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Synthesis and characterization of novel indanone-based spiro-dihydrobenzofuran derivatives

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Abstract: In this study, the synthesis and characterization of novel indanone-based spiro-dihydrobenzofuran derivatives were examined. Firstly, chalcone-like compounds **4a-k**, (*E*)-2-benzylidene-2,3-dihydro-1*H*-inden-1-one derivatives, were synthesized by the base-catalyzed addition of benzaldehyde derivatives to 2,3-dihydro-1*H*-inden-1-one. Then Mn(OAc)₃-mediated addition of dimedone (**2**) to the chalcone-like compounds gave two novel spiro-dihydrobenzofuran isomers: (3*S*)-6,6-dimethyl-3-aryl-6,7-dihydro-3*H*-spiro [benzofuran-2,2'-indene]-1',4(3'*H*,5*H*)-dione (**5a-k**) and (2'*S*)-6,6-dimethyl-2-aryl-6,7-dihydro-2*H*-spiro[benzofuran-3,2'-indene]-1',4(3'*H*,5*H*)-dione (**6a-k**) in good yields. The isomers were separated by column chromatography and their structures were elucidated on the basis of spectral data (NMR, IR) and elemental analysis.

Key words: Indanone, spirobenzofuran, chalcone-like compound, Mn(OAc)₃, dimedone

1. Introduction

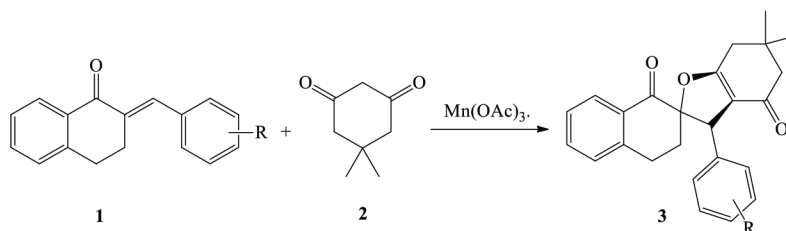
Benzofuran derivatives are an important class of heterocyclic compounds having biological activity, such as dihydrofuran [1,2]. Benzofuran [3] and spiro-benzofuran [4] derivatives have advantageous structural skeletons in medicinal chemistry for drug discovery [5]. They are found in the structures of many natural and significant pharmaceuticals [6–10]. Moreover, they have a wide spectrum of biological activity such as antifungal [11], antibacterial [12], antitumor [13,14], antimicrobial [15–18], antiinflammatory [19,20], antihyperglycemic, analgesic, antiparasitic, and kinase inhibitory [21–26].

The synthesis, characterization, and isolation of spiro-benzofuran derivatives are of interest to chemists due to the wide range of biological activity and many methods have been used for their synthesis [27–30]. Among these methods, manganese(III) acetate-catalyzed oxidative free radical addition of 1,3-dicarbonyls to related olefins is one of the most useful [20,31–35].

In addition, indanones are also an important group amongst the compounds exhibiting pharmacological properties and are often used as starting materials in synthesis [36], drug intermediates, ligands of olefinic polymerization catalysts, and discotic liquid crystals [37].

In our previous study, we reported the Mn(OAc)₃-mediated oxidative free radical addition of dimedone (**2**) to (*E*)-2-(benzylidene)-3,4-dihydronaphthalen-1(2*H*)-one derivatives (**1**). From this reaction, tetralone-based spirodihydrobenzofuran derivatives (**3**) were obtained by regioselective addition of dimedone to the β -carbon atom of the α,β -unsaturated unit following oxidative cyclization in good yields [38].

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As part of our previous work, the current study reports the oxidative free radical addition of dimesone (**2**) to (*E*)-2-benzylidene-2,3-dihydro-1H-inden-1-one derivatives (**4a–k**) mediated by Mn(OAc)₃.

2. Materials and methods

2.1. General

All chemicals were purchased from Sigma-Aldrich and Fluka. Melting points were measured on an Electrothermal 9100 apparatus. IR spectra (KBr disc) were recorded on a Jasco FT/IR-430 spectrometer. ¹H and ¹³C NMR spectra were recorded on a Bruker Avance DPX-400 instrument. TMS (¹H NMR, δ (0.00)) and CDCl₃ (δ (77.0)) served as internal standards for ¹³C NMR spectroscopy, *J* values are given in Hz. Elemental analyses were conducted using a LECO CHNS 932 Elemental Analyzer.

2.2. Synthesis

2.2.1. General procedure for the synthesis of (*E*)-2-benzylidene-2, 3-dihydro-1H-inden-1-one (chalcone-like compounds) derivatives (**4a–k**)

The chalcone-like compounds, (*E*)-2-benzylidene-2,3-dihydro-1H-inden-1-one derivatives (**4a–k**), were synthesized using our previously published procedure [39].

2.2.2. General procedure for the synthesis of indano-based spiro-didhydrobenzofuran derivatives (**5a–k** and **6a–k**) [38]

A solution of Mn(OAc)₃ (10 mmol) in AcOH (10 mL) was heated for 2 h at 80 °C under N₂ atmosphere. After the temperature had dropped to 60 °C, to this solution was added solution of **4a–k** (1 mmol) and dimesone (**2**) (3 mmol) in AcOH (10 mL) dropwise over 25 min. The mixture was refluxed for 3 h under N₂ atmosphere. The reaction mixture was extracted with CH₂Cl₂, dried over anhydrous Na₂SO₄, and concentrated under reduced pressure. The crude products were separated on a silica gel column eluting with ethyl acetate/hexane (3:7). The first product was the isomer **3**.

