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Synthesis of substituted trisphenols by use of a double acidic ionic liquid under solvent-free conditions

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ABSTRACT

3-methyl-1-(4-sulfobutyl)-1-*H*-imidazol-3ium hydrogen sulfate, as a dual acidic ionic liquid (DAIL), was found to be an efficient catalyst for the simple, rapid and green synthesis of substituted trisphenols from the condensation of different substituted phenols and 2,6-bis (methylol) phenols (BMP). DAIL catalyst efficiently promoted the reaction between phenols and BMPs with a variety of functionalities. Use of a non-corrosive and reusable catalyst, high yields of the products, short reaction times and solvent-free conditions are as worthwhile advantages of the present method.

Keywords*: 3-methyl-1-(4-sulfobutyl)-1-H-imidazol-3ium hydrogensulfate, Trisphenol, 2,6-Bis(methylol)phenol, Dual acidic ionic liquid, Solvent-free.*

1. Introduction

Trisphenols are an important and most widely used class of polyhydroxy aromatic compounds (PHA). The presence of especial functional groups (hydroxyl groups) in a suitable arrangement for chelating metal ions of enzymes, renders these compounds as potent antibiotics [1]. PHAs have been used as drugs in treatment of many deceases [2-6]. Also they play important role in organic synthesis, especially calixarenes and crown ethers [7,8]. Moreover, these compounds are used as organic photoluminscent devices [9] and positive photoresist materials in semiconductor industries [10]. These compounds also have another important property; they can be used as antioxidants in polymer industries.

Moshfegh et al. synthesized some antibacterial derivatives of trisphenols and reported that the presence of halogen atoms in the structure of these compounds enhances their biological activity [11,12].
Inspite of the aforementioned wide applications of trisphenols in different industries, few methods have been reported for the preparation of these useful compounds [11-16]. Additionally, each of these methods suffers from disadvantages such as low yields of the products, long reaction times, use of corrosive, mineral acid catalyst, use of large excess phenols, tedious work-up process and use of toxic solvents. Therefore, it is still desirable to seek a green protocol that uses a highly efficient and reusable catalyst for the preparation of trisphenolic compounds. Ionic liquids (ILs) as catalyst or reaction media have attracted increasing attention due to their particular properties such as non-volatility, environmentally friendly nature, high polarity, high thermal and chemical stability and ease of recovery and reuse [17]. Among them, BrØnsted acidic ILs have attracted considerable interest, because they have the combined advantages of both mineral and solid acids [18]. Recently dual acidic ionic liquids with enhanced acidity have been intensively studied [19].

Owing to the importance of the described compounds and in continuation of our interest towards the development of green methodologies for the synthesis of organic compounds [20-25], here in we report a facile, efficient and green procedure for the synthesis of substituted trisphenolic compounds using a dual acidic ionic liquid (DAIL), 3-methyl-1-(4-sulfobutyl)-1-*H*-imidazol-3ium hydrogen sulfate, as catalyst (Scheme 1).

2. Experimental

The chemicals and solvents were purchased from Merck chemical company. Melting points were determined using melting point IA 8103 apparatus. FT-IR spectra were obtained with KBr pellets in the

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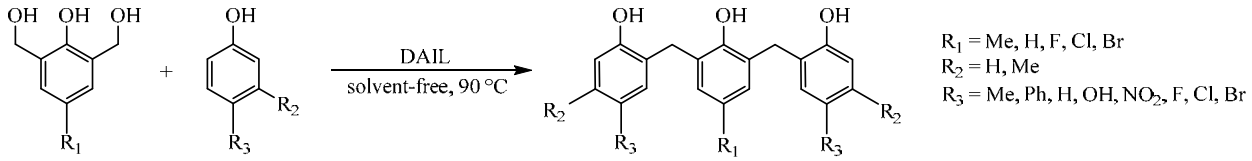


Scheme 1. Synthesis of 2,6-bis-(2-hydroxy benzyl) phenol derivatives in the presence of DAIL.

range of 400-4000 cm^{-1} with a Nicolet-860 spectrometer. ^1H and ^{13}C NMR spectra were measured on a Bruker DRX-300 spectrometer at 300 and 75 MHz, respectively and TMS as an internal standard. Elemental analysis for C, H, and N were performed using a Heraeus CHN rapid analyzer.

