Multicomponent synthesis of 1-[aryl(*p*-tolylsulfanyl)methyl]naphthalen-2-ols using *p*-toluenesulfonic acid as a catalyst

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Three-component reaction between 2-naphthol, an aromatic aldehyde and thiols catalysed by *p*-toluene sulfonic acid (*p*-TSA) provided a simple and efficient one-pot route for the synthesis of 1-[aryl(arylsulfanyl)methyl]naphthalen-2-ol derivatives in excellent yields.

Keywords: 2-naphthol, aromatic aldehydes, thiols, three-component reaction, *p*-toluene sulfonic acid

Multi-component reactions are useful and efficient methods in organic synthesis. The major advantages of these reactions are a single purification step, higher yields than stepwise assembly, the use of simple and diverse precursors to construct complex molecules and the use of only a single promoter or catalyst. Thus, the development of new multi-component reactions is a popular area of research in organic chemistry and from a green chemistry point of view.[1–3]

Ortho-quinone methides have been employed in many tandem processes,[4–6] but there are only a few reports on their reactions with nucleophiles.[7–9] There are some recent reports from the three-component reaction between 2-naphthol, aromatic aldehydes and nucleophiles such as amides or ureas using different catalysts.[10–13] These reactions have been reported to proceed by the nucleophilic addition of amide or urea derivative on the intermediate *ortho*-quinone methides. In continuation of our previous work on three-component reactions between an aldehyde, an enolic system, such as substituted 2-naphthols, 4-hydroxycoumarin or 2-hydroxy-3-naphthoic acid and a nucleophile,[14–17] here we describe the three-component reaction between 2-naphthol, aromatic aldehydes and thiols in the presence of catalytic amounts of *p*-toluene sulfonic acid (*p*-TSA).

Results and discussion

Thus, reaction between 2-naphthol, benzaldehyde and thiol in the presence of *p*-TSA in refluxing 1,2-dichloroethane after 2 h afforded 1-[phenyl(phenylsulfanyl)methyl]naphthalen-2-ol (**4a**) in 90% yield (Scheme 1).

To determine the optimum quantity of *p*-TSA the reaction of 2-naphthol (1 equiv.), benzaldehyde (1 equiv.), and thiol (1 equiv.) was carried out under the above conditions using different quantities of catalyst. The use of 5 mol% of catalyst resulted in the highest yield in 2 h. We prepared a range of 1-[aryl(arylsulfanyl)methyl]naphthalen-2-ols **4** under the optimised reaction conditions: 2-naphthol **1** (1 mmol), aryl aldehydes **2** (1 mmol), and thiols **3** (1 mmol) in the presence of *p*-TSA (0.05 mmol). In all cases, aromatic aldehydes with either electron-donating or electron-withdrawing groups gave the desired products in 85–92% yields. (Scheme 2)

We also examined the reaction between 2-naphthol, aromatic aldehydes and thiol in the absence of *p*-TSA in the same conditions, but no product was isolated from the reaction mixtures.

Products **4a–h** were all new compounds and their structures were deduced from their elemental analyses and spectral data. The mass spectrum of compound **4a** showing a molecular ion peak at 342 confirmed that compound **4a** is a triadduct of 2-naphthol, benzaldehyde and thiol. The ^{1}H NMR spectrum of compound **4a** displayed a sharp single signal at $\delta = 5.46$ ppm for methine proton, along with charactristic signals at $\delta = 7.15–7.83$ ppm for the aromatic protons. A singlet was observed at $\delta = 10.21$ ppm, disappeared by addition of D_2O, for OH proton. ^{13}C NMR spectrum of compound **4a** showed 19 distinct signals in agreement with the proposed structure.

A possible mechanism for the formation of 1-[aryl(arylsulfanyl)methyl]naphthalen-2-ols **4a–h** has been proposed in Scheme 3. As reported in the literature,[13,18–20] the reaction of 2-naphthol with aromatic aldehydes in the presence of an acid catalyst is known to give orthoquinone methides. The same orthoquinone methides, generated *in situ*, have been reacted with thiol via conjugate addition to form 1-[aryl(arylsulfanyl)methyl]naphthalen-2-ol derivatives.

