Preliminary Communication

T.A. Jenifer Vijay, Nagarakere C. Sandhya, C.S. Pavankumar, Kanchugarakoppal S. Rangappa* and Kempegowda Mantelingu*

Ligand- and catalyst-free intramolecular C-S bond formation: direct access to indalothiochromen-4-ones

DOI 10.1515/hc-2014-0206
Received January 9, 2015; accepted March 10, 2015

Abstract: An efficient ligand- and catalyst-free intramolecular *S*-arylation leading to the direct synthesis of indalothiochromen-4-ones from simple dithioesters under mild conditions has been developed. This method is particularly noteworthy given its experimental simplicity, high generality, and good functional group toleration.

Keywords: dithioesters; indalothiochromen-4-ones; *S*-arylation; Vilsmeier-Haack reaction.

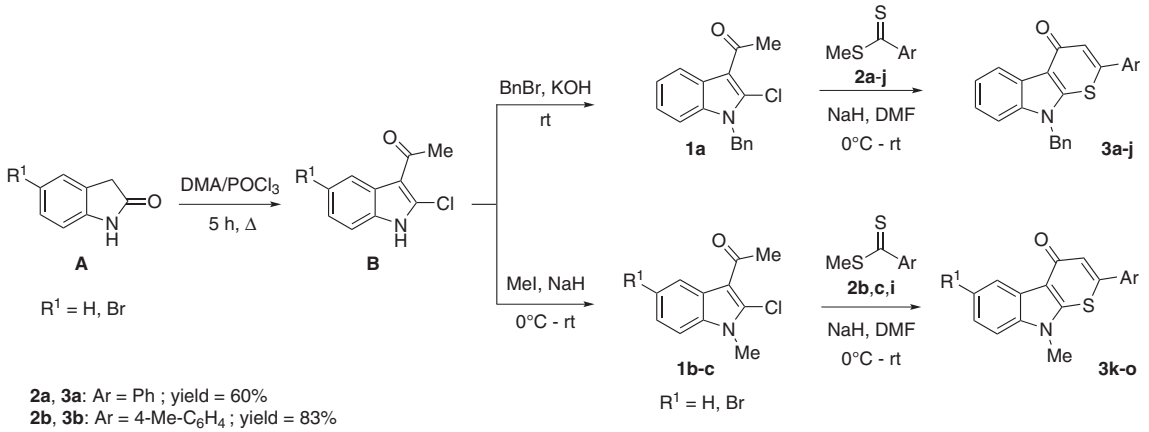
The indole subunits have always fascinated the researchers for their recurrent presence in most of the biologically active natural products [1–5]. The polycyclic annulated indole compounds have drawn the interest of chemists to design their synthesis and study their interaction with enzymes in biological systems [6–10]. For example, polycyclic indole alkaloids such as ajmaline [11], ervincidine [12], alistonitrine [13], MGM-16, and mitragynine [14] are important in both biology and medicinal chemistry.

A wide range of sulfur-heterocyclic scaffolds such as thiopyrans and fused-thiopyran derivatives, including benzothiopyrans, have been reported for their biological activity [15–19]. Annulation of the indole ring to the thiopyran makes it even more interesting in the synthetic and biological perspective [9, 20, 21]. On the basis of these considerations and our interest in developing new synthetic strategies for the synthesis of biologically viable heterocycles [22–28], we herein report an improved method for the synthesis of indalothiochromen-4-ones.

The literature reports reveal only a few synthetic methods for the construction of indalothiochromen-4-ones. The earliest report on the synthesis of such compounds is the reaction of propiolic acid and 3-mercaptoindole followed by treatment with phosphoric acid [29], but this method has not attracted much attention. Indoline-2-thione was exploited more as a starting material than any other reactants [21, 30–33]. The *thio*-Claisen rearrangement of 2-(4′-aryloxybut-2′-ynylthio)-1-methylindole derived from indoline-2-thione and 1-aryloxy-4-chlorobut-2-yne has also been reported [34]. On the other hand, the use of dithioesters as a sulfur source to afford indalothiochromen-4-ones has not been explored yet to the best of our knowledge. Herein, we report the new and efficient synthesis of indalothiochromen-4-ones by the reaction of simple 1-(2-chloro-1*H*-indol-3-yl)ethanone and dithioesters under basic conditions at room temperature.