2.1. General procedure for the synthesis of 2,6-(2-hydroxy-benzyl)-phenol derivatives

In a 10 mL round bottom flask, a mixture of 3-methyl-1-(4-sulfobutyl)-1-H-imidazol-3ium hydrogen sulfate (0.2 mmol), BMP (1 mmol) and substituted phenol (3 mmol) was heated at 90 °C and stirred until TLC monitoring indicated no further progress (20 to 40 minutes according to Table 2). Subsequently the reaction mixture was cooled to room temperature and acetonitrile (5 mL) was added. The catalyst was removed by filtration and the filtrates were evaporated under reduced pressure. Then the residue was suspended in boiling water and decanted to remove the unreacted phenol. The product was then purified by column chromatography (hexane/ethyl acetate) to obtain the desired product.

Spectral data of the synthesized compounds

2,6-Bis-(5-bromo-2-hydroxy-benzyl)-4-chlorophenol (Table 2, entry 1):

White solid. m.p.= 251-252 °C [15]; found 251-253 °C. IR (KBr): $\bar{\nu}$ = 3150, 3020, 2990, 1600, 1220 cm^{-1}. ^{1}HNMR (300 MHz, DMSO-d_6): δ= 3.82 (s, 4H, CH_2), 6.76-7.21 (m, 8H, aromatic), 7.93 (s, 1H, OH), 9.68 (brs, 2H, OH) ppm. ^{13}CNMR (75 MHz, DMSO-d_6): δ= 29.6, 110.1, 117.0, 122.9, 127.2, 128.9, 129.4, 129.8, 132.4, 151.4, 154.3 ppm. Anal. calc. for $C_{20}H_{15}Br_2ClO_3$: C 48.1, H 3.03%; found: C 48.25, H 3.07%.

2,6-Bis-(2-hydroxy-4,5-di-methyl-benzyl)-4-methyl phenol (Table 2, entry 2):

White solid. m.p.= 198-200 °C. IR (KBr): $\bar{\nu}$ = 3425, 3036, 2988, 1612, 1506, 1475, 1282 cm^{-1}. ^{1}HNMR (300 MHz, DMSO-d_6): δ= 1.97 (s, 3H, 4-CH_3), 2.02 (s, 6H, benzyl-5-CH_3), 2.08 (s, 6H, benzyl-4-CH_3), 3.71 (s, 4H, CH_2), 6.59-6.73 (m, 6H, aromatic), 8.14 (s, 1H, OH), 9.21 (s, 2H, OH) ppm. ^{13}CNMR (75 MHz, DMSO-d_6): δ= 18.5, 19.2, 20.4, 29.3, 116.2, 123.9, 126.11, 127.4, 127.7, 128.0, 131.3, 134.3, 149.6, 152.2 ppm. Anal. calc. for $C_{25}H_{28}O_3$: C 79.78, H 7.44%; found: C 79.87, H 7.50%.

2,6-Bis-(2-hydroxy-5-methyl-benzyl)-4-methylphenol (Table 2, entry 3):

White solid. M.p.= 214-216 °C [15]; found 215-217 °C. IR (KBr): $\bar{\nu}$ = 3265, 3090, 3000, 2919, 1604, 1505, 1392 cm^{-1}. ^{1}HNMR (300 MHz, DMSO-d_6): δ= 2.05 (s, 3H, CH_3), 2.12 (s, 6H, 2CH_3), 3.8 (s, 4H, CH_2), 6.63–6.80 (m, 8H, aromatic), 8.19 (s, 1H, OH), 9.35 (s, 2H, OH) ppm. ^{13}CNMR (75 MHz, DMSO-d_6): δ= 20.3, 20.4, 29.6, 114.7, 115.0, 126.7, 127.3, 127.4, 127.5, 127.5, 128.3, 129.7, 149.9, 152.2 ppm. Anal. calc. for $C_{23}H_{24}O_3$: C 79.28, H 6.94%; found: C 79.27, H 7.00%.

