Eco-friendly water as a solvent for the one-pot synthesis of 2-aminothiazoles

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ABSTRACT

An efficient one-pot environmentally benign greener synthetic method for the preparation of 2-aminothiazole derivatives from aldehydes, ketones and β-keto esters using aqueous hydrobromic acid and hydrogen peroxide as bromine source in water solvent.

Key words: Green synthesis, Hantzsch’s synthesis, aldehydes, ketones, β-keto esters, hydrobromic acid, hydrogen peroxide, thiourea.

INTRODUCTION

The thiazole derivatives plays very important role in medicinal chemistry and has found broad application in drug developments for the treatment of antibacterial [1-3], antifungal [4], antiviral [5-6], anti-HIV [7-8], anti-inflammatory [9-11], anticanic [12-14], pesticidal [15], antiprotozoal [16], antituberculosis [17-18], anthelmintic [19], anticonvulsant [20], Diauretics [21] etc.

There are several synthetic methods have been reported for the preparation of 2-aminothiazole derivatives, typically the most prevalent method is Hantzsch’s synthesis [22]. This method involves the reaction of α-halocarbonyl compounds which are highly lachrymator and very difficult to isolate. Many improved process for synthesis of thiazole derivatives have been reported from α-diazo ketones [23], α-tosyloxyketones [24], alkene using IBX and Iodine [25], 1H-1-(1'-alkynyl)-5-methyl-1,2,3-benzodithiole-3,3-dioxide with thioamide [26], N,N′-diformylaminomethyl aryl ketones with phosphorous pentasulfide [27], active methylene isocyanides [28], with Lawesson’s reagent [29], and catalyst such as ammonium-12-molybdophosphate in methanol [30], β-cyclodextrin in water [31], proparglyic alcohols with different catalysts [32], iodine [33], also from microwave reaction [34-36]. However the above methods suffered from handling of lachrymatory α-halocarbonyl compounds, harsh reaction and cumbersome for the product isolation, using organic solvents for reaction and using expensive catalyst.

In recent years water is obvious choice for chemical reaction due to its environmentally benign new solvent. It plays a major role in green synthesis as an attractive and alternative to conventional solvents. Water is making economically and environmentally friendly solvent for many reactions. The greener synthetic methods of bromination on ketones in water using aqueous hydrobromic acid and hydrogen peroxide is known in literature [37] and involves the high atom economy, use less corrosive materials and eliminate liquid bromine handling. However water has not been studied extensively for chemical reaction especially the synthetic organic chemistry because of solubility of the organic compounds and most of the reaction required anhydrous condition.
As part of our research to develop a methodology for 2-aminothiazole derivatives using green chemistry with one-pot synthesis in water as solvent, we have developed a simple and an efficient greener one pot synthesis of 2-aminothiazole derivatives by Hantzsch’s reaction from aldehydes, ketones and β-ketoesters in water with out handling of α-bromocarbonyl derivatives which are highly lachrymator.

**EXPERIMENTAL SECTION**

Commercial reagents were used as received. Analytical TLC is conducted on E-Merck 60F254 aluminum-packed silica gel plates (0.2mm). Developed plates are visualized using UV light or Iodine chamber. Column chromatography was performed using 60-120 mesh silica gel and executed under nitrogen pressure (flash chromatography) conditions, using commercial grade solvents, as eluents. Melting points were determined on a Micro Química model APF 301 apparatus and are uncorrected. Infrared spectra were recorded on Bomen Michelson model 102 FTIR or Hartman & Braun MB, and the most intense or representative bands are reported (in cm\(^{-1}\)). \(^1\)H and \(^{13}\)C NMR spectra were obtained on a Bruker DRX-400 spectrometer at 400 MHz, and on a Bruker ARX-200 spectrometer at 100 respectively, with CDCl\(_3\), DMSO-d\(_6\) and D\(_2\)O as solvent. Chemical shifts are in ppm downfield from a tetramethylsilane internal standard. Mass spectra were recorded on a Perkin-Elmer mass spectrometer operating at 70 eV.

1. **General Procedure for making 2-aminothiazole derivatives from Ketones and β-keto esters**

To a stirred solution of Ketones (1a-1j) / β-keto esters (1k-1n) in water at room temperature, was added aqueous hydrobromic acid (48%, 2.0 eq.). The mixture was cooled to 0-10 °C and added slowly of aqueous hydrogen peroxide solution (50%, 1.0eq.), warmed the reaction mass to ambient temperature and stirred for 2-16 hr. till the bromine colour was faded. Added thiourea derivatives (3a-3c) (1.0 eq.) and heated to 90-95 °C. Once the reaction was completed cooled gradually to 0-10 °C and stirred. Filtered the product washed with chilled water and dried the product.