The starting materials *N*-alkyl/aryl indoles **1a-c** were synthesized according to the reported method [35]. Initially, the Vilsmeier-Haack reaction of oxindoles (**A**) yielded 3-acetyl 2-chloro indoles (**B**). These products were next, either benzylated or methylated using benzyl bromide and methyl iodide, respectively (Scheme 1). The starting materials dithioesters were also synthesized by the known method with slight modifications. The aryl halides were converted into Grignard reagents, which were further allowed to react with carbon disulfide to form a thiocarbonyl-thio salt. Subsequently, treatment of the thiocarbonyl-thio salt with an alkyl halide yielded the desired dithioesters **2a-j** [36]. As can be seen from Scheme 1, 1-(2-chloro-1*H*-indol-3-yl)ethanone (**1a**) was treated with dithioester **2a** in DMF in the presence of sodium hydride at room temperature to furnish 2-phenyl-thiopyrano[2,3-*b*]

***Corresponding authors: Kanchugarakoppal S. Rangappa and Kempegowda Mantelingu,** Department of Studies in Chemistry, Manasagangothri, University of Mysore, Mysore 570006, India, e-mail: rangappaks@gmail.com (K.S. Rangappa); kmantelingu@yahoo.com (K. Mantelingu)
T.A. Jenifer Vijay, Nagarakere C. Sandhya and C.S. Pavankumar: Department of Studies in Chemistry, Manasagangothri, University of Mysore, Mysore 570006, India



2a, **3a**: Ar = Ph ; yield = 60%
2b, **3b**: Ar = 4-Me-C_6H_4 ; yield = 83%
2c, **3c**: Ar = 4-OMe-C_6H_4; yield = 78%
2d, **3d:** Ar = 3,4-$(OMe)_2$-C_6H_3; yield = 62%
2e, **3e:** Ar = 3,4,5-$(OMe)_3C_6H_2$; yield = 76%
2f, **3f:** Ar = 4-Cl-C_6H_4; yield = 67%
2g, **3g:** Ar = 4-Br-C_6H_4; yield = 61%
2h, **3h:** Ar = 4-F-C_6H_4; yield = 53%
2i, **3i**: Ar = thiophen-2-yl; yield = 63%
2j, **3j**: Ar = benzo[*b*]thiophen-3-yl; yield = 56%

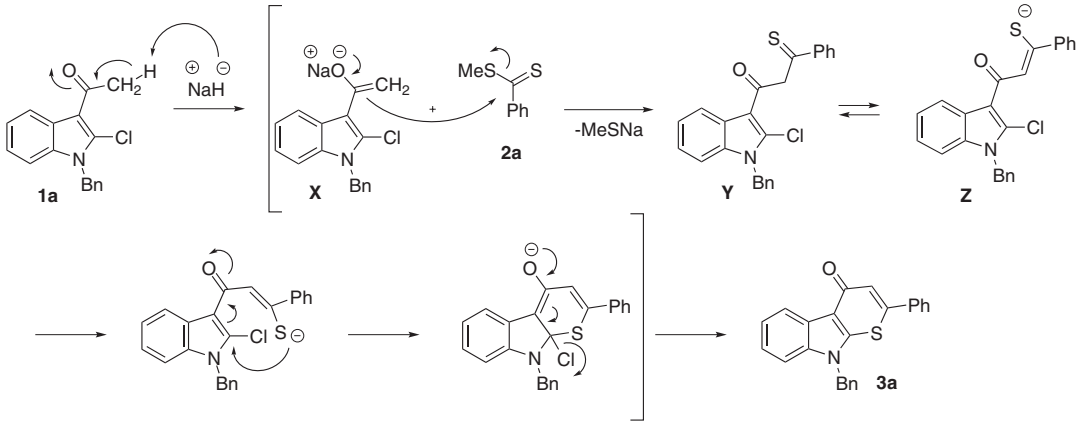
2b, 3k: R^1 = H; Ar = 4-Me-C_6H_4; yield = 58%
2c, 3l: R^1 = H; Ar = 4-OMe-C_6H_4; yield = 51%
2i, 3m: R^1 = H; Ar = thiophen-2-yl; yield = 63%
2b, 3n: R^1 = Br; Ar = 4-Me-C_6H_4; yield = 52%
2c, 3o: R^1 = Br; Ar = 4-OMe-C_6H_4; yield = 48%