4-Fluoro-2,6-bis-(5-fluoro-2-hydroxy-benzyl)phenol (Table 2, entry 4):

White solid. m.p.= 216-218 °C. IR (KBr): $\bar{\nu}$ = 3250, 3050, 2950, 1600, 1220 cm^{-1}. ^{1}HNMR (300 MHz, DMSO-d6): δ= 3.83 (s, 4H, CH2), 6.59–6.99 (m, 8H, aromatic), 8.5 (brs, 1H, OH), 9.-56 (brs, 2H, OH). ^{13}CNMR (75 MHz, DMSO-d_6): δ= 30.0, 113.3 (d, $^2J_{C\text{-}F}$=22.3 Hz), 113.8 (d, $^2J_{C\text{-}F}$=22.4 Hz), 115.6 (d, $^3J_{C\text{-}F}$=7.9 Hz), 116.3 (d, $^2J_{C\text{-}F}$=22.6 Hz), 127.9 (d, $^3J_{C\text{-}F}$=7.0 Hz), 129.3 (d, $^3J_{C\text{-}F}$=7.5 Hz), 148.6, 151.1, 155.5 (d, $^1J_{C\text{-}F}$=232.1 Hz), 155.6 (d, $^1J_{C\text{-}F}$=232.7 Hz). Anal. calc. for $C_{20}H_{15}F_3O_3$: C 66.67, H 4.20%; found: C 66.61, H 4.25%.

2,6-Bis-(5-chloro-2-hydroxy-benzyl)- 4-fluorophenol (Table 2, entry 5):

White solid. m.p.= 205–207 °C. IR (KBr): $\bar{\nu}$ = 3228, 2945, 1610, 1487, 1238 cm^{-1}. ^{1}HNMR (300 MHz, DMSO-d_6): δ= 3.82 (s, 4H, CH_2), 6.59-7.35 (m, 8H, aromatic), 8.46 (brs, 1H, OH), 9.85 (brs, 2H, OH) ppm. ^{13}CNMR (75 MHz, DMSO-d_6): δ= 29.8, 113.9 (d, $^2J_{C\text{-}F}$=22.4 Hz), 116.4, 122.4, 126.9, 128.3, 128.5, 129.2 (d, $^3J_{C\text{-}F}$=7.5 Hz), 129.50, 153.9, 155.9 (d, $^1J_{C\text{-}F}$=233.2 Hz) ppm. Anal. calc. for $C_{20}H_{15}Cl_2FO_3$: C 61.06, H 3.82%; found: C 61.01, H 3.89%.

4-Chloro-2,6-bis-(2-hydroxy-5-nitro-benzyl)phenol (Table 2, entry 6):

Yellow solid. m.p.= 220-225 °C [14]; found 221-223 °C. IR (KBr): $\bar{\nu}$ = 3350, 3090, 2925, 1630, 1590, 1500, 1280 cm^{-1}. ^{1}HNMR (300 MHz, DMSO-d_6): δ= 3.86 (s, 4H), 8.77-6.67 (m, 8H), 8.86 (brs, H), 11.15 (brs, 2H) ppm. ^{13}CNMR (75 MHz, DMSO-d_6): δ= 161.5, 151.0, 141.0, 130.2, 129.6, 125.3, 123.4, 122.8, 117.21, 112.4, 17.7 ppm. Anal. calc. for $C_{20}H_{15}ClN_2O_7$: C 55.74, H 3.48, N 6.50%; found: C 55.72, H 3.40, N 6.59%.

3,3-(5-Chloro-2-hydroxy-1,3-phenylene)bis(methylene) bis(biphenyl-4-ol) (Table 2, entry 7):

White solid. m.p.= 143-45 °C [15]; found 144–145 °C. IR (KBr): $\bar{\nu}$ = 3200, 3030, 2910, 1610, 1600, 1520, 1490, 1220 cm^{-1}. ^{1}HNMR (300 MHz, DMSO-d_6): δ= 3.87 (s, 4H), 6.7–7.61 (m, 18H), 8.82 (s, 1H), 9.79 (s, 2H) ppm. ^{13}CNMR (75 MHz, DMSO-d_6): δ= 33.3, 115.8, 117.3, 125.2, 125.8, 126.0, 126.7, 128.3, 128.6, 129.7, 129.8, 130.9, 140.6, 157.2, 159.7 ppm. Anal. calc. for $C_{32}H_{25}ClO_3$: C 77.96, H 5.11%; found: C 78.81, H 5.18%.

