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Facile One Pot Synthesis of 4,5-Disubstituted 1,2,3-Thiadiazoles using Acid Halides *via* Diazo Intermediate Formation

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In this work, a competent straightforward one-pot synthesis of 4,5-disubstituted 1,2,3-thiadiazoles was carried out using acid halides. The reaction proceeds through the conversion of acid halides into diazo carbonyl compounds, which further involve in the nucleophilic addition with CS_2 and alkylation on sulphur by alkyl halides results in substituted thiadiazoles. This process is highly regioselective and operationally simple for generating various substituted thiadiazole molecules. This protocol offers several advantages for accessing the medicinally significant thiadiazole moieties with promising yields under mild reaction conditions, furthermore it involves a simple purification and also the removal of toxic reagents.

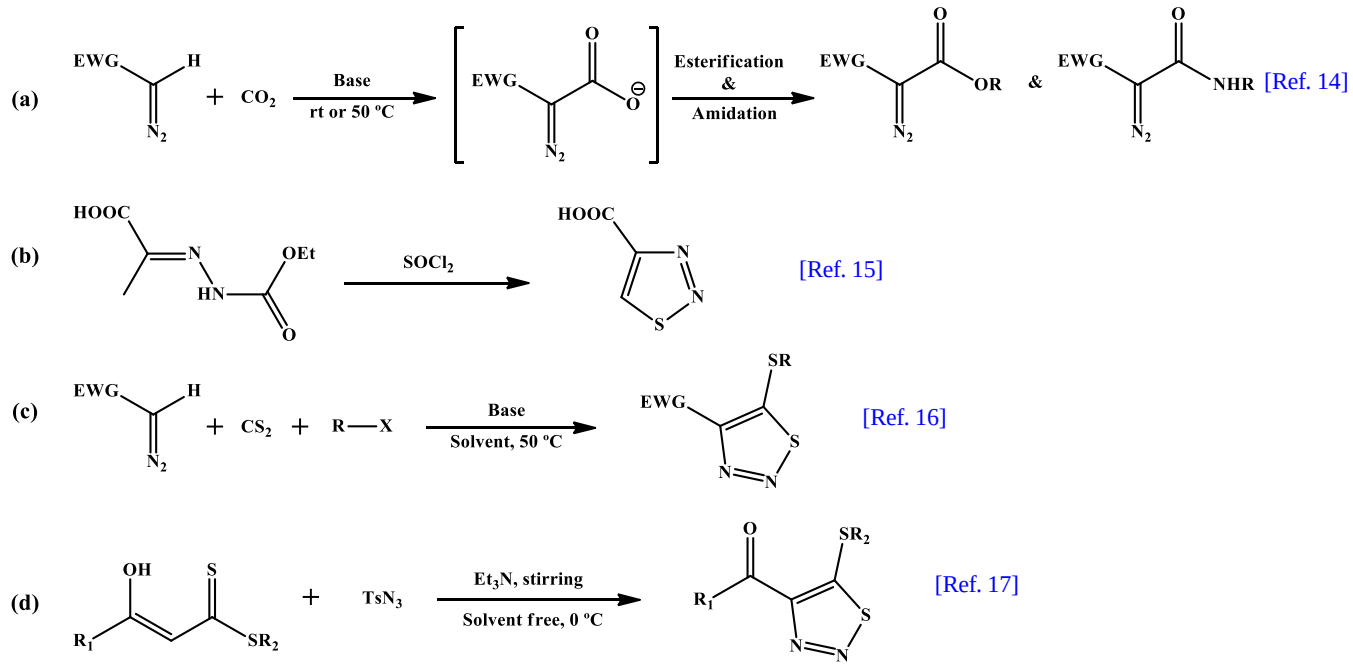
Keywords: Acid halides, α-Diazo carbonyl compounds, Carbon disulphide, One pot reaction, Disubstituted 1,2,3-thiadiazoles.

INTRODUCTION

Synthetic organic chemistry plays a vital role across many areas of our modern technological society. Its relevance remains especially strong in the realm of new drug discovery and it continues to form a foundational component of the chemical industry. 1,2,3-Thiadiazoles [1,2] represent a group of versatile heterocycles that are integral to various pharmaceutical ingredients [3,4]. Their distinguished biological activities have been resulted in the discovery of numerous potent drugs in the fields of pharmaceutical industry such as anti-HIV, antibiotics, antiviral, neurodegenerative drugs and in agriculture [5-11]. Also, these 1,2,3-thidiazoles exhibit potential optoelectronic properties [12,13].