Scheme 1 Synthesis route of 2-aryl/heteroaryl-thiopyrano[2,3-*b*]indol-4-(9*H*)–ones.

indol-4-(9*H*)-one thiochromone (**3a**) in good yield. The mildest conditions possible under which the reaction of compound **1a** with dithioester **2a** would proceed with a synthetically useful rate were investigated. The reaction conducted under reflux in DMF in the presence of NaH (1.5 Eq) required 24 h to reach completion and provided the desired product **3a** in 40% yield. The use of other bases than NaH, including K_2CO_3, TEA, KOH**,** *t*-BuOK, and MeONa, gave rise to significantly lower yields or no product **3a** at all.

Therefore, the reaction was optimized by varying the amount of the base NaH, solvent, and temperature. The reaction was found to proceed efficiently at room temperature with the highest yield of 60% of **3a** obtained in the presence of 2.5 Eq of NaH. A decrease in the amount of NaH to 2.0 Eq had negative effect on the yield of **3a** (55%), whereas the use of 3.0 Eq did not lead to any significant increase in the yield compared to the application of 2.5 Eq of NaH. Screening of various solvents, including toluene, THF, diethyl ether and DMF, showed that DMF is the most suitable medium. The reaction of **1a** with **2a** showed no improvement upon raising the temperature. Subsequently, the reactions of *N*-alkyl/aryl indole derivatives **1a-c** with wide range of dithioesters **2a-j** were evaluated under the optimized conditions. In all cases, the products were obtained in moderate to good yield at room temperature.

Interestingly, the LCMS analysis of crude product **3h** suggested a contamination with a trace amount of



Scheme 2

9-benzyl-2-(4-(methylthio)phenyl)thiopyrano[2,3-*b*]indol-4(9*H*)-one [28, 37] (not shown). The suggested S_NAr substitution reaction of the halogen atom by the methylthio group did not take place with 4-chlorophenyl and 4-bromophenyl substituted indalothiochromen-4-ones **3f,g**. The heterocyclic dithioesters of benzothiophene **2i** and thiophene **2j** underwent the reaction with **1a** and **1c**, efficiently furnishing the corresponding indalothiochromen-4-ones **3i, 3j,** and **3m** in 63%, 56%, and 63% yields, respectively. 6-Bromo substituted indalothiochromen-4-ones **3n** and **3o** were obtained in the respective yields of 52% and 48%. The structures of all these products were characterized and confirmed by spectral analyses.

We propose that the reaction proceeds according to the mechanism shown in Scheme 2, exemplified by the particular reaction of **1a** with **2a**. The carbanion intermediate **X** undergoes a reaction with dithioester **2a** to afford 1,3-thioketone **Y**, which then undergoes keto-enol tautomerization to generate another intermediate product **Z**. Finally, an intramolecular addition of mercapto group in **Z** followed by elimination of halide ion led to the formation of the observed product **3a**.

Experimental details

All materials were purchased from known commercial sources and used without further purification. Thin layer chromatography (TLC) analysis was performed with silica gel $60F_{254}$ aluminum sheets (Merck). Mixtures of hexanes and ethyl acetate in different ratios were used in TLC analysis. Melting points were determined in open capillaries and are uncorrected. Infrared (IR) spectra were recorded on FT-IR spectrometer in KBr pellets. ^{1}H NMR (400 MHz) and ^{13}C NMR (100 MHz) spectra were collected at NMR Facility, IOE, University of Mysore.

One-pot synthesis of indalothiochromen-4-ones 3a-o

A solution of *N,N*-dimethylformamide (DMF, 10.5 mL, 3 Eq) in dichloromethane (20 mL) was treated dropwise at 0°C with a solution of phosphorus oxychloride (11 mL, 3 Eq) in dichloromethane (20 mL). The mixture was stirred for 15 min, then treated slowly with a solution of 2-oxindole (**A**, 5 g, 1 Eq) in chloroform (20 mL), and stirred under reflux for 5 h. After the addition of crushed ice and stirring for an additional 20 min, the separation of two layers was observed. The aqueous layer was adjusted to pH 7 with sodium acetate. The mixture was left at room temperature overnight, and then the resultant precipitate of product **B** was collected by filtration, washed with water, and dried [35].