### 2-Amino-4-methylthiazole Hydrobromide (4a)

Followed general procedure by using Acetone (1a) and Thiourea (3a).

\[ \delta (6.17, s, 1H), 2.02, (s, 3H) \]

\[ \delta (169.91, 136.03, 130.18, 101.80, 121.80, 101.79, 12.71) \]

\[ IR (KBr,cm\(^{-1}\)) : 3315, 3236, 3184, 3135, 3106, 1618, 1430, 1415, 1390, 1139, 971, 783, 725, 712 \]

\[ MS (m/z) = 114.17 [M+1]^+ ; MP : 180.3-182.7 °C \]

### 2-Amino-4,5-dimethylthiazole Hydrobromide (4b-i) & 2-Amino-4-ethylthiazole (4b-ii)

Followed general procedure by using Methyl ethyl ketone (1b) and Thiourea (3a).

\[ \delta (1.94, s, 3H), 1.91, (s, 3H) \]

\[ \delta (168.44, 130.26, 113.12, 9.79, 9.12) \]

\[ IR (KBr,cm\(^{-1}\)) : 3341, 3231, 3191, 3144, 1614, 1429, 1187, 977, 879, 775, 634, 594, 554; MS (m/z) = 129.2 [M+1]^+ ; MP : 282.2-290.1 °C \]

### 2-Amino-4-ethyl-5-methylthiazole Hydrobromide (4c)

Followed general procedure by using Diethyl ketone (1c) and Thiourea (3a).

\[ \delta (2.30-2.35, q, 2H, J=7.6, 15.1 Hz), 1.97, (s, 3H), 0.91-0.95, (t, 3H, J=7.6Hz); \]

\[ \delta (168.05, 135.84, 113.05, 18.72, 12.30, 9.78) \]

\[ IR (KBr,cm\(^{-1}\)) : 3349, 3147, 2755, 1611, 1566, 1445, 1430, 1061, 964, 783, 714, 632, 533; MS (m/z) = 143.1 [M+1]^+ ; MP : 157.3-160.8 °C \]

### 2-Amino-4-isopropylthiazole Hydrobromide (4d)

Followed general procedure by using Methyl isopropyl ketone (1d) and Thiourea (3a).

\[ \delta (6.18, s, 1H), 2.63-2.72, (m, 1H), 1.01-1.03, (d, J=6.9 Hz); \]

\[ \delta (170.35, 146.39, 99.71, 27.61, 20.12, 12.30, 9.78) \]

\[ IR (KBr,cm\(^{-1}\)) : 3400, 3263, 3109, 2755, 1626, 1570, 1468, 1234, 1117, 1068, 901, 741, 721, 641; MS (m/z) = 143.1 [M+1]^+ ; MP : 69.1-74.2°C \]
2-Amino-4-tert-butyIthiazole Hydrobromide (4e)
Followed general procedure by using Pinacolone (1e) and Thiourea (3a), \(^1\H-NMR (D_2O): \delta 6.22\) (s,1H), 1.08\) (s,9H); \(^1^3\C-NMR (D_2O): \delta 170.67, 149.06, 99.66, 32.67, 27.81\(3\)C); IR (KBr,\cm): 3444, 3245, 3099, 2964, 1628, 1564, 1461, 1222, 1202, 894, 756, 654; MS (m/z) = 157.1 [M+1]+; MP : 1245.-127.8°C

2-Amino-4-isoo-butylthiazole Hydrobromide (4f)
Followed general procedure by using methyl isobutyl ketone (1f) and Thiourea (3a), \(^1\H-NMR (CDCl_3): \delta 2.34-2.32\) (d,2H,J=7.0Hz), 1.96-1.89\) (m,4H); IR (KBr,\cm): 3383, 3268, 3125, 1633, 1570, 1449, 770; MS (m/z) = 177.2 [M+1]+; MP : 188.2-193.7°C

