NH), 8.73 (d, 1H, *J* = 7.8 Hz, H-1), 7.74 (brd, 1H, *J* = 7.8 Hz, H-4), 7.69 (d, 1H, *J* = 8.0 Hz, H-11), 7.49 (t, 1H, *J* = 7.8 Hz, H-3), 7.46 (t, 1H, *J* = 8.0 Hz, H-10), 7.40 (t, 1H, *J* = 7.8 Hz, H-2), 7.37 (d, 1H, *J* = 2.0 Hz, Ar-2'H), 7.33 (dd, 1H, *J* = 8.2 and 2.0 Hz, Ar-6'H), 7.27 (dd, 1H, *J* = 8.2 Hz, Ar-5'H), 7.15 (d, 1H, *J* = 8.0 Hz, H-8), 7.06 (t, 1H, *J* = 8.0 Hz, H-9), 3.92 (s, 3H, *O*CH3), 3.80 (s, 3H, *O*CH3);^{13}C-NMR (125 MHz, DMSO-*d*6): δ 151.0 (2 x q), 149.5 (2 x q), 128.9 (CH), 127.4 (2 x q), 125.4 (2 x CH), 125.1 (CH), 123.4 (2 x q), 122.5 (CH), 122.4 (CH), 122.3 (CH), 121.9 (CH), 120.9 (CH), 113.0 (CH), 112.6 (CH), 56.3 (CH3), 56.2 (CH3); IR (KBr, cm^{-1}): 2932, 1573, 1510, 1446, 1365, 1263, 1224, 1139, 1028; HRMS [M+H]$^+$ found = 411.1164; $C_{25}H_{18}N_2O_2S$ required 411.1167.

7-(4-Methoxyphenyl)-5*H*-thiopyrano[2,3-*b*:4,5-*b'*]diindole (9e): brown powder (25 mg, 29%); ^{1}H-NMR (500 MHz, DMSO-*d*6): δ 12.67 (brs, 1H, NH), 8.73 (d, 1H, *J* = 7.8 Hz, H-1), 7.75 – 7.70 (m, 3H, Ar-6'H, Ar-2'H and H-4), 7.69 (brd, 1H, *J* = 7.8 Hz, H-11), 7.49 (t, 1H, *J* = 7.8 Hz, H-3), 7.46 (t, 1H, *J* = 7.8 Hz, H-10), 7.41 (t, 1H, *J* = 7.8 Hz, H-2), 7.27 – 7.24 (m, 2H, Ar-5' and -3'H), 7.09 (d, 1H, *J* = 7.8 Hz, H-8), 7.04 (t, 1H, *J* = 7.8 Hz, H-9), 3.93 (s, 3H, *O*CH3); ^{13}C-NMR (125 MHz, DMSO-*d*6): δ 161.5 (q), 142,4 (q), 131.3 (2 x CH), 129.0 (CH), 128.9 (CH) 127.4 (q), 125.5 (CH),125.4 (CH), 123.8 (2 x q), 123.4 (2 x q), 122.4 (CH), 122.1 (CH), 121.9 (CH), 120.9 (CH), 115.3 (2 x CH), 108.5 (2 x q), 56.0 (CH3); IR (KBr, cm^{-1}): 1616, 1504, 1462, 1361, 11249, 1105, 1028, 748; HRMS [M-H]$^-$ found = 379.0911; $C_{24}H_{16}N_2OS$ required 379.0904.

7-(3,5-Dimethoxyphenyl)-2,9-dimethoxy-5*H*-thiopyrano[2,3-*b*:4,5-*b'*]diindole (9f): brown powder (15 mg, 15%); ^{1}H-NMR (500 MHz, DMSO-*d*6): δ 12.80 (brs, 1H, NH), 8.18 (brs, 1H, H-1), 7.70 – 7.55 (m, 2H, H-11 and H-4), 7.16 – 7.03 (m, 2H, H-10 and H-3), 6.90 (d, 2H, *J* = 2.3 Hz, Ar-2’ and 6’H), 6.84 (t, 1H, *J* = 2.3 Hz, Ar-4’H), 6.58 (brs, 1H, H-8), 3.95 (s, 3H, *O*CH_3), 3.84 (s, 6H, 2 x *O*CH_3), 3.60 (s, 3H, *O*CH_3);^{13}C-NMR (125 MHz, DMSO-d_6): δ 161.5 (q), 136.4 (q), 119.0 (CH), 115.3 (CH), 114.9 (CH), 112.9 (CH), 107.6 (3 x CH), 104.5 (CH), 102.6 (CH), 56.3 (CH_3), 56.2 (2 x CH_3), 55.6 (CH_3); IR (KBr, cm^{-1}): 2936, 1623, 1589, 1460, 1350, 1207, 1153, 1057; HRMS $[M+H]^+$ found = 471.1378; $C_{27}H_{22}N_2O_4S$ required 471.1378.

2,9-Dimethoxy-7-phenyl-5*H*-thiopyrano[2,3-*b*:4,5-*b'*]diindole (9g): red powder (30 mg, 25%); ^{1}H-NMR (500 MHz, DMSO-d_6): δ 12.52 (brs, 1H, NH), 8.19 (brd, 1H, *J* = 1.7 Hz, H-1), 7.80 – 7.68 (m, 5H, Ph-H), 7.63 (d, 1H, *J* = 8.7 Hz, H-4), 7.59 (d, 1H, *J* = 8.7 Hz, H-11), 7.12 (dd, 1H, *J* = 8.7 and 2.4 Hz, H-3), 7.07 (dd, 1H, *J* = 8.7 and 2.4 Hz, H-10), 6.35 (d, 1H, *J* = 2.4 Hz, H-8), 3.95 (s, 3H, *O*CH_3), 3.53 (s, 3H, *O*CH_3); ^{13}C-NMR (125 MHz, DMSO-d_6): δ 131.3 (CH), 129.7 (5 x CH), 127.6 (CH), 115.4 (CH), 114.9 (CH), 107.2 (CH), 104.6 (CH), 56.2 (CH_3), 55.5 (CH_3); IR (KBr, cm^{-1}): 2827, 1614, 1464, 1336, 1203 1026; HRMS $[M+H]^+$ found = 411.1165; $C_{25}H_{18}N_2O_2S$ required 411.1167.

7-Phenyl-5*H*-thiopyrano[2,3-*b*:4,5-*b'*]diindole (9h): orange powder (50 mg, 47%); ^{1}H-NMR (500 MHz, DMSO-d_6): δ 12.85 (brs, 1H, NH), 8.74 (d ,1H, *J* = 7.5 Hz, H-1), 7.79 – 7.78 (m, 2H, Ph-H), 7.76 – 7.69 (m, 5H, Ph-H and H-11 and H-4), 7.52 (t, 1H, *J* = 8.0 Hz, H-3), 7.49 (m, 1H, H-10), 7.42 (t, 1H, *J* = 8.0 Hz, H-2), 7.01 (t, 1H, *J* = 7.5 Hz, H-9), 6.92 (d, 1H, *J* = 7.5 Hz, H-8); ^{13}C-NMR (125 MHz, DMSO-d_6): δ 131.2 (CH), 129.9 (3 x CH), 129.8 (3 x CH), 129.1 (CH), 125.5 (CH), 122.4 (CH), 122.1 (CH), 122.0 (CH), 121.0 (CH); IR (KBr, cm^{-1}): 1613, 1448, 1360, 1228, 752; HRMS $[M+H]^+$ found = 351.0952; $C_{23}H_{14}N_2S$ required 351.0956.

4,11-Dibromo-7-[4-(trifluoromethyl)phenyl]-5*H*-thiopyrano[2,3-*b*:4,5-*b'*]diindole (9i): red powder (18 mg, 63%); ^{1}H-NMR (500 MHz, DMSO-d_6): δ 13.20 (s, 1H, NH), 8.75 (brs, 1H, H-1), 8.20 – 7.94 (m, 4H, Ar-H), 7.85 – 7.60 (m, 2H, H-10 and H-3), 7.56 – 7.31 (m, 1H, H-2), 7.20 – 6.70 (m, 2H, H-8 and H-9); ^{13}C-NMR (125 MHz, DMSO-d_6): δ 141.4 (q), 138.8 (q), 132.0 (CH), 131.5 (q), 131.0 (2 x CH), 128.1 (CH), 127.0 (2 x CH), 124.4 (q), 123.4 (CH), 123.2 (CH), 122.1 (CH), 121.2 (CH); IR (KBr, cm^{-1}): 1564, 1377, 1324, 1168, 1122; HRMS $[M+H]^+$ found = 574.9036; $C_{24}H_{11}Br_2F_3N_2S$ required 574.9040.