Next, a mixture of compound **B** (2.5 g) and potassium hydroxide (1.25 g, 1.5 Eq) in dry DMF (10 mL) was stirred for 10 min before treatment with benzyl bromide (1.4 mL, 1.1 Eq). The mixture was stirred at room temperature until substrate **B** was completely consumed, as monitored by TLC analysis. The mixture was then poured into water and extracted with ethyl acetate. The organic extract was dried over sodium sulfate and concentrated. The residue of product **1a** was crystallized from diethyl ether.

A solution of compound **1** (1.0 mmol, 1.0 Eq) in DMF (2 mL) was added at 0°C to a 60% suspension of NaH in mineral oil (2.5 mmol, 2.5 Eq), and the mixture was stirred for 15 min at room temperature. Then a solution of dithioester **2** (1.0 mmol, 1.0 Eq) in DMF (2 mL) was added over a period of 10 min at 0°C, and the mixture was stirred at room temperature for an additional 7 h. The progress of the reaction was monitored by TLC. The mixture was poured into water and extracted with ethyl acetate (2×25 mL). The combined organic layers were washed with brine (25 mL) and dried over anhydrous sodium sulfate. The solvent was removed under reduced pressure, and the crude product was passed through a small plug of silica eluting with hexane/ethyl acetate (8:2) to afford indalothiochromen-4-ones **3a-o**. Representative products are characterized as follows. Characterization of all compounds is given in Supplementary Information.

9-Benzyl-2-phenylthiopyrano[2,3-*b*]indol-4(9*H*)-one (3a) Compound **3a** was obtained by the reaction of **1a** and **2a** in 60% yield as a pale brown solid; mp 164–166°C; ^{1}H NMR ($CDCl_3$): δ 8.65 (d, *J* = 4.8 Hz, 1H), 7.60 (t, *J* = 3.6 Hz, 2H), 7.46–7.45 (m, 3H), 7.38–7.36 (m, 3H), 7.29–7.25 (m, 4H), 7.14 (d, *J* = 6.4 Hz, 2H), 5.43 (s, 2H); ^{13}C NMR ($CDCl_3$): δ 178.6, 143.9, 142.9, 137.9, 136.5, 134.6, 130.3, 129.0, 127.2, 127.0, 126.6, 124.7, 122.7, 122.4, 114.2, 108.9, 48.2; IR: 1597, 1481, 1474, 1419, 1334, 873, 750, 743, 717, 612 cm^{-1}; MS (ESI): *m/z* = 368.1 (M^+). Anal. Calcd for $C_{24}H_{17}NOS$: C, 78.45; H, 4.66; N, 3.81. Found: C, 78.43; H, 4.64; N, 3.79.

9-Benzyl-2-(3,4,5-trimethoxyphenyl)thiopyrano[2,3-*b*]indol-4(9*H*)-one (3e) Compound **3e** was obtained by the reaction of **1a** and **2e** in 76% yield as pale yellow solid; mp 169–171°C; ^{1}H NMR (DMSO-d_6): δ 8.43 (d, *J* = 7.7 Hz, 1H), 7.76 (d, *J* = 8.1 Hz, 1H), 7.42 (t, *J* = 7. 2 Hz, 1H), 7.44–7.23 (m, 7H), 7.02 (s, 2H), 5.73 (s, 2H), 3.89 (s, 6H), 3.73 (s, 3H); ^{13}C NMR (DMSO-d_6): δ 177.8, 153.8, 144.1, 142.7, 138.1, 136.0, 131.8, 129.3, 128.4, 127. 5, 126.2, 125.0, 124.4, 122.6, 121.8, 110.7, 105.1, 60.6, 56.6, 48.0; IR: 1599, 1505, 1479, 1420, 1332, 1249, 1126, 1008, 829, 758, 667 cm^{-1}; MS (ESI): *m/z* = 458.7 (M^+). Anal. Calcd for $C_{24}H_{16}ClNOS$: C, 70.88; H, 5.07; N, 3.06. Found: C, 70.85; H, 5.05; N, 3.05.