2.3. Spectral characterization of the synthesized compounds (**5a–k** and **6a–k**)

2.3.1. (3*S*)-3-(4-bromophenyl)-6, 6-dimethyl-6, 7-dihydro-3*H*-spiro[benzofuran-2, 2'- indene]-1', 4 (3'*H*,5*H*)-dione (**5a**)

Yield 45%, mp: 167–170 °C. IR (KBr, cm⁻¹): 3404, 2959, 2870, 2310, 2246, 1724, 1644, 1487, 1466, 1389, 1348, 1300, 1218, 1010. ¹H NMR (400 MHz, CDCl₃) δ (ppm): 7.84 (d, *J* = 7.6 Hz, 1H), 7.61 (d, *J* = 7.6 Hz, 1H), 7.46 (d, *J* = 7.6 Hz, 1H), 7.42 (d, *J* = 8.4 Hz, 2H), 7.26 (d, *J* = 7.6 Hz, 1H), 6.88 (d, *J* = 8.4 Hz, 2H), 4.43 (bs, 1H), 3.10 (d, *J* = 17.6 Hz, 1H), 2.80 (d, *J* = 17.6 Hz, 1H), 2.54–2.51 (m, 2H), 2.36 (d, *J* = 16.0

Hz, 1H), 2.27 (d, $J = 16.4$ Hz, 1H), 1.23 (bs, 6H). ^{13}C NMR (100 MHz, CDCl_3) δ (ppm): 199.9, 193.4, 176.2, 150.3, 137.3, 136.2, 133.1, 131.9 (4C), 129.8, 128.4, 126.3, 125.4, 121.6, 115.0, 95.3, 51.1, 49.6, 37.7, 35.8, 34.2, 28.8. Anal. calc. for $\text{C}_{24}\text{H}_{21}\text{BrO}_3$: C, 65.91; H, 4.84. Found: C, 65.86; H, 4.77.

2.3.2. (2'S)-2-(4-bromophenyl)-6, 6-dimethyl-6, 7-dihydro-2H-spiro[benzofuran-3, 2'-indene]-1', 4 (3'H,5H)-dione (6a)

Yield: 40%, mp: 178–181 °C. IR (KBr, cm^{-1}): 3404, 2960, 2868, 2348, 1702, 1650, 1628, 1490, 1464, 1396, 1284, 1226, 1151, 1071, 1015. ^1H NMR (400 MHz, CDCl_3) δ (ppm): 7.56 (t, $J = 7.4$ Hz, 1H), 7.44 (d, $J = 7.6$ Hz, 1H), 7.39 (d, $J = 7.6$ Hz, 1H), 7.28 (d, $J = 9.2$ Hz, 2H), 7.26 (d, $J = 7.6$ Hz, 1H), 6.98 (d, $J = 8.4$ Hz, 2H), 5.69 (bs, 1H), 4.13 (d, $J = 17.2$ Hz, 1H), 3.21 (d, $J = 17.6$ Hz, 1H), 2.59 (m, 2H), 2.34 (d, $J = 16.0$ Hz, 1H), 2.22 (d, $J = 16.0$ Hz, 1H), 1.27 (bs, 3H), 1.22 (bs, 3H). ^{13}C NMR (100 MHz, CDCl_3) δ (ppm): 202.6, 193.9, 178.0, 151.5, 135.8, 135.0, 133.8, 131.2 (2C), 127.6, 127.5 (2C), 125.8, 124.1, 122.4, 115.3, 94.4, 61.7, 51.1, 39.1, 38.0, 34.7, 29.4, 27.7. Anal. calc. for $\text{C}_{24}\text{H}_{21}\text{BrO}_3$: C, 65.91; H, 4.84. Found: C, 65.83; H, 4.80.

2.3.3. (3S)-3-(4-chlorophenyl)-6, 6-dimethyl-6, 7-dihydro-3H-spiro[benzofuran-2, 2'-indene]-1', 4 (3'H,5H)-dione(5b)

Yield: 40%, mp: 161–164 °C. IR (KBr, cm^{-1}): 3432, 2959, 2871, 2361, 1724, 1635 1604, 1541, 1490, 1468, 1389, 1300, 1218, 1090. ^1H NMR (400 MHz, CDCl_3) δ (ppm): 7.85 (d, $J = 7.6$ Hz, 1H), 7.63 (t, $J = 7.6$ Hz, 1H), 7.43 (t, $J = 7.4$ Hz, 1H), 7.28 (d, $J = 8.4$ Hz, 3H), 6.94 (d, $J = 8.4$ Hz, 2H), 4.44 (bs, 1H), 3.10 (d, $J = 17.6$ Hz, 1H), 2.80 (d, $J = 17.6$ Hz, 1H), 2.54–2.51 (m, 2H), 2.36 (d, $J = 16.0$ Hz, 1H), 2.27 (d, $J = 16.4$ Hz, 1H), 1.23 (bs, 6H). ^{13}C NMR (100 MHz, CDCl_3) δ (ppm): 200.0, 193.4, 176.1, 150.3, 136.8, 136.2, 133.4, 133.1, 129.5 (2C), 129.0 (2C), 128.4, 126.3, 125.4, 115.0, 95.4, 51.2, 49.5, 37.7, 35.8, 34.2, 28.8, 28.7. Anal. calc. for $\text{C}_{24}\text{H}_{21}\text{ClO}_3$: C, 73.37; H, 5.39. Found: C, 73.24; H, 5.18.

2.3.4. (2'S)-2-(4-chlorophenyl)-6, 6-dimethyl-6, 7-dihydro-2H-spiro[benzofuran-3, 2'-indene]-1', 4 (3'H,5H)-dione (6b)

Yield: 40%, mp: 172–175 °C. IR (KBr, cm^{-1}): 3434, 2960, 2893, 2345, 1703, 1653, 1632, 1606, 1495, 1465, 1397, 1227, 1194, 1151, 1093, 1071. ^1H NMR (400 MHz, CDCl_3) δ (ppm): 7.56 (t, $J = 7.4$ Hz, 1H), 7.44 (d, $J = 7.6$ Hz, 1H), 7.38 (d, $J = 7.6$ Hz, 1H), 7.24 (t, $J = 7.6$ Hz, 1H), 7.13 (d, $J = 8.4$ Hz, 2H), 7.04 (d, $J = 8.4$ Hz, 2H), 5.70 (bs, 1H), 4.13 (d, $J = 17.2$ Hz, 1H), 3.21 (d, $J = 17.2$ Hz, 1H), 2.59 (m, 2H), 2.34 (d, $J = 16.0$ Hz, 1H), 2.23 (d, $J = 16.4$ Hz, 1H), 1.27 (bs, 3H), 1.22 (bs, 3H). ^{13}C NMR (100 MHz, CDCl_3) δ (ppm): 202.6, 193.9, 178.0, 151.5, 135.8, 135.0, 134.2, 133.2, 128.2 (2C), 127.6, 127.3 (2C), 125.8, 124.0, 115.3, 94.4, 61.8, 51.1, 39.1, 38.0, 34.7, 29.4, 27.7. Anal. calc. for $\text{C}_{24}\text{H}_{21}\text{ClO}_3$: C, 73.37; H, 5.39. Found: C, 73.28; H, 5.27.