4,11-Dibromo-7-(3,5-dimethoxyphenyl)-5*H*-thiopyrano[2,3-*b*:4,5-*b'*]diindole (9j): brown powder (20 mg, 32%); ^{1}H-NMR (500 MHz, DMSO-d_6): δ 13.15 (s, 1H, NH), 8.74 (d, 1H, *J* = 7.8 Hz, H-1), 7.75 (dd, 1H, *J* = 7.8 and 0.9 Hz, H-3), 7.68 (dd, 1H, *J* = 7.8 and 0.7 Hz, H-10), 7.43 (t, 1H, *J* = 7.8 Hz, H-2), 7.10 (d, 1H, *J* = 7.8 Hz, H-8), 6.99 (t, 1H, *J* = 7.8 Hz, H-9), 6.94 (d, 2H, *J* = 2.2 Hz, Ar-2’ and 6’H), 6.85 (t, 1H, *J* = 2.2 Hz, Ar-4’H), 3.83 (s, 6H, 2 x *O*CH_3);^{13}C-NMR (125 MHz, DMSO-d_6): δ 161.5 (2 x q), 156.1 (q), 154.9 (q), 143.2 (q), 136.4 (q), 131.7 (CH), 129.8 (q), 128.0 (CH), 126.1 (q), 124.8 (q), 123.3 (CH), 123.2 (CH), 122.1 (CH), 121.6 (CH), 112.6 (q), 110.5 (q), 107.7 (2 x CH), 104.4 (q), 102.9 (CH), 56.2 (2 x CH_3);

IR (KBr, cm^{-1}): 3244, 1599, 1565, 1375, 1317, 1222, 1190, 1149, 1059; HRMS [M+H]$^+$ found = 566.9376; $C_{22}H_{16}Br_2N_2O_2S$ required 566.9377.

4,11-Dibromo-7-(3-bromophenyl)-5*H*-thiopyrano[2,3-*b*:4,5-*b'*]diindole (9k): red powder (20 mg, 50%); ^{1}H-NMR (500 MHz, DMSO-*d*$_6$): δ 13.17 (brs, 1H, NH), 8.74 (d, 1H, *J* = 7.7 Hz, H-1), 8.08 (t, 1H, *J* = 1.9 Hz, Ar-2'H), 7.99 – 7.95 (m, 1H, Ar-4'H), 7.84 – 7.80 (m, 1H, Ar-6'H), 7.75 (d, 1H, *J* = 7.7 Hz, H-3), 7.68 (t, 1H, *J* = 8.0 Hz, Ar-5'H), 7.67 (d, 1H, *J* = 7.8 Hz, H-10), 7.42 (t, 1H, *J* = 7.7 Hz, H-2), 6.95 (t, 1H, *J* = 7.8 Hz, H-9), 6.86 (d, 1H, *J* = 7.8 Hz, H-8); ^{13}C-NMR (125 MHz, DMSO-*d*$_6$): δ 141.3 (q), 136.9 (q), 134.2 (CH), 132.3 (CH), 132.1 (CH), 131.9 (CH), 129.0 (CH), 127.9 (CH), 123.2 (CH), 123.1 (CH), 123.0 (q), 122.1 (CH), 121.1 (CH); IR (KBr, cm^{-1}): 1566, 1375, 1234, 1120, 1047, 785, 746; HRMS [M+H]$^+$ found = 584.8265; $C_{23}H_{11}Br_3N_2S$ required 584.8271.

4,11-Dibromo-7-(4-methoxyphenyl)-5*H*-thiopyrano[2,3-*b*:4,5-*b'*]diindole (9l): red powder (16 mg, 41%); ^{1}H-NMR (500 MHz, DMSO-*d*$_6$): δ 13.12 (brs, 1H, NH), 8.75 (d, 1H, *J* = 7.8 Hz, H-1), 7.76 – 7.71 (m, 3H, Ar-2'and 6'H and H-3), 7.67 (dd, 1H, *J* = 7.7 and 0.8 Hz, H-10), 7.43 (t, 1H, *J* = 7.8 Hz, H-2), 7.29 – 7.24 (m, 2H, Ar-3' and 5'H), 7.09 (dd, 1H, *J* = 7.7 and 0.7 Hz, H-8), 6.96 (t, 1H, *J* = 7.7 Hz, H-9), 3.93 (s, 3H, *O*CH$_3$); ^{13}C-NMR (125 MHz, DMSO-*d*$_6$): δ 131.6 (CH), 131.3 (2 x CH), 128.0 (CH), 123.3 (CH), 123.1 (CH), 122.0 (CH), 121.3 (CH), 115.4 (2 x CH), 56.0 (CH$_3$; IR (KBr, cm^{-1}): 1604, 1560, 1504, 1369, 1247, 1172, 1120, 1026; HRMS [M+H]$^+$ found = 536.9266; $C_{24}H_{14}Br_2N_2OS$ required 536.9272.

2,9-Dimethoxy-7-[4-(trifluoromethyl)phenyl]-5*H*-thiopyrano[2,3-*b*:4,5-*b'*]diindole (9m): brown powder (10 mg, 30%); ^{1}H-NMR (500 MHz, DMSO-*d*$_6$): δ 12.45 (brs, 1H, NH), 8.19 (brs, 1H, H-1), 8.11 (d, 2H, *J* = 8.1 Hz, Ar-3' and 5'H), 8.04 (d, 2H, *J* = 8.1 Hz, Ar-2' and 6'H), 7.70 – 7.55 (m, 2H, H-11 and H-4), 7.13 (d, 1H, *J* = 8.5 Hz, H-3), 7.09 (d, 1H, *J* = 7.8 Hz, H-10), 6.23 (s, 1H, H-8), 3.95 (s, 3H, *O*CH$_3$), 3.53 (s, 3H, *O*CH$_3$); ^{13}C-NMR (125 MHz, DMSO-*d*$_6$): δ 131.0 (2 x CH), 126.8 (2 x CH), 119.3 (CH), 115.8 (CH), 115.1 (CH), 113.0 (CH), 106.9 (CH), 104.5 (CH), 56.2 (CH$_3$), 55.4 (CH$_3$); IR (KBr, cm^{-1}): 1615, 1469, 1323, 1211, 1130, 1066; HRMS [M+H]$^+$ found = 479.1040; $C_{26}H_{17}F_3N_2O_2S$ required 479.1041

4,11-Dibromo-7-phenyl-5*H*-thiopyrano[2,3-*b*:4,5-*b'*]diindole (9n): red powder (16 mg, 52%); ^{1}H-NMR (500 MHz, DMSO-*d*$_6$): δ 13.15 (s, 1H, NH), 8.75 (d ,1H, *J* = 7.8 Hz, H-1), 7.83 – 7.70 (m, 6H, Ph-H and H-3), 7.66 (dd, 1H, *J* = 7.2 Hz, H-10), 7.44 (t, 1H, *J* = 7.8 Hz, H-2), 6.95-6.88 (m, 2H, H-9 and H-8), ^{13}C-NMR (125 MHz, DMSO-*d*$_6$): δ 131.7 (CH), 131.4 (CH), 130.0 (2 x CH), 129.7 (2 x CH), 128.0 (CH), 123.4 (CH), 123.1 (CH), 122.0 (CH), 121.2 (CH); IR (KBr, cm^{-1}): 1607, 1562, 1425, 1377, 1228, 1116, 1045, 754; HRMS [M+H]$^+$ found = 506.9161; $C_{23}H_{12}Br_2N_2S$ required 506.9166.