2,6-Bis-(2-hydroxy benzyl)phenol (Table 2, entry 8):

Light brown solid. m.p.= 160-161°C. IR (KBr): $\bar{\nu}$ = 3318, 3022, 2980, 1588, 1459, 1223 cm^{-1}. ^{1}HNMR (300 MHz, DMSO-d_6): δ= 3.85 (s, 4H, CH_2), 6.60-7.04 (m, 11H, aromatic), 8.54 (brs, 1H, OH), 9.58 (brs, 2H, OH) ppm. ^{13}CNMR (75 MHz, DMSO-d_6): δ= 29.6, 110.1, 117.0, 122.9, 127.2, 128.9, 129.4, 129.8, 132.4, 151.4, 154.3 ppm. Anal. calc. for $C_{20}H_{18}O_3$: C 78.43, H 5.88%; found: C 78.39, H 5.95%.

4-Bromo-2,6-bis-(5-fluoro-2-hydroxy-benzyl)phenol (Table 2, entry 9):

White solid. m.p.= 234-236 °C [15]; found 232-234 °C. IR (KBr): $\bar{\nu}$ = 3200, 2940, 1600, 1500, 1450, 1235 cm^{-1}. ^{1}HNMR (300 MHz, $CDCl_3$): δ= 3.80 (s, 4H), 6.75-7.02 (m, 8H), 9.36 (brs, 3H) ppm. ^{13}CNMR (75 MHz, $CDCl_3$): δ= 29.7, 110.6, 113.2 (d, $^2J_{C\text{-}F}$ = 22.4 Hz), 115.5 (d, $^3J_{C\text{-}F}$ = 8.0 Hz), 116.28 (d, $^2J_{C\text{-}F}$ = 22.7 Hz), 127.0, 127.7, 129.9 (d, $^3J_{C\text{-}F}$ = 6.6 Hz), 151.0, 151.9, 155.4 (d, $^1J_{C\text{-}F}$ = 232.5 Hz) ppm. Anal. calc. for $C_{20}H_{15}BrF_2O_3$: C 56.97, H 3.60%; found: C 56.64, H 3.55%.

4-Chloro-2,6-bis-(2-hydroxy-5-methyl-benzyl)phenol (Table 2, entry 10):

White solid. m.p.= 136-140 °C [14]; found 137-139 °C. IR (KBr): $\bar{\nu}$ = 3208, 3018, 2876, 1605, 1448, 810 cm^{-1}. ^{1}HNMR (300 MHz, DMSO-d_6): δ= 2.13 (s, 6H, CH_3), 3.77 (s, 4H, CH_2), 6.68-6.83 (m, 8H, aromatic), 8.69 (brs, 1H, OH), 9.34 (brs, 2H, OH) ppm. ^{13}CNMR (75 MHz, DMSO-d_6): δ= 20.1, 29.6, 114.8, 122.6, 125.6, 126.7, 127.5, 127.6, 130.1, 130.9, 151.1, 152.4 ppm. Anal. calc. for $C_{22}H_{21}ClO_3$: C 71.64, H 5.74%; found: C 71.70, H 5.70%.

4-Chloro-2,6-bis-(5-chloro-2-hydroxy-benzyl)phenol (Table 2, entry 11):

Yellow solid. m.p.= 234-238 °C [14]; found 233-235 °C. IR (KBr): $\bar{\nu}$ = 3150, 3010, 2980, 1610, 1220 cm^{-1}. ^{1}HNMR (300 MHz, DMSO-d_6): δ= 3.82 (s, 4H, CH_2), 6.67–7.09 (m, 8H, aromatic), 8.82 (brs, 1H, OH), 9.82 (brs, 2H, OH) ppm. ^{13}CNMR (75 MHz, DMSO-d_6): δ= 29.6, 116.4, 122.4, 122.8, 126.9, 127.2, 128.4, 129.4, 129.5, 151.4, 153.9 ppm. Anal. calc. for $C_{20}H_{15}Cl_3O_3$: C 58.63, H 3.69%; found: C 58.60, H 3.62%.