2-Amino-4-phenylthiazole Hydrobromide (4g)
Followed general procedure by using Methyl isopropyl ketone (1g) and Thiourea (3a), \(^1\H-NMR (CDCl_3): \delta 6.04\) (s,1H), 5.00\) (br,s,1H), 3.57-3.53\) (m,1H), 2.83-2.76\) (m,1H), 1.23-1.21\) (d,6H,J=6.47Hz), 1.20-1.19\) (d,6H,J=6.98Hz); \(^1^3\C-NMR (CDCl_3): \delta 159.73, 147.88, 47.84, 47.84, 30.89, 22.82\(2\)C, 22.01\(2\)C); IR (KBr,\cm): 3223, 2964, 2930, 2871, 1539, 1464, 1384, 1635, 1338, 1255, 1213, 1172, 1125, 1067, 991, 837, 757, 703, 681; MS (m/z) = 185.2 [M+1]+; MS (m/z) = 199.3 [M+1]+
Isopropyl-(4-phenylthiazole-2-yl)-amine (4n)
Followed general procedure by using Acetophenone (1g) and Isopropylthiourea (3b), purified through column chromatography. \(^{1}H\)NMR (CDCl\(_3\)): δ 7.82-7.80 (d,2HJ=7.5Hz), 7.39-7.35 (m,2H), 7.30-7.26 (m,1H), 6.70(s,1H), 5.29-5.27 (d,br,1H), 3.72-3.67 (m,1H), 1.28-1.27 (d,6HJ=6.4Hz); \(^{13}C\)NMR (CDCl\(_3\)): δ 169.12, 151.36, 135.06, 128.63(2C), 127.63, 126.16(2C), 100.43, 48.12, 22.73(2C); IR (Neat cm\(^{-1}\)): 3186, 3075, 2965, 2930, 2888, 1571, 1460, 1437, 1337, 1291, 1274, 1170, 1057, 770, 704; MS (m/z) = 219.1 [M+1]\(^+\)

Isopropyl-(4,5,6,7-tetrahydrobenzothiazole-2-yl)-amine (4o)
Followed general procedure by using Cyloheptanone (1i) and Isopropylthiourea (3b), purified through column chromatography. \(^{1}H\)NMR (CDCl\(_3\)): δ 5.02 (s,br,1H), 3.61-3.57 (m,1H), 2.54-2.52 (m,4H), 1.78-1.75 (m,4H), 1.22-1.11 (d,6HJ=6.4Hz); \(^{13}C\)NMR (CDCl\(_3\)): δ 166.66, 145.36, 115.39, 47.69, 35.59, 26.69, 23.58, 23.15, 22.94(2C); IR (Neat cm\(^{-1}\)): 3217, 2967, 2930, 2854, 1536, 1446, 1364, 1211, 1177, 1070; MS (m/z) = 197.3 [M+1]\(^+\)

(4-Isopropylthiazol-2-yl)-phenylamine Hydrobromide (4p)
Followed general procedure by using Methyl acetoacetate (1d) and Phenylthiourea (3c), \(^{1}H\)NMR (DMSO-d\(_6\)): δ 7.56-7.54 (d,2HJ=7.9Hz), 7.39-7.35 (t,2HJ=7.7Hz), 7.09-7.06 (t,2HJ=7.7Hz), 6.50 (s,1H), 1.26 (s,9H); \(^{13}C\)NMR (DMSO-d\(_6\)): δ 140.38, 129.72, 123.71, 119.31, 100.27, 34.27, 29.49(3C); IR (KBr,cm\(^{-1}\)): 3079, 2970, 1608, 1582, 1521, 1494, 1195, 764, 701; MS (m/z) = 233.2 [M+1]\(^+\)

(4-Tert-butythiazol-2-yl)-phenylamine (4q)
Followed general procedure by using Pinacolone (1e) and Phenylthiourea (3c), \(^{1}H\)NMR (DMSO-d\(_6\)): δ 7.16-7.15 (d,br,1H), 4.27-4.21 (q,2HJ=7.1,14.2Hz), 3.56 ( m,1H), 2.51 (s,br,1H), 1.33-1.29 (t,3HJ=7.08Hz), 1.27-1.25 (d,6HJ=6.3Hz); \(^{13}C\)NMR (DMSO-d\(_6\)): δ 169.71, 160.54, 157.06, 106.74, 61.65, 27.05, 20.91(2C), 14.37; IR (KBr,cm\(^{-1}\)): 3352, 3043, 3008, 1617, 1580, 1534, 1497, 768, 750; MS (m/z) = 253.2 [M+1]\(^+\)

