DOI: 10.1002/cjoc.201500572

Efficient One-Pot Access to 2,9-Dihydrothiopyrano[2,3-*b*]indole Scaffolds Showing Large Stokes Shifts

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A simple, mild and efficient one-pot approach for the construction of 2-aryl-3-nitro-2,9-dihydrothiopyrano-[2,3-*b*]indole derivatives has been realized in CH_2Cl_2 medium at ambient temperature *via* three-component tandem reaction of *N*-protected-2-chloro-3-formylindoles, sodium hydrosulfide and *β*-substituted nitroolefins/*δ*-substituted nitrodienes using DABCO (10 mol%) as an organocatalyst, followed by dehydration in the presence of activated molecular sieves (4 Å). The significant advantages of this protocol are simple operation, shorter reaction time, high atom economy, good to high yields (73%—89%) and wider substrate scope. In addition, all the synthesized compounds have shown the large positive Stokes shift values (5632—6081 cm^{-1}).

Keywords one-pot MCR, 2,9-dihydrothiopyrano[2,3-*b*]indole, organocatalysis, molecular sieves, large Stokes shifts

Introduction

Highly efficient synthesis of sulfur-containing polycyclic indole derivatives is a subject of growing interest in recent times because these building blocks play important roles in organic synthesis, pharmaceuticals and material science.[1] Owing to their importance in various fields, a substantial amount of efforts have been devoted for the preparations of these frameworks.[1,2] Even with such a progress, the synthesis of dihydrothiopyrano-[2,3-*b*]indole derivative has been considerably less explored.[3] Towards the access of these compounds (Scheme 1), Zhou *et al*.[3a] published organocatalytic one-pot method for the synthesis of enantioenriched version of 3-formyl-2-aryl-2,9-dihydrothiopyrano[2,3-*b*]indoles from 2-mercapto-3-formylindoles (Scheme 1a). In 2015, an enantioselective synthesis of 4,9-dihydothiopyrano[2,3-*b*]indole scaffolds has been realized via an organocatalytic cascade thio-Michael-cyclization of indoline-2-thione with 2-benzylidemalononitrile as reported by Wang *et al*. (Scheme 1b).[3b] In our effort, we reported a first two-step synthetic method for the synthesis of 2,9-dihydrothiopyrano[2,3-*b*]indole derivative through a three-component reaction between *N*-Boc-2-chloro-3-formylindole, $NaSH{\bullet}H_2O$ and aryl-substituted-nitrostyrene in the presence of organic base, and the resulting product was dehydrated by $MeSO_2Cl$/Et_3N reagent system.[3c] Therefore, it is an ample scope to develop our previous methodology towards the synthesis of 2,9-dihydrothiopyrano[2,3-*b*]indole scaffold in a one-pot, efficient and economical manner. In this regard, we seemed that the dehydration step may perform by using activated molecular sieves (MS) which have been extensively used for drying the liquids and gases[4] as well as promoting various organic transformations.[5]

As part of our continued interest towards the synthesis of polycyclic indole derivatives,[6] herein, we wish to report a mild, convenient, practical and general one-pot method for the synthesis of *N*-protected-2-aryl-3-nitro-2,9-dihydrothiopyrano[2,3-*b*]indole scaffolds via a tandem aromatic nucleophilic thiolation/thio-Michael/Henry reaction of *N*-protected-2-chloro-3-formylindoles, $NaSH{\bullet}H_2O$ with substituted nitroolefins/nitrodienes in CH_2Cl_2 at room temperature, followed by *in situ* dehydration using activated molecular sieves (Scheme 1c).

Experimental

General

All reactions were carried out under air and monitored by TLC using Merck 60 F_{254} pre coated silica gel plates (0.25 mm thickness) and the products were visualized by UV detection. Flash chromatography was carried out with silica gel (200—300 mesh). FT-IR spectra were recorded on a Bruker Tensor-27 spectrometer. ^1H NMR and ^{13}C NMR spectra were recorded on a Bruker Avance (III) 400 MHz spectrometer. Data for ^1H NMR are reported as a chemical shift, multiplicity (s=singlet, d=doublet, q=quartet, m=multiplet), coupling constant *J* (Hz), integration, and assignment, data for ^{13}C are reported as a chemical shift. High resolutions mass

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Received August 7, 2015; accepted September 9, 2015; published online October 28, 2015.
Supporting information for this article is available on the WWW under http://dx.doi.org/10.1002/cjoc.201500572 or from the author.

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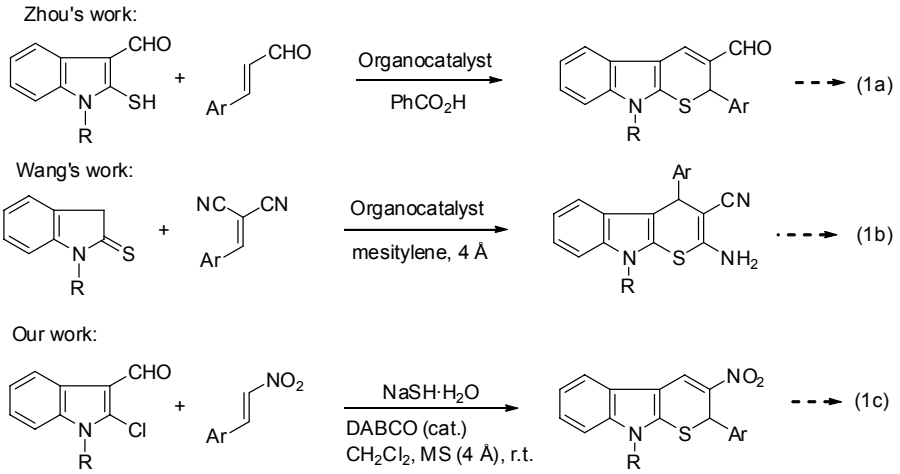
Scheme 1 Various techniques for the synthesis of dihydrothiopyrano[2,3-*b*]indoles



spectral analyses (HRMS) were carried out using ESI-TOF-MS. Absorption spectra were recorded using Varian UV-Vis spectrophotometer (model: cary 100). Emission spectra were recorded in a fluoromax-4p fluorimeter from Horiba Yovin (model: FM-100).

