TÜBİTAK

Turkish Journal of Chemistry

http://journals.tubitak.gov.tr/chem/

Research Article

Turk J Chem
(2019) 43: 1445 – 1457
© TÜBİTAK
doi:10.3906/kim-1904-13

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

Meliha Burcu GÜDERE, Neşe DÜRÜ, Yakup BUDAK, Mustafa CEYLAN*
Department of Chemistry, Faculty of Arts and Sciences, Gaziosmanpaşa University, Tokat, Turkey

Received: 09.04.2019 • **Accepted/Published Online:** 11.09.2019 • **Final Version:** 07.10.2019

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

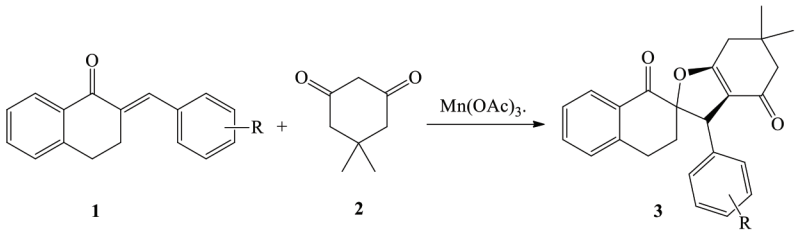
Benzofuran derivatives are an important class of heterocyclic compounds having biological activity, such as dihydrofuran [1,2]. Benzofuran [3] and spiro-benzofuran [4] derivatives have advantageous structural skeletons in medicinal chemistry for drug discovery [5]. They are found in the structures of 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].

*Correspondence: mustafa.ceylan@gop.edu.tr



1 2 3

As part of our previous work, the current study reports the oxidative free radical addition of dimedone (**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. ^{1}H and ^{13}C NMR spectra were recorded on a Bruker Avance DPX-400 instrument. TMS (^{1}H NMR, δ (0.00)) and $CDCl_3$ (δ (77.0)) served as internal standards for ^{13}C 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-1*H*-inden-1-one (chalcone-like compounds) derivatives (4a–k)

The chalcone-like compounds, (*E*)-2-benzylidene-2,3-dihydro-1*H*-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-didyhrobenzofuran 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 N_2 atmosphere. After the temperature had dropped to 60 °C, to this solution was added solution of **4a**–**k** (1 mmol) and dimedone (**2**) (3 mmol) in AcOH (10 mL) dropwise over 25 min. The mixture was refluxed for 3 h under N_2 atmosphere. The reaction mixture was extracted with CH_2Cl_2, dried over anhydrous Na_2SO_4, 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. **^{1}H NMR (400 MHz, $CDCl_3$) 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 $C_{24}H_{21}BrO_3$: 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-2*H*-spiro[benzofuran-3, 2'-indene]-1', 4 (3'*H*,5*H*)-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. **^{1}H 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 $C_{24}H_{21}BrO_3$: C, 65.91; H, 4.84. Found: C, 65.83; H, 4.80.

2.3.3. (3*S*)-3-(4-chlorophenyl)-6, 6-dimethyl-6, 7-dihydro-3*H*-spiro[benzofuran-2, 2'-indene]-1', 4 (3'*H*,5*H*)-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. **^{1}H 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 $C_{24}H_{21}ClO_3$: 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-2*H*-spiro[benzofuran-3, 2'-indene]-1', 4 (3'*H*,5*H*)-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. **^{1}H 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 $C_{24}H_{21}ClO_3$: C, 73.37; H, 5.39. Found: C, 73.28; H, 5.27.

2.3.5. (3*S*)-3-(4-methoxyphenyl)-6, 6-dimethyl-6, 7-dihydro-3*H*-spiro[benzofuran-2, 2'-indene]-1', 4 (3'*H*,5*H*)-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. **^{1}H 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 $C_{25}H_{24}O_4$: 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-2*H*-spiro[benzofuran-3, 2'-indene]-1', 4 (3'*H*,5*H*)-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. **^{1}H 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 $C_{25}H_{24}O_4$: C, 77.30; H, 6.23. Found: C, 77.20; H, 6.13.