9-Benzyl-2-(4-fluorophenyl)thiopyrano[2,3-*b*]indol-4(9*H*)-one (3h) Compound **3h** was obtained by the reaction of **1a** and **2h** in 53% yield as creamy solid; mp 155–157°C; ^{1}H NMR ($CDCl_3$): δ 8.59 (d, *J* = 4.8 Hz, 1H), 7.61–7.57 (m, 2H), 7.42–7.25 (m, 7H), 7.20–7.13 (m, 4H), 5.47 (s, 2H); ^{13}C NMR ($CDCl_3$): δ 165.3, 162.8, 138.0, 134.3, 132.3, 129.2, 128.3, 126.1, 125.1, 124.3, 122.7, 116.4, 109.0, 48.4; IR: 1607, 1486, 1452, 1230, 1162, 1107, 1334, 833, 746, 559 cm^{-1}; MS (ESI): *m/z* = 386.6 (M^+). Anal. Calcd for $C_{24}H_{16}ClNOS$: C, 74.78; H, 4.18; N, 3.63. Found: C, 74.76; H, 4.16; N, 3.62.

2-(Benzo[*b*]thiophen-3-yl)-9-benzylthiopyrano[2,3-*b*]indol-4(9*H*)-one (3j) Compound **3j** was obtained by the reaction of **1a** and **2j** in 56% yield as amber solid; mp 145–149°C; ^{1}H NMR ($CDCl_3$): δ 8.47 (d, *J* = 7.2 Hz, 1H), 8.01 (d, *J* = 8.0 Hz, 2H), 7.85–7.75 (m, 4H), 7.42–7.31 (m, 5H), 7.25–7.18 (m, 2H), 7.12 (d, *J* = 7.6 Hz, 1H), 5.51 (s, 2H); ^{13}C NMR ($CDCl_3$): δ 182.1, 147.8, 141.1, 137.5, 135.9, 132.1, 129.3, 128.8, 128.6, 127.6, 126.6, 125.1, 124.6, 122.5, 122.2, 121.4, 119.8, 112.5, 110.9, 109.9, 60.7; IR: 1586, 1480, 1424, 1419, 1266, 1117, 755, 752, 733, 401 cm^{-1}; MS (ESI): *m/z* = 423.8 (M^+). Anal. Calcd for $C_{26}H_{17}NOS_2$: C, 73.73; H, 4.05; N, 3.31. Found: C, 73.72; H, 4.03; N, 3.30.

6-Bromo-9-methyl-2-(*p*-tolyl)thiopyrano[2,3-*b*]indol-4(9*H*)-one (3n) Compound **3n** was obtained by the reaction of **1c** and **2b** in 52% yield as pale brown solid; mp 168–170 °C; ^{1}H NMR ($CDCl_3$): δ 8.73 (s, 2H), 8.59 (d, *J* = 6.8 Hz, 1H), 7.41 (dd, *J* = 6.6, 1.2 Hz, 2H), 7.34–7.29 (m, 2H), 6.94 (d, *J* = 8.8 Hz, 1H), 3.81 (s, 3H), 2.12 (s, 3H); ^{13}C NMR ($CDCl_3$): δ 176.8, 147.9, 138.0, 136.4, 134.8, 129.0, 128.8, 128.7, 126.3, 124.7, 123.5, 121.1, 113.8, 111.8, 110.2, 36.6, 21.3; IR: 1594, 1480, 1424, 1363,1234, 1194, 1052, 1016, 851, 810, 732, 705 cm^{-1}; MS (ESI): *m/z* = 322.12 (M^+). Anal. Calcd for $C_{19}H_{14}BrNOS$: C, 59.38; H, 3.67; N, 3.64. Found: C, 59.36; H, 3.66; N, 3.63.

Supplementary material

Experimental procedures for **1a-c** and **2a-j** and characterization of the remaining products **3** are available as supplementary material on the journal's website.

Acknowledgments: The Ministry of Human Resource Development (MHRD) and the University Grant Commission (UGC), New Delhi, India, are acknowledged for recognizing the University of Mysore as the Institute of Excellence and for the financial assistance. We also thank NMR Facility, IOE, University of Mysore, Manasagangotri, Mysore, India, for spectral data.