General procedure for the synthesis of 9-(*N*-*tert*-butoxycarbonyl)-2-phenyl-3-nitro-2,9-dihydrothiopyrano[2,3-*b*]indole (3aa)

A mixture of *N*-protected-2-chloro-3-formylindole (0.25 mmol), NaSH•H_2O (0.3 mmol), *β*-nitrostyrenes (0.3 mmol), DABCO (10.0 mol%) and activated molecular sieves (300 mg, 4 Å) was stirred in DCM (2.0 mL) at room temperature. The reaction mixture was monitored by TLC (Thin Layer Chromatography). Upon completion of the reaction, the product was directly purified by column chromatography over silica gel using EtOAc/hexane as an eluent to afford the corresponding pure product.

All the products were synthesized in Table 2 and Scheme 2 by the above procedure and characterized by their corresponding spectroscopic data (IR, ^{1}H NMR and ^{13}C NMR, HRMS).

9-(*N*-*tert*-Butoxycarbonyl)-2-phenyl-3-nitro-2,9-dihydrothiopyrano[2,3-*b*]indole (3aa) Yield 82%; m.p. 150 ℃; ^{1}H NMR (400 MHz, $CDCl_3$) *δ*: 8.54 (s, 1H), 8.00－8.01 (m, 1H), 7.64－7.66 (m, 1H), 7.30－7.36 (m, 4H), 7.24－7.26 (m, 2H), 5.78 (s, 1H), 1.68 (s, 9H); ^{13}C NMR (100 MHz, $CDCl_3$) *δ*: 148.7, 139.2, 138.2, 136.5, 134.3, 128.6, 128.3, 127.3, 126.2, 126.1, 124.4, 124.0, 111.7, 115.0, 112.3, 86.7, 42.2, 27.8; IR (KBr) *v*: 3443, 2924, 2852, 1721, 1618, 1495, 1480, 1446, 1402, 1361, 1321 cm^{-1}; HRMS (ESI) *m*/*z* calcd for $C_{22}H_{20}N_2O_4S$ [M＋Na]$^+$: 431.1036, found 431.1037.

9-(*N*-*tert*-Butoxycarbonyl)-2-(4-methylphenyl)-3-nitro-2,9-dihydrothiopyrano[2,3-*b*]indole (3ab) Yield 80%; m.p. 160 ℃; ^{1}H NMR (400 MHz, $CDCl_3$) *δ*: 8.52 (s, 1H), 7.98－8.00 (m, 1H), 7.63－7.65 (m, 1H), 7.29－7.34 (m, 2H), 7.19－7.23 (m, 2H), 7.04－7.06 (m, 2H), 5.75 (s, 1H), 2.27 (s, 3H), 1.69 (s, 9H); ^{13}C NMR (100 MHz, $CDCl_3$) *δ*: 149.0, 138.6, 136.8, 136.6, 134.7, 129.6, 127.6, 126.4, 126.3, 124.7, 124.3, 117.0, 115.3, 112.5, 86.9, 42.3, 28.1, 21.1; IR (KBr) *v*: 3442, 2961, 2924, 1736, 1626, 1580, 1507, 1491, 1479, 1444, 1400, 1370, 1355, 1315 cm^{-1}; HRMS (ESI) *m*/*z* calcd for $C_{23}H_{22}N_2O_4S$ [M＋Na]$^+$: 445.1192, found 445.1230.

9-(*N*-*tert*-Butoxycarbonyl)-2-(4-methoxyphenyl)-3-nitro-2,9-dihydrothiopyrano[2,3-*b*]indole (3ac) Yield 81%; m.p. 150 ℃; ^{1}H NMR (400 MHz, $CDCl_3$) *δ*: 8.51 (s, 1H), 8.00－8.02 (m, 1H), 7.63－7.66 (m, 1H), 7.30－7.34 (m, 2H), 7.22－7.25 (m, 1H), 6.75－6.78 (m, 2H), 5.74 (s, 1H), 3.73 (s, 3H), 1.69 (s, 9H); ^{13}C NMR (100 MHz, $CDCl_3$) *δ*: 159.8, 149.0, 138.5, 136.8, 134.9, 131.7, 127.7, 127.6, 126.2, 124.7, 124.3, 116.9, 115.3, 114.2, 112.4, 86.9, 55.2, 42.1, 28.1; IR (KBr) *v*: 3435, 2981, 2836, 1732, 1625, 1609, 1581, 1510, 1479, 1443, 1399, 1371, 1356, 1315 cm^{-1}; HRMS (ESI) *m*/*z* calcd for $C_{23}H_{22}N_2O_5S$ [M＋Na]$^+$: 461.1142, found 461.1087.

9-(*N*-*tert*-Butoxycarbonyl)-2-(2-methoxyphenyl)-3-nitro-2,9-dihydrothiopyrano[2,3-*b*]indole (3ad) Yield 77%; m.p. 157 ℃; ^{1}H NMR (400 MHz, $CDCl_3$) *δ*: 8.62 (s, 1H), 7.96 (d, *J*＝8.04 Hz, 1H), 7.65 (d, *J*＝7.04 Hz, 1H), 7.28－7.35 (m, 2H), 7.21－7.23 (m, 1H), 7.01－7.03 (m, 1H), 6.91－6.94 (m, 1H), 6.74－6.76 (m, 1H), 6.25 (s, 1H), 3.95 (s, 3H), 1.66 (s, 9H); ^{13}C NMR (100 MHz, $CDCl_3$) *δ*: 155.3, 149.0, 140.6, 136.8, 133.2, 129.6, 127.7, 127.6, 126.7, 126.6, 124.5, 124.2, 120.3, 116.9, 115.3, 111.9, 111.1, 86.7, 55.7, 36.1, 28.1; IR (KBr) *v*: 3440, 2977, 2928, 1730, 1622, 1598, 1582, 1489, 1445, 1403, 1370, 1357, 1320 cm^{-1}; HRMS (ESI) *m*/*z* calcd for $C_{23}H_{22}N_2O_5S$ [M＋Na]$^+$: 461.1142, found 461.1137.