2.3.7. (3*S*)-6, 6-dimethyl-3-(p-tolyl)-6, 7-dihydro-3*H*-spiro[benzofuran-2, 2'-indene]-1', 4 (3'*H*,5*H*)-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. **^{1}H 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 $C_{25}H_{24}O_3$: 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-2*H*-spiro[benzofuran-3,2'-indene]-1', 4 (3'*H*,5*H*)-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. **^{1}H 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 $C_{25}H_{24}O_3$: 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. **^{1}H NMR (400 MHz, $CDCl_3$)** 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). **^{13}C NMR (100 MHz, $CDCl_3$)** 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 $C_{24}H_{21}ClO_3$: 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. **^{1}H NMR (400 MHz, $CDCl_3$)** 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). **^{13}C NMR (100 MHz, $CDCl_3$)** 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 $C_{24}H_{21}ClO_3$: 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. **^{1}H 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 (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). **^{13}C NMR (100 MHz, $CDCl_3$)** 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 $C_{25}H_{24}O_4$: 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. **^{1}H NMR (400 MHz, $CDCl_3$)** 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). **^{13}C NMR (100 MHz, $CDCl_3$)**

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. **^{1}H 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. **^{1}H 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. **^{1}H 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-2*H*-spiro[benzofuran-3, 2'-indene]-1', 4 (3'*H*,5*H*)-dione (6i)

Yield: 38%, mp: 220–223 °C. **IR (KBr, cm^{-1}):** 3433, 2960, 2873, 2347, 1592, 1527, 1468, 1451, 1403, 1239, 1046. **^{1}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}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 $C_{24}H_{20}ClNO_5$: C, 65.83; H, 4.60; N, 3.20. Found: C, 65.75; H, 4.54; N, 3.08.

2.3.17. (3*S*)-3-(2, 4-dimethoxyphenyl)-6, 6-dimethyl-6, 7-dihydro-3*H*-spiro[benzofuran-2, 2'-indene]-1', 4 (3'*H*,5*H*)-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}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}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 $C_{26}H_{26}O_5$: 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-2*H*-spiro [benzofuran-3, 2'-indene]-1', 4(3'*H*,5*H*)-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}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}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 $C_{26}H_{26}O_5$: C, 74.62; H, 6.26. Found: C, 74.51; H, 6.18.

2.3.19. (3*S*)-3-(2, 5- dimethoxyphenyl)-6, 6-dimethyl-6, 7-dihydro-3*H*-spiro [benzofuran-2, 2'-indene]-1', 4 (3'*H*,5*H*)-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}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}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-2*H*-spiro[benzo-furan-3,2'-indene]-1', 4 (3'*H*,5*H*)-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. **^{1}H 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.

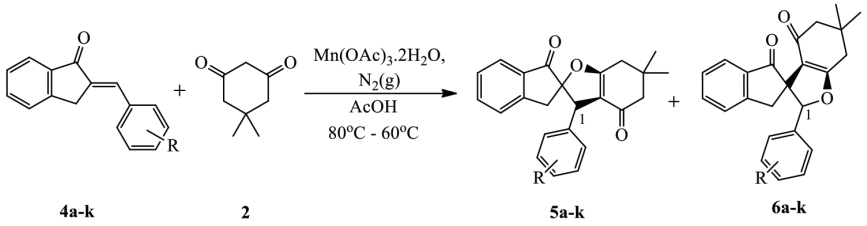
In our previous study [38], we investigated the $Mn(OAc)_3$-mediated oxidative free radical addition of dimedone to 2-(benzylidene)-3,4-dihydronaphthalen-1(2*H*)-one derivatives. We determined that the dimedone was regioselectively added to the β-carbon atom of the α,β-unit of the starting materials and the tetralone-based spirodihydrobezofuran derivatives occurred by oxidative cyclization as a single isomer in good yield. In the present study, the addition of dimedone to 2-(benzyliden)-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 dimedon to the β- and α-carbon atoms of the α,β-unsaturated unit in the structure of 2-(benzyliden)-2,3-dihydro-1*H*-inden-1-one (**4a**–**k**), respectively. A distinction between these structures has been made on the basis of ^{1}H 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 ^{1}H NMR spectra.