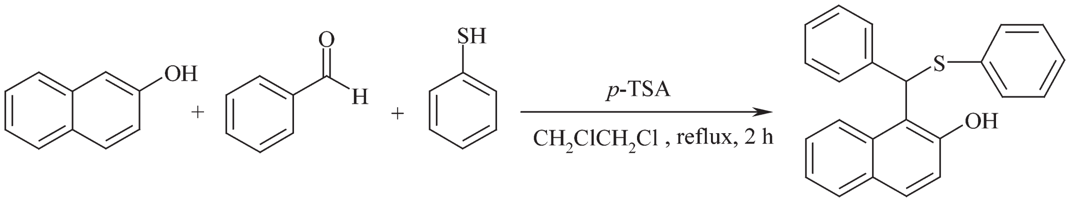
In conclusion, we report here a simple and efficient one-pot synthesis of 1-[aryl(arylsulfanyl)methyl]naphthalen-2-ol derivatives by three-component reaction between 2-naphthol, an aromatic aldehyde and thiols catalysed by *p*-toluenesulfonic acid. The advantages of this method are available starting materials, short reaction times, easy and clean work-up, and excellent yields.

Experimental

All melting points are uncorrected. Elemental analyses were performed at the analytical laboratory of Science and Research Unit of the Islamic Azad University. Mass spectra were recorded on a FINNIGAN-MAT 8430 mass spectrometer operating at an ionisation potential of 70 eV. IR spectra were recorded on a Shimadzu IR-470 spectrometer. ^{1}H and ^{13}C NMR spectra were recorded on Bruker DRX-500 Avance spectrometer at solution in DMSO using TMS as internal standard. The chemicals used in this work were purchased from Fluka (Buchs, Switzerland) and were used without further purification.

General procedure

A magnetically stirred solution of thiols (1mmol), 2-naphthol (1 mmol), aldehyde (1 mmol) and *p*-TSA (0.05 mmol) in 15 mL 1,2-dichloroethane was refluxed for 2 h. The mixture was poured into water (50 mL).



Scheme 1 Condensation of benzaldehyde, 2-naphthol and thiol catalysed by *p*-TSA.

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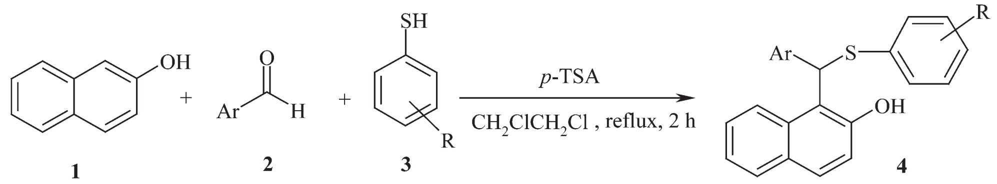
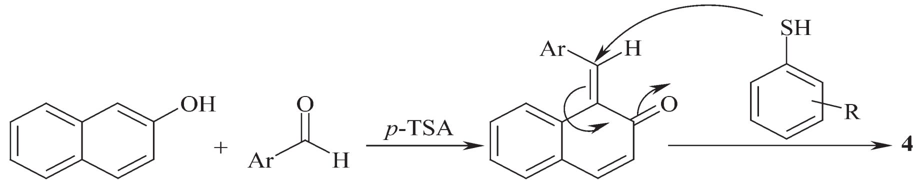


4	Ar	R	%Yield *
a	C_6H_5	H	90
b	4-Cl C_6H_4	CH_3	88
c	4-Br C_6H_4	H	89
d	2-Cl C_6H_4	H	90
e	3-NO_2 C_6H_4	CH_3	85
f	4-NO_2 C_6H_4	CH_3	86
g	4-CH_3O C_6H_4	H	89
h	2-CH_3O C_6H_4	CH_3	92

*Yields refer to the pure isolated prodoucts

Scheme 2 Three-component reaction between aromatic aldehydes, 2-naphthol and thiols catalysed by *p*-TSA.