9-(*N*-*tert*-Butoxycarbonyl)-2-(4-benzyloxy-3-methoxyphenyl)-3-nitro-2,9-dihydrothiopyrano[2,3-*b*]indole (3ae) Yield 74%; m.p. 135 ℃; ^{1}H NMR (400 MHz, $CDCl_3$) *δ*: 8.51 (s, 1H), 7.99 (d, *J*＝7.52 Hz, 1H), 7.62－7.64 (m, 1H), 7.27－7.37 (m, 7H), 6.88－6.89 (m, 1H), 6.72－6.75 (m, 1H), 6.67－6.69 (m, 1H), 5.73 (s, 1H), 5.06 (s, 2H), 3.80 (s, 3H), 1.68 (s, 9H); ^{13}C NMR (100 MHz, $CDCl_3$) *δ*: 149.7, 149.0, 148.6, 138.6,

136.8, 136.7, 134.8, 132.3, 128.5, 127.8, 127.5, 127.1, 124.7, 124.3, 118.7, 116.9, 115.3, 113.5, 112.5, 110.3, 87.0, 70.8, 56.0, 42.5, 28.1; IR (KBr) *v*: 3441, 2925, 2853, 1717, 1620, 1510, 1492, 1481, 1461, 1444, 1400, 1371, 1358, 1320 cm^{-1}; HRMS (ESI) *m*/*z* calcd for $C_{30}H_{28}N_2O_6S$ $[M+Na]^+$: 567.1560, found 567.1678.

9-(*N*-*tert*-Butoxycarbonyl)-2-(4-chlorophenyl)-3-nitro-2,9-dihydrothiopyrano[2,3-*b*]indole (3af) Yield 85%; m.p. 155 ℃; ^1H NMR (400 MHz, $CDCl_3$) *δ*: 8.53 (s, 1H), 8.00－8.02 (m, 1H), 7.64－7.67 (m, 1H), 7.32－7.36 (m, 2H), 7.21－7.27 (m, 3H), 5.75 (s, 1H), 1.69 (s, 9H); ^{13}C NMR (100 MHz, $CDCl_3$) *δ*: 148.9, 138.2, 138.0, 136.8, 134.5, 134.3, 129.1, 127.8, 127.5, 126.6, 124.9, 124.4, 117.1, 115.4, 112.5, 87.2, 41.9, 28.1; IR (KBr) *v*: 3441, 2977, 2924, 1732, 1627, 1581, 1506, 1490, 1443, 1400, 1372, 1356, 1316 cm^{-1}; HRMS (ESI) *m*/*z* calcd for $C_{22}H_{19}N_2O_4ClS$ $[M+Na]^+$: 465.0646, found 465.0687.

9-(*N*-*tert*-Butoxycarbonyl)-2-(2-chlorophenyl)-3-nitro-2,9-dihydrothiopyrano[2,3-*b*]indole (3ag) Yield 84%; m.p. 180 ℃; ^1H NMR (400 MHz, $CDCl_3$) *δ*: 8.65 (s, 1H), 7.99－8.02 (m, 1H), 7.66－7.68 (m, 1H), 7.44－7.46 (m, 1H), 7.33－7.37 (m, 1H), 7.28－7.32 (m, 1H), 7.18－7.22 (m, 1H), 7.11－7.14 (m, 1H), 7.05－7.09 (m, 1H), 6.25 (s, 1H), 1.67 (s, 9H); ^{13}C NMR (100 MHz, $CDCl_3$) *δ*: 148.8, 139.2, 136.9, 135.7, 133.2, 131.8, 130.5, 129.6, 127.9, 127.4, 127.1, 124.8, 124.4, 116.9, 115.4, 112.0, 87.2, 39.3, 28.1; IR (KBr) *v*: 3434, 2981, 2930, 1726, 1622, 1581, 1572, 1510, 1496, 1467, 1444, 1397, 1365, 1354 cm^{-1}; HRMS (ESI) *m*/*z* calcd for $C_{22}H_{19}ClN_2O_4S$ $[M+K]^+$: 481.0386, found 481.0370.

9-(*N*-*tert*-Butoxycarbonyl)-2-(4-cyanophenyl)-3-nitro-2,9-dihydrothiopyrano[2,3-*b*]indole (3ah) Yield 87%; m.p. 158 ℃; ^1H NMR (400 MHz, $CDCl_3$) *δ*: 8.55 (s, 1H), 7.97－8.00 (m, 1H), 7.64－7.66 (m, 1H), 7.54－7.56 (m, 2H), 7.42－7.44 (m, 2H), 7.31－7.38 (m, 2H), 5.79 (s, 1H), 1.68 (s, 9H); ^{13}C NMR (100 MHz, $CDCl_3$) *δ*: 148.9, 144.4, 137.9, 136.8, 133.5, 132.8, 129.9, 127.2, 127.1, 125.1, 124.6, 118.2, 117.2, 115.4, 112.6, 112.5, 87.4, 42.1, 28.1; IR (KBr) *v*: 3441, 2924, 2853, 2228, 1711, 1620, 1581, 1504, 1479, 1444, 1397, 1370, 1358, 1321 cm^{-1}; HRMS (ESI) *m*/*z* calcd for $C_{23}H_{19}N_3O_4S$ $[M+H]^+$: 434.1169, found 434.1222.

9-(*N*-*tert*-Butoxycarbonyl)-2-(4-nitrophenyl)-3-nitro-2,9-dihydrothiopyrano[2,3-*b*]indole (3ai) Yield 86%; m.p. 155 ℃; ^1H NMR (400 MHz, $CDCl_3$) *δ*: 8.57 (s, 1H), 8.09－8.12 (m, 2H), 7.98－8.00 (m, 1H), 7.65－7.67 (m, 1H), 7.48－7.50 (m, 2H), 7.31－7.39 (m, 2H), 5.84 (s, 1H), 1.68 (s, 9H); ^{13}C NMR (100 MHz, $CDCl_3$) *δ*: 148.9, 147.9, 146.2, 137.8, 136.8, 133.5, 127.4, 127.3, 127.2, 125.2, 124.6, 124.2, 117.2, 115.4, 112.6, 87.5, 41.9, 28.1; IR (KBr) *v*: 3440, 2982, 2926, 2854, 1716, 1674, 1622, 1604, 1581, 1528, 1504, 1489, 1443, 1401, 1369, 1355, 1321 cm^{-1}; HRMS (ESI) *m*/*z* calcd for $C_{22}H_{19}N_3O_6S$ $[M+Na]^+$: 476.0887, found 476.0878.