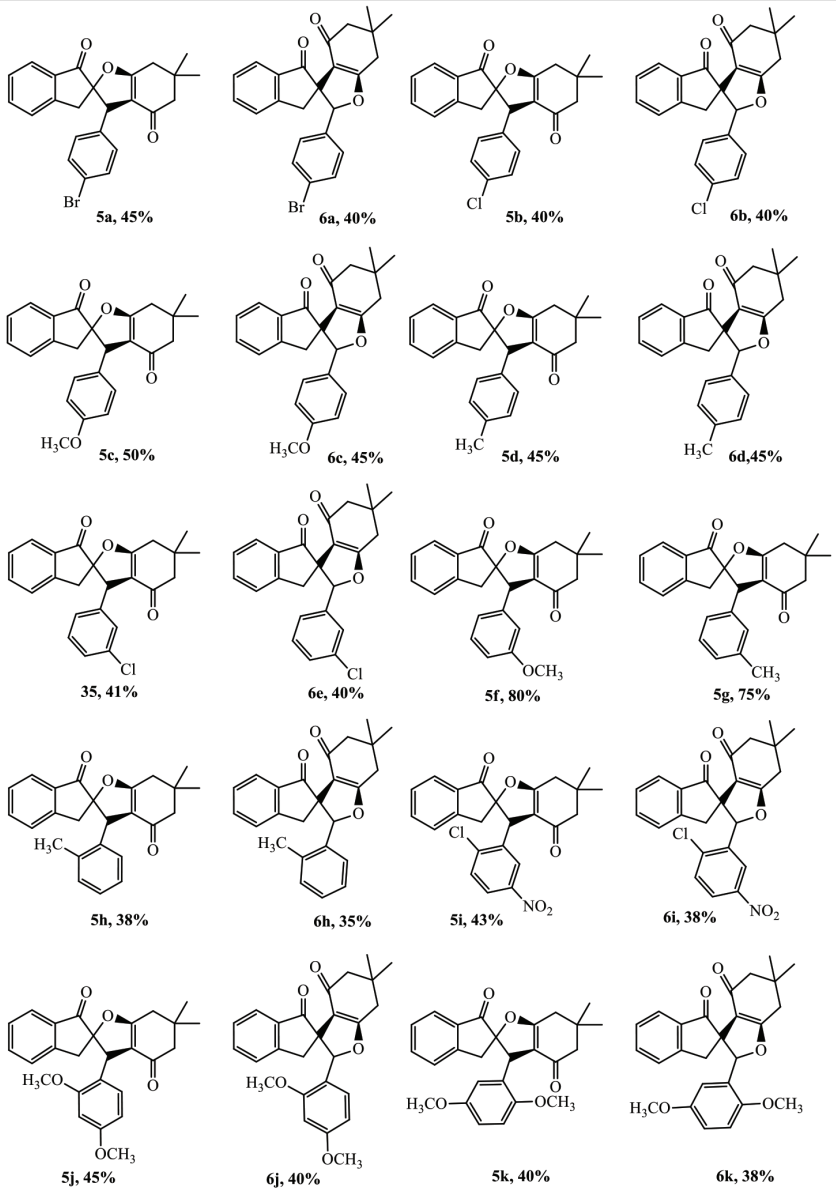
4. Conclusion

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.





Acknowledgments

The authors are indebted to the Gaziosmanpaşa University Scientific Research Projects Commission (Project No: BAP-2015/42) and the Scientific and Technological Research Council of Turkey (TÜBİTAK; BİDEP-2210-C) for their financial support.