2,9-Dichloro-7-[4-(trifluoromethyl)phenyl]-5*H*-thiopyrano[2,3-*b*:4,5-*b'*]diindole (9o): brown powder (18 mg, 67%); ^{1}H-NMR (500 MHz, DMSO-*d*$_6$): δ 12.82 (brs, 1H, NH), 8.74 (brs, 1H, H-1), 8.12 (d, 2H, *J* = 8.0 Hz, Ar-3' and 5'H), 8.05 (d, 2H, *J* = 8.0 Hz, Ar-2' and 6'H), 7.77 (d, 1H, *J* = 8.6 Hz, H-4), 7.75 –

7.65 (m, 1H, H-11), 7.52 (d, 1H, *J* = 8.6 Hz, H-3), 7.50 (d, 1H, *J* = 8.6 Hz, H-10), 6.71 (brs, 1H, H-8); ^{13}C-NMR (125 MHz, DMSO-d_6): δ 139.0 (q), 131.7 (q), 131.3 (q), 130.9 (2 x CH), 129.0 (CH), 127.0 (2 x CH), 126.7 (CH), 125.7 (CH), 125.4 (CH), 124.3 (q), 121.4 (2 x CH); IR (KBr, cm^{-1}): 1614, 1440, 1323, 1160, 1107, 1068; HRMS [M+H]$^+$ found = 487.0049; $C_{24}H_{11}Cl_2F_3N_2S$ required 487.0050.

2,9-Dichloro-7-(3,5-dimethoxyphenyl)-5*H*-thiopyrano[2,3-*b*:4,5-*b'*]diindole (9p): brown powder (19 mg, 32%); ^{1}H-NMR (500 MHz, DMSO-d_6): δ 13.01 (brs, 1H, NH), 8.73 (brs, 1H, H-1), 7.77 (d, 1H, *J* = 8.6 Hz, H-4), 7.71 (d, 1H, *J* = 8.2 Hz, H-11), 7.55 – 7.48 (m, 2H, H-10 and H-3), 7.05 (t, 1H, *J* = 1.3 Hz, H-8), 6.96 (d, 2H, *J* = 2.1 Hz, Ar-2' and 6'H), 6.88 (t, 1H, *J* = 2.1 Hz, Ar-4'H), 3.85 (s, 6H, 2 x *O*CH_3); ^{13}C-NMR (125 MHz, DMSO-d_6): δ 128.8 (CH), 125.6 (2 x CH), 125.6 (CH), 121.9 (2 x CH), 107.7 (2 x CH), 103.1 (CH), 56.3 (2 x CH_3); IR (KBr, cm^{-1}): 2925, 1589, 1437, 1346, 1205, 1159, 1058; HRMS [M+H]$^+$ found = 479.0388; $C_{25}H_{16}Cl_2N_2O_2S$ required 479.0388.

4,11-Dichloro-7-[4-(trifluoromethyl)phenyl]-5*H*-thiopyrano[2,3-*b*:4,5-*b'*]diindole (9q): brown powder (30 mg, 67%); ^{1}H-NMR (500 MHz, DMSO-d_6): δ 13.39 (brs, 1H, NH), 8.74 (d, 1H, *J* = 7.5 Hz, H-1), 8.12 (d, 2H, *J* = 8.0 Hz, Ar-3' and 5'H), 8.08 (d, 2H, *J* = 8.0 Hz, Ar-2' and 6'H), 7.65 (d, 1H, *J* = 7.5 Hz, H-3), 7.55 (d, 1H, *J* = 7.6 Hz, H-10), 7.51 (t, 1H, *J* = 7.5 Hz, H-2), 7.03 (t, 1H, *J* = 7.6 Hz, H-9), 6.81 (d, 1H, *J* = 7.6 Hz, H-8);^{13}C-NMR (125 MHz, DMSO-d_6): δ 138.6 (q), 131.0 (2 x CH), 129.2 (CH), 127.0 (2 x CH), 125.4 (CH), 123.3 (CH), 123.2 (CH), 121.8 (CH), 120.7 (CH), 110.4 (q); IR (KBr, cm^{-1}): 3138, 1599, 1566, 1373, 1323, 1166, 1120, 1066; HRMS [M+H]$^+$ found = 487.0047; $C_{24}H_{11}Cl_2F_3N_2S$ required 487.0050.

4,11-Dichloro-7-(3,5-dimethoxyphenyl)-5*H*-thiopyrano[2,3-*b*:4,5-*b'*]diindole (9r): brown powder (20 mg, 26%); ^{1}H-NMR (500 MHz, DMSO-d_6): δ 13.30 (s, 1H, NH), 8.69 (d, 1H, *J* = 7.7 Hz, H-1), 7.62 (dd, 1H, *J* = 7.7 and 0.9 Hz, H-3), 7.55 – 7.51 (m, 1H, H-8), 7.49 (t, 1H, *J* = 7.7 Hz, H-2), 7.08 – 7.05 (m, 2H, H-10 and H-9), 6.94 (d, 2H, *J* = 2.2 Hz, Ar-2' and 6'H), 6.85 (t, 1H, *J* = 2.2 Hz, Ar-4'H), 3.83 (s, 6H, 2 x *O*CH_3); ^{13}C-NMR (125 MHz, DMSO-d_6): δ 161.5 (q), 156.1 (q), 153.4 (q), 136.4 (q), 128.8 (CH), 125.1 (q), 125.0 (CH), 123.3 (CH), 123.0 (CH), 121.6 (CH), 121.1 (CH), 107.7 (2 x CH), 102.9 (CH), 56.2 (2 x CH_3); IR (KBr, cm^{-1}): 2931, 1593, 1566, 1421, 1369, 1153, 1062; HRMS [M+H]$^+$ found = 479.0387; $C_{25}H_{16}Cl_2N_2O_2S$ required 479.0388.

Representative procedure for the synthesis of 12-aryl-5*H*-thiopyrano[2,3-*b*:6,5-*b*']diindoles (10) and 12-aryl-7,12-dihydro-5*H*-thiopyrano[2,3-*b*:6,5-*b*']diindoles (13): General procedure: To a solution of indoline-2-thione (**1**, 1.0 mmol) and the corresponding aldehyde (0.4 mmol) in EtOH (2 mL) were added pyridine (0.4 mmol) and the reaction mixture was stirred at 145 °C for 45 min in an *Anton-Paar* microwave reactor. After completion of the reaction, the reaction mixture was evaporated to Celite and the residue was subjected to column chromatography over silica (eluent: heptane – EtOAc, gradient) to yield the title product.

12-[4-(Trifluoromethyl)phenyl]-5*H*-thiopyrano[2,3-*b*:6,5-*b'*]diindole (10a): orange powder (140 mg, 42%); ^{1}H-NMR (500 MHz, DMSO-d_6): δ 13.4 (brs, 1H, NH), 8.18 (d, 2H, *J* = 8.0 Hz, Ph-3' and 5'H), 7.91 (d, 2H, *J* = 8.0 Hz, Ph-2' and 6'H), 7.64 (d, 2H, *J* = 8.0 Hz, H-8 and H-4), 7.32 (t, 2H, *J* = 8.0 Hz, H-9 and H-3), 6.98 (t, 2H, *J* = 8.0 Hz, H-10 and H-2), 6.38 (d, 2H, *J* = 8.0 Hz, H-11 and H-1); ^{13}C-NMR (125 MHz, DMSO-d_6): δ 145.6 (q), 141.8 (q), 130.2 (q), 128.9 (2 x CH), 127.3 (2 x CH), 125.6 (4 x CH), 124.8 (q), 121.6 (2 x CH), 120.6 (2 x CH); IR (KBr, cm^{-1}): 3062, 1487, 1450, 1396, 1322, 1193, 1174, 1126, 1104, 1064; HRMS [M+H]$^+$ found = 419.0826; $C_{24}H_{13}F_3N_2S$ required 419.0830.

12-(3,5-Dimethoxyphenyl)-5*H*-thiopyrano[2,3-*b*:6,5-*b'*]diindole (10b): orange powder (10 mg, 31%); ^{1}H-NMR (500 MHz, DMSO-d_6): δ 13.30 (brs, 1H, NH), 7.65 – 7.60 (m, 2H, H-8 and H-4), 7.35 – 7.29 (m, 2H, H-9 and H-3), 7.05 – 7.00 (m, 2H, H-10 and H-2), 6.88 (t, 1H, *J* = 2.3 Hz, Ar-4'H), 6.77 (d, 2H, *J* = 2.3 Hz, Ar-2' and 6'H), 6.70 (brd, 2H, *J* = 7.7 Hz, H-11 and H-1), 3.81 (s, 6H, 2 x *O*CH$_3$); ^{13}C-NMR (125 MHz, DMSO-d_6): δ 162.1 (2 x q), 147.2 (q), 139.4 (q), 125.6 (2 x CH), 125.5 (2 x CH), 121.6 (2 x CH), 121.1 (2 x CH), 105.2 (2 x CH), 101.4 (CH), 56.1 (2 x CH$_3$); IR (KBr, cm^{-1}): 1589, 1552, 1448, 1396, 1361, 1192, 1155, 1101, 1057; HRMS [M+H]$^+$ found = 411.1165; $C_{25}H_{18}N_2O_2$ S required 411.1167.