Pechmanm & Nold [14] reported the synthesis of α-diazo esters and α-diazo amides through the addition of diazo compounds to CO_2 followed by esterification or amidation (**Scheme-Ia**). Alternatively, Hurd *et al.* [15] reported the synthesis of substituted 1,2,3-thiadiazoles by reaction of acyl hydrazone with thionyl chloride and obtained moderate yields only (Hurd-Mori synthesis) (**Scheme-Ib**). The addition of diazo compounds to carbon disulphide followed by addition of alkyl halides in presence of base to provide substituted thiadiazoles were achieved by Zhang *et. al.* [16] and provided only poor to mode-rate yields (**Scheme-Ic**). Moreover, Singh *et al.* [17] synthesized 4,5-disubstituted 1,2,3-thiadiazoles through cycloaddition of α-enolic dithioesters with tosyl azide (**Scheme-Id**). Wolff [18] also reported the synthesis of 5-alkyl-4-carbalkoxy-1,2,3-thiadiazoles using α-diazo carbonyl compounds by reacting with Lawesson's reagent.

The previously reported methods generally involve the addition of diazo compounds to carbon dioxide through *ipso*-C–H bond formation without using transition metals, while preserving the diazo functional group [19]. The resulted intermediate α-diazo carboxylate is further converted into the corresponding esters and amides. Similarly carbon disulfide which acts as electrophile instead of CO_2 to provide corresponding analogue, has been extensively employed as a sulphur source for the synthesis of a wide range of valuable sulphur containing heterocyclic compounds used in the agricultural and pharmaceutical applications [20,21]. On the other side, the focus on green synthetic strategies for forming and breaking carbon–carbon (C–C) and carbon–heteroatom (C–X) bonds is most important element of environment friendly organic synthesis. There is a strong push towards environ-mentally sustainable practices, which aims to find alternative methods that reduce the stringent requirements for chemical reactions.



Scheme-I: Existing reports for the synthesis of 4,5-disubstituted 1,2,3-thiadiazoles

Keeping in view of adverse effects of solvents and hazardous chemicals on the environment and human health, we carried out the present work by minimizing the amount of solvent used in the multistep one-pot synthesis of 1,2,3-thiadiazoles. As a continuation to our previous investigations, herein the conversion of acid halides into diazo compounds, followed by the addition of CS_2 and alkyl halides in presence of DBU base, which led to formation of 4,5-disubstituted 1,2,3-thiadiazoles under mild conditions *via in situ* reactions.

EXPERIMENTAL

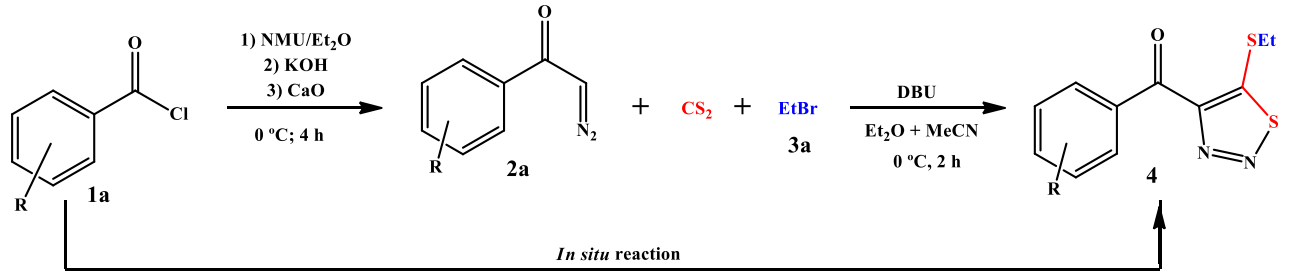
The commercially available starting materials benzoyl chlorides, *N*-nitroso-*N*-methylurea (NMU), carbon disulphide (CS_2) and alkyl bromides were procured from Sigma-Aldrich, USA and used as received without further purification. IR spectra were recorded in KBr using a Bruker Alpha II FT-IR spectrometer in the 4000-400 cm^{-1} range. ^1H and ^{13}C NMR spectra were obtained on a Bruker Avance III NMR spectrometer operating at 400/500 MHz for ^1H and 100/125 MHz for ^{13}C, with chemical shifts in ppm. Mass spectra were recorded using a Thermo-Scientific LCQ Fleet ESI-MS instrument. Melting points were measured using a Stuart SMP30 digital melting point apparatus and are uncorrected.