References

1. Logoglu E, Yılmaz M, Katircioglu H, Yakut M, Mercan S. Synthesis and biological activity studies of furan derivatives. Medicinal Chemistry Research 2010; 19: 490-497. doi: 10.1007/s00044-009-9206-8
2. Nevagi RJ, Dighe SN, Dighe SN. Biological and medicinal significance of benzofuran. European Journal of Medicinal Chemistry 2015; 97: 561-581. doi: 10.1016/j.ejmech.2014.10.085
3. Masubuchi M, Kawasaki K, Ebiike H, Ikeda Y, Tsuji S et al. Design and synthesis of novel benzo-furans as a new class of antifungal agents targeting fungal N-myristoyltransferase. Part 1 Bioorganic & Medicinal Chemistry Letters 2001; 11: 1833-1837. doi: 10.1016/S0960-894X(01)00319-5
4. Dhotare BB, Choudhary MK, Nayak SK. $SbCl_3$-catalyzed solvent-free Friedel–Crafts reaction of phenols with mandelic acids to 3-aryl benzofuran-2(3H)-ones: synthesis of spirocyclic 2,3-dihydrobenzofuran-2-ones. Synthetic Communications 2016; 46 (21): 1772-1780. doi: 10.1080/00397911.2016.1226341
5. Dawood KM. Benzofuran derivatives: a patent review. Expert Opinion on Therapeutic Patents 2013; 23 (9): 1133-1156. doi: 10.1517/13543776.2013.801455
6. Pertino MW, Theoduloz CJ, Rodriguez A, Lazo V, Yanez Y et al. Gastroprotective effect of carnosic acid γ-lactone derivatives. Journal of Natural Products 2010; 73: 639-643. doi: 10.1021/np900822x
7. Nicolaou KC, Wu TR, Kang Q, Chen DYK. Total synthesis of hopeahainol A and hopeanol. Angewandte Chemie International Edition 2009; 48: 3440-3443. doi: 10.1002/anie.200900438
8. Ge HM, Zhu CH, Shi DH, Zhang LD, Xie DQ, et al. Hopeahainol A: an acetylcholinesterase inhibitor from *Hopea hainanensis*. Chemistry European Journal 2008; 14: 376-381. doi: 10.1002/chem.200700960
9. Sontag B, Ruth M, Spiteller P, Arnold N, Steglich W et al. Chromogenic meroterpenoids from the mushrooms *Russula ochroleuca* and *R. viscida*. European Journal of Organic Chemistry 2006; 4: 1023-1033. doi: 10.1002/ejoc.200500714
10. Yang L, Qin L. H, Bligh SWA, Bashall A, Zhang CF et al. A new phenanthrene with a spirolactone from *Dendrobium chrysanthum* and its anti-inflammatory activities. Bioorganic & Medicinal Chemistry 2006; 14: 3496-3501. doi: 10.1016/j.bmc. 2006.01.004
11. Masubuchi M, Ebiike H, Kawasaki K, Sogabe S, Morikami K et al. Synthesis and biological activities of benzofuran antifungal agents targeting fungal N-myristoyltransferase Bioorganic & Medicinal Chemistry 2003; 11: 4463-4478. doi: 10.1016/S0968-0896(03)00429-2
12. Abdel-Aziz HA, Mekawey AA. I, Dawood KM. Convenient synthesis and antimicrobial evaluation of some novel 2-substituted-3-methylbenzofuran derivatives. European Journal of Medicinal Chemistry 2009; 44: 3637-3644. doi: 10.1016/j.ejmech.2009.02.020
13. Konicek BW, Stephens JR, McNulty AM, Robichaud N, Peery RB et al. Therapeutic inhibition of MAP Kinase interacting kinase blocks eukaryotic initiation factor 4E phosphorylation and suppresses outgrowth of experimental lung metastases. Cancer Research 2011; 71: 1849-1857. doi: 10.1158/0008-5472.CAN-10-3298
14. Galal SA, Abd El-All AS, Abdullah MM, El-Diwani HI. Synthesis of potent antitumor and antiviral benzofuran derivatives. Bioorganic & Medicinal Chemistry Letters 2009; 19 (9): 2420-2428. doi: 10.1016/j.bmcl.2009.03.069