Scheme 3 Suggested mechanism for formation of compounds **4a–h**.

The solid product was filtered and recrystallised from ethyl acetate/haxane mixture to give the pure product.

1-[Phenyl(phenylsulfanyl)methyl]naphthalen-2-ol (**4a**): White solid, m.p. 143–145 °C, IR (KBr) (ν_{max} cm^{-1}): 3465, 1593, 1511. Anal. Calcd for $C_{23}H_{18}OS$: C, 80.67; H, 5.30. Found: C, 80.60; H, 5.34%. MS (*m/z*, %): 342 (10). ^{1}H NMR (500 MHz, d$_6$-DMSO): δ 5.46 (1H, s, CH), 7.28–7.32 (3H, m, 3CH naphthol moiety), 7.38 (1H, d, $^3J_{HH}$ = 8 Hz, CH naphthol moiety), 7.78 (1H, d, $^3J_{HH}$ = 8 Hz, CH naphthol moiety), 7.83 (1H, d, $^3J_{HH}$ = 8 Hz, CH naphthol moiety), 7.15–7.39 (10H, m, 10CH phenyl moieties), 10.21 (1H, broad s, OH) ppm. ^{13}C NMR (125.8 MHz, d$_6$-DMSO): δ 46.82 (CH), 118.85, 119.50, 123.48, 124.11, 127.15, 129.38, 129.31, 130.19, 133.02 and 153.78 (naphthol moiety), 126.81, 127.24, 127.72, 128.30, 128.86 130.35, 141.76 and 143.27 (phenyl moieties) ppm.

1-[4-Chlorophenyl(p-tolylsulfanyl)methyl]naphthalen-2-ol (**4b**): White solid, m.p. 156–158 °C, IR (KBr) (ν_{max} cm^{-1}): 3460, 1590, 1505. Anal. Calcd for $C_{24}H_{19}ClOS$: C, 73.74; H, 4.90. Found: C, 73.79; H, 4.76%. MS (*m/z*, %): 390 (4). ^{1}H NMR (500 MHz, d$_6$-DMSO): δ 2.28 (3H, s, CH_3), 5.63 (1H, s, CH), 7.21–7.33 (3H, m, 3CH naphthol moiety), 7.35 (1H, d, $^3J_{HH}$ = 8 Hz, CH naphthol moiety), 7.74 (1H, d, $^3J_{HH}$ = 8 Hz, CH naphthol moiety), 7.79 (1H, d, $^3J_{HH}$ = 8 Hz, CH naphthol moiety), 7.18–7.48 (8H, m, 8CH phenyl moieties), 10.24 (1H, broad s, OH) ppm. ^{13}C NMR (125.8 MHz, d$_6$-DMSO): δ 21.53 (CH_3), 47.38 (CH), 118.75, 119.47, 123.40, 124.22, 127.28, 129.37, 129.42, 130.35, 133.06 and 153.75 (naphthol moiety), 126.15, 127.16, 127.82, 128.33, 128.92 130.44, 142.07 and 143.28 (phenyl moieties) ppm.

1-[4-Bromophenyl(phenylsulfanyl)methyl]naphthalen-2-ol (**4c**): White solid, m.p. 129–131 °C, IR (KBr) (ν_{max} cm^{-1}): 3457, 1582, 1501. Anal. Calcd for $C_{23}H_{17}BrOS$: C, 65.56; H, 4.07. Found: C, 65.42; H, 4.15%. MS (*m/z*, %): 421 (5). ^{1}H NMR (500 MHz, d$_6$-DMSO): δ 5.65 (1H, s, CH), 7.24–7.32 (3H, m, 3CH naphthol moiety), 7.34 (1H, d, $^3J_{HH}$ = 8 Hz, CH naphthol moiety), 7.74 (1H, d, $^3J_{HH}$ = 8 Hz, CH naphthol moiety), 7.76 (1H, d, $^3J_{HH}$ = 8 Hz, CH naphthol moiety), 7.22–7.45 (8H, m, 8CH phenyl moieties), 10.27 (1H, broad s, OH) ppm. ^{13}C NMR (125.8 MHz, d$_6$-DMSO): δ 47.36 (CH), 119.54, 119.82, 123.32, 123.88, 127.42, 129.65, 130.22, 130.76, 132.95 and 153.38 (naphthol moiety), 126.27, 127.19, 127.76, 128.44, 128.90 130.37, 142.13 and 143.16 (phenyl moieties) ppm.