2.3.5. (3S)-3-(4-methoxyphenyl)-6, 6-dimethyl-6, 7-dihydro-3H-spiro[benzofuran-2, 2'-indene]-1', 4 (3'H,5H)-dione (5c)

Yield: 50%, mp: 146–149 °C. IR (KBr, cm^{-1}): 3404, 2955, 2884, 2347, 1703, 1655, 1632, 1517, 1460, 1422, 1391, 1396, 1348, 1303, 1252, 1232, 1178, 1052, 1027. ^1H NMR (400 MHz, CDCl_3) δ (ppm): 7.84 (d, J

= 9.6 Hz, 1H), 7.55 (t, $J = 10$ Hz, 1H), 7.46–7.36 (m, 4H), 6.68 (d, $J = 12$ Hz, 2H), 4.41 (bs, 1H), 3.72 (bs, 3H), 3.08 (d, $J = 23.2$ Hz, 1H), 2.84 (d, $J = 23.2$ Hz, 1H), 2.58 (bs, 2H), 2.51 (bs, 2H), 1.28 (bs, 3H), 1.22 (bs, 3H). ^{13}C NMR (100 MHz, CDCl_3) δ (ppm): 200.5, 193.3, 175.6, 150.9, 136.5, 136.3, 136.2, 133.0, 130.6, 128.3, 127.4, 127.3, 126.3 (2C), 125.3, 115.5, 97.4, 55.4, 45.5, 37.7, 36.1, 34.2, 28.9, 28.8, 19.6. Anal. calc. for $\text{C}_{25}\text{H}_{24}\text{O}_4$: C, 77.30; H, 6.23. Found: C, 77.15; H, 6.17.

2.3.6. (2'S)-2-(4-methoxyphenyl)-6, 6-dimethyl-6, 7-dihydro-2H-spiro[benzofuran-3, 2'-indene]-1', 4 (3'H,5H)-dione (6c)

Yield: 45%, mp: 157–160 °C. IR (KBr, cm^{-1}): 3609, 3407, 3962, 2893, 2347, 1725, 1712, 1632, 1609, 1512, 1466, 1421, 1388, 1348, 1302, 1267, 1243, 1221, 1143, 1026, 1000. ^1H NMR (400 MHz, CDCl_3) δ (ppm): 7.53 (t, $J = 9.8$ Hz, 1H), 7.37 (d, $J = 10.0$ Hz, 1H), 7.24 (d, $J = 8.8$ Hz, 1H), 7.04 (d, $J = 11.2$ Hz, 1H), 6.91 (d, $J = 11.6$ Hz, 2H), 6.83 (d, $J = 12.0$ Hz, 2H), 5.68 (bs, 1H), 4.11 (d, $J = 22.8$ Hz, 1H), 3.79 (bs, 3H), 3.18 (d, $J = 23.2$ Hz, 1H), 2.58 (bs, 2H), 2.51 (bs, 2H), 1.24 (bs, 3H), 1.23 (bs, 3H). ^{13}C NMR (100 MHz, CDCl_3) δ (ppm): 200.3, 193.9, 177.9, 153.3, 135.8, 134.7, 134.0, 133.3, 129.9, 128.1, 127.6, 127.5, 125.7, 125.6, 123.9, 114.9, 91.0, 62.2, 55.1, 40.5, 38.0, 34.7, 29.1, 28.1, 19.2. Anal. calc. for $\text{C}_{25}\text{H}_{24}\text{O}_4$: C, 77.30; H, 6.23. Found: C, 77.20; H, 6.13.

2.3.7. (3S)-6, 6-dimethyl-3-(p-tolyl)-6, 7-dihydro-3H-spiro[benzofuran-2, 2'-indene]-1', 4 (3'H,5H)-dione (5d)

Yield: 45%, mp: 145–147 °C. IR (KBr, cm^{-1}): 3432, 3037, 2955, 2869, 2348, 1726, 1634, 1509, 1468, 1394, 1299, 1218, 1143, 1113, 1001. ^1H NMR (400 MHz, CDCl_3) δ (ppm): 7.84 (d, $J = 10.0$ Hz, 1H), 7.60 (d, $J = 11.0$ Hz, 1H), 7.43 (t, $J = 10.6$ Hz, 1H), 7.24 (d, $J = 10.4$ Hz, 1H), 7.10 (d, $J = 10.4$ Hz, 2H), 6.87 (d, $J = 10.8$ Hz, 2H), 4.42 (bs, 1H), 3.74 (d, $J = 9.6$ Hz, 1H), 3.08 (d, $J = 23.6$ Hz, 1H), 2.84 (d, $J = 23.6$ Hz, 1H), 2.53 (d, $J = 9.6$ Hz, 2H), 2.29 (bs, 1H), 2.19 (bs, 3H), 1.24 (bs, 3H), 1.23 (bs, 3H). ^{13}C NMR (100 MHz, CDCl_3) δ (ppm): 199.6, 193.4, 180.2, 147.0, 141.0, 139.8, 139.2, 136.0, 133.1, 129.4 (2C), 128.0 (3C), 126.3, 106.2, 97.6, 51.2, 44.9, 34.7, 32.9, 30.1, 28.8, 28.7, 26.3. Anal. calc. for $\text{C}_{25}\text{H}_{24}\text{O}_3$: C, 80.62; H, 6.49. Found: C, 80.54; H, 6.39.