12-Phenyl-5*H*-thiopyrano[2,3-*b*:6,5-*b'*]diindole (10c): brown powder (25 mg, 52%); ^{1}H-NMR (500 MHz, DMSO-d_6): δ 13.33 (brs, 1H, NH), 7.82 – 7.75 (m, 3H, Ph-3', 4' and 5'H), 7.64 – 7.58 (m, 4H, H-8, H-4, Ph-2' and 6'H), 7.32 – 7.27 (m, 2H, H-9 and H-3), 6.97 – 6.91 (m, 2H, H-10 and H-2), 6.48 (brd, 2H, *J* = 7.8 Hz, H-11 and H-1); ^{13}C-NMR (125 MHz, DMSO-d_6): δ 147.4 (q), 137.5 (q), 130.2 (2 x CH), 129.8 (CH), 127.5 (2 x CH) 125.4 (2 x CH), 121.4 (2 x CH), 120.9 (2 x CH), 115.3 (2 x CH); IR (KBr, cm^{-1}): 1496, 1440, 1392, 1354, 1300, 1193, 1176, 1100; HRMS [M+H]$^+$ found = 351.0948; $C_{23}H_{14}N_2S$ required 351.0956.

2,10-Dimethoxy-12-[4-(trifluoromethyl)phenyl]-5*H*-thiopyrano[2,3-*b*:6,5-*b'*]diindole (10d): red powder (25 mg, 26%); ^{1}H-NMR (500 MHz, DMSO-d_6): δ 13.13 (brs, 1H, NH), 8,2 (d, 2H, *J* = 8.0 Hz, Ph-3' and 5'H), 7.92 (d, 2H, *J* = 8.0 Hz, Ph-2' and 6'H), 7.52 (d, 2H, *J* = 8.7 Hz, H-8 and H-4), 6.93 (dd, 2H, *J* = 8.7 and 2.4 Hz, H-9 and H-3), 5.85 (brs, 2H, H-11 and H-1), 3,44 (s, 6H, 2 x *O*CH$_3$); ^{13}C-NMR (125 MHz, DMSO-d_6): δ 154.7 (q), 145.5 (q), 141.5 (q), 129.1 (2 x CH), 127.2 (2 x CH), 115.8 (2 x CH), 113.5 (2 x CH), 104.1 (2 x CH), 55.1 (2 x CH$_3$); IR (KBr, cm^{-1}): 1615, 1492, 1398, 1322, 1172, 1124; HRMS [M+H]$^+$ found = 479.1036; $C_{26}H_{17}F_3N_2O_2S$ required 479.1041.

12-(3-Bromo-5-chlorophenyl)-5*H*-thiopyrano[2,3-*b*:6,5-*b*']diindole (10e): orange powder (120 mg, 52%); ^{1}H-NMR (500 MHz, DMSO-d_6): δ 13.39 (brs, 1H, NH), 8.21 (t, 1H, *J* = 1.7 Hz, Ar-4'H), 7.96 (t, 1H, *J* = 1.7 Hz, Ar-2'H), 7.89 (t, 1H, *J* = 1.7 Hz, Ar-6'H), 7.66 (d, 2H, *J* = 7.8 Hz, H-8 and H-4), 7.35 (t, 2H, *J* = 7.8 Hz, H-9 and H-3), 7.08 (t, 2H, *J* = 7.8 Hz, H-10 and H-2), 6.56 (d, 2H, *J* = 7.8 Hz, H-11 and H-

1); ^{13}C-NMR (125 MHz, DMSO-d_6): δ 143.7 (q), 141.0 (q), 136.1 (q), 132.3 (CH), 129.6 (CH), 127.2 (CH), 125.7 (2 x CH), 125.5 (2 x CH), 124.1 (q), 121.8 (2 x CH), 120.6 (2 x CH); IR (KBr, cm^{-1}): 1552, 1491, 1450, 1392, 1357, 1300, 1192, 1103; HRMS [M+H]$^+$ found = 462.9668; $C_{23}H_{12}BrClN_2S$ required 462.9671.

12-(3,4-Dimethoxyphenyl)-5*H*-thiopyrano[2,3-*b*:6,5-*b'*]diindole (10f): orange powder (15 mg, 22%); ^{1}H-NMR (500 MHz, DMSO-d_6): δ 13.25 (brs, 1H, NH), 7.61 (d, 2H, *J* = 8.0 Hz, H-8 and H-4), 7.35 (d, 1H, *J* = 8.1 Hz, Ar-5'H), 7.30 (dd, 2H, *J* = 8.1 and 1.1 Hz, H-9 and H-3), 7.20 (d, 1H, *J* = 2.0 Hz, Ar-2'H), 7.13 (dd, 1H, *J* = 8.1 and 2.0 Hz , Ar-6'H), 7.01 (d, 2H, *J* = 8.1 and 1.1 Hz, H-10 and H-2), 6.65 (d, 2H, *J* = 8.1 Hz, H-11 and H-1), 3.97 (s, 3H, *O*CH$_3$), 3.71 (s, 3H, *O*CH$_3$); ^{13}C-NMR (125 MHz, DMSO-d_6): δ 150.2 (q), 149.6 (q), 147.6 (q), 129.6 (q), 125.3 (2 x CH), 121.4 (2 x CH), 121.1 (2 x CH), 119.7 (CH), 115.4 (2 x CH), 113.0 (CH), 111.1 (CH), 56.3 (CH$_3$), 56.1 (CH$_3$); IR (KBr, cm^{-1}): 1512, 1446, 1394, 1357, 1247, 1192, 1172, 1141, 1103; HRMS [M+H]$^+$ found = 411.1164; $C_{25}H_{18}N_2O_2S$ required 411.1167.

3,9-*Bis*(trifluoromethyl)-12-[4-(trifluoromethyl)phenyl]-5*H*-thiopyrano[2,3-*b*:6,5-*b'*]diindole (10g): brown powder (25 mg, 48%); ^{1}H-NMR (500 MHz, DMSO-d_6): δ 13.88 (brs, 1H, NH), 8.21 (d, 2H, *J* = 8.0 Hz, Ar-3' and 5'H), 8.00 – 7.97 (m, 2H, H-8 and H-4), 7.94 (d, 2H, *J* = 8.0 Hz Ar-2' and 6'H), 7.37 (dd, 2H, *J* = 8.3 and 1.2 Hz, H-10 and H-2), 6.54 (d, 2H, *J* = 8.3 Hz, H-11 and H-1); ^{13}C-NMR (125 MHz, DMSO-d_6): δ 147.8 (q), 140.6 (q), 138.4 (q), 128.8 (2 x CH), 127,5 (2 x CH), 126.5 (q), 124.0 (q), 121.2 (2 x CH), 118.4 (2 x CH), 112,7 (2 x CH); IR (KBr, cm^{-1}): 1489, 1402, 1321, 1163, 1184, 1055, 916; HRMS [M+H]$^+$ found = 555.0574; $C_{26}H_{11}F_9N_2S$ required 555.0577.

12-(3,5-Dimethoxyphenyl)-3,9-bis(trifluoromethyl)-5*H*-thiopyrano[2,3-*b*:6,5-*b'*]diindole (10h): tan powder (25 mg, 33%); ^{1}H-NMR (500 MHz, DMSO-d_6): δ 13.82 (brs, 1H, NH), 8.00 (brs, 2H, H-8 and H-4), 7.43 (brd, 2H, *J* = 8.1 Hz, H-10 and H-2), 6.92 (t, 1H, *J* = 2.2 Hz, Ar-4'H), 6.86 (brd, 2H, *J* = 8.1 Hz, H-11 and H-1), 6.83 (d, 2H, *J* = 2.2 Hz, Ar-2'and 6'H), 3.81 (s, 6H, 2 x *O*CH$_3$); ^{13}C-NMR (125 MHz, DMSO-d_6): δ 162.2 (q), 149.4 (q), 138.4 (q), 126.6 (q), 123.8 (q), 121,7 (2 x CH), 118.3 (2 x CH), 104.9 (2 x CH), 102.1 (CH), 56.2 (2 x CH$_3$); IR (KBr, cm^{-1}): 1595, 1398, 1319, 1159, 1114, 1055; HRMS [M+H]$^+$ found = 547.0911; $C_{27}H_{16}F_6N_2O_2S$ required 547.0915.