General reaction procedure for synthesis of 4,5-disubstituted-1,2,3-thiadiazoles (4a-q): In a 40 mL vial containing a stir bar and *N*-nitroso-*N*-methyl urea (2.9 mmol), a mixture of KOH, (3.2 mmol) and diethyl ether (6 mL) were added was added portion wise in a glove box. The vial was then removed from the glove box, cooled to 0 °C in an ice bath and stirred slowly. After 30 min the stirring, the reaction was stopped and the obtained yellow ethereal solution of diazomethane. Then, a solution of aroyl chloride (1.0 mmol) in diethyl ether (1 mL) was added dropwise to the stirred reaction mixture over 4 h, during which the intense yellow colour gradually disappeared. Subsequently, a mixture of 1,8-diazabicycloundec-7-ene (DBU, 1.6 mmol, 1.2 equiv.), CS_2 (1.0 mmol, 2.2 equiv.) and alkyl bromide (0.75 mmol, 1.5 equiv.) dissolved in 2 mL of diethyl ether–MeCN mixture was added dropwise to the reaction mixture. The vial was then sealed and stirred at 0 °C for 2 h until the reaction was complete, as monitored by TLC. Finally, the reaction mixture was washed with 20 mL of ethyl acetate and water (3 × 20 mL). The organic layer was separated and dried over Na_2SO_4 later solvent was evaporated using rotavapor (**Scheme-II**). The obtained residue was purified by column chromatography with silica gel using EtOAc–hexane as eluent. The solid product obtained was recrystallized from CH_3OH–$CHCl_3$ mixture (1:1) to obtain the pure compound.