2.3.8. (2'S)-6, 6-dimethyl-2-(p-tolyl)-6, 7-dihydro-2H-spiro[benzofuran-3,2'-indene]-1', 4 (3'H,5H)-dione (6d)

Yield: 45%, mp: 152–155 °C. IR (KBr, cm^{-1}): 3433, 3030, 2958, 2929, 2869, 2348, 1703, 1654, 1643, 1607, 1515, 1463, 1428, 1395, 1273, 1229, 1188, 1147, 1070. ^1H NMR (400 MHz, CDCl_3) δ (ppm): 7.53 (d, $J = 9.8$ Hz, 1H), 7.43 (d, $J = 10.0$ Hz, 1H), 7.37 (d, $J = 10.0$ Hz, 1H), 7.20 (d, $J = 9.8$ Hz, 1H), 6.98 (d, $J = 4.8$ Hz, 4H), 5.71 (bs, 1H), 4.11 (d, $J = 22.8$ Hz, 1H), 3.22 (d, $J = 23.2$ Hz, 1H), 2.59 (d, $J = 1.6$ Hz, 2H), 2.32 (d, $J = 6.0$ Hz, 1H), 2.23 (bs, 3H), 2.19 (bs, 1H), 1.27 (bs, 3H), 1.22 (bs, 3H). ^{13}C NMR (100 MHz, CDCl_3) δ (ppm): 202.9, 194.0, 178.3, 157.8, 151.5, 138.1, 136.0, 134.7, 131.6, 128.7, 127.3, 125.8, 123.9, 118.3, 115.4, 113.0, 95.4, 61.7, 51.2, 39.1, 38.0, 34.7, 29.4, 27.8, 21.1. Anal. calc. for $\text{C}_{25}\text{H}_{24}\text{O}_3$: C, 80.62; H, 6.49. Found: C, 80.56; H, 6.34.

2.3.9. (3*S*)-3-(3-chlorophenyl)-6,6-dimethyl-6,7-dihydro-3*H*-spiro[benzofuran-2, 2'-indene]-1', 4(3'*H*,5*H*)-dione (5e)

Yield: 41%, mp: 136–139 °C. IR (KBr, cm⁻¹): 3405, 2959, 2879, 2344, 1735, 1639, 1470, 1433, 1393, 1300, 1226, 1214, 1116, 1004. ¹H NMR (400 MHz, CDCl₃) δ (ppm): 7.85 (d, *J* = 7.6 Hz, 1H), 7.63 (t, *J* = 7.4 Hz, 1H), 7.45 (t, *J* = 7.4 Hz, 1H), 7.26–7.23 (m, 3H), 6.99 (bs, 1H), 6.90 (d, *J* = 6.4 Hz, 1H), 4.43 (bs, 1H), 3.12 (d, *J* = 17.6 Hz, 1H), 2.79 (d, *J* = 17.6 Hz, 1H), 2.53 (m, 2H), 2.36 (d, *J* = 16.4 Hz, 1H), 2.29 (d, *J* = 16.0 Hz, 1H), 1.24 (bs, 3H), 1.23 (bs, 3H). ¹³C NMR (100 MHz, CDCl₃) δ (ppm): 199.8, 193.3, 176.2, 150.3, 140.4, 136.2, 134.7, 133.0, 130.0, 128.4, 128.2, 127.9, 126.4, 126.3, 125.4, 115.0, 95.4, 51.2, 49.6, 37.7, 38.8, 34.3, 28.7 (2C). Anal. calc. for C₂₄H₂₁ClO₃: C, 73.37; H, 5.39. Found: C, 73.25; H, 5.30.

2.3.10. (2'*S*)-2-(3-chlorophenyl)-6, 6-dimethyl-6, 7-dihydro-2*H*-spiro[benzofuran-3, 2'-indene]-1', 4(3'*H*,5*H*)-dione (6e)

Yield: 40%, mp: 143–147 °C. IR (KBr, cm⁻¹): 3444, 2954, 2348, 1700, 1654, 1633, 1600, 1475, 1427, 1398, 1273, 1227, 1145, 1077. ¹H NMR (400 MHz, CDCl₃) δ (ppm): 7.59–7.55 (td, *J* = 7.4 Hz, 1.2 Hz, 1H), 7.46 (d, *J* = 7.6 Hz, 1H), 7.39 (d, *J* = 8.0 Hz, 1H), 7.25 (t, *J* = 7.6 Hz, 1H), 7.15 (d, *J* = 8.0 Hz, 1H), 7.10 (bs, 1H), 7.07 (d, *J* = 7.6 Hz, 1H), 6.94 (d, *J* = 7.6 Hz, 1H), 5.70 (bs, 1H), 4.15 (d, *J* = 17.2 Hz, 1H), 3.23 (d, *J* = 17.2 Hz, 1H), 2.60–2.55 (m, 2H), 2.34 (d, *J* = 16.0 Hz, 1H), 2.22 (d, *J* = 16.0 Hz, 1H), 1.27 (bs, 3H), 1.23 (bs, 3H). ¹³C NMR (100 MHz, CDCl₃) δ (ppm): 202.4, 193.9, 177.9, 157.5, 151.4, 136.8, 135.0, 134.1, 129.2, 128.5, 127.6, 126.1, 125.9, 124.0, 123.8, 115.3, 94.2, 61.8, 51.2, 39.1, 37.9, 34.7, 29.4, 27.8. Anal. calc. for C₂₄H₂₁ClO₃: C, 73.37; H, 5.39. Found: C, 73.27; H, 5.27.

2.3.11. (3*S*)-3-(3-methoxyphenyl)-6,6-dimethyl-6,7-dihydro-3*H*-spiro[benzofuran-2,2'-indene]-1', 4(3'*H*,5*H*)-dione (5f)

Yield: 80%, mp: 155–158 °C. IR (KBr, cm⁻¹): 3449, 2994, 2958, 2928, 2830, 2347, 1715, 1642, 1605, 1581, 1465, 1420, 1390, 1348, 1300, 1267, 1221, 1154, 1140, 1051. ¹H NMR (400 MHz, CDCl₃) δ (ppm): 7.85 (d, *J* = 7.6 Hz, 1H), 7.61 (t, *J* = 7.6 Hz, 1H), 7.44 (d, *J* = 7.4 Hz, 1H), 7.25 (d, *J* = 7.6 Hz, 1H), 7.21 (d, *J* = 8.0 Hz, 1H), 6.81 (d, *J* = 7.6 Hz, 1H), 6.59 (d, *J* = 7.6 Hz, 1H), 6.51 (bs, 1H), 4.43 (bs, 1H), 3.73 (bs, 3H), 3.08 (d, *J* = 17.6 Hz, 1H), 2.83 (d, *J* = 17.6 Hz, 1H), 2.54–2.53 (m, 2H), 2.37 (d, *J* = 16.0 Hz, 1H), 2.29 (d, *J* = 16.4 Hz, 1H), 1.25 (bs, 3H), 1.23 (bs, 3H). ¹³C NMR (100 MHz, CDCl₃) δ (ppm): 200.3, 193.4, 176.0, 159.8, 150.7, 139.8, 136.0, 133.2, 129.8, 128.3, 126.3, 125.3, 120.5, 115.1, 113.9, 112.9, 95.6, 55.1, 51.2, 50.1, 37.7, 35.8, 34.2, 28.9, 28.7. Anal. calc. for C₂₅H₂₄O₄: C, 77.30; H, 6.23. Found: C, 77.25; H, 6.09.