9-(*N*-*tert*-Butoxycarbonyl)-2-furyl-3-nitro-2,9-dihydrothiopyrano[2,3-*b*]indole (3aj) Yield 89%; m.p. 145 ℃; ^1H NMR (400 MHz, $CDCl_3$) *δ*: 8.44 (s, 1H), 8.01－8.03 (m, 1H), 7.62－7.64 (m, 1H), 7.33－7.36 (m, 1H),7.30－7.33 (m, 2H), 6.20－6.21 (m, 1H), 6.14－6.15 (m, 1H), 5.91 (s, 1H), 1.70 (s, 9H); ^{13}C NMR (100 MHz, $CDCl_3$) *δ*: 150.4, 149.0, 143.3, 138.5, 136.8, 132.2, 127.6, 126.8, 124.8, 124.3, 117.1, 115.3, 112.7, 110.6, 108.2, 87.1, 36.8, 28.1; IR (KBr) *v*: 3448, 2923, 2852, 1728, 1611, 1579, 1470, 1393, 1359, 1328 cm^{-1}; HRMS (ESI) *m*/*z* calcd for $C_{20}H_{18}N_2O_5S$ $[M+Na]^+$: 421.0829, found 421.0864.

9-(*N*-Ethoxycarbonyl)-2-phenyl-3-nitro-2,9-dihydrothiopyrano[2,3-*b*]indole (3ba) Yield 80%; m.p. 180 ℃; ^1H NMR (400 MHz, $CDCl_3$) *δ*: 8.53 (s, 1H), 8.00－8.02 (m, 1H), 7.64－7.66 (m, 1H), 7.34－7.38 (m, 2H), 7.30－7.32 (m, 3H),7.23－7.24 (m, 2H), 5.80 (s, 1H), 4.53 (q, *J*＝7.28, 14.16 Hz, 2H), 1.50 (t, *J*＝7.0, 14.28 Hz, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) *δ*: 150.5, 146.1, 139.3, 138.2, 136.6, 134.9, 128.9, 128.6, 127.6, 126.4, 124.9, 124.5, 117.1, 115.4, 112.9, 64.9, 42.5, 14.2; IR (KBr) *v*: 3442, 2952, 2924, 1733, 1620, 1581, 1503, 1480, 1445, 1399, 1377, 1346, 1318 cm^{-1}; HRMS (ESI) *m*/*z* calcd for $C_{20}H_{16}N_2O_4S$ $[M+Na]^+$: 403.0723, found 403.0733.

9-(*N*-*tert*-Butoxycarbonyl)-2-phenyl-6-chloro-3-nitro-2,9-dihydrothiopyrano[2,3-*b*]indole (3ca) Yield 83%; m.p. 160 ℃; ^1H NMR (400 MHz, $CDCl_3$) *δ*: 8.47 (s, 1H), 8.04－8.05 (m, 1H), 7.54 (d, *J*＝8.28 Hz, 1H), 7.29－7.33 (m, 4H), 7.26－7.27 (m, 2H), 5.78 (s, 1H), 1.68 (s, 9H); ^{13}C NMR (100 MHz, $CDCl_3$) *δ*: 148.6, 139.3, 138.8, 137.1, 135.0, 130.7, 129.1, 128.9, 128.7, 126.4, 126.0, 124.8, 117.6, 115.8, 112.1, 87.7, 42.4, 28.1; IR (KBr) *v*: 3441, 2925, 2854, 1737, 1628, 1507, 1491, 1470, 1454, 1422, 1403, 1372, 1348 cm^{-1}; HRMS (ESI) *m*/*z* calcd for $C_{22}H_{19}ClN_2O_4S$ $[M+Na]^+$: 465.0646, found 465.0712.

9-(*N*-*tert*-Butoxycarbonyl)-2-styryl-3-nitro-2,9-dihydrothiopyrano[2,3-*b*]indole (3ak) Yield 81%; m.p. 148 ℃; ^1H NMR (400 MHz, $CDCl_3$) *δ*: 8.37 (s, 1H), 8.03－8.04 (m, 1H), 7.61－7.63 (m, 1H), 7.22－7.32 (m, 7H), 6.54 (d, *J*＝15.56 Hz, 1H), 6.24 (dd, *J*＝7.28, 15.4 Hz, 1H), 5.34 (d, *J*＝6.8 Hz, 1H), 1.72 (s, 9H); ^{13}C NMR (100 MHz, $CDCl_3$) *δ*: 149.1, 138.4, 136.8, 135.7, 133.7, 132.1, 128.5, 128.2, 127.6, 126.8, 125.9, 124.8, 124.3, 123.9, 117.1, 115.4, 112.9, 87.1, 41.2, 28.2; IR (KBr) *v*: 1731, 1619, 1579, 1502, 1489, 1478, 1443, 1398, 1369, 1356, 1318, 1286 cm^{-1}; HRMS (ESI) *m*/*z* calcd for $C_{24}H_{22}N_2O_4S$ $[M+Na]^+$: 457.1192, found 457.1196.