2,2-(5-Chloro-2-hydroxy-1,3-phenylene)bis(methylene) dibenzene-1,4-diol (Table 2, entry 12):

Light-brown crystals. m.p.= 178-180 °C [14], found 178–180 °C. IR (KBr): $\bar{\nu}$ = 3200, 3020, 2990, 1610, 1600, 1500, 1450, 1250, 850 cm^{-1}. ^{1}HNMR (300 MHz, DMSO-d_6): δ= 3.89 (s, 4H, CH_2), 6.49-6.83 (m, 8H, aromatic), 8.65 (s, 2H, OH), 8.77 (brs, 1H, OH), 9.00 (brs, 2H, OH) ppm. ^{13}CNMR (75 MHz, DMSO-d_6): δ= 29.7, 113.6, 115.5, 116.8, 122.7, 126.7, 126.8, 130.0, 147.0, 149.7, 151.2 ppm. Anal. calc. for $C_{20}H_{17}ClO_5$: C 64.44, H 4.60%; found: C 64.39, H 4.64%.

4-Chloro-2,6-bis-(5-fluoro-2-hydroxy-benzyl)phenol (Table 2, entry 13):

White solid. m.p.= 223-226 °C [15]; found 223-225 °C. IR (KBr): $\bar{\nu}$ = 3190, 1600, 1495, 1445, 1235, 1190 cm^{-1}. ^{1}HNMR (300 MHz, DMSO-d_6): δ= 3.8 (s, 4H, CH_2), 6.77-6.89 (m, 8H, aromatic), 8.75 (s, 1H, OH), 9.57 (s, 2H, OH) ppm. ^{13}CNMR (75 MHz, DMSO-d_6): δ= 29.7, 113.2 (d, $^2J_{C\text{-}F}$=22.2 Hz), 115.5 (d, $^3J_{C\text{-}F}$=8.0 Hz), 116.3 (d, $^2J_{C\text{-}F}$=22.7 Hz), 122.9, 127.1, 127.7 (d, $^3J_{C\text{-}F}$=7.1 Hz), 129.5, 151.1, 151.3, 155.4 (d, $^1J_{C\text{-}F}$=232.2 Hz) ppm. Anal. calc. for $C_{20}H_{15}ClF_2O_3$: C 63.75, H 4.01%; found: C 63.77, H 3.82%.

4-Bromo-2,6-bis-(5-bromo-2-hydroxy-benzyl)phenol (Table 2, entry 14):

Yellow solid. m.p.= 235-236 °C [14]; found 236-238 °C. IR (KBr): $\bar{\nu}$ = 3200, 3090, 2950, 1600, 1250 cm^{-1}. ^{1}HNMR (300 MHz, DMSO-d_6): δ= 3.81 (s, 4H, CH_2), 6.76-7.20 (m, 8H, aromatic), 8.8 (s, 1H, OH), 9.89 (s, 2H, OH) ppm. ^{13}CNMR (75 MHz, DMSO-d_6): δ= 29.4, 110.0, 110.7, 117.0, 128.9, 129.8, 129.9, 130.0, 132.3, 151.8, 154.3 ppm. Anal. calc. for $C_{20}H_{15}Br_3O_3$: C 44.23, H 2.78%; found: C 44.19, H 2.76%.

2,6-Bis-(5-chloro-2-hydroxy-benzyl)-4-methylphenol (Table 2, entry 15):

White solid. m.p.= 239-240 °C [15]; found 235-237 °C. IR (KBr): δ= 3135, 3030, 2930, 1600, 1485, 1420, 1390 cm^{-1}. ^{1}HNMR (300 MHz, DMSO-d_6): δ= 2.06 (s, 3H, CH_3), 3.8 (s, 4H, CH_2), 6.63-7.19 (m, 8H, aromatic), 8.32 (brs, 1H, OH), 9.8 (brs, 2H, OH) ppm. ^{13}CNMR (75 MHz, DMSO-d_6): δ= 20.3, 29.6, 116.2, 122.3, 126.4, 126.7, 127.7, 128.0 129.2, 129.5, 144.9, 153.7 ppm. Anal. calc. for $C_{21}H_{18}Cl_2O_3$: C 64.79, H 4.66%; found: C 64.86, H 4.61%.