2.3.12. (3*S*)-6, 6-dimethyl-3-(*m*-tolyl)-6, 7-dihydro-3*H*-spiro[benzofuran-2, 2'-indene]-1', 4(3'*H*,5*H*)-dione (5g)

Yield: 75%, mp: 157–160 °C. IR (KBr, cm⁻¹): 3457, 3018, 2957, 2867, 2347, 1716, 1659, 1641, 1603, 1464, 1423, 1391, 1349, 1298, 1236, 1219, 1154, 1110, 1046. ¹H NMR (400 MHz, CDCl₃) δ (ppm): 7.75 (d, *J* = 10.0 Hz, 1H), 7.51 (d, *J* = 10.0 Hz, 1H), 7.34 (d, *J* = 10.0 Hz, 1H), 7.14 (d, *J* = 10.4 Hz, 1H), 7.08 (d, *J* = 10.0 Hz, 1H), 6.97 (dd, *J* = 10.4 Hz, 1H), 6.70 (d, *J* = 11.2 Hz, 1H), 4.32 (bs, 1H), 2.98 (d, *J* = 23.6 Hz, 1H), 2.71 (d, *J* = 23.2 Hz, 1H), 2.47 (d, *J* = 23.6 Hz, 1H), 2.40 (d, *J* = 23.6 Hz, 2H), 2.27 (d, *J* = 21.6 Hz, 1H), 2.19 (bs, 3H), 2.18 (d, *J* = 21.6 Hz, 1H), 1.57 (bs, 3H), 1.14 (bs, 3H). ¹³C NMR (100 MHz, CDCl₃)

δ (ppm): 200.3, 193.4, 175.8, 150.7, 138.3, 1348.1, 136.0, 128.6, 128.4, 128 (2C), 126.3 (2C), 125.3 (2C), 115.4, 95.7, 51.2, 50.0, 37.7, 35.8, 34.7, 28.9, 28.7, 21.4. Anal. calc. for $C_{25}H_{24}O_3$: C, 80.62; H, 6.49. Found: C, 80.49; H, 6.37.

2.3.13. (3*S*)-6, 6-dimethyl-3-(*o*-tolyl)-6, 7-dihydro-3*H*-spiro[benzofuran-2, 2'-indene]-1', 4 (3'*H*,5*H*)-dione (5h)

Yield: 38%, mp: 163–166 °C. IR (KBr, cm^{-1}): 3438, 3047, 2953, 2928, 2346, 1725, 1649, 1608, 1465, 1422, 1383, 1342, 1299, 1230, 1133, 1050. 1H NMR (400 MHz, $CDCl_3$) δ (ppm): 7.85 (d, $J = 7.6$ Hz, 1H), 7.61 (t, $J = 7.6$ Hz, 1H), 7.44 (t, $J = 7.4$ Hz, 1H), 7.25 (t, $J = 7.8$ Hz, 1H), 7.20–7.14 (m, 2H), 7.09 (d, $J = 7.2$ Hz, 1H), 7.04 (d, $J = 7.4$ Hz, 1H), 4.78 (bs, 1H), 3.05 (d, $J = 17.6$ Hz, 1H), 2.75 (d, $J = 18.0$ Hz, 1H), 2.52 (m, 2H), 2.36 (d, $J = 16.0$ Hz, 1H), 2.30 (d, $J = 16.4$ Hz, 1H), 1.93 (bs, 3H), 1.26 (bs, 3H), 1.24 (bs, 3H). ^{13}C NMR (100 MHz, $CDCl_3$) δ (ppm): 200.5, 193.3, 175.6, 150.9, 136.5, 136.3, 136.2, 133.0, 130.6, 128.3, 127.4, 127.3, 126.3 [5(2C)], 125.3, 115.5, 95.4, 51.3, 45.5, 37.7, 36.1, 34.2, 28.9, 28.8, 19.6. Anal. calc. for $C_{25}H_{24}O_3$: C, 80.62; H, 6.49. Found: C, 80.56; H, 6.33.

2.3.14. (2'*S*)-6, 6-dimethyl-2-(*o*-tolyl)-6, 7-dihydro-2*H*-spiro[benzofuran-3, 2'-indene]-1', 4 (3'*H*,5*H*)-dione (6h)

Yield: 35%, mp: 178–181 °C. IR (KBr, cm^{-1}): 3416, 3029, 2961, 2946, 2929, 2867, 2348, 1717, 1645, 1604, 1492, 1466, 1420, 1395, 1368, 1340, 1291, 1266, 1227, 1191, 1143, 1071, 1013. 1H NMR (400 MHz, $CDCl_3$) δ (ppm): 7.53 (t, $J = 7.4$ Hz, 1H), 7.42 (d, $J = 7.4$ Hz, 1H), 7.34 (d, $J = 7.4$ Hz, 1H), 7.32 (d, $J = 8.8$ Hz, 1H), 7.23 (d, $J = 7.4$ Hz, 1H), 7.20 (d, $J = 7.4$ Hz, 1H), 7.08 (t, $J = 7.4$ Hz, 1.2 Hz, 1H), 6.86 (d, $J = 7.2$ Hz, 1H), 6.04 (bs, 1H), 4.07 (d, $J = 16.8$ Hz, 1H), 3.34 (d, $J = 17.2$ Hz, 1H), 2.63 (d, $J = 17.6$ Hz, 1H), 2.56 (d, $J = 17.6$ Hz, 1H), 2.31 (m, 2H), 1.90 (bs, 3H), 1.31 (bs, 3H), 1.23 (bs, 3H). ^{13}C NMR (100 MHz, $CDCl_3$) δ (ppm): 202.3, 193.9, 177.9, 151.3, 135.8, 134.7, 134.0, 133.3, 129.9, 128.1, 127.6, 127.5, 125.7, 125.6, 123.9, 114.9, 92.8, 62.2, 51.1, 40.5, 38.0, 34.7, 29.1, 28.1, 19.2. Anal. calc. for $C_{25}H_{24}O_3$: C, 80.62; H, 6.49. Found: C, 80.59; H, 6.38.