9-(*N*-Ethoxycarbonyl)-2-styryl-3-nitro-2,9-dihydrothiopyrano[2,3-*b*]indole (3bk) Yield 83%; m.p. 181 ℃; ^1H NMR (400 MHz, $CDCl_3$) *δ*: 8.43 (s, H), 8.10－8.12 (m, 1H), 7.68－7.70 (m, 1H), 7.40－7.42 (m, 2H), 7.27－7.35 (m, 5H), 6.60 (d, *J*＝15.56 Hz, 1H), 6.29 (dd, *J*＝7.28, 15.6 Hz, 1H), 5.42 (d, *J*＝7.52 Hz, 1H), 4.64 (q, *J*＝7.0, 14.28 Hz, 2H), 1.61 (t, *J*＝2.76, 6.28 Hz, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) *δ*: 150.6, 138.2, 136.6, 135.6, 134.0, 132.3, 128.5, 128.3, 127.7,

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126.8, 125.7, 124.9, 124.6, 123.7, 117.2, 115.4, 113.3, 64.9, 41.2, 14.3; IR (KBr) *v*: 1736, 1640, 1610, 1579, 1498, 1485, 1446, 1397, 1376, 1348, 1319, 1298 cm^{-1}; HRMS (ESI) *m*/*z* calcd for $C_{22}H_{18}N_2O_4S$ $[M+H]^+$: 407.1060, found 407.1061.

9-(*N*-*tert*-Butoxycarbonyl)-2-(4-methoxystyryl)-3-nitro-2,9-dihydrothiopyrano[2,3-*b*]indole (3al) Yield 74%; m.p. 150 ℃; ^1H NMR (400 MHz, $CDCl_3$) δ: 8.36 (s, 1H), 8.02－8.04 (m, 1H), 7.61－7.62 (m, 1H), 7.20－7.35 (m, 4H), 6.75－6.77 (m, 2H), 6.48 (d, *J*= 15.56 Hz, 1H), 6.09 (dd, *J*=7.8, 15.68 Hz, 1H), 5.31 (d, *J*=7.52 Hz, 1H), 3.75 (s, 3H), 1.71 (s, 9H); ^{13}C NMR (100 MHz, $CDCl_3$) δ: 159.7, 149.1, 138.5, 136.8, 133.9, 131.6, 128.4, 128.1, 127.7, 125.7, 124.8, 124.3, 121.7, 117.0, 115.4, 113.9, 112.9, 87.0, 55.3, 41.4, 28.2; IR (KBr) *v*: 1732, 1618, 1606, 1510, 1478, 1445, 1398, 1370, 1355, 1317, 1291 cm^{-1}; HRMS (ESI) *m*/*z* calcd for $C_{25}H_{24}N_2O_5$ $[M+Na]^+$: 487.1298, found 487.1274.

9-(*N*-Ethoxycarbonyl)-2-(4-methoxystyrene)-3-nitro-2,9-dihydrothiopyrano[2,3-*b*]indole (3bl) Yield 76%; m.p. 158 ℃; ^1H NMR (400 MHz, $CDCl_3$) δ: 8.35 (s, 1H), 8.04－8.05 (m, 1H), 7.61－7.63 (m, 1H), 7.33－7.35 (m, 2H), 7.20－7.22 (m, 2H), 6.75－6.77 (m, 2H), 6.48 (d, *J*=15.56 Hz, 1H), 6.08 (dd, *J*=7.80, 15.56 Hz, 1H), 5.32 (d, *J*=7.52 Hz, 1H), 4.57 (q, *J*= 7.04, 14.04 Hz, 2H), 3.75 (s, 3H), 1.53 (t, *J*=2.76, 6.28 Hz, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ: 159.7, 150.6, 138.3, 136.6, 134.2, 131.8, 128.3, 128.1, 127.7, 125.5, 124.9, 124.5, 121.5, 117.1, 115.4, 113.9, 113.3, 64.9, 55.2, 41.4, 14.3; IR (KBr) *v*: 1734, 1638, 1606, 1579, 1510, 1490, 1446, 1397, 1375, 1349, 1321, 1291 cm^{-1}; HRMS (ESI) *m*/*z* calcd for $C_{23}H_{20}N_2O_5S$ $[M+Na]^+$: 459.0985, found 459.0995.

9-(*N*-*tert*-Butoxycarbonyl)-2-(2-methoxystyryl)-3-nitro-2,9-dihydrothiopyrano[2,3-*b*]indole (3am) Yield 74%; m.p. 158 ℃; ^1H NMR (400 MHz, $CDCl_3$) δ: 8.36 (s, 1H), 8.03－8.05 (m, 1H), 7.61－7.63 (m, 1H), 7.29－7.31 (m, 3H), 7.14－7.18 (m, 1H), 6.89 (d, *J*= 15.8 Hz, 1H), 6.77－6.83 (m, 2H), 6.26 (dd, *J*=7.52, 15.72 Hz, 1H), 5.34 (d, *J*=7.28 Hz, 1H), 3.74 (s, 3H), 1.71 (s, 9H); ^{13}C NMR (100 MHz, $CDCl_3$) δ: 157.0, 149.0, 138.5, 136.8, 133.9, 129.3, 127.7, 127.2, 126.9, 125.8, 124.7, 124.6, 124.3, 123.9, 120.5, 117.0, 115.3, 113.0, 110.9, 86.9, 55.4, 41.8, 28.2; IR (KBr) *v*: 1731, 1619, 1598, 1579, 1488, 1464, 1444, 1398, 1371, 1355, 1317, 1292 cm^{-1}; HRMS (ESI) *m*/*z* calcd for $C_{25}H_{24}N_2O_5S$ $[M+Na]^+$: 487.1298, found 487.1289.

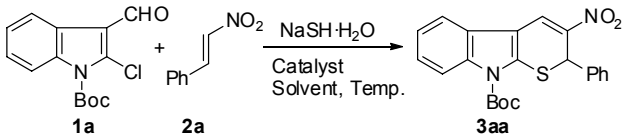
9-(*N*-*tert*-Butoxycarbonyl)-2-styryl-6-chloro-3-nitro-2,9-dihydrothiopyrano[2,3-*b*]indole (3ck) Yield 79%; m.p. 160 ℃; ^1H NMR (400 MHz, $CDCl_3$) δ: 8.30 (s, 1H), 8.08 (s, 1H), 7.50－7.52 (m, 1H), 7.19－7.32 (m, 6H), 6.52 (d, *J*=15.56 Hz, 1H), 6.21 (dd, *J*= 7.28, 15.56 Hz, 1H), 5.33 (d, *J*=7.28 Hz, 1H), 1.71 (s, 9H); ^{13}C NMR (100 MHz, $CDCl_3$) δ: 148.6, 138.7, 137.1, 135.5, 134.1, 132.3, 130.7, 128.5, 128.3, 126.8, 126.1, 125.4, 124.8, 123.6, 117.6, 115.8, 112.4, 87.7, 41.2, 28.1; IR (KBr) *v*: 1732, 1618, 1490, 1470, 1423, 1395, 1371, 1350, 1313, 1274 cm^{-1}; HRMS (ESI) *m*/*z* calcd for $C_{24}H_{21}N_2O_4ClS$ $[M+H]^+$: 469.0983, found 469.0995.