4-Bromo-2,6-bis-(5-chloro-2-hydroxy-benzyl)phenol (Table 2, entry 16):

Pale-yellow solid. m.p.= 235-236 °C [15], found 234-236 °C. IR (KBr): $\bar{\nu}$ = 3439, 3050, 2950, 1584, 1448 cm^{-1}. ^{1}HNMR (300 MHz, DMSO-d_6): δ= 3.82 (s, 4H, CH_2), 6.81-7.09 (m, 8H, aromatic), 8.8 (brs, 1H, OH), 9.87 (brs, 2H, OH) ppm. ^{13}CNMR (75 MHz, DMSO-d_6): δ= 29.5, 110.7, 116.4, 122.4, 126.9, 128.3, 129.5, 130.0, 130.1, 151.9, 153.9 ppm. Anal. calc. for $C_{20}H_{15}BrCl_2O_3$: C 52.89, H 3.33%; found: C 52.80, H 3.38%.

3. Results and Discussion

At the beginning 3-methyl-1-(4-sulfobutyl)-1-H-imidazol-3ium hydrogen sulfate (Fig. 1) and different BMPs with the structures shown in Fig. 2, were synthesized based on the procedures in the literature [26,27].

The catalytic activity of DAIL was then investigated in the synthesis of different substituted trisphenols. The reaction between 4-chloro-2,6-bis-(hydroxymethyl)-phenol (1c) and 4-bromophenol (2a) was chosen as a model reaction to find the optimization conditions for the preparation of 2,6-bis-(5-bromo-2-hydroxy-benzyl)-4-chloro-phenol (3a). The results of this study are summarized in Table 1.

It was found that when the reaction was carried out in the absence of the catalyst, no product was observed; even after 3h (Table 1, entry 13). In order to show the effect of solvent on this reaction, the reaction was tested using different solvents such as n-hexane, acetonitrile, toluene and under solvent-free conditions in the presence of 3-methyl-1-(4-sulfobutyl)-1-H-imidazol-3ium hydrogen sulfate (Table 1, entries1-4). It was found that the best result was obtained under solvent-free conditions. To determine the optimum temperature, the reaction was carried out under solvent-free conditions at 70 to 100°C. At 70°C, the yield of the reaction was 68% and it was increased to 90% at 90°C (Table 1, entry 6). No improvement was seen in the yield and reaction time at higher temperature (Table1, entry 7). In order to optimize the best molar ratio of phenol to BMP, the model reaction was performed using different amounts of *p*-bromophenol (Table 1, entries 6,8,9). The results indicate that the best ratio is 3 mmol of phenol per each mmol of BMP. Finally to determine the amount of the catalyst, the model reaction was carried out using different amounts of 3-methyl-1-(4-sulfobutyl)-1-*H*-imidazol-3ium hydrogen sulfate (Table 1, entries 6, 10-13). The best result obtained when we used 0.2 equivalent of the catalyst (Table 1, entry 6).

After optimization of the reaction conditions, a series of trisphenols as a class of polyhydroxy aromatic compounds were synthesized. The results were summarized in Table 2.

Considering Table 2, it is clear that 3-methyl-1-(4-sulfobutyl)-1-H-imidazol-3ium hydrogen sulfate is an effective catalyst for the synthesis of trisphenolic compounds using the reaction of phenols and BMPs. As can be seen from Table 2, the reactions proceeded efficiently and the desired products were obtained in good yields. It is noteworthy to mention that the effect of the nature of the substituents on the aromatic rings, showed no obvious effect on this condensation, because all the products were obtained in high yields and short reaction times. The selectivity of this method was examined by using 3,4-di-methylphenol as an asymmetric phenol which has two different ortho sites adjacent to hydroxyl group. The results indicated in Table 2 revealed that the less hindered ortho site is alkylated selectively (Table 2, entry 2).

Comparison of the efficiency of 3-methyl-1-(4-sulfobutyl)-1-H-imidazol-3ium hydrogen sulfate catalyst with other catalytic systems in the condensation reaction of 4-chloro-2,6-bis-(hydroxy methyl)-phenol and *p*-bromophenol to prepare 2,6-bis-(5-bromo-2-hydroxy-benzyl)-4-chlorophenol is presented in Table 3. As this Table shows, 3-methyl-1-(4-sulfobutyl)-1-H-imidazol-3ium hydrogen sulfate was found to be more active and efficient than other catalysts.