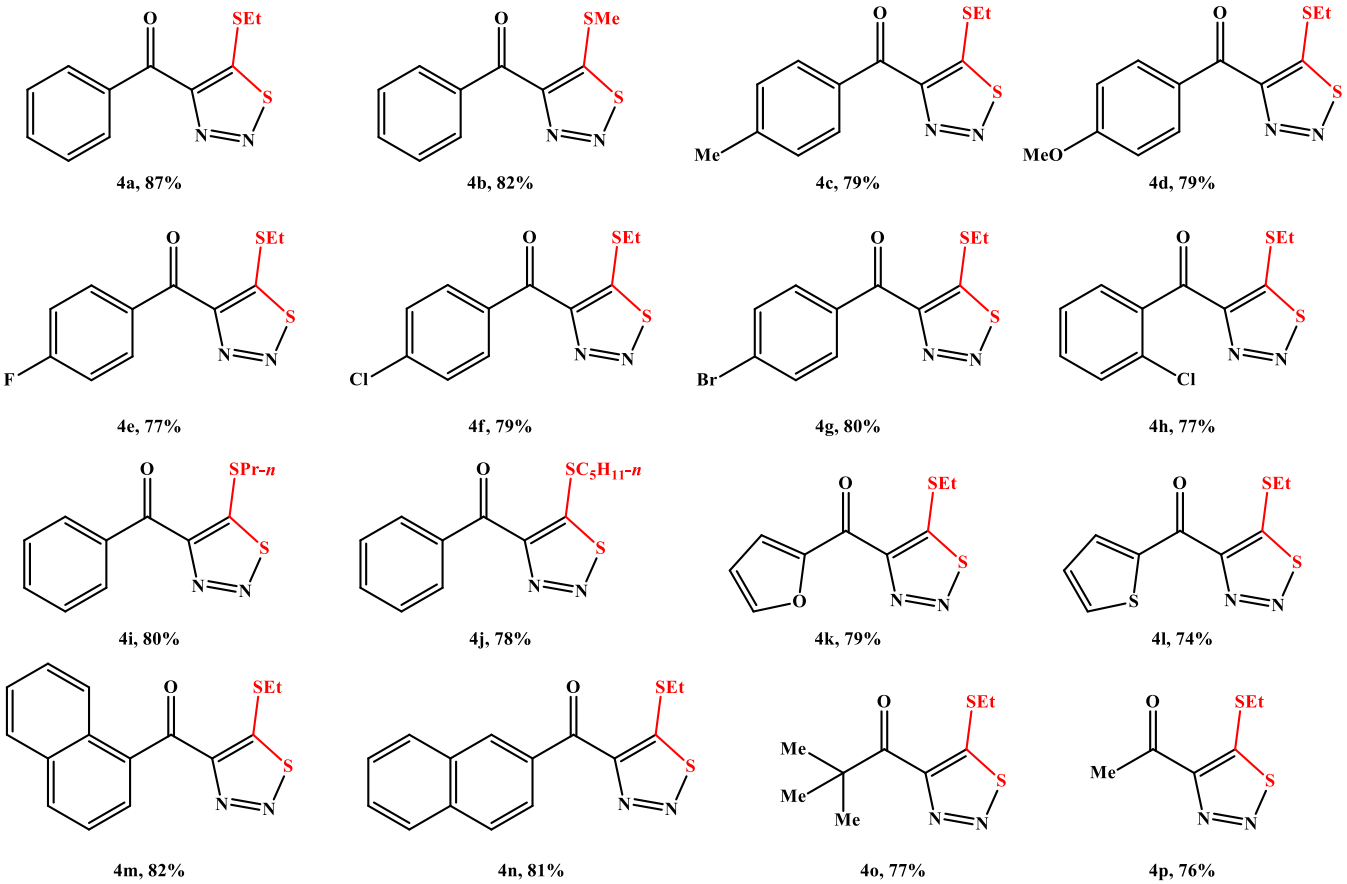
(5-(Ethylthio)-1,2,3-thiadiazol-4-yl)(phenyl)methanone (4a): White solid; m.p.: 102-103 °C; yield: 87%; ^1H NMR (400 MHz, $CDCl_3$, δ ppm): 8.33 (q, *J* = 2.8 Hz, 1H), 7.59-7.52 (m, 4H), 3.14 (q, *J* = 7.2 Hz, 2H), 1.57 (t, *J* = 7.2 Hz, 3H); ^{13}C NMR (100 MHz, $CDCl_3$, δ ppm): 186.81, 168.17, 153.39, 137.03, 133.01, 130.86, 128.57, 33.32, 13.29; IR (KBr, ν_{max}, cm^{-1}): 3035, 2910, 2895, 1618, 1542, 1419, 1323, 1231, 1051, 853; HRMS (ESI) *m/z* calcd. for $C_{11}H_{11}N_2OS_2$ [M+H^+], 251.0312; Found 251.0301.

(5-(Methylthio)-1,2,3-thiadiazol-4-yl)(phenyl)methanone (4b): White solid; m.p.: 108-110 °C; yield: 82%; ^1H NMR (400 MHz, $CDCl_3$, δ ppm): 8.38 (d, *J* = 7.2 Hz, 2H), 7.62 (t, *J* = 7.4 Hz, 1H), 7.53 (t, *J* = 7.6 Hz, 2H), 2.72 (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$, δ ppm): 185.84, 170.41, 153.22, 137.07, 133.25, 130.68, 128.40, 21.90; IR (KBr, ν_{max}, cm^{-1}): 3070, 2910, 1628, 1558, 1582, 1447, 1392, 1218, 1087; HRMS (ESI) *m/z* calcd. for $C_{10}H_8N_2OS_2Na^+$ [M+Na^+], 258.9975; Found 258.9863.

(5-(Ethylthio)-1,2,3-thiadiazol-4-yl)(*p*-tolyl)methanone (4c): White solid; m.p.: 165-168 °C; yield: 79%; ^1H NMR (400 MHz, $CDCl_3$, δ ppm): 8.30 (d, *J* = 8.2 Hz, 2H), 7.33 (d, *J* = 8.1 Hz, 2H), 3.10 (q, *J* = 7.4 Hz, 2H), 2.45 (s, 3H), 1.53 (t, *J* = 7.4 Hz, 3H); ^{13}C NMR (100 MHz, $CDCl_3$, δ ppm):



[a]Reaction conditions: Reactions were carried out using 2a (1.0 mmol) (based on 1a uses), RBr 3a (1.5 eq.), base (1.2 eq.), solvent (2 mL), reaction time 6 h (*in situ*), temperature 0 °C, sealed.