1-[2-Chlorophenyl(phenylsulfanyl)methyl]naphthalen-2-ol (**4d**): White solid, m.p. 150–152 °C, IR (KBr) (ν_{max} cm^{-1}): 3462, 1590, 1504. Anal. Calcd for $C_{23}H_{17}ClOS$: C, 73.30; H, 4.55. Found: C, 73.35; H, 4.62%. MS (*m/z*, %): 376 (7). ^{1}H NMR (500 MHz, d$_6$-DMSO): δ 5.58 (1H, s, CH), 7.23–7.35 (3H, m, 3CH naphthol moiety), 7.61 (1H, d, $^3J_{HH}$ = 8 Hz, CH naphthol moiety), 7.75 (1H, d, $^3J_{HH}$ = 8 Hz, CH naphthol moiety), 7.80 (1H, d, $^3J_{HH}$ = 8 Hz, CH naphthol moiety), 7.20–7.42 (9H, m, 9CH phenyl moieties), 10.08 (1H, broad s, OH) ppm. ^{13}C NMR (125.8 MHz, d$_6$-DMSO): δ 47.38 (CH), 118.04, 119.71, 123.53, 124.62, 127.15, 129.18, 130.24, 130.60, 133.52 and 154.37 (naphthol moiety), 125.93, 127.18, 127.90, 128.35, 128.97 130.44, 131.04 133.06, 140.32, and 143.19 (phenyl moieties) ppm.

1-[3-Nitrophenyl(p-tolylsulfanyl)methyl]naphthalen-2-ol (**4e**): White solid, m.p. 161–163 °C, IR (KBr) (ν_{max} cm^{-1}): 3466, 1594, 1500. Anal. Calcd for $C_{24}H_{19}NO_3S$: C, 71.80; H, 4.77; N, 3.49%. Found: C, 71.85; H, 4.70; N, 3.61. MS (*m/z*, %): 401 (8). ^{1}H NMR (500 MHz, d$_6$-DMSO): δ 2.32 (3H, s, CH_3), 5.66 (1H, s, CH), 7.31 (1H, t, $^3J_{HH}$ = 8 Hz, CH naphthol moiety), 7.48 (1H, d, $^3J_{HH}$ = 8 Hz, CH naphthol moiety), 7.52 (1H, t, $^3J_{HH}$ = 8 Hz, CH naphthol moiety), 7.64 (1H, d, $^3J_{HH}$ = 8 Hz, CH naphthol moiety), 7.83 (1H, d, $^3J_{HH}$ = 8 Hz, CH naphthol moiety), 7.86 (1H, d, $^3J_{HH}$ = 8 Hz, CH naphthol moiety), 7.19–8.12 (8H, m, 8CH phenyl moieties), 10.35 (1H, broad s, OH) ppm. ^{13}C NMR (125.8 MHz, d$_6$-DMSO): δ 21.62 (CH_3), 47.73 (CH), 118.53, 119.24, 123.50, 124.08, 127.65, 129.28, 129.72, 130.54, 133.60 and 154.27 (naphthol moiety), 121.24, 122.17, 127.18, 128.98 130.42, 130.82, 132.90, 143.21 146.12 and 148.51, (phenyl moieties) ppm.