The reusability of the catalyst was tested by separating it from the reaction mixture by use of acetonitrile. After completion of the reaction, the reaction mixture was extracted with acetonitrile (2×5 mL) and the remained catalyst dried in an oven at 80 °C for 2h. Then it directly reused for the next run. The recovered catalyst can be reused without significant loss of its activity for at least 6 runs (Fig. 3).

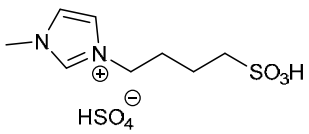


Fig. 1. The DAIL synthesized and used in this study: 3-methyl-1-(4-sulfobutyl)-1-*H*-imidazol-3ium hydrogensulfate.

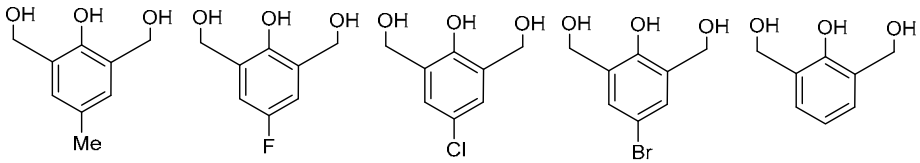
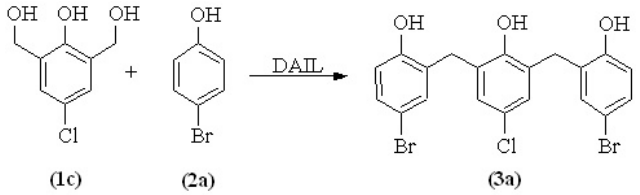


Fig. 2. The chemical structure of the synthesized BMPs.

Table 1. Optimization of the reaction conditions for the DAIL catalyzed reaction of 4-chloro-2,6-bis-(hydroxymethyl)-phenol and *p*-bromophenol.



(1c) (2a) (3a)

Entry	Molar ratios of phenol/BMP/catalyst	Solvent	Temp. (°C)	Time (min)	Yield (%)[a]
1	3/1/0.2	n-Hexane	68	120	Trace
2	3/1/0.2	Toluene	110	120	34
3	3/1/0.2	Acetonitrile	82	120	51
4	3/1/0.2	Solvent-free	70	40	68
5	3/1/0.2	Solvent-free	80	20	78
6	3/1/0.2	Solvent-free	90	20	90
7	3/1/0.2	Solvent-free	100	60	71
8	2/1/0.2	Solvent-free	90	60	75
9	4/1/0.2	Solvent-free	90	20	85
10	3/1/0.1	Solvent-free	90	60	66
11	3/1/0.15	Solvent-free	90	45	79
12	3/1/0.25	Solvent-free	90	20	87
13	3/1/0	Solvent-free	90	180	-

[a]Isolated yield.

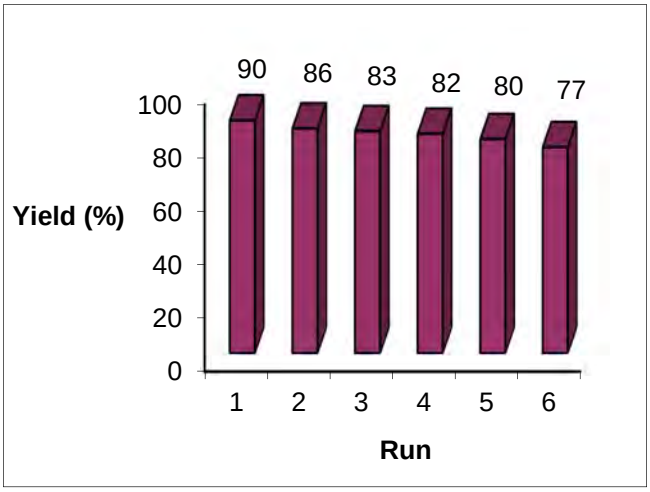
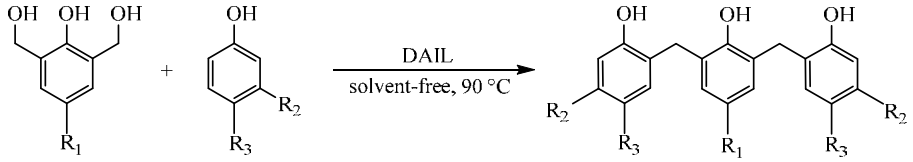


Fig. 3. Reusability of the catalyst in the synthesis of 2,6-bis-(5-bromo-2-hydroxy-benzyl)-4-chlorophenol.