9-(N-*tert*-Butoxycarbonyl)-2-(4-methoxystyryl)-6-chloro-3-nitro-2,9-dihydrothiopyrano[2,3-*b*]indole (3cl) Yield 73%; m.p. 162 ℃; ^1H NMR (400 MHz, $CDCl_3$) δ: 8.31 (s, 1H), 8.11 (s, 1H), 7.52－7.54 (m, 1H), 7.23－7.34 (m, 3H), 6.78－6.80 (m, 2H), 6.50 (d, *J*= 15.32 Hz, 1H), 6.10 (dd, *J*=6.76, 16.20 Hz, 1H), 5.33 (d, *J*=6.28 Hz, 1H), 3.77 (s, 3H), 1.74 (s, 9H); ^{13}C NMR (100 MHz, $CDCl_3$) δ: 159.8, 148.6, 138.8, 137.1, 134.3, 131.8, 130.7, 128.3, 128.1, 126.1, 125.2, 124.8, 121.4, 117.6, 115.8, 113.9, 112.4, 87.6, 55.3, 41.4, 28.1; IR (KBr) *v*: 1738, 1621, 1605, 1510, 1490, 1467, 1422, 1401, 1371, 1344, 1296 cm^{-1}; HRMS (ESI) *m*/*z* calcd for $C_{25}H_{23}N_2O_5ClS$ $[M+Na]^+$: 521.0908, found 521.0907.

Results and Discussion

At the beginning, we chose a model reaction between compound **1a**, *β*-nitrostyrene (**2a**) and $NaSH{\bullet}H_2O$ in methanol at room temperature using DABCO as an organocatalyst. After 24 h, a little amount (18%, Entry 1 and Table 1) of dihydrothiopyrano[2,3-*b*]indole was obtained as characterized by its spectroscopic data (^1H NMR, ^{13}C NMR, IR and HRMS). In order to access the better yield of **3aa**, we did the several reactions in common organic solvents or neat conditions using easily available basic catalysts such as DABCO, DBU, Et_3N, Al_2O_3 and KF-Al_2O_3 at 60 ℃. The results showed that

Table 1 Optimization of reaction[a]



1a **2a** **3aa**

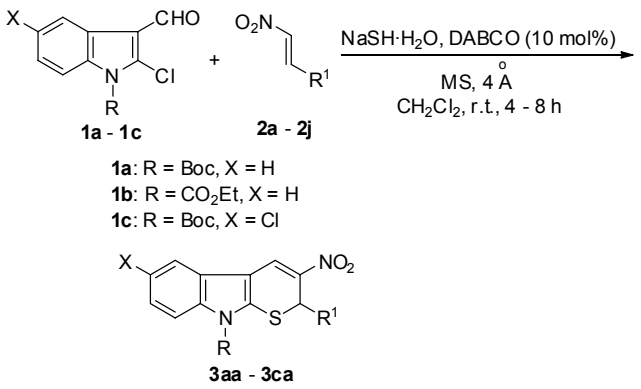
Entry	Catalyst	Solvent	*T*/℃	*t*/h	Yield[b]/%
1	DABCO	MeOH	rt	24	18
2	DABCO	MeOH	60	24	21
3	DABCO	EtOH	60	24	24
4	DABCO	THF	60	24	27
5	DBU	EtOH	60	24	31
6	Et_3N	EtOH	60	24	19
7[c]	Al_2O_3	Nil	60	4	32
8[c]	KF-Al_2O_3	Nil	60	4	37
9	DABCO	$CHCl_3$	r.t.	24	42
10	DABCO	CH_2Cl_2	r.t.	24	51
11[d]	DABCO	CH_2Cl_2	r.t.	4	82

[a] Unless otherwise specified, all reactions were carried out at room temperature with **1a** (0.25 mmol), **2a** (0.3 mmol) and $NaSH{\bullet}H_2O$ (0.3 mmol) using 10 mol% catalysts in the specified solvents (2.0 mL). [b] Isolated yields after column chromatography. [c] 500 mg was used. [d] 300 mg activated molecular sieves was used.

in all the cases unsatisfactory yields (19%—37%, Entries 2—8) were obtained. However, the yields (41%—55%) of **3aa** were improved when the reaction was carried out in chlorinated solvents (CH_2Cl_2 and $CHCl_3$) at room temperature for 24 h in the presence of DABCO. Gratifyingly, high yield (82%, Entry 11) of **3aa** was obtained in CH_2Cl_2 with short span of time (4 h) when the reaction was performed in the presence of activated molecular sieves (4 Å) as dehydrating agent.

Having optimal reaction conditions in hand, a series of 2-aryl-3-nitro-2,9-dihydrothiopyrano[2,3-*b*]indole derivatives were synthesized involving the reaction of several *N*-protected-2-chloro-3-formylindoles, NaSH•H_2O with aryl-substituted-*β*-nitrostyrenes in our established reaction conditions. The obtained results were collected in Table 2. By this procedure, several indole derivatives (**1a**—**1c**) annulated smoothly with aryl-substituted-*β*-nitrostyrene possessing electron donating (Me, OMe, OBn) and electron withdrawing (Cl, NO_2, CN) substituents on aryl rings to provide the corresponding *N*-protected-2-aryl-3-nitro-2,9-dihydrothiopyrano[2,3-*b*]indole derivatives in good to high yields (74%—86% **3aa**—**3ai** and **3ba** — **3ca)** within 4 — 8 h. Interestingly, heteroaryl-substituted *β*-nitroolefin (**2j**) was found to be a good thio-Michael-acceptor in our present conditions, resulting in excellent yield (89%) of corresponding product **3aj**. Moreover, several sensitive functional groups such as Cl, OMe, OBn, Boc, CO_2Et, NO_2, CN, furan, *etc*. were unaffected under the present conditions.