2,10-Dichloro-12-[4-(trifluoromethyl)phenyl]-5*H*-thiopyrano[2,3-*b*:6,5-*b'*]diindole (10i): red powder (15 mg, 58%); ^{1}H-NMR (500 MHz, DMSO-d_6): δ 13.67 (brs, 1H, NH), 8.25 (d, 2H, *J* = 8.0 Hz, Ar-5' and 3'H), 7.94 (d, 2H, *J* = 8.0 Hz, Ar-6' and 2'H), 7.68 (d, 2H, *J* = 8.5 Hz, H-8 and H-4), 7.37 (dd, 2H, *J* = 8.5 and 2.1 Hz, H-9 and H-3), 6.25 (brs, 2H, H-11 and H-1); ^{13}C-NMR (125 MHz, DMSO-d_6): δ 146.3 (q), 140.9 (q), 130.8 (q), 130.5 (q), 128.9 (2 x CH), 127.4 (2 x CH), 126.5 (q), 125.8 (q), 125.6 (2 x CH), 125.4 (2 x CH), 119.8 (2 x CH); IR (KBr, cm^{-1}): 1396, 1354, 1323, 1300, 1276, 1192, 1151, 1103, 1068; HRMS [M+H]$^+$ found = 487.0047; $C_{24}H_{11}Cl_2F_3N_2S$ required 487.0050.

12-(3,5-Dimethoxyphenyl)-2,10-dimethoxy-5*H*-thiopyrano[2,3-*b*:6,5-*b'*]diindole (10j): red powder (11 mg, 18%); ^{1}H-NMR (500 MHz, DMSO-d_6): δ 13.01 (brs, 1H, NH), 7.50 (d, 2H, *J* = 8.7 Hz, H-8 and H-4), 6.94 (dd, 2H, *J* = 8.7 and 2.5 Hz, H-9 and H-3), 6.88 (t, 1H, *J* = 2.3 Hz, Ar-4'H), 6.78 (d, 2H, *J* = 2.3 Hz, Ar-6' and 2'H), 6.22 (d, 2H, *J* = 2.5 Hz, H-11 and H-1), 3.81 (s, 6H, 2 x *O*CH$_3$), 3.53 (s, 6H, 2 x *O*CH$_3$); ^{13}C-NMR (125 MHz, DMSO-d_6): δ 162.3 (q), 154.6 (q), 147.0 (q), 139.0 (q), 115.8 (2 x CH), 113.0 (2 x CH), 105.2 (2 x CH), 105.0 (2 x CH), 101.3 (CH), 56.2 (2 x CH$_3$), 55.4 (2 x CH$_3$); IR (KBr, cm^{-1}): 1583, 1452, 1396, 1350, 1313, 1280, 1178, 1165, 1136, 1062, 1033; HRMS [M+H]$^+$ found = 471.1379; $C_{27}H_{22}N_2O_4S$ required 471.1378.

2,10-Dimethoxy-12-phenyl-5*H*-thiopyrano[2,3-*b*:6,5-*b'*]diindole (10k): red powder (25 mg, 24%); ^{1}H-NMR (500 MHz, DMSO-d_6): δ 13.11 (brs, 1H, NH), 7.86 – 7.70 (m, 3H, Ar-3', 4' and 5'H), 7.64 – 7.58 (m, 2H, Ar-2' and 6'H), 7.50 (d, 2H, *J* = 8.7 Hz, H-8 and H-4), 6.92 (dd, 2H, *J* = 8.7 and 2.4 Hz, H-9 and H-3), 5.98 (d, 2H, *J* = 2.4 Hz, H-11 and H-1), 3.45 (s, 6H, 2 x *O*CH$_3$); ^{13}C-NMR (125 MHz, DMSO-d_6): δ 129.7 (3 x CH), 127.6 (2 x CH), 115.8 (2 x CH), 113.1 (2 x CH), 104.7 (2 x CH), 55.3 (2 x CH$_3$); IR (KBr, cm^{-1}): 2901, 1462, 1398, 1352, 1213, 1178, 1128, 1089; HRMS [M+H]$^+$ found = 411.1165; $C_{25}H_{18}N_2O_2S$ required 411.1167.

2,10-Dimethoxy-12-(4-methoxyphenyl)-5*H*-thiopyrano[2,3-*b*:6,5-*b'*]diindole (10l): red powder (35 mg, 20%); ^{1}H-NMR (500 MHz, DMSO-d_6): δ 13.12 (brs, 1H, NH), 7.55 – 7.48 (m, 4H, Ar-2' and 6'H, H-8 and H-4), 7.38 – 7.33 (m, 2H, Ar-3' and 5'H), 6.93 (dd, 2H, *J* = 8.7 and 2.5 Hz, H-9 and H-3), 6.10 (d, 2H, *J* = 2.5 Hz, H-11 and H-1), 3.94 (s, 3H, *O*CH$_3$), 3.50 (s, 6H, 2 x *O*CH$_3$); ^{13}C-NMR (125 MHz, DMSO-d_6): δ 160.4 (q), 154.6 (q), 147.7 (q), 129.2 (q), 129.1 (2 x CH), 115.8 (2 x CH), 115.5 (2 x CH), 113.0 (2 x CH), 105.0 (2 x CH), 56.0 (CH$_3$), 55.4 (2 x CH$_3$); IR (KBr, cm^{-1}): 2825, 1510, 1454, 1433, 1396, 1344, 1317, 1284, 1247, 1213, 1178, 1126, 1087, 1031; HRMS [M+H]$^+$ found = 441.1270; $C_{26}H_{20}N_2O_3S$ required 441.1273.

4,8-Dibromo-12-(3,5-dimethoxyphenyl)-5*H*-thiopyrano[2,3-*b*:6,5-*b'*]diindole (10m): red powder (15 mg, 32%); ^{1}H-NMR (500 MHz, DMSO-d_6): δ 13.44 (brs, 1H, NH), 7.55 (d, 2H, *J* = 7.5 Hz, H-9 and H-3), 7.03 – 6.95 (m, 2H, H-10 and H-2), 6.89 (t, 1H, *J* = 2.3 Hz, Ar-4'H), 6.77 (d, 2H, *J* = 2.3 Hz, Ar-2H' and 6'H), 6.72 (brs, 2H, H-11 and H-1), 3.82 (s, 6H, 2 x *O*CH$_3$); ^{13}C-NMR (125 MHz, DMSO-d_6): δ 162.2 (2 x q), 148.8 (q), 138.5 (q), 128.0 (2 x CH), 122.9 (2 x CH), 120.4 (2 x CH), 105.1 (2 x CH), 101.7 (CH), 56.1 (2 x *O*CH$_3$); IR (KBr, cm^{-1}): 2922, 1587, 1489, 1423, 1382, 1355, 1332, 1311, 1244, 1193, 1163, 1124, 1057; HRMS [M+H]$^+$ found = 566.9375; $C_{25}H_{16}$ $Br_2N_2O_2S$ required 566.9377.

4,8-Dibromo-12-(3-bromophenyl)-5*H*-thiopyrano[2,3-*b*:6,5-*b'*]diindole (10n): red powder (22 mg, 68%); ^{1}H-NMR (500 MHz, DMSO-d_6): δ 13.49 (brs, 1H, NH), 8.01 – 7.97 (m, 1H, Ar-4'H), 7.94 – 7.84 (m, 1H, Ar-2'H), 7.83 – 7.73 (m, 2H, Ar-5'H), 7.72 – 7.64 (m, 1H, Ar-6'H), 7.56 (d, 2H, *J* = 2.3 Hz, H-9 and H-3), 6.97 (brs, 2H, H-10 and H-2), 6.53 (brs, 2H, H-11 and H-1); ^{13}C-NMR (125 MHz, DMSO-*d*$_6$): δ 146.9 (q), 138.9 (q), 133.1 (CH), 132.5 (CH), 130.4 (CH), 128.4 (2 x CH), 126.9 (CH), 123.3 (q), 123.0 (2 x CH), 120.0 (2 x CH); IR (KBr, cm^{-1}): 2970, 2900, 1379, 1357, 1255, 1192, 1163, 1124, 1053; HRMS $[M+H]^+$ found = 584.8264; $C_{23}H_{11}Br_3N_2$ required 584.8271.