Table 2. Synthesis of some substituted trisphenols in the presence of 3-methyl-1-(4-sulfobutyl)-1-H-imidazol-3ium hydrogensulfate.



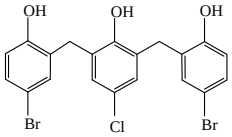
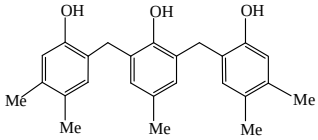
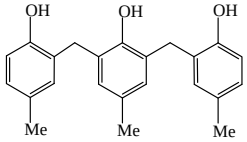
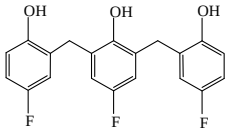
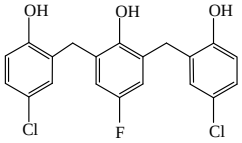
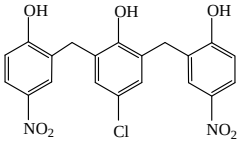
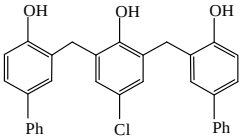
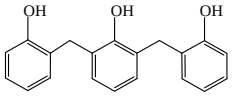
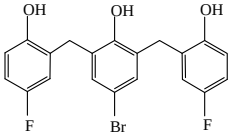
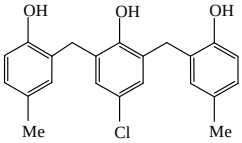
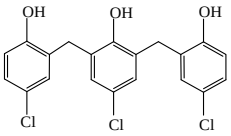
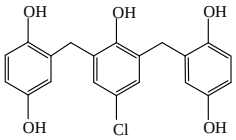
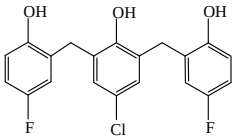
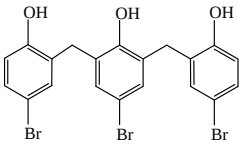
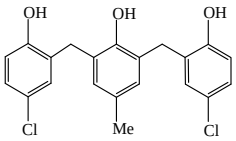
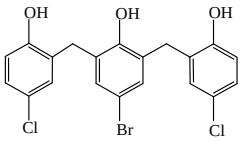
Entry	R_1	R_2	R_3	Product	Time (min)	Yield (%)[a]
1	Cl	H	Br		20	90
2	Me	Me	Me		40	80
3	Me	H	Me		25	85
4	F	H	F		25	86
5	F	H	Cl		25	90
6	Cl	H	NO_2		40	79
7	Cl	H	Ph		40	80
8	H	H	H		30	83
9	Br	H	F		30	85

Table 2. *(Continued).*

10	Cl	H	Me		20	88
11	Cl	H	Cl		25	83
12	Cl	H	OH		20	88
13	Cl	H	F		30	82
14	Br	H	Br		35	85
15	Me	H	Cl		30	83
16	Br	H	Cl		20	86

[a]Isolated yield.

Table 3. Comparison of the activity of various catalysts in the condensation reaction of 4-chloro-2,6-bis-(hydroxymethyl)-phenol and 4-bromophenol.

Entry	Catalyst	Solvent	Time	Yield (%)	Ref.
1	3-methyl-1-(4-sulfobutyl)-1-*H*-imidazol-3ium hydrogensulfate	Solvent-free	20 min	90	This work
2	HCl	Methanol	12 h	68	[12]
3	$ZnCl_2$/Microwave	Solvent-free	42 s	90	[14]
4	Silica sulfuric acid	1,4-Dioxane	1.5 h	85	[15]
5	Tungstosilicic acid	H_2O	6 h	85	[13]

4. Conclusions

In conclusion, we have established a new and efficient method for preparation of substituted trisphenols using a dual acidic ionic liquid, 3-methyl-1-(4-sulfobutyl)-1-*H*-imidazol-3ium hydrogen sulfate, as catalyst. High yields of the products, short reaction times, easy work up, use of an ecofriendly and reusable catalyst and solvent-free conditions are as worthwhile advantages of this method.

Acknowledgements

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