2-Amino-5-carboxyethyl-4-methylthiazole Hydrobromide (4s)
Followed general procedure by using Ethyl acetoacetate (1k) and Thiourea (3a), \(^{1}H\)NMR (DMSO-d\(_6\)): δ 10.45 (br,1H), 7.90-7.88 (d,2HJ=7.56Hz), 7.74-7.72 (d,2HJ=7.7Hz), 7.46-7.28 (m,6H), 6.99-6.95 (t,1HJ=7.12Hz), 6.49 (br,2H); \(^{13}C\)NMR (DMSO-d\(_6\)): δ 168.66, 160.71, 147.54, 107.83, 61.77, 14.40, 14.07; IR (KBr,cm\(^{-1}\)): 3085, 2816, 2774, 1705, 1615, 1555, 1288, 1268, 1096, 788, 715, 657, 619; MS (m/z) = 187.1[M+1]\(^+\); MP : 210.5-212.8°C.

2-Amino-5-carboxyethyl-4-isopropylthiazole Hydrobromide (4t)
Followed general procedure by using Isopropylacetoacetate (1l) and Thiourea (3a), \(^{1}H\)NMR (DMSO-d\(_6\)): δ 4.22-4.14 (q,2HJ=7.0,14.1Hz), 3.85-3.78 (m,1H), 1.23-1.17(m,9H); \(^{13}C\)NMR (DMSO-d\(_6\)): δ 169.71, 160.54, 157.06, 106.74, 61.65, 27.05, 20.91(2C), 14.37; IR (KBr,cm\(^{-1}\)): 3352, 3043, 3008, 1723, 1714, 1645, 1615, 1567, 1463, 1367, 1340, 1329, 1087, 1019; MS (m/z) = 215.2[M+1]\(^+\); MP : 105.9-109.8°C.

Isopropyl-(5-carboxyethyl-4-methylthiazole-2-yl)-amine Hydrobromide (4u)
Followed general procedure by using Ethyl acetoacetate (1m) and Isopropylthiourea (3b), \(^{1}H\)NMR (DMSO-d\(_6\)): δ 6.15 (br,1H), 4.27-4.21 (q,2HJ=7.1,14.2Hz), 3.56 (m,1H), 2.51 (s,3H), 1.33-1.29 (t,3HJ=7.08Hz), 1.27-1.25 (d,6HJ=6.3Hz); \(^{13}C\)NMR (DMSO-d\(_6\)): δ 170.45, 162.79, 159.72, 108.84, 30.33, 48.41, 22.42(2C), 14.49, 14.45; IR (KBr,cm\(^{-1}\)): 3188, 3073, 2975, 1699, 1573, 1465, 1440, 1369, 1260, 1174, 1082, 757; MS (m/z) = 229.1[M+1]\(^+\).
II. General Procedure for making 2-aminothiazole derivatives from aldehydes

To a stirred solution of aldehydes (5a-5f) in water at room temperature, was added aqueous hydrobromic acid (48%, 2.0 eq.). The mixture was cooled to 0-10°C and added slowly of aqueous hydrogen peroxide solution (50%, 1.0eq.), warmed the reaction mass to ambient temperature and stirred for 2-16 hr. till the bromine colour was faded. Added thiourea (3a-3b) (1.0 eq.) and heated to 90-95°C. Once the reaction was completed cooled gradually to 0-10°C and stirred. Basified the mass and extracted in Ethyl acetate. The organic extracts were concentrated and purified through column chromatography using silica gel 60-120 mesh. Using Ethyl acetate/hexane as eluent to afford the product 7.

2-Amino-thiazole (7a)
Followed general procedure by using Acetaldehyde solution (5a) and Thiourea (3a).

$^1$H-NMR (DMSO-d$_6$): $\delta$ 6.92-6.90 (d, 1H, J=3.7Hz), 6.87 (br,s, 2H), 6.50-6.51 (d, 1H, J=3.7Hz);

$^{13}$C-NMR (DMSO-d$_6$): $\delta$ 168.92, 138.64, 106.61;

IR (KBr, cm$^{-1}$): 3410, 3288, 3119, 1626, 1519, 1489, 1323, 1275, 1200, 1029, 758, 693, 514; MS (m/z) = 101.1 [M+1]$^+$; MP : 80.1-84.4°C

2-Amino-5-methylthiazole (7b)
Followed general procedure by using Propionaldehyde (5b) and Thiourea (3a).