4,8-Dibromo-12-(4-methoxyphenyl)-5*H*-thiopyrano[2,3-*b*:6,5-*b'*]diindole (10o): red powder (18 mg, 50%); ^{1}H-NMR (500 MHz, DMSO-*d*$_6$): δ 13.57 (brs, 1H, NH), 7.57 – 7.50 (m, 4H, Ar-2’ and 6’H, H-9 and H-3), 7.35 – 7.30 (m, 2H, Ar-3’ and 5’H), 6.95 (t, 2H, *J* = 7.7 Hz, H-10 and H-2), 6.58 (brs, 2H, H-11 and H-1), 3.96 (s, 3H, *O*CH$_3$); ^{13}C-NMR (125 MHz, DMSO-*d*$_6$): δ 129.0 (2 x CH), 127.8 (2 x CH), 122.8 (2 x CH), 120.3 (2 x CH), 115.6 (2 x CH), 55.9 (CH$_3$); IR (KBr, cm^{-1}): 1606, 1483, 1377, 1352, 1163, 1118; HRMS $[M+H]^+$ found = 536.9268; $C_{24}H_{14}Br_2N_2OS$ required 536.9272.

4,8-Dibromo-12-[4-(trifluoromethyl)phenyl]-5*H*-thiopyrano[2,3-*b*:6,5-*b'*]diindole (10p): red powder (20 mg, 52%); ^{1}H-NMR (500 MHz, DMSO-*d*$_6$): δ 13.51 (brs, 1H, NH), 8.17 (d, 2H, *J* = 8.0 Hz, Ar-3’ and 5’H), 7.90 (d, 2H, *J* = 8.0 Hz, Ar-2’ and 6’H), 7.56 (dd, 2H, *J* = 7.7 and 0.7 Hz, H-9 and H-3), 7.02 – 6.80 (m, 2H, H-10 and H-2), 6.49 – 6.20 (m, 2H, H-11 and H-1); ^{13}C-NMR (125 MHz, DMSO-*d*$_6$): δ 147.1 (q), 140.9 (q), 130.9 (q), 128.9 (2 x CH), 128.6 (2 x CH), 127.3 (2 x CH), 124.6 (q), 123.0 (2 x CH), 119.9 (2 x CH); IR (KBr, cm^{-1}): 1705, 1487, 1379, 1321, 1165, 1124, 1066; HRMS $[M+H]^+$ found = 574.9034; $C_{24}H_{11}Br_2F_3N_2S$ required 574.9040.

4,8-Dibromo-12-phenyl-5*H*-thiopyrano[2,3-*b*:6,5-*b'*]diindole (10q): red powder (41 mg, 72%); ^{1}H-NMR (500 MHz, DMSO-*d*$_6$): δ 13.45 (brs, 1H, NH), 7.86 – 7.58 (m, 5H, Ph-H), 7.54 (d, 2H, *J* = 7.6 Hz, H-9 and H-3), 7.05 – 6.80 (m, 2H, H-10 and H-2), 6.61 – 6.26 (m, 2H, H-11 and H-1); ^{13}C-NMR (125 MHz, DMSO-*d*$_6$): δ 130.2 (5 x CH), 128.0 (2 x CH), 122.8 (2 x CH), 120.3 (2 x CH); IR (KBr, cm^{-1}): 1566, 1487, 1377, 1354, 1165, 1120; HRMS $[M+H]^+$ found = 506.9160; $C_{23}H_{12}Br_2N_2S$ required 506.9166.

4,8-Dibromo-12-(pyridin-4-yl)-5*H*-thiopyrano[2,3-*b*:6,5-*b'*]diindole (10r): red powder (18 mg, 34%); ^{1}H-NMR (500 MHz, DMSO-*d*$_6$): δ 13.71 (brs, 1H, NH), 9.07 – 8.97 (m, 2H, Py-2’ and 6’H), 7.80 – 7.70 (m, 2H, Py-3’ and 5’H), 7.58 (brd, 2H, *J* = 7.1 Hz, H-9 and H-3), 6.97 (brs, 2H, H-10 and H-2), 6.46 (brs, 2H, H-11 and H-1);^{13}C-NMR (125 MHz, DMSO-*d*$_6$): δ 151.8 (2 x CH), 129.7 (CH), 127.3 (CH), 123.0 (2 x CH), 122.7 (2 x CH), 120.7 (CH), 119.1 (CH); IR (KBr, cm^{-1}): 1607, 1571, 1492, 1357, 1165, 1124; HRMS $[M+H]^+$ found = 507.9111; $C_{22}H_{11}Br_2N_3S$ required 507.9118.

4,8-Dichloro-12-phenyl-5*H*-thiopyrano[2,3-*b*:6,5-*b'*]diindole (10s): red powder (25 mg, 49%); ^{1}H-NMR (500 MHz, DMSO-*d*$_6$): δ 13.76 (brs, 1H, NH), 7.83 – 7.77 (m, 3H, Ph-3’, 4’ and 5’H), 7.65 – 7.59 (m, 2H, Ph-2’ and 6’H), 7.41 (d, 2H, *J* = 7.8 Hz, H-9 and H-3), 7.02 – 6.92 (m, 2H, H-10 and H-2), 6.41 (brs, 2H, H-11 and H-1); ^{13}C-NMR (125 MHz, DMSO-*d*$_6$): δ 148.9 (q), 136.6 (q), 130.4 (2 x CH), 130.2 (CH), 127.4

(2 x CH), 125.2 (2 x CH), 122.5 (2 x CH), 119.7 (2 x CH); IR (KBr, cm^{-1}): 1615, 1548, 1500, 1425, 1382, 1352, 1159, 1138; HRMS $[M+H]^+$ found = 419.0174; $C_{23}H_{12}Cl_2N_2S$ required 419.0176.

4,8-Dichloro-12-(3,5-dimethoxyphenyl)-5*H*-thiopyrano[2,3-*b*:6,5-*b'*]diindole (10t): yellow powder (18 mg, 37%); ^{1}H-NMR (500 MHz, DMSO-*d*$_6$): δ 13.58 (s, 1H, NH), 7.41 (d, 2H, *J* = 7.5 Hz, H-9 and H-3), 7.15 – 7.05 (m, 2H, H-10 and H-2), 6.92 – 6.87 (m, 1H, Ar-4'H), 6.83 – 6.76 (m, 2H, Ar-2' and 6'H), 6.75 – 6.50 (m, 2H, H-11 and H-1), 3.82 (s, 6H, 2 x *O*CH$_3$); ^{13}C-NMR (125 MHz, DMSO-*d*$_6$): δ 125.3 (2 x CH), 122.6 (2 x CH), 119.9 (2 x CH), 105.5 (2 x CH), 102.0 (CH), 56.2 (2 x CH$_3$); IR (KBr, cm^{-1}): 2926, 1589, 1491, 1382, 1359, 1197, 1157, 1139, 1055; HRMS $[M+H]^+$ found = 479.0385; $C_{25}H_{16}Cl_2N_2O_2S$ required 479.0388.

5-Methyl-7-[4-(trifluoromethyl)phenyl]-5*H*-thiopyrano[2,3-*b*:4,5-*b'*]diindole (11): To a solution of 7-[4-(trifluoromethyl)phenyl]-5*H*-thiopyrano[2,3-*b*:4,5-*b*']diindole (**9a**, 20 mg, 0.047 mmol) in THF (0.3 mL) was added KO^{t}Bu (8.0 mg, 0.07 mmol) and stirred at room temperature for 15 min. Then to the reaction mixture iodomethane (4 μL, 0.062 mmol) was added dropwise at room temperature and reaction mixture was stirred for 1 h. After completion of the reaction, the reaction mixture was evaporated to Celite and the residue was subjected to column chromatography over silica (eluent: heptane – EtOAc, gradient) to yield the title product (13 mg, 62%) as a brown powder.^{1}H-NMR (500 MHz, DMSO-*d*$_6$): δ 8.74 (d, 1H, *J* = 7.7 Hz, H-1), 8.11 (d, 2H, *J* = 8.3 Hz, Ar-3' and 5'H), 8.06 (d, 2H, *J* = 8.0 Hz, Ar-2' and 6'H), 7.87 (d, 1H, *J* = 8.2 Hz, H-4), 7.75 (d, 1H, *J* = 7.7 Hz, H-11), 7.58 (td, 1H, *J* = 8.2 and 1.2 Hz, H-3), 7.52 – 7.44 (m, 2H, H-10 and H-2), 7.02 (t, 1H, *J* = 7.7 Hz, H-9), 6.91 (d, 1H, *J* = 7.7 Hz, H-8), 4.05 (s, 3H, *N*Me) ;^{13}C-NMR (125 MHz, DMSO-*d*$_6$): δ 158.0 (q), 155.9 (q), 139.3 (q), 139.0 (q), 138.3 (q), 137.2 (q), 131.3 (q), 131.0 (2 x CH), 130.4 (q), 129.5 (CH), 126.9 (2 x CH), 125.4 (CH), 124.5 (q), 124.3 (q) 123.2 (q), 122.8 (CH), 122.0 (2 x CH), 121.9 (CH), 119.1 (CH), 110.5 (CH), 108.9 (q), 31.8 (*N*Me); IR (KBr^{-1}): 1572, 1404, 1371, 1321, 1165, 1122, 1068; HRMS $[M+H]^+$ found = 433.0981; $C_{25}H_{15}F_3N_2S$ required 433.0986.