15. Xia L, Idhayadhulla A, Lee YR, Kim SH, Wee YJ. Synthesis and biological valuation of diverse tetrahydrobenzofuran-4-ones as potent antibacterial agents. Journal of Industrial and Engineering Chemistry 2015; 22: 378-383. doi: 10.1016/j.jiec.2014.07.035

16. Findik E, Dingil A, Karaman I, Budak Y, Ceylan M. Synthesis of multi-substituted 4,5-dihydrofuran derivatives from (S)-Limonene and 1,3-dicarbonyl compounds and their biological activities. E-Journal of Chemistry 2009; 6: 53-59.

17. Manna K, Agarwal YK. Microwave assisted synthesis of new indophenazine 1,3,5-trisubstruted pyrazoline derivatives of benzofuran and their antimicrobial activity. Bioorganic & Medicinal Chemistry Letters 2009; 19 (10): 2688-2692. doi: 10.1016/j.bmcl.2009.03.161

18. Karaburun NG, Benkli K, Tunali Y, Uçucu U, Demirayak S. Synthesis and antifungal activities of some aryl [3-(imidazol-1-yl/triazol-1-ylmethyl) benzofuran-2-yl] ketoximes. European Journal of Medicinal Chemistry 2006; 41: 651-656. doi: 10.1016/j.ejmech.2005.12.013

19. Chakrabarthi JK, Eggleton RJ, Gallagher PT, Harvey J, Hicks TA. 5-Acyl-3-substituted benzofuran-2(3H)-ones as potential antiinflammatory agents. Journal of Medicinal Chemistry 1987; 30 (9): 1663-1668. doi: 10.1021/jm00392a024

20. Santana L, Teijeira M, Uriarte E, Teran C, Liñares B et al. AM1 theoretical study, synthesis and biological evaluation of some benzofuran analogues of anti-inflammatory arylalkanoic acids. European Journal of Pharmaceutical Sciences 1999; 7: 161-166. doi: 10.1016/S0928-0987(98)00019-0

21. Shamsuzzaman KH. Bioactive benzofuran derivatives: a review. European Journal of Medicinal Chemistry 2015; 97: 483-504. doi: 10.1016/j.ejmech.2014.11.039

22. Naik R, Harmalkar DS, Xu X, Jang K, Lee K. Bioactive benzofuran derivatives: moracins A-Z in medicinal chemistry. European Journal of Medicinal Chemistry 2015; 90: 379-393. doi: 10.1016/j.ejmech.2014.11.047

23. Radadiya A, Shah A. Bioactive benzofuran derivatives: an insight on lead developments, radioligands and advances of the last decade. European Journal of Medicinal Chemistry 2015; 97: 356-376. doi: 10.1016/j.ejmech.2015.01.021

24. Nevagi RJ, Dighe SN, Dighe SN. Biological and medicinal significance of benzofuran. European Journal of Medicinal Chemistry 2015; 97: 561-581. doi: 10.1016/j.ejmech.2014.10.085

25. Rizzo S, Riviere C, Piazzi L, Bisi A, Gobbi S et al. Benzofuran-based hybrid compounds for the inhibition of cholinesterase activity, β amyloid aggregation, and Aβ neurotoxicity. Journal of Medicinal Chemistry 2008; 51: 2883-2886. doi: 10.1021/jm8002747

26. Dixit M, Tripathi BK, Tamrakar AK, Srivastava AK, Kumar B et al. Synthesis of benzofuran scaffold-based potential PTP-1B inhibitors. Bioorganic & Medicinal Chemistry 2007; 15: 727-734. doi: 10.1016/j.bmc.2006.10.053

27. Nakamura I, Mizushima Y, Yamagishi U, Yamamoto Y. Synthesis of 2,3-disubstituted benzofurans and indoles by p-Lewis acidic transition metal-catalyzed cyclization of ortho-alkynylphenyl O,O- and N,O-acetals. Tetrahedron 2007; 63: 8670-8676. doi: 10.1016/j.tet.2007.03.039