2.3.15. (3*R*)-3-(2-chloro-5-nitrophenyl)-6, 6-dimethyl-6, 7-dihydro-3*H*-spiro[benzofuran-2, 2'-indene]-1', 4 (3'*H*, 5*H*)-dione (5i)

Yield: 43%, mp: 210–213 °C. IR (KBr, cm^{-1}): 3441, 3079, 2348, 1708, 1604, 1527, 1464, 1347, 1268, 1095, 1048. 1H NMR (400 MHz, $CDCl_3$) δ (ppm): 8.21 (d, $J = 8.4$ Hz, 1H), 7.97 (d, $J = 12.0$ Hz, 1H), 7.82 (d, $J = 12.0$ Hz, 1H), 7.69 (d, $J = 11.6$ Hz, 1H), 7.56 (d, $J = 9.6$ Hz, 1H), 7.50 (d, $J = 10.4$ Hz, 1H), 7.16 (d, $J = 10.4$ Hz, 1H), 6.98 (d, $J = 9.6$ Hz, 1H), 4.57 (bs, 1H), 3.74 (d, $J = 9.6$ Hz, 1H), 3.34 (m, 2H), 2.19 (m, 2H), 1.57 (bs, 6H). ^{13}C NMR (100 MHz, $CDCl_3$) δ (ppm): 200.7, 198.2, 173.6, 149.2, 146.8, 139.1, 137.8, 137.5, 133.2, 131.2, 128.1, 127.2, 126.3 (2C), 124.4, 105.0, 97.7, 51.7, 39.7, 36.7, 34.7, 33.7, 27.5 (2C). Anal. calc. for $C_{24}H_{20}ClNO_5$: C, 65.83; H, 4.60; N, 3.20. Found: C, 65.79; H, 4.51; N, 3.14.

2.3.16. (2'S)-2-(2-chloro-5-nitrophenyl)-6, 6-dimethyl-6, 7-dihydro-2H-spiro[benzofuran-3, 2'-indene]-1', 4 (3'H,5H)-dione (6i)

Yield: 38%, mp: 220–223 °C. IR (KBr, cm^{-1}): 3433, 2960, 2873, 2347, 1592, 1527, 1468, 1451, 1403, 1239, 1046. $^1\text{H NMR}$ (400 MHz, CDCl_3) δ (ppm): 8.02 (d, $J = 8.0$ Hz, 1H), 7.79 (d, $J = 10.4$ Hz, 1H), 7.56 (d, $J = 10.0$ Hz, 1H), 7.55 (d, $J = 10.0$ Hz, 1H), 7.43 (d, $J = 11.6$ Hz, 1H), 7.38 (d, $J = 9.6$ Hz, 1H), 7.22 (d, $J = 10.4$ Hz, 1H), 5.05 (bs, 1H), 3.01 (d, $J = 23.6$ Hz, 1H), 2.62 (d, $J = 23.6$ Hz, 1H), 2.46 (m, 2H), 2.30 (m, 2H), 1.23 (bs, 3H), 1.16 (bs, 3H). $^{13}\text{C NMR}$ (100 MHz, CDCl_3) δ (ppm): 199.1, 193.3, 177.0, 150.4, 146.9, 141.3, 138.2, 136.4, 132.8, 130.6, 128.5, 126.3, 125.5, 123.7, 113.1, 94.6, 51.1, 46.2, 37.8, 36.3, 34.3, 28.8, 28.7, 27.5. Anal. calc. for $\text{C}_{24}\text{H}_{20}\text{ClNO}_5$: C, 65.83; H, 4.60; N, 3.20. Found: C, 65.75; H, 4.54; N, 3.08.

2.3.17. (3S)-3-(2, 4-dimethoxyphenyl)-6, 6-dimethyl-6, 7-dihydro-3H-spiro[benzofuran-2, 2'-indene]-1', 4 (3'H,5H)-dione (5j)

Yield: 45%, mp: 170–173 °C. IR (KBr, cm^{-1}): 3423, 2950, 2839, 2345, 1716, 1643, 1588, 1507, 1467, 1386, 1274, 1228, 1209, 1152, 1124, 1036. $^1\text{H NMR}$ (400 MHz, CDCl_3) δ (ppm): 7.52 (t, $J = 9.8$ Hz, 1H), 7.37 (t, $J = 10.0$ Hz, 2H), 7.23 (d, $J = 9.6$ Hz, 2H), 6.75 (d, $J = 11.2$ Hz, 1H), 6.32 (dd, $J = 11.2$ Hz, 3.2 Hz, 1H), 5.97 (d, $J = 3.2$ Hz, 1H), 4.81 (bs, 1H), 3.98–3.81 (m, 1H), 3.72–3.69 (m, 1 H), 3.64 (bs, 3H), 3.48 (d, $J = 22.4$ Hz, 1H), 2.92 (bs, 3H) 2. 58 (d, $J = 23.6$ Hz, 1H), 2.36 (d, $J = 22.4$ Hz, 1H), 2.24 (d, $J = 21.6$ Hz, 1H), 1.23 (bs, 3H), 1.12 (bs, 3H). $^{13}\text{C NMR}$ (100 MHz, CDCl_3) δ (ppm): 200.3, 193.9, 177.2, 159.9, 156.6, 150.1, 135.2, 134.6, 129.2, 126.3, 125.7, 123.6, 125.7, 116.8, 112.9, 103.5, 97.8, 96.18, 55.2, 51.6, 49.8, 43.3, 39.7, 34.4, 34.2, 27.8. Anal. calc. for $\text{C}_{26}\text{H}_{26}\text{O}_5$: C, 74.62; H, 6.26. Found: C, 74.53; H, 6.11.