5-Methyl-7-[4-(trifluoromethyl)phenyl]-7,12-dihydro-5*H*-thiopyrano[2,3-*b*:4,5-*b'*]diindole (12): To a solution of 5-methyl-7-[4-(trifluoromethyl)phenyl]-5*H*-thiopyrano[2,3-*b*:4,5-*b*']diindole (**12**, 10 mg, 0.023 mmol) in MeOH (0.1 mL) was cooled to 0 °C. To the reaction mixture was added NaBH$_4$ (2 mg, 0.046 mmol) in small portions at 10 °C. The reaction mixture was stirred at room temperature for 1 h. Once the reaction was completed the reaction mixture was purified by preparative HPLC to yield the title product (5 mg, 50%) as a yellow powder. ^{1}H-NMR (500 MHz, DMSO-*d*$_6$): δ 11.54 (s, 1H, NH), 8.21 – 8.17 (m, 1H, H-1), 7.58 (d, 2H, *J* = 8.2 Hz, Ar-3' and 5'H), 7.50 – 7.41 (m, 4H, H-11, H-4, Ar-2' and 6'H), 7.27 – 7.17 (m, 3H, H-8, H-3 and H-2), 7.03 (td, 1H, *J* = 8.2 and 1.2 Hz, H-10), 6.94 (td, 1H, *J* = 8.2 and 1.2 Hz, H-9), 6.26 (s, 1H, H-7), 3.67 (s, 3H, *N*Me);^{13}C-NMR (125 MHz, DMSO-*d*$_6$): δ 148.6 (q), 137.8 (q), 136.9 (q), 133.0 (q), 131.6 (q), 128.2 (q), 128.0 (2 x CH), 126.0 (2 x CH), 125.8 (q), 124.6 (q),123.3 (q), 121.6 (CH), 120.8 (2 x CH), 120.0 (CH), 118.6 (CH), 117.2 (CH), 111.8 (CH), 110.3 (CH), 104.3 (q), 101.0 (q), 42.7 (CH), 31.2 (CH_3).

1,11-Dimethoxy-12-[4-(trifluoromethyl)phenyl]-7,12-dihydro-5*H*-thiopyrano[2,3-*b*:6,5-*b'*]diindole (13a): brown powder (10 mg, 18%); ^{1}H-NMR (500 MHz, DMSO-*d*$_6$): δ 11.50 (s, 2H, 2 x NH), 7.55 (d, 2H, *J* = 8.2 Hz, Ar-2' and 6'H), 7.47 (d, 2H, *J* = 8.2 Hz, Ar- 3' and 5'H), 6.93 (t, 2H, *J* = 8.0 Hz, H-9 and H-3), 6.87 (d, 2H, *J* = 8.0 Hz, H-8 and H-4), 6.43 (d, 2H, *J* = 8.0 Hz, H-10 and H-2), 6.38 (s, 1H, H-12), 3.87 (s, 6H, 2 x *O*CH_3); ^{13}C-NMR (125 MHz, DMSO-*d*$_6$): δ 154.5 (q), 153.2 (2 x q), 138.9 (2 x q), 129.5 (2 x CH), 126.4 (q), 124.8 (2 x CH), 124.7 (q), 122.4 (2 x CH), 121.0 (2 x q), 116.6 (2 x q), 111.5 (2 x q) 104.5 (2 x CH), 100.2 (2 x CH), 55.2 (2 x CH_3), 39.3 (CH); IR (KBr, cm^{-1}): 3404, 3350, 1504, 1429, 1323, 1257, 1138, 1101, 1099, 1066; HRMS $[M+H]^+$ found = 481.1194; $C_{26}H_{19}F_3N_2O_2S$ required 481.1197.

1,11-Dichloro-12-[4-(trifluoromethyl)phenyl]-7,12-dihydro-5*H*-thiopyrano[2,3-*b*:6,5-*b'*]diindole (13b): brown powder (110 mg, 78%); ^{1}H-NMR (500 MHz, DMSO-*d*$_6$): δ 12.10 (s, 2H, 2 x NH), 7.67 (d, 2H, *J* = 8.3 Hz, Ar-2' and 6'H), 7.53 (d, 2H, *J* = 8.3 Hz Ar-3' and 5'H), 7.33 (dd, 2H, *J* = 7.4 and 1.6 Hz, H-8 and H-4), 7.06 (t, 2H, *J* = 7.4 Hz, H-9 and H-3), 7.05 – 7.01 (m, 3H, H-12, H-10 and H-2); ^{13}C-NMR (125 MHz, DMSO-*d*$_6$): δ 152.7 (q), 138.9 (2 x q), 128.9 (2 x CH), 127.0 (q), 126.1 (2 x q), 125.5 (2 x CH), 124.3 (q), 123.3 (2 x q), 123.0 (2 x q), 122.6 (2 x CH), 120.9 (2 x CH), 111.4 (2 x q), 110.7 (2 x CH), 36.4 (CH); ^{19}F-NMR (DMSO-*d*$_6$): δ -60.8; IR (KBr, cm^{-1}): 3381, 1417, 1325, 1130, 1066; HRMS $[M+H]^+$ found = 489.0204; $C_{24}H_{13}Cl_2F_3N_2S$ required 489.0207.

1,11-Dichloro-12-(3,5-dimethoxyphenyl)-7,12-dihydro-5*H*-thiopyrano[2,3-*b*:6,5-*b'*]diindole (13c): brown powder (70 mg, 80%); ^{1}H-NMR (500 MHz, DMSO-*d*$_6$): δ 12.10 (s, 2H, 2 x NH), 7.32 (dd, 2H, *J* = 7.3 and 1.9 Hz, H-8 and H-4), 7.06 (t, 2H, *J* = 7.3 Hz, H-9 and H-3), 7.04 (d, 2H, *J* = 7.4 Hz, H-10 and H-2), 6.84 (s, 1H, H-12), 6.62 (d, 2H, *J* = 2.2 Hz, Ar-2' and 6'H), 6.19 (t, 1H, *J* = 2.2 Hz, Ar-4'H), 3.59 (s, 6H, 2 x *O*CH_3); ^{13}C-NMR (125 MHz, DMSO-*d*$_6$): δ 160.4 (2 x q), 150.1 (q), 138.9 (2 x q), 126.0 (2 x q), 123.4 (2 x q), 123.0 (2 x q), 122.4 (2 x CH), 120.8 (2 x CH), 112.1 (2 x q), 110.6 (2 x CH), 106.6 (2 x CH), 97.1 (CH), 55.3 (2 x CH_3), 36.3 (CH); IR (KBr, cm^{-1}): 3290, 2972, 1595, 1421, 1334, 1139, 1057, 748; HRMS $[M+H]^+$ found = 481.0540; $C_{25}H_{18}Cl_2N_2O_2S$ required 481.0544.