28. Sakai N, Uchida N, Konakahara T. Facile and efficient synthesis of polyfunctionalized benzofurans: three-component coupling reactions from an alkynylsilane, an o-hydroxybenzaldehyde derivative, and a secondary amine by a Cu(I)–Cu(II) cooperative catalytic system. Tetrahedron Letters 2008; 49: 3437-3440. doi: 10.1016/j.tetlet.2008.03.111

29. Abu-Hashem AA, Hussein HAR, Aly AS, Goudac MA. Synthesis of benzofuran derivatives via different methods. Synthetic Communications 2014; 44: 2285-2312. doi: 0.1080/00397911.2014.894528

30. Bosiak MJA. Convenient synthesis of 2-arylbenzo[b]furans from aryl halides and 2-halophenols by catalytic one-pot cascade method. ACS Catalysis. 2016; 6: 2429-2434. doi: 10.1021/acscatal.6b00190

31. Çalışkan R, Ali MF, Şahin E, Watson WH, Balci M. Unusual manganese(III)- mediated oxidative free radical additions of 1,3-dicarbonyl compounds to benzonorbornadiene and 7-heterobenzonorbornadienes:? mechanistic studies. The Journal of Organic Chemistry 2007; 72: 3353-3359. doi: 10.1021/jo0625711

32. Südemen MB, Zengin M, Genç H, Balcı M. Reaction of cycloheptatriene derivatives with 1,3-diketones in the presence of $Mn(OAc)_3$. Turkish Journal of Chemistry 2011; 35: 1-11. doi: 10.3906/kim-1011-776

33. Çalışkan R, Pekel T, Watson W, Balci M. Unusual oxidative free-radical additions of 1,3-dicarbonyl compounds to benzonorbornadiene and oxabenzonorbornadiene. Tetrahedron Letters 2005; 46: 6227-6230. doi: 10.1016/j.tetlet.2005.07.051

34. Findik E, Ceylan M. Manganese(III) acetate catalyzed oxidative radical additions of α,β-dicarbonyl compounds to 1- and 2-phenylcyclohepta-1,3,5-triene. Helvetica Chimica Acta 2011; 94: 1431-1439. doi: 10.1002/hlca.201000463

35. Ceylan M, Fındık E. Synthesis of 3-aryl-2-benzoylbenzofuran derivatives using manganese(III) acetate-mediated addition of dimedon to chalcone derivatives. Synthetic Communications 2008; 38: 1070-1077. doi: 10.1080/00397910701862782

36. Camps P, Domingo LR, Formosa X, Galdeano C, Gonzalez D et al. Highly diastereoselective one-pot synthesis of spiro{cyclopenta[a]indene-2,2'-indene}diones from 1-indanones and aromatic aldehydes. The Journal of Organic Chemistry 2006; 71: 3464-3471. doi: 10.1021/jo0600095

37. Pinkerton AB, Cube RV, Hutchinson JH, James JK, Gardner MF et al. Allosteric potentiators of the metabotropic glutamate receptor 2 (mGlu2). Part 3: Identification and biological activity of indanone containing mGlu2 receptor potentiators Bioorganic & Medicinal Chemistry Letters 2005; 15: 1565-1571. doi: 10.1016/j.bmcl.2005.01.077

38. Ergüntürk D, Gürdere MB, Budak Y, Ceylan M. Synthesis, characterization, and investigations of antimicrobial activity of 6,6-dimethyl-3-aryl-3′,4′,6,7-tetrahydro-1′H,3H-spiro[benzofuran-2,2′-naphthalene]-1′,4(5H)-dione. Synthetic Communications 2017; 47: 1501-1506. doi: 10.1080/00397911.2017.1334918

39. Şahin B, Gürdere MB, Ceylan M. Michael addition of malononitrile to indenones: synthesis and characterization of 2-(1-oxo-2,3-dihydro-1H-inden-2-yl) (aryl) (methyl)malononitrile derivatives. Synthetic Communications 2017; 47: 1090-1095. doi: 10.1080/00397911.2017.1312450