Table 2 One-pot synthesis of 2-aryl-3-nitro-2,9-dihydrothiopyrano[2,3-*b*]indole derivatives (**3aa**–**3ca**)[a]



Entry	R	R^1	X	Name	Yield[b]/%
1	Boc	Ph	H	**3aa**	82
2	Boc	4-MeC_6H_4	H	**3ab**	80
3	Boc	4-$MeOC_6H_4$	H	**3ac**	81
4	Boc	2-$MeOC_6H_4$	H	**3ad**	77
5	Boc	3-MeO-4-$BnOC_6H_3$	H	**3ae**	74
6	Boc	4-ClC_6H_4	H	**3af**	85
7	Boc	2-ClC_6H_4	H	**3ag**	84
8	Boc	4-CNC_6H_4	H	**3ah**	87
9	Boc	4-$NO_2C_6H_4$	H	**3ai**	86
10	Boc	2-Furyl	H	**3aj**	89
11	CO_2Et	Ph	H	**3ba**	80
12	Boc	Ph	Cl	**3ca**	83

[a] Unless otherwise specified, all the reactions were carried out at room temperature with compound (**1a**—**1c**, 0.25 mmol), nitrostyrenes (**2a**—**2j**, 0.3 mmol), NaSH•H_2O (0.3 mmol), DABCO (10 mol%) and molecular sieves 4 Å (300 mg) in CH_2Cl_2 (2.0 mL). [b] Isolated yields after column chromatography.

In order to expand towards more substrate possibility, we employed the chemically challenging nitrodienes as Michael acceptors for this one-pot MCR. As is evident from Scheme 2, the thio-Michael reaction between 2-mercapto-3-formylindoles (*in situ* generated from the reaction between **1a**—**1c** and NaSH•H_2O) and *δ*-aryl-substituted nitrodienes (**2k**—**2m**) occurred exclusively at the *β*-positions of nitrodienes in our present conditions. As a result, all the reactions led to the corresponding (*E*)-2-styryl-substituted-3-nitro-2,9-dihydrothiopyrano[2,3-*b*]indole (**3ak** — **3cl**) in good to high (73%—84%) yields as shown in Scheme 2.

Physical appearance of all the synthesized compounds is red in color which prompted us to evaluate their spectroscopic properties. In this line, we began to examine the solvatochromic effects of compound **3ai** in various organic solvents (spectroscopic grade). The results are plotted systematically in Figure **1a**. The compound **3ai** shows maximum absorption bands in the visible region at around 460—464 nm (approximately) in THF, ethyl acetate, ethanol and methanol. Whereas,

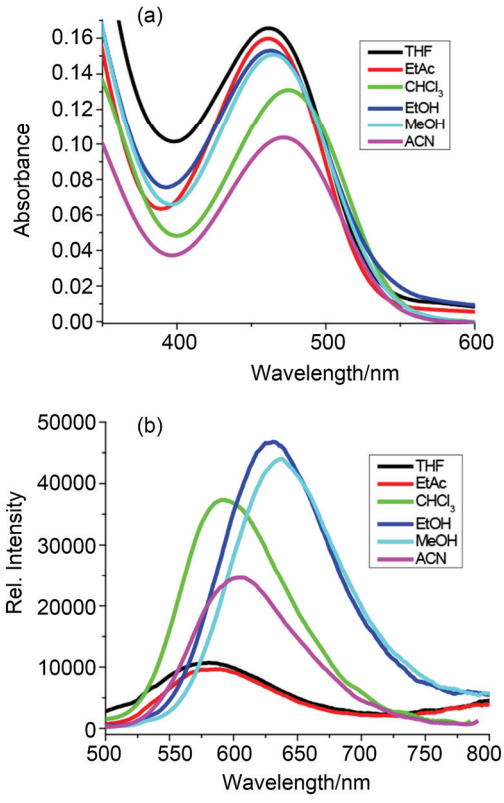


Figure 1 Solvatochromic effects of compound **3ai** in absorption and emission spectra (excited at 460 nm).

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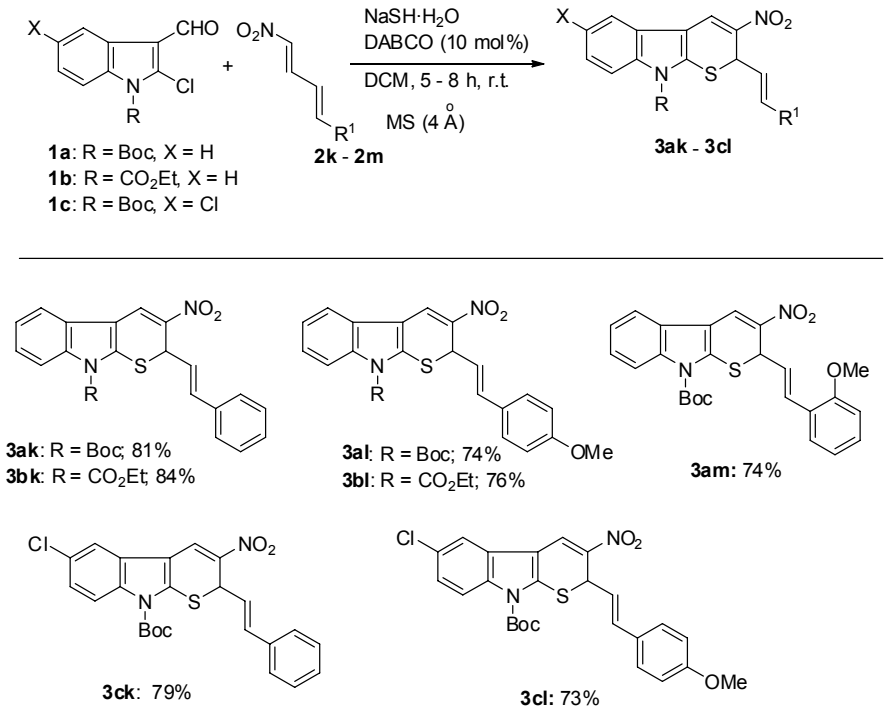
Scheme 2 One-pot synthesis of (*E*)-2-styryl-substituted-3-nitro-2,9-dihydrothiopyrano[2,3-*b*]indole scaffolds (**3ak**—**3cl**)



small red shifts (10—16 nm) are shown in acetonitrile (λ_{max} 470 nm) and chloroform (λ_{max} 476 nm) solvents. On the other hand, the emission maxima for **3ai** are strongly influenced by solvent polarity and exhibit bathochromic shifts as well as positive Stokes shifts with increasing polarity of solvents (Figure 1b).