Scheme-II: Substrate scope of one-pot synthesis of 4,5-disubstituted 1,2,3-thiadiazoles (**4a-p**)

185.44, 168.12, 153.60, 144.17, 134.57, 130.86, 129.12, 33.16, 21.80, 13.27; IR (KBr, ν_{max}, cm^{-1}): 3070, 2955, 1625, 1600, 1565, 1414, 1392, 1210, 1076.

(5-(Ethylthio)-1,2,3-thiadiazol-4-yl)(4-methoxyphenyl)-methanone (4d): White solid; m.p.: 165-167 °C; yield: 78%; ^{1}H NMR (400 MHz, $CDCl_3$, δ ppm): 8.46 (d, *J* = 9.0 Hz, 2H), 7.01 (d, *J* = 9.0 Hz, 2H), 3.91 (s, 3H), 3.10 (q, *J* = 7.4 Hz, 2H), 1.53 (t, *J* = 7.4 Hz, 3H); ^{13}C NMR (100 MHz, $CDCl_3$, δ ppm): 184.08, 167.89, 163.79, 153.71, 133.25, 129.89, 113.70, 55.56, 33.13, 13.28; IR (KBr, ν_{max}, cm^{-1}): 3075, 2954, 2916, 1639, 1596, 1555, 1426, 1393, 1255, 1173, 1085.

(5-(Ethylthio)-1,2,3-thiadiazol-4-yl)(4-fluorophenyl)-methanone (4e): White solid; m.p.: 138-140 °C, yield: 77%; ^{1}H NMR (500 MHz, $CDCl_3$, δ ppm): 7.81 (d, *J* = 8.3 Hz, 2H), 7.47 (d, *J* = 8.3 Hz, 2H), 3.01 (q, *J* = 7.4 Hz, 2H), 1.40 (t, *J* = 7.4 Hz, 3H); ^{13}C NMR (125 MHz, $CDCl_3$, δ ppm): 188.67, 164.27, 142.84, 139.92, 136.17, 130.04, 129.18, 126.44, 113.25, 30.50, 14.25; IR (KBr, ν_{max}, cm^{-1}): 3075, 2984, 2916, 1619, 1596, 1565, 1426, 1393, 1255, 1173, 1085.

(4-Chlorophenyl)(5-(ethylthio)-1,2,3-thiadiazol-4-yl)-methanone (4f): Pale yellow solid; m.p.: 146-148 °C; yield: 79%; ^{1}H NMR (500 MHz, $CDCl_3$, δ ppm): 7.73 (d, *J* = 8.3 Hz, 2H), 7.47 (d, *J* = 8.3 Hz, 2H), 3.01 (q, *J* = 7.4 Hz, 2H), 1.40 (t, *J* = 7.4 Hz, 3H); ^{13}C NMR (125 MHz, $CDCl_3$, δ ppm): 182.82, 152.87, 139.92, 136.17, 131.62, 130.04, 129.18, 30.50, 14.25; IR (KBr, ν_{max}, cm^{-1}): 3070, 2950, 1620, 1602, 1563, 1414, 1394, 1183, 1076; HRMS (ESI) *m/z* calcd. for $C_{11}H_{10}ClN_2OS_2^+$ [M + H], 284.9923; Found 284.9905.

(4-Bromophenyl)(5-(ethylthio)-1,2,3-thiadiazol-4-yl)-methanone (4g): Yellow solid; m.p.: 170-171 °C; yield: 80%; ^{1}H NMR (500 MHz, $CDCl_3$, δ ppm): 8.28 (d, *J* = 8.6 Hz, 2H), 7.67 (d, *J* = 8.6 Hz, 2H), 3.11 (q, *J* = 7.4 Hz, 2H), 1.54 (t, *J* =

7.4 Hz, 3H). ^{13}C NMR (125 MHz, $CDCl_3$, δ ppm): 186.39, 136.67, 132.74, 128.68, 126.71, 54.22, 29.73, 14.16; (KBr, ν_{max}, cm^{-1}): 3070, 2950, 1620, 1602, 1563, 1414, 1394, 1183, 1076; HRMS (ESI) *m/z* calcd. for $C_{11}H_9N_2BrOS_2Na^+$ [M + Na^+], 350.9237; Found 350.9225.