2.3.18. (2'S)-2-(2, 4-dimethoxyphenyl)-6, 6-dimethyl-6, 7-dihydro-2H-spiro [benzofuran-3, 2'-indene]-1', 4(3'H,5H)-dione (6j)

Yield: 40%, mp: 162–165 °C. IR (KBr, cm^{-1}): 3439, 3057, 2958, 2874, 2348, 1689, 1631, 1596, 1580, 1507, 1464, 1409, 1327, 1298, 1272, 1231, 1181, 1160, 1153, 1116, 1094, 1083. $^1\text{H NMR}$ (400 MHz, CDCl_3) δ (ppm): 7.84 (d, $J = 7.6$ Hz, 1H), 7.51 (t, $J = 7.6$ Hz, 1H), 7.35 (t, $J = 7.6$ Hz, 1H), 7.30 (d, $J = 8.4$ Hz, 1H), 7.20 (d, $J = 7.6$ Hz, 1H), 6.54 (d, $J = 8.4$ Hz, 1H), 6.23 (bs, 1H), 6.12 (bs, 1H), 3.81 (bs, 3H), 2.99 (m, 4H), 2.70–2.51 (m, 3H), 2.28 (d, $J = 16.0$ Hz, 1H), 2.15 (d, $J = 16.0$ Hz, 1H), 1.20 (bs, 3H), 1.25 (bs, 3H). $^{13}\text{C NMR}$ (100 MHz, CDCl_3) δ (ppm): 206.9, 193.2, 176.4, 160.8, 156.8, 152.8, 136.1, 134.4, 126.9, 126.5, 125.7, 123.7, 117.4, 117.4, 104.0, 97.7, 90.4, 60.8, 55.3, 53.8, 51.0, 37.9, 35.7, 34.3, 29.1, 28.2. Anal. calc. for $\text{C}_{26}\text{H}_{26}\text{O}_5$: C, 74.62; H, 6.26. Found: C, 74.51; H, 6.18.

2.3.19. (3S)-3-(2, 5- dimethoxyphenyl)-6, 6-dimethyl-6, 7-dihydro-3H-spiro [benzofuran-2, 2'-indene]-1', 4 (3'H,5H)-dione (5k)

Yield: 40%, mp: 137–140 °C. IR (KBr, cm^{-1}): 3440, 2956, 2867, 2839, 2347, 1731, 1628, 1501, 1465, 1420, 1402, 1352, 1329, 1298, 1225, 1042. $^1\text{H NMR}$ (400 MHz, CDCl_3) δ (ppm): 7.77 (d, $J = 10.0$ Hz, 1H), 7.50 (t, $J = 9.8$ Hz, 1H), 7.33 (t, $J = 9.8$ Hz, 1H), 7.14 (d, $J = 10.0$ Hz, 1H), 6.65 (dd, $J = 6.2$ Hz, 4.2 Hz, 1H), 6.53 (d, $J = 12.0$ Hz, 1H), 6.48 (d, $J = 4.0$ Hz, 1H), 4.85 (bs, 1H), 3.66 (bs, 3H), 3.04 (bs, 3H), 2.88 (d, $J = 24.0$ Hz, 1H), 2.70 (d, $J = 24.0$ Hz, 1H), 2.40 (m, 2H), 2.29 (bs, 2H), 1.19 (bs, 3H), 1.14 (bs, 3H). $^{13}\text{C NMR}$ (100 MHz, CDCl_3) δ (ppm): 201.1, 193.5, 176.5, 153.5, 151.3, 151.2, 135.6, 133.5, 127.8, 127.2,

125.9, 125.0, 115.3, 112.9, 112.1, 110.4, 95.2, 55.6, 54.6, 51.4, 44.3, 37.9, 36.4, 34.1, 28.9, 28.8. Anal. calc. for $C_{26}H_{26}O_5$: C, 74.62; H, 6.26. Found: C, 74.58; H, 6.20.

2.3.20. (2'S)-2-(2, 5-dimethoxyphenyl)-6, 6-dimethyl-6, 7-dihydro-2H-spiro[benzo-furan-3,2'-indene]-1', 4 (3'H,5H)-dione (6k)

Yield: 38%, mp: 147–150 °C. IR (KBr, cm^{-1}): 3440, 3014, 2956, 2867, 2347, 1731, 1628, 1502, 1646, 1420, 1402, 1352, 1329, 1298, 1225, 1120, 1042. 1H NMR (400 MHz, $CDCl_3$) δ (ppm): 7.86 (d, $J = 10$ Hz, 1H), 7.52 (d, $J = 9.6$ Hz, 1H), 7.23 (d, $J = 10$ Hz, 2H), 6.62 (d, $J = 12$ Hz, 1H), 6.57 (d, $J = 4$ Hz, 2H), 6.04 (bs, 1H), 3.88 (d, $J = 22$ Hz, 1H), 3.79 (bs, 3H), 3.50 (d, $J = 22.4$ Hz, 1H), 3.02 (bs, 3H), 2.38 (bs, 2H), 2.25 (bs, 2H), 1.24 (bs, 3H), 1.23 (bs, 3H). ^{13}C NMR (100 MHz, $CDCl_3$) δ (ppm): 202.3, 193.9, 177.9, 151.3, 135.8, 134.7, 134.0, 133.3, 129.9, 128.1, 127.6, 127.5, 125.7, 125.6, 123.9, 114.9, 92.8, 62.2, 51.1, 40.5, 38.0, 34.7, 29.1, 28.1, 19.2, 19.0. Anal. calc. for $C_{26}H_{26}O_5$: C, 74.62; H, 6.26. Found: C, 74.49; H, 6.23.

3. Results and discussion

Firstly, the starting materials, chalcone-like derivatives, 2-(benzylidene)-2,3-dihydro-1*H*-inden-1-one (**4a–k**), were synthesized from the Claisen–Schmidt condensation of 2,3-dihydro-1*H*-inden-1-one (1-indanone) with benzaldehyde derivatives according to our recently published procedure [39]. The structures of compounds **4a–k** were elucidated by spectroscopic data (NMR, IR, and elemental analysis) and comparison with authentic samples of them [39].