References

[1] Negi, A.; Singla, R.; Singh, V. Indole based alkaloid in cancer: an overview. *PharmaTutor* **2014**, *2*, 76–82.

[2] Aygun, A.; Pindur, U. Chemistry and biology of new marine alkaloids from the indole and annelated indole series. *Curr. Med. Chem.* **2003**, *10*, 1113–1127.

[3] Srivastava, A.; Pandeya, S. N. Indole a versitile nucleus in pharmaceutical field. *Int. J. Current Pharm. Rev. Res.* **2011**, *1*, 1–17.

[4] Lounasmaa, M.; Tolvanen, A. Simple indole alkaloids and those with a nonrearranged monoterpenoid unit. *Nat. Prod. Rep.* **2000**, *17*, 175–191.

[5] Vine, K. L.; Matesic, L.; Locke, J. M.; Ranson, M.; Skropeta, D. Cytotoxic and anticancer activities of isatin and its derivatives: a comprehensive review. *Anticancer. Agents Med. Chem.* **2009**, *9*, 397–414.

[6] Takada, S.; Ishizuka, N.; Sasatani, T.; Makisumi, Y,; Jyoyama, H.; Hatakeyama, H.; Asanuma F.; Hirose, K. Studies on fused indoles. II. Structural modifications and analgesic activity of 4-aminomethyltetrahydrothiopyrano [2, 3-*b*] indoles. *Chem. Pharm. Bull. (Tokyo)* **1984**, *32*, 877–886.

[7] El-Agrody, A. M.; Fouda, A. M.; Al-Dies, A.-A. M. Studies on the synthesis, *in vitro* antitumor activity of 4*H*-benzo[*h*]chromene, 7*H*-benzo[*h*]chromene[2,3-*d*]pyrimidine derivatives and structure-activity relationships of the 2-,3- and 2,3-positions. *Med. Chem. Res.* **2014**, *23*, 3187–3199.

[8] Parmar, N. J.; Labana, B. M.; Barad, H. A.; Kant, R.; Gupta, V. K. An efficient domino Knoevenagel/hetero-Diels-Alder route to some novel thiochromenoquinoline-fused polyheterocycles. *Monatshefte für Chemie* **2014**, *145*, 1179–1189.

[9] Takada, S.; Makisumi, Y. Studies on fused indoles. I. Novel synthesis of 4-aminomethyltetrahydrothiopyrano [2, 3-*b*] indoles through a thio-claisen rearrangement. *Chem. Pharm. Bull. (Tokyo)* **1984**, *32*, 872–876.

[10] Chu, X.-Q.; Zi, Y.; Lu, X.-M.; Wang, S.-Y.; Ji, S.-J. Intramolecular Pd-catalyzed C–H functionalization: construction of fused tetracyclic bis-indole alkaloid analogues. *Tetrahedron* **2014**, *70*, 232–238.

[11] Mullish, B. H.; Fofaria, R. K.; Smith, B. C.; Lloyd, K.; Lloyd, J.; Goldin, R. D.; Dhar, A. Severe cholestatic jaundice after a single administration of ajmaline; a case report and review of the literature. *BMC Gastroenterol.* **2014**, *14*, 60–70.

[12] Rallapalli, S. K.; Namjoshi, O. A.; Tiruveedhula, V. V. N. P. B.; Deschamps, J. R.; Cook, J. M. Stereospecific total synthesis of the indole alkaloid ervincidine. Establishment of the C-6 hydroxyl stereochemistry. *J. Org. Chem.* **2014**, *79*, 3776–3780.

[13] Zhu, G.-Y.; Yao, X.-J.; Liu, L.; Bai, L.-P.; Jiang, Z.-H. Alistonitrine A, a caged monoterpene indole alkaloid from Alstonia scholaris. *Org. Lett.* **2014**, *16*, 1080–1083.

[14] Matsumoto, K.; Narita, M.; Muramatsu, N.; Nakayama, T.; Misawa, K.; Kitajima, M.; Tashima, K.; Devi, L. A.; Suzuki, T.; Takayama, H.; et al. Orally active opioid μ/δ dual agonist MGM-16, a derivative of the indole alkaloid mitragynine, exhibits potent antiallodynic effect on neuropathic pain in mice. *J. Pharmacol. Exp. Ther.* **2014**, *348*, 383–392.