(2-Chlorophenyl)(5-(ethylthio)-1,2,3-thiadiazol-4-yl)-methanone (4h): Yellow solid; m.p.: 104-106 ºC; yield: 77%; ^{1}H NMR (400 MHz, $CDCl_3$, δ ppm): 7.68 (dd, *J* = 6.6, 2.2 Hz, 1H), 7.59-7.53 (m, 2H), 7.45 (dd, *J* = 10.4, 4.8 Hz, 1H), 3.14 (q, *J* = 7.4 Hz, 2H), 1.57 (t, *J* = 5.6 Hz, 3H); ^{13}C NMR (100 MHz, $CDCl_3$, δ ppm): 186.95, 169.51, 153.08, 138.18, 131.81, 131.74, 130.15, 129.76, 126.42, 33.32, 13.29; IR (KBr, ν_{max}, cm^{-1}): 3070, 2950, 1620, 1602, 1563, 1414, 1394, 1183, 1076; HRMS (ESI) *m/z* calcd. for $C_{11}H_{10}ClN_2OS_2$ [M + H^+], 284.9923; Found 284.9914.

Phenyl(5-(propylthio)-1,2,3-thiadiazol-4-yl)methanone (4i): Yellow liquid; yield: 80%; ^{1}H NMR (500 MHz, $CDCl_3$, δ ppm): 8.26 (t, *J* = 9.0 Hz, 2H), 7.54-7.51 (m, 1H), 7.47-7.44 (m, 2H), 3.08 (t, *J* = 7.3 Hz, 2H), 1.88 (m, 2H), 1.05 (t, *J* = 7.0 Hz, 3H); ^{13}C NMR (125 MHz, $CDCl_3$, δ ppm): 185.87, 168.84, 153.46, 137.20, 133.18, 130.68, 128.37, 41.10, 21.51, 13.43; IR (KBr, ν_{max}, cm^{-1}): 3030, 2908, 2898, 1619, 1543, 1419, 1323, 1231, 1051, 853; HRMS (ESI) *m/z* calcd. for $C_{12}H_{13}N_2OS_2$ [M+H^+], 265.0469; Found 265.0456.

(5-(Pentylthio)-1,2,3-thiadiazol-4-yl)(phenyl)methanone (4j): White solid; m.p.: 68-70 ºC; yield: 78%; ^{1}H NMR (500 MHz, $CDCl_3$, δ ppm): 8.36 (d, *J* = 7.1 Hz, 2H), 7.62 (t, *J* = 7.4 Hz, 1H), 7.53 (t, *J* = 7.7 Hz, 2H), 3.08 (t, *J* = 7.3 Hz, 2H), 1.88 (dt, *J* = 15.0, 7.4 Hz, 2H), 1.42-1.40 (m, 2H), 1.39 (dq, *J* = 14.4, 7.2 Hz, 2H), 0.94 (t, *J* = 7.3 Hz, 3H); ^{13}C NMR (125 MHz, $CDCl_3$, δ ppm): 185.87, 168.84, 153.46, 137.20, 133.18, 130.68, 128.37, 39.27, 30.98, 27.85, 22.18, 13.88; IR (KBr, ν_{max}, cm^{-1}): 3030, 2908, 2898, 1619, 1543, 1419, 1323, 1231, 1051, 853; HRMS (ESI) *m/z* calcd. for $C_{14}H_{17}N_2OS_2$ [M + H^+], 293.0782; Found 293.0762.

(5-(Ethylthio)-1,2,3-thiadiazol-4-yl)(furan-2-yl)methanone (4k): White solid; m.p.: 97-99 ºC; yield: 79%; ^{1}H NMR (400 MHz, $CDCl_3$, δ ppm): 8.07 (d, J = 3.3 Hz, 1H), 7.70 (s, 1H), 6.57 (d, J = 1.8 Hz, 1H), 3.10 (q, *J* = 7.6 Hz, 2H), 1.53 (t, *J* = 7.6 Hz, 3H); ^{13}C NMR (100 MHz, $CDCl_3$, δ ppm): 172.03, 169.36, 151.63, 151.06, 148.02, 122.89, 112.54, 30.50, 14.25; IR (KBr, ν_{max}, cm^{-1}): 3089, 2979, 1666, 1587, 1516, 1418, 1268, 1049.