1,11-Dichloro-12-phenyl-7,12-dihydro-5*H*-thiopyrano[2,3-*b*:6,5-*b'*]diindole (13d): orange powder (15 mg, 31%); ^{1}H-NMR (500 MHz, DMSO-*d*$_6$): δ 12.01 (s, 2H, 2 x NH), 7.49 – 7.44 (m, 2H, Ph-2' and 6'H), 7.31 (dd, 2H, *J* = 7.4 and 1.6 Hz, H-8 and H-4), 7.15 – 7.10 (m, 2H, Ph-H-3' and 5'H), 7.06 – 7.00 (m, 5H, Ph-4'H, H-10, H-9, H-3 and H-2), 6.93 (s, 1H, H-12); ^{13}C-NMR (125 MHz, DMSO-*d*$_6$): δ 148.2 (q), 138.9 (2 x q), 128.4 (2 x CH), 128.1 (2 x CH), 126.2 (CH), 125.9 (2 x q), 123.4 (2 x q), 123.1 (2 x q), 122.4 (2 x CH), 120.7 (2 x CH), 112.4 (2 x q), 110.5 (2 x CH), 36.3 (CH); IR (KBr, cm^{-1}): 3370, 1560, 1417, 1328, 1184, 769, 738, 704; HRMS $[M+H]^+$ found = 421.0328; $C_{23}H_{14}Cl_2N_2S$ required 421.0333.

1,11-Dichloro-12-(4-nitrophenyl)-7,12-dihydro-5*H*-thiopyrano[2,3-*b*:6,5-*b'*]diindole (13e): tan powder (22 mg, 35%); ^{1}H-NMR (500 MHz, DMSO-*d*$_6$): δ 12.13 (s, 2H, 2 x NH), 8.07 – 8.02 (m, 2H, Ar-5' and 3'H), 7.74 – 7.70 (m, 2H, Ar-6' and 2'H), 7.33 (dd, 2H, *J* = 7.2 and 1.7 Hz, H-8 and H-4), 7.06 (t, 2H, *J* = 7.2 Hz, H-9 and H-3), 7.05 (s, 1H, H-12), 7.04 (dd, 2H, *J* = 7.2 and 1.7 Hz, H-10 and H-2); ^{13}C-NMR (125 MHz, DMSO-*d*$_6$): δ 155.6 (q), 146.1 (q), 138.9 (2 x q), 129.4 (2 x CH), 126.1 (2 x q), 124.0 (2 x CH), 123.2 (2 x q), 122.9 (2 x q), 122.7 (2 x CH), 120.9 (2 x CH), 110.9 (2 x q), 110.7 (2 x CH), 36.5 (CH); IR (KBr, cm^{-1}): 3387, 1510, 1421, 1334, 1188, 769, 738, 773, 734; HRMS [M-H]$^-$ found = 464.0033; $C_{23}H_{13}Cl_2N_3S$ required 464.0027.

Isolated and identified by-products for the support the suggested reaction pathway. All these compounds were isolated from the reactions run under the conditions for preparing of **10** after purification by preparative HPLC. No systematic isolation was attempted, they were identified only to support our mechanistic considerations.

2,3-*Bis*[4-(trifluoromethyl)phenyl]-8*H*-thieno[2,3-*b*]indole (14): yellow powder; ^{1}H-NMR (500 MHz, DMSO-*d*$_6$): δ 11.92 (s, 1H, NH), 7.89 (d, 2H, *J* = 8.2, 3-Ph-3' and 5'H), 7.72 (d, 2H, *J* = 8.2, 3-Ph-2' and 6'H), 7.67 (d, 2H, *J* = 8.3, 2-Ph-3' and 5'H), 7.56 – 7.52 (m, 1H, H-7), 7.42 (d, 2H, *J* = 8.3, 2-Ph-2' and 6'H), 7.28 (d, 1H, *J* = 8.0, H-4), 7.22 (td, 1H, *J* = 7.7 and 1.2 Hz ,H-6), 7.02 (td, 1H, *J* = 7.7 and 1.2 Hz, H-5); ^{13}C-NMR (125 MHz, DMSO-*d*$_6$): δ 142.2 (q), 140.8 (q), 140.1 (q), 138.9 (q), 131.0 (2 x CH), 130.4 (q), 129.7 (2 x CH) 128.7 (q), 128.5 (q), 127.5 (q), 126.4 (2 x CH),126.2 (2 x CH), 125.8 (q), 124.7 (q), 124.4 (q), 123.1 (CH), 121.7 (q), 119.8 (CH), 118.4 (CH), 112.5 (CH); ^{19}F-NMR (DMSO-*d*$_6$): δ -60.9, -61.0; IR (KBr, cm^{-1}): 3081, 1601, 1579, 1492, 1475, 1411, 1230. HRMS [M+H]$^+$ found = 462.0748; $C_{24}H_{13}F_6NS$ required 462.0751.

2,2'-Disulfanediyl *bis*(6-methoxy-3-{[4-(trifluoromethyl)phenyl]methyl}-1*H*-indole) (15): yellow powder; ^{1}H-NMR (500 MHz, DMSO-*d*$_6$): δ 11.52 (s, 2H, 2 x NH), 7.20 (d, 2H, *J* = 8.7 Hz, 2 x H-4), 7.06 (d, 4H, *J* = 8.2 Hz, 2 x Ar-3' and 2 x 5'H), 6.98 (d, 4H, *J* = 8.2 Hz, 2 x Ar-2' and 2 x 6'H), 6.77 (d, 2H, *J* = 2.1 Hz, 2 x H-7), 6.61 (dd, 2H, *J* = 8.7 and 2.1 Hz, 2 x H-5), 3.79 (s, 4H, 2 x CH_2), 3.72 (s, 6H, 2 x *O*CH_3); ^{13}C-NMR (125 MHz, DMSO-*d*$_6$): δ 157.9 (2 x q), 145.6 (2 x q), 125.3 (2 x q), 139.3 (2 x q), 129.2 (4 x CH), 126.8 (2 x q), 125.1 (4 x CH), 123.6 (2 x q), 122.4 (2 x q), 121.4 (2 x q), 120.8 (2 x CH), 111.0 (2 x CH), 94.3 (2 x CH), 55.6 (2 x CH_3), 30.3 (2 x CH_2); IR (KBr, cm^{-1}): 3396, 2904, 1624, 1321, 1159, 1119, 1064; HRMS [M-H]$^-$ found = 671.1265; $C_{16}H_{10}N_2S$ required 671.1261.

5,7-Dihydrothieno[2,3-*b*:5,4-*b'*]diindole (17): yellow powder; ^{1}H-NMR (500 MHz, DMSO-*d*$_6$): δ 12.15 (s, 2H, NH), 7.50 – 7.47 (m, 2H, H-8 and H-4), 7.35 – 7.29 (m, 2H, H-9 and H-3), 7.29 – 7.26 (m, 2H, H-11 and H-1), 7.07 (m, 2H, H-10 and H-2); ^{13}C-NMR (125 MHz, DMSO-*d*$_6$): δ 136.7 (2 x q), 127.4 (2 x q), 125.3 (2 x q), 125.0 (2 x CH), 120.7 (2 x CH), 120.6 (2 x CH), 119.7 (2 x q), 112.6 (2 x CH); IR (KBr, cm^{-1}): 3380, 2962, 1614, 1560, 1259, 12018, 796, 740; HRMS [M+H]$^+$ found = 263.0635; $C_{16}H_{10}N_2S$ required 263.0643.

1,12-Dichloro-13-[4-(trifluoromethyl)phenyl]-8,13-dihydro-5*H*-[1,2]dithiepino[3,4-*b*:7,6-*b'*]diindole (19): brown powder; ^{1}H-NMR (500 MHz, DMSO-*d*$_6$): δ 12.17 (s, 2H, NH), 8.03 (s, 1H, H-13), 7.56 (d, 2H, *J* = 8.4 Hz, Ar-3' and 5'H), 7.36 (dd, 2H, *J* = 7.9 and 1.0 Hz, H-9 and H-4), 7.26 (d, 2H, *J* = 8.4 Hz, Ar-2' and 6'H), 7.15 (t, 2H, *J* = 7.9 Hz, H-10 and H-3), 7.10 (dd, 2H, *J* = 7.9 and 1.0 Hz, H-11 and H-2); ^{13}C-NMR (125 MHz, DMSO-*d*$_6$): δ 153.3 (q), 137.3 (2 x q), 131.5 (2 x q), 128.7 (2 x CH), 126.3 (q), 125.3 (q), 125.2 (2 x CH), 124.2 (q), 124.0 (2 x q), 123.3 (2 x CH), 121.8 (2 x CH), 115.1 (2 x q), 111.3 (2 x CH), 36.1 (CH); IR (KBr, cm^{-1}): 3395, 1707, 1419 1323, 1114, 1062; HRMS [M-H]$^-$ found = 518.9779; $C_{24}H_{13}Cl_2$ F_3NS_2 required 518.9770.

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