$^1$H-NMR (CDCl$_3$): $\delta$ 6.67 (s, 1H), 5.42 (br,s, 2H), 2.26 (s, 3H);

$^{13}$C-NMR (CDCl$_3$): $\delta$ 167.08, 135.06, 122.75, 11.86; IR (KBr, cm$^{-1}$): 3424, 3263, 3112, 3056, 1617, 1512, 1443, 1432, 1310, 1050, 858, 848; MS (m/z) = 115.2 [M+1]$^+$; MP : 90.5-96.7°C

2-Amino-5-ethylthiazole (7c)
Followed general procedure by using Butyraldehyde (5c) and Thiourea (3a).

$^1$H-NMR (CDCl$_3$): $\delta$ 6.73 (s, 1H), 4.90 (br,s, 2H), 2.69-2.64 (q, 2H, J=7.4, 14.8 Hz), 1.25-1.22 (t, J=7.5 Hz);

$^{13}$C-NMR (CDCl$_3$): $\delta$ 166.88, 133.27, 130.51, 20.42, 15.57; IR (KBr, cm$^{-1}$): 3444, 3272, 3109, 2966, 2872, 1618, 1518, 1314, 1196, 1057, 843, 570; MS (m/z) = 129.2 [M+1]$^+$; MP : 43.5-51.3°C

2-Amino-5-propylthiazole (7d)
Followed general procedure by using Valeraldehyde (5d) and Thiourea (3a).

$^1$H-NMR (CDCl$_3$): $\delta$ 6.73 (s, 1H), 4.78 (br,s, 2H), 2.62-2.58(t, 2H), 1.63-1.57(q, 2H, J=7.34, 14.7 Hz), 0.96-0.92 (t, J=7.3 Hz);

$^{13}$C-NMR (CDCl$_3$): $\delta$ 166.84, 134.03, 129.08, 33.24, 26.64, 21.89, 13.62; MS (m/z) = 157.1 [M+1]$^+$; MP : 157.1 [M+1]$^+$

2-Amino-5-isopropylthiazole (7f)
Followed general procedure by using Isovaleraldehyde (5f) and Thiourea (3a).

$^1$H-NMR (CDCl$_3$): $\delta$ 6.73 (s, 1H), 4.80 (br,s, 2H), 3.05-2.96 (m, 2H), 1.26-1.25 (d, 2H, J=6.8 Hz);

$^{13}$C-NMR (CDCl$_3$): $\delta$ 168.12, 113.36, 128.24, 47.70, 22.92(2C), 20.61, 15.84; IR (KBr,cm$^{-1}$): 3198, 2966, 1582, 1556, 1467, 138, 1332, 1301, 1169, 847; MS (m/z) = 171.1 [M+1]$^+$
Isopropyl-(5-isopropylthiazol-2-yl)-amine (7i)
Followed general procedure by using Isovaleraldehyde (5e) and Isopropyl thiourea (3a). $^1$H-NMR (CDCl$_3$): $\delta$ 6.73 (s,1H), 5.13-5.12 (br,1H), 3.69-3.64 (m,1H), 3.02-2.96 (m,1H), 1.27-1.24(d,12H); $^{13}$C-NMR (CDCl$_3$): $\delta$ 167.67, 134.42, 132.44, 47.64, 27.69, 24.42(2C), 22.99(2C); IR (KBr,cm$^{-1}$) : 3186, 3085, 2966, 2870, 1579, 1554, 1463, 1363, 1345, 1170, 1127, 848; MS (m/z) = 185.2 [M+1]$^+$

**RESULT AND DISCUSSION**
We have started our synthesis initially with easily available ketone reagent such as acetone (1a). The addition of aqueous H$_2$O$_2$ to the acetone in HBr solution at lower temperature gives the formation of $\alpha$-bromoacetone (2a) which are highly lachrymator. The condensation of in-situ prepared $\alpha$-bromo acetone with thiourea (3a) to get 2-amino-4-methylthiazole hydrobromide (4a) by simply cooling and filtering.