For example, in case of non-polar aprotic solvents such as THF, EtOAc, $CHCl_3$ and CH_3CN, emission bands are shown at 580 nm, 592 nm, and 604 nm respectively. The emission bands of **3ai** are further increased to 629 nm and 638 nm when emission spectra are recorded in high polar solvents such as EtOH and MeOH respectively. Thus, it is clearly indicated that the maximum Stokes shift value (5877 cm^{-1} or 174 nm) of compound **3ai** is observed in MeOH as compared to other solvents (4116—5841 cm^{-1} or 120—169 nm) recorded for this experiment.

In order to evaluate the general trends of these absorption and fluorescence spectra, we recorded all the synthesized 2,9-dihydrothiopyrano[2,3-*b*]indole derivatives (**3aa**—**3cl**) in Table 2 and Scheme 2 in MeOH medium under similar conditions. The absorption and emission bands as well as their corresponding Stokes shift values are summarized in Table 3. As shown in Table 3, the UV-visible absorption maxima are shown at 456—465 nm which is almost independent nature of substituents and their positions on aryl rings (Entries 1—19, Table **3** and Figure 2). Similarly, all the compounds emit within the range at 623—641 nm, resulting in large positive Stokes shifts (5632—6081 cm^{-1}, Table 3). Therefore, the large Stokes shifts of 2,9-dihydrothiopyrano annulated indole derivatives may find out the potential application in material science.[7]

Table 3 Absorption and fluorescence spectra of compounds **3aa**—**3cl**[a]

Entry	Product	λ_a/nm	λ_e[b]/nm	SS[c]/nm	SS/cm^{-1}
1	**3aa**	464	641	177	5950
2	**3ab**	456	631	175	6081
3	**3ac**	465	644	179	5977
4	**3ad**	469	643	174	5769
5	**3ae**	460	630	170	5866
6	**3af**	461	630	169	5818
7	**3ag**	465	630	165	5632
8	**3ah**	463	631	168	5750
9	**3ai**	464	638	174	5877
10	**3aj**	458	623	165	5782
11	**3ak**	465	641	176	5904
12	**3al**	458	629	171	5935
13	**3am**	461	631	170	5844
14	**3ba**	460	634	174	5966
15	**3bk**	461	631	170	5844
16	**3bl**	461	630	169	5818
17	**3ca**	461	632	171	5869
18	**3ck**	460	633	173	5941
19	**3cl**	458	631	173	5986

[a] All the compounds were recorded their UV and fluorescence spectra in MeOH. [b] Excited at 460 nm. [c] SS indicates Stokes Shift.

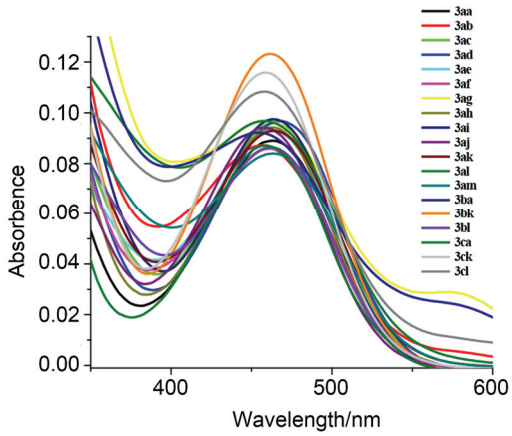


Figure 2 UV-Vis spectra of compounds **3aa**—**3cl**.

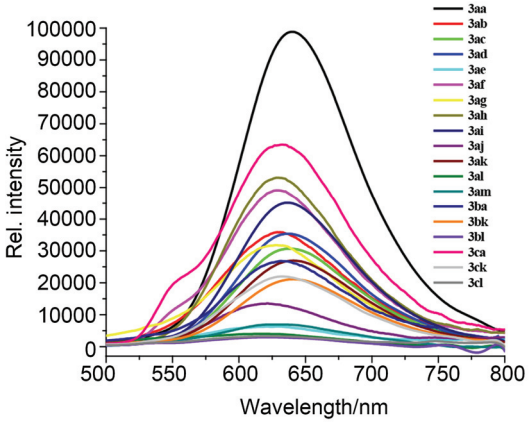


Figure 3 Emission spectra of compounds **3aa**—**3cl**.

Conclusions

In conclusion, we have reported a one-pot direct method for the construction of unknown functionalized *N*-protected-2-aryl/styryl-substituted-3-nitro-2,9-dihydrothiopyrano[2,3-*b*]indoles in CH_2Cl_2 via a tandem aromatic nucleophilic thiolation/thio-Michael/Henry reaction between *N*-protected-2-chloro-3-formylindoles, $NaSH•H_2O$ and substituted-nitroolefins/nitrodienes in the presence of DABCO, followed by *in situ* dehydration using activated molecular sieves (4 Å). The current one-pot process has several advantageous points such as mild reaction conditions, high yielding, no toxic by-products, broad substrate scope, construction of three new bonds (C—S, C—C and C=C) by single operation. In addition, various sensitive functional groups were tolerated in our mild conditions. Moreover, our synthesized compounds have shown the high positive Stokes shift values ($\leqslant$6081 cm^{-1}). Additional applications of these synthesized compounds are under progress which will be documented in due course.

Acknowledgement

The authors thank the DST, Govt. of India research grant (Project No. SB/S1/OC-19/2013). S. Singh is thankful to her UGC fellowship.

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(Lu, Y.)