[15] Van Vliet, L. A.; Rodenhuis, N.; Dijkstra, D.; Wikström, H.; Pugsley, T. A.; Serpa, K. A.; Meltzer, L. T.; Heffner, T. G.; Wise, L. D.; Lajiness, M. E.; et al. Synthesis and pharmacological evaluation of thiopyran analogues of the dopamine D3 receptor-selective agonist (4aR,10bR)-(+)-*trans*-3,4,4a,10b-tetrahydro-4-*n*-propyl-2*H*,5*H* [1*b*]enzopyrano[4,3-*b*]-1,4-oxazin-9-ol (PD 128907). *J. Med. Chem.* **2000**, *43*, 2871–2882.

[16] Brown, M. J.; Carter, P. S.; Fenwick, A. S.; Fosberry, A. P.; Hamprecht, D. W.; Hibbs, M. J.; Jarvest, R. L.; Mensah, L.; Milner, P. H.; O'Hanlon, P. J.; et al. The antimicrobial natural product chuangxinmycin and some synthetic analogues are potent and selective inhibitors of bacterial tryptophanyl tRNA synthetase. *Bioorg. Med. Chem. Lett.* **2002**, *12*, 3171–3174.

[17] Sugita, Y.; Hosoya, H.; Terasawa, K.; Yokoe, I.; Fujisawa, S.; Sakagami, H. Cytotoxic activity of benzothiepins against human oral tumor cell lines. *Anticancer Res.* **2001**, *21*, 2629–2632.

[18] Quaglia, W.; Pigini, M.; Piergentili, A.; Giannella, M.; Gentili, F.; Marucci, G.; Carrieri, A.; Carotti, A.; Poggesi, E.; Leonardi, A.; et al. Structure-activity relationships in 1,4-benzodioxan-related compounds. 7. Selectivity of 4-phenylchroman analogues for α(1)-adrenoreceptor subtypes. *J. Med. Chem.* **2002**, *45*, 1633–1643.

[19] Carter, J. S.; Rogier, J. D. J.; Talley, J. J. Dihydrobenzopyrans, dihydrobenzothiopyrans, and tetrahydroquinolines for the treatment of cox-2-mediated disorders. *J. Med. Chem*. **2001, *44***, 211-220.

[20] Voskressensky, L. G.; Festa, A. A.; Varlamov, A. V. Domino reactions based on Knoevenagel condensation in the synthesis of heterocyclic compounds. Recent advances. *Tetrahedron* **2014**, *70*, 551–572.

[21] Majumdar, K. C.; Ponra, S.; Ghosh, T. Green approach to highly functionalized thiopyrano derivatives via domino multi-component reaction in water. *RSC Adv.* **2012**, *2*, 1144–1150.