1-[4-Nitrophenyl(p-tolylsulfanyl)methyl]naphthalen-2-ol (**4f**): White solid, m.p. 155–157 °C, IR (KBr) (ν_{max} cm^{-1}): 3465, 1592, 1503. Anal. Calcd for $C_{24}H_{19}NO_3S$: C, 71.80; H, 4.77; N, 3.49%. Found: C, 71.85; H, 4.70; N, 3.61. MS (*m/z*, %): 401 (4). ^{1}H NMR (500 MHz, d_6-DMSO): δ 2.30 (3H, s, CH_3), 5.64 (1H, s, CH), 7.40–7.45 (3H, m, 3CH naphthol moiety), 7.34 (1H, d, $^3J_{HH}$ = 8 Hz, CH naphthol moiety), 7.80 (1H, d, $^3J_{HH}$ = 8 Hz, CH naphthol moiety), 7.83 (1H, d, $^3J_{HH}$ = 8 Hz, CH naphthol moiety), 7.23–8.11 (8H, m, 8CH phenyl moieties), 10.36 (1H, broad s, OH) ppm. ^{13}C NMR (125.8 MHz, d_6-DMSO): δ 21.60 (CH_3), 47.69 (CH), 118.52, 119.31, 123.54, 124.05, 127.63, 129.22, 129.76, 130.50, 133.62 and 154.21 (naphthol moiety), 114.92, 127.12, 127.56, 128.84, 130.36, 143.16 146.47 and 150.85 (phenyl moieties) ppm.

1-[4-Methoxyphenyl(phenylsulfanyl)methyl]naphthalen-2-ol (**4g**): White solid, m.p. 166–168 °C, IR (KBr) (ν_{max} cm^{-1}): 3474, 1599, 1508. Anal. Calcd for $C_{24}H_{20}O_2S$: C, 77.39; H, 5.41. Found: C, 77.50; H, 5.45%. MS (*m/z*, %): 372 (9). ^{1}H NMR (500 MHz, d_6-DMSO): δ 3.62 (3H, s, OCH_3), 5.32 (1H, s, CH), 7.21–7.35 (3H, m, 3CH naphthol moiety), 7.30 (1H, d, $^3J_{HH}$ = 8 Hz, CH naphthol moiety), 7.75 (1H, d, $^3J_{HH}$ = 8 Hz, CH naphthol moiety), 7.81 (1H, d, $^3J_{HH}$ = 8 Hz, CH naphthol moiety), 7.23–7.58 (9H, m, 9CH phenyl moieties), 10.38 (1H, broad s, OH) ppm. ^{13}C NMR (125.8 MHz, d_6-DMSO): δ 47.62 (CH), 55.82 (OCH_3), 119.54, 119.82, 123.32, 123.88, 127.42, 129.62, 129.92, 130.78, 133.02 and 154.25 (naphthol moiety), 114.52, 127.19, 128.58, 128.93, 129.07, 133.42, 143.12 and 146.05 (phenyl moieties) ppm.

1-[2-Methoxyphenyl(p-tolylsulfanyl)methyl]naphthalen-2-ol (**4h**): White solid, m.p. 163–165 °C, IR (KBr) (ν_{max} cm^{-1}): 3470, 1596, 1507. Anal. Calcd for $C_{25}H_{22}O_2S$: C, 77.69; H, 5.74. Found: C, 77.60; H, 5.63%. MS (*m/z*, %): 386 (7). ^{1}H NMR (500 MHz, d_6-DMSO): δ 2.27 (3H, s, CH_3), 3.36 (3H, s, OCH_3), 5.37 (1H, s, CH), 6.95–7.30 (3H, m, 3CH naphthol moiety), 7.32 (1H, d, $^3J_{HH}$ = 8 Hz, CH naphthol moiety), 7.50 (1H, d, $^3J_{HH}$ = 8 Hz, CH naphthol moiety), 7.64 (1H, d, $^3J_{HH}$ = 8 Hz, CH naphthol moiety), 7.21–7.45 (8H, m, 8CH phenyl moieties), 9.96 (1H, broad s, OH) ppm. ^{13}C NMR (125.8 MHz, d_6-DMSO): δ 21.58 (CH_3), 47.67 (CH), 55.64 (OCH_3), 119.30, 119.71, 123.16, 124.26, 126.85, 129.24, 130.12, 130.80, 133.16 and 153.85 (naphthol moiety), 111.60, 120.42, 127.22, 128.27, 128.61, 128.96, 129.16, 130.61, 143.17 and 157.32 (phenyl moieties) ppm.

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