Encouraged by the above result recourse has been taken to study various ketones (1b-1j) and $\beta$-keto esters (1k-1n) with aqueous hydrobromic acid and hydrogen peroxide solution to afford $\alpha$-bromo carbonyl compounds (2b-2n). This $\alpha$-bromocarbonyl compounds reacted with thiourea (3a), isopropylthiourea (3b) and phenylthiourea (3c) and furnished the desired 2-aminothiazole derivatives (4a-4v). All the experiments were carried out using very simple, cheapest, commercially easily available ketones and $\beta$-keto esters. These process made for us to avoid the handling of $\alpha$-bromo carbonyl derivatives with simple operation to get the required derivatives. These reaction are briefly summarized in **Scheme-1** and the results are summarized in **Table-1**

![Scheme-1](image)

**Table-1 : Synthesis of 2-aminothiazole derivatives from Ketones and $\beta$-Keto esters**

<table>
<thead>
<tr>
<th>Entry</th>
<th>Ketone / $\beta$-Keto ester</th>
<th>Thiourea deri.</th>
<th>2-Aminothiazoles</th>
</tr>
</thead>
<tbody>
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<td>1</td>
<td>1a</td>
<td>3a</td>
<td>$R$ - $R''$ - $R'''$ - CH$_3$ - COOEt - H</td>
</tr>
<tr>
<td>2</td>
<td>1b</td>
<td>3a</td>
<td>$R$ - $R''$ - $R'''$ - CH$_3$ - COOEt - H</td>
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<tr>
<td>3</td>
<td>1c</td>
<td>3a</td>
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<tr>
<td>4</td>
<td>1d</td>
<td>3a</td>
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<tr>
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<td>3a</td>
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<tr>
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<td>1f</td>
<td>3a</td>
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<td>1g</td>
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<tr>
<td>8</td>
<td>1h</td>
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<tr>
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</tbody>
</table>
Similarly we have studied to the various aldehydes (5a-5f) with aqueous hydrobromic acid and hydrogen peroxide solution, followed by reaction with thiourea derivatives (3a-3b) to furnish the required 2-aminothiazole derivatives (7a-7j) in good yields. These reaction are briefly summarized in Scheme-2 and the results are summarized in Table-2.

![Diagram of reaction](image)

**Scheme-2**

<table>
<thead>
<tr>
<th>Entry</th>
<th>Aldehydes</th>
<th>Thiourea der.</th>
<th>2-Aminothiazoles</th>
<th>R</th>
<th>R'</th>
<th>Yield (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>5a</td>
<td>3a</td>
<td>7a</td>
<td>H</td>
<td>H</td>
<td>72</td>
</tr>
<tr>
<td>2</td>
<td>5b</td>
<td>3a</td>
<td>7b</td>
<td>CH₃</td>
<td>H</td>
<td>76</td>
</tr>
<tr>
<td>3</td>
<td>5c</td>
<td>3a</td>
<td>7c</td>
<td>CH₂CH₃</td>
<td>H</td>
<td>58</td>
</tr>
<tr>
<td>4</td>
<td>5d</td>
<td>3a</td>
<td>7d</td>
<td>CH₂CH₂CH₃</td>
<td>H</td>
<td>61</td>
</tr>
<tr>
<td>5</td>
<td>5e</td>
<td>3a</td>
<td>7e</td>
<td>CH(CH₃)₂</td>
<td>H</td>
<td>75</td>
</tr>
<tr>
<td>6</td>
<td>5f</td>
<td>3a</td>
<td>7f</td>
<td>CH₃(CH₂)₃</td>
<td>H</td>
<td>71</td>
</tr>
<tr>
<td>7</td>
<td>5b</td>
<td>3b</td>
<td>7g</td>
<td>CH₃</td>
<td>CH(CH₃)₂</td>
<td>75</td>
</tr>
<tr>
<td>8</td>
<td>5e</td>
<td>3b</td>
<td>7h</td>
<td>CH₂CH₂CH₃</td>
<td>CH(CH₃)₂</td>
<td>64</td>
</tr>
<tr>
<td>9</td>
<td>5d</td>
<td>3b</td>
<td>7i</td>
<td>CH₂CH₃</td>
<td>CH₃(CH₂)₃</td>
<td>72</td>
</tr>
<tr>
<td>10</td>
<td>5e</td>
<td>3b</td>
<td>7j</td>
<td>CH₂CH₃</td>
<td>CH₃(CH₂)₃</td>
<td>70</td>
</tr>
</tbody>
</table>

**CONCLUSION**

In summary, we report a high yield one-pot procedure in water alone for the synthesis of 2-amino thiazole derivatives. With this we have demonstrated a simple experimental procedure, convenient, eco-friendly and highly efficient green one pot synthesis of 2-aminothiazole derivatives in water from easily available carbonyl derivatives. The present method provides several advantages such as avoiding handling of α-bromocarbonyl compounds which are difficult to make and isolate due to its high lacrimary and use of highly polar, toxic organic solvents and catalyst.

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