[22] Raghavendra, G. M.; Ramesha, A. B.; Revanna, C. N.; Nandeesh, K. N.; Mantelingu, K.; Rangappa, K. S. One-pot tandem approach for the synthesis of benzimidazoles and benzothiazoles from alcohols. *Tetrahedron Lett.* **2011**, *52*, 5571–5574.
[23] Vinayaka, A. C.; Sadashiva, M. P.; Wu, X.; Biryukov, S. S.; Stoute, J. A.; Rangappa, K. S.; Gowda, D. C. Facile synthesis of antimalarial 1,2-disubstituted 4-quinolones from 1,3-bisarylmonothio-1,3-diketones. *Org. Biomol. Chem.* **2014**, *12*, 8555–8561.
[24] Ramesha, A. B.; Raghavendra, G. M.; Nandeesh, K. N.; Rangappa, K. S.; Mantelingu, K. Tandem approach for the synthesis of imidazo[1,2-a]pyridines from alcohols. *Tetrahedron Lett.* **2013**, *54*, 95–100.
[25] Kumar, S. V.; Yadav, S. K.; Raghava, B.; Saraiah, B.; Ila, H.; Rangappa, K. S.; Hazra A. Cyclocondensation of arylhydrazines with 1,3-bis(het)arylmonothio-1,3-diketones and 1,3-bis(het) aryl-3-(methylthio)-2-propenones: synthesis of 1-aryl-3,5-bis(het)arylpyrazoles with complementary regioselectivity. *J. Org. Chem.* **2013**, *78*, 4960–4973.
[26] Revanna, C. N.; Raghavendra, G. M.; Jenifer Vijay, T. A.; Rangappa, K. S.; Badregowda, D. G.; Mantelingu, K. Propylphosphonic anhydride-catalyzed tandem approach for Biginelli reaction starting from alcohols. *Chem. Lett.* **2014**, *43*, 178–180.
[27] Nandeesh, K. N.; Raghavendra, G. M.; Revanna, C. N.; Jenifer Vijay, T. a.; Rangappa, K. S.; Mantelingu, K. Recyclable, graphite-catalyzed, four-component synthesis of functionalized pyrroles. *Synth. Commun.* **2014**, *44*, 1103–1110.
[28] Jenifer Vijay, T. A.; Nandeesh, K. N.; Raghavendra, G. M.; Rangappa, K. S.; Mantelingu, K. Transition metal free intramolecular S-arylation: one-pot synthesis of thiochromen-4-ones. *Tetrahedron Lett.* **2013**, *54*, 6533–6537.
[29] Brown, E. R. Indolothiopyrones. *US 4032537 A 19770628*, **1977**.
[30] Majumdar, K. C.; Ponra, S.; Nandi, R. K. One-pot efficient green synthesis of spirooxindole-annulated thiopyran derivatives via Knoevenagel condensation followed by Michael addition. *Tetrahedron Lett.* **2012**, *53*, 1732–1737.
[31] Suzuki, T.; Matsuhisa, A.; Miyata, K.; Yanagisawa, I.; Ohta, M. Novel 5-hydroxytryptamine (5-HT3) receptor antagonists. Synthesis and structure-activity relationships of 9-methyl-2, 3, 4, 9-tetrahydrothiopyrano[2, 3-*b*]indol-4-one derivatives. *Chem. Pharm. Bull. (Tokyo)* **1997**, *45*, 101–106.
[32] Kopecky, J.; Smejkal, J. The synthesis of 1,4-dihydroxy- and 1,4-dihalogenobicyclo[2.2.2]octanes. *Tetrahedron Lett.* **1967**, *8*, 3889–3891.
[33] Majumdar, K. C.; Taher, A.; Ray, K. Domino-Knoevenagel-hetero-Diels-Alder reactions: an efficient one-step synthesis of indole-annulated thiopyranobenzopyran derivatives. *Tetrahedron Lett.* **2009**, *50*, 3889–3891.
[34] Majumdar, K. C.; Alam, S. Regioselective unusual formation of spirocyclic 4-{2′-benzo(2′,3′-dihydro)furo}-9-methyl-2,3,9-trihydrothiopyrano[2,3-*b*]indole by 4-exo-trig aryl radical cyclization and rearrangement. *Org. Lett.* **2006**, *8*, 4059–4062.
[35] Monge, A.; Palop, J.; Ramirez, C.; Font, M.; Fernandez-Alvarez, E. New 5*H*-1,2,4-triazino[5,6-*b*]indole and aminoindole derivatives. Synthesis and studies as inhibitors of blood platelet aggregation, anti-hypertensive agents and thromboxane synthetase inhibitors. *Eur. J. Med. Chem.* **1991**, *26*, 179–188.
[36] Perrier, S.; Takolpuckdee, P. Macromolecular design via reversible addition-fragmentation chain transfer (RAFT)/xanthates (MADIX) polymerization. *J. Polym. Sci. Part A Polym. Chem.* **2005**, *43*, 5347–5393.
[37] Li, M.; Cao, H.; Wang, Y.; Lv, X.-L.; Wen, L. One-pot multicomponent cascade reaction of N,S-ketene acetal: solvent-free synthesis of imidazo[1,2-*a*]thiochromeno[3,2-*e*]pyridines. *Org. Lett.* **2012**, *14*, 3470–3473.

Supplemental Material: The online version of this article (DOI: 10.1515/hc-2014-0206) offers supplementary material, available to authorized users.