Then the compounds (**4a–k**) were reacted with the dimedone (**2**) in the presence of $Mn(OAc)_3$ in acetic acid at 60 °C for 2 h. The reaction resulted in the formation of two isomeric spirobenzofuran derivatives (**5a–k** and **6a–k**) in a ratio of almost 1:1 (Table). In the case of compounds **4f** and **4g**, the single isomers **5f** and **5g** were formed, respectively, in both reactions. The isomers **5a–k** and **6a–k** were separated by silica gel column chromatography eluting with ethyl acetate/hexane (3:7). The structures of the compounds were explained on the basis of spectral data (NMR and IR) and elemental analysis. All spectral data were in good agreement with the proposed structures of the compounds.

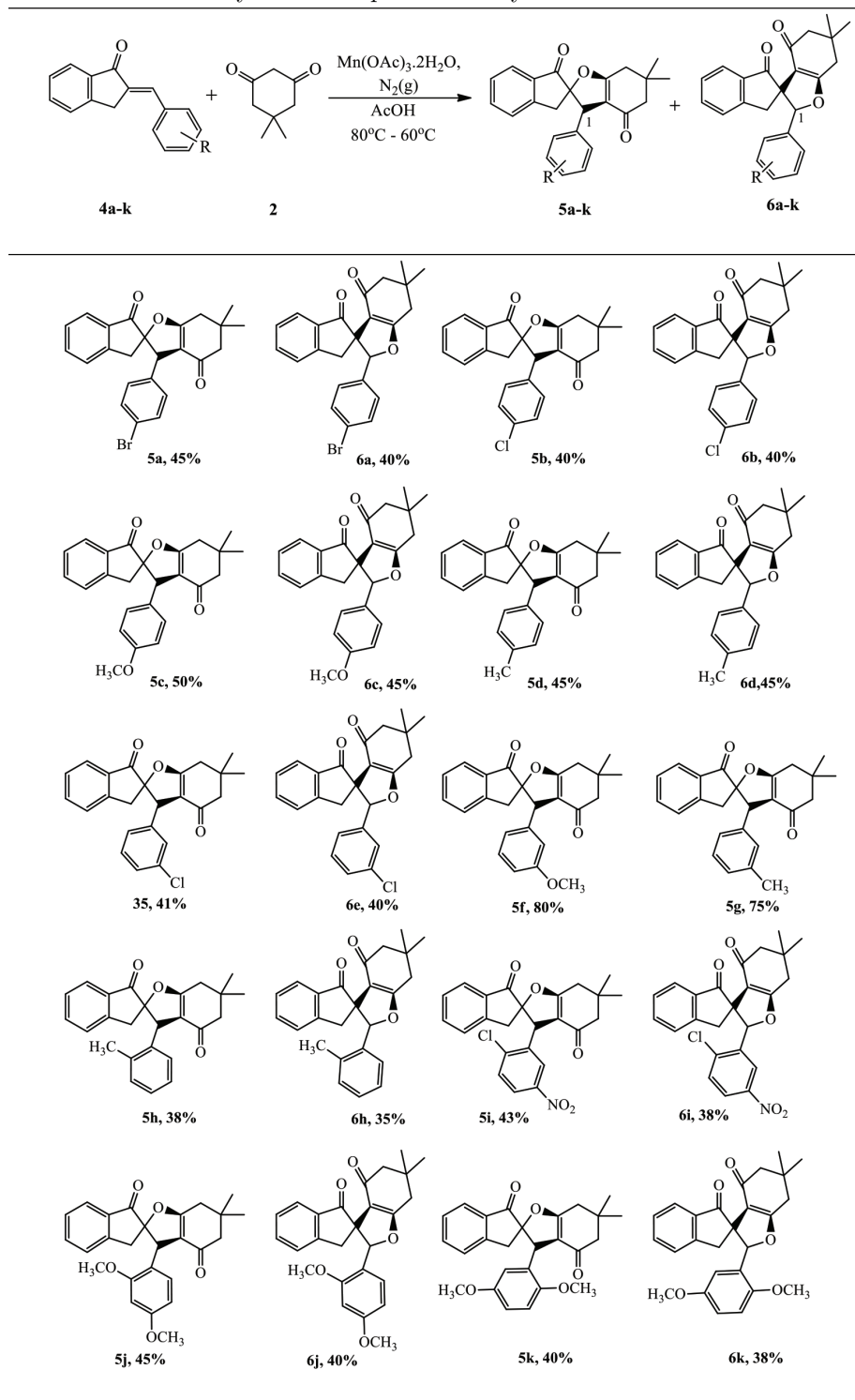
In our previous study [38], we investigated the $Mn(OAc)_3$ -mediated oxidative free radical addition of dimedone to 2-(benzylidene)-3,4-dihydronaphthalen-1(2*H*)-one derivatives. We determined that the dimedone was regioselectively added to the β -carbon atom of the α,β -unit of the starting materials and the tetralone-based spirodihydrobenzofuran derivatives occurred by oxidative cyclization as a single isomer in good yield. In the present study, the addition of dimedone to 2-(benzylidene)-2,3-dihydro-1*H*-inden-1-one (**4a–k**) gave the two isomeric indanone-based spirodihydrobenzofuran derivatives. Formation of the two isomers can be explained by the addition of dimedone to the β - and α -carbon atoms of the α,β -unsaturated unit in the structure of 2-(benzylidene)-2,3-dihydro-1*H*-inden-1-one (**4a–k**), respectively. A distinction between these structures has been made on the basis of 1H NMR spectral studies. The benzylic proton C1-H of isomers **5** and **6** resonated in the upfield region at δ 4.32–4.85 ppm and in the downfield region at δ 5.05–6.12 ppm as expected, respectively, in their 1H NMR spectra.

4. Conclusion

Two novel series of isomeric indanone-based spirodihydrobenzofuran derivatives, (3*S*)-6,6-dimethyl-3-aryl-6,7-dihydro-3*H*-spiro[benzofuran-2,2'-indene]-1',4(3'*H*,5*H*)-dione (**5a–k**) and (2'*S*)-6,6-dimethyl-2-aryl-6,7-dihydro-

2*H*-spiro[benzofuran-3,2'-indene]-1',4(3'*H*,5*H*)-dione (**6a-k**), were synthesized using Mn(OAc)₃-mediated oxidative free radical additions between indanone-based chalcone-like compounds **4a-k** and dimedone (**2**) in a ratio of almost 1:1.

Table. Synthesis of spirobenzodihydrofurane derivatives.



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