(5-(Ethylthio)-1,2,3-thiadiazol-4-yl)(thiophen-2-yl)-methanone (4l): White solid; m.p.: 121-123 ºC; yield 74%; ^{1}H NMR (400 MHz, $CDCl_3$, δ ppm): 8.61 (d, *J* = 3.4 Hz, 1H), 7.78 (d, *J* = 4.4 Hz, 1H), 7.24 (dd, *J* = 5.4, 4.1 Hz, 1H), 3.14 (q, *J* = 7.4 Hz, 2H), 1.41 (t, *J* = 5.6 Hz, 3H); ^{13}C NMR (100 MHz, $CDCl_3$, δ ppm): 177.14, 169.68, 152.24, 142.22, 136.20, 135.30, 128.57, 33.32, 14.06; IR (KBr, ν_{max}, cm^{-1}): 3087, 2980, 1656, 1599, 1507, 1420, 1270, 1057, 838.

(5-(Ethylthio)-1,2,3-thiadiazol-4-yl)(naphthalen-1-yl)-methanone (4m): Pale yellow solid; m.p.: 74-76 ºC; yield: 82%; ^{1}H NMR (400 MHz, $CDCl_3$, δ ppm): 8.33 (dd, *J* = 7.9, 1.8 Hz, 1H), 8.03 (dd, *J* = 12.7, 5.3 Hz, 2H), 7.93-7.91 (m, 1H), 7.60-7.53 (m, 3H), 3.14 (q, *J* = 7.4 Hz, 2H), 1.57 (t, *J* = 5.6 Hz, 3H); ^{13}C NMR (100 MHz, $CDCl_3$, δ ppm): 188.78, 168.17, 154.47, 135.30, 133.80, 132.48, 130.86, 129.76, 128.57, 127.57, 126.42, 125.41, 124.38, 33.32, 13.29; IR (KBr, ν_{max}, cm^{-1}): 3049, 2909, 1629, 1505, 1436, 1409, 1274, 1058; HRMS (ESI) *m/z* calcd. for $C_{15}H_{12}N_2OS_2Na^+$ [M + Na^+], 323.0288; Found 323.0275.

(5-(Ethylthio)-1,2,3-thiadiazol-4-yl)(naphthalen-2-yl)-methanone (4n): Yellow solid; m.p.: 70-72 ºC; yield: 81%; ^{1}H NMR (400 MHz, $CDCl_3$, δ ppm): 8.45 (1H), 8.16-8.11 (m, 3H), 7.93-7.91 (m, 1H), 7.75-7.73 (m, 1H), 3.14 (q, *J* = 7.4 Hz, 2H), 1.57 (t, *J* = 5.6 Hz, 3H); ^{13}C NMR (100 MHz, $CDCl_3$, δ ppm): 189.75, 168.17, 154.47, 139.32, 133.80, 132.48, 130.86, 129.76, 128.57, 127.57, 126.42, 125.41, 124.38, 32.29, 13.29; IR (KBr, ν_{max}, cm^{-1}): 3049, 2909, 1629, 1505, 1436, 1409, 1274, 1058; HRMS (ESI) *m/z* calcd. for $C_{15}H_{12}N_2OS_2Na^+$ [M + Na^+], 323.0288; Found 323.0268.

1-(5-(Ethylthio)-1,2,3-thiadiazol-4-yl)-2,2-dimethyl-propan-1-one (4o): Yellow liquid; yield: 77%; ^{1}H NMR (500 MHz, $CDCl_3$, δ ppm): 2.66 (s, 3H), 1.49 (s, 9H); ^{13}C NMR (125 MHz, $CDCl_3$, δ ppm): 199.88, 169.54, 151.78, 44.87, 26.83, 21.90; IR (KBr, ν_{max}, cm^{-1}): 2967, 1634, 1592, 1392, 1218, 1007.

1-(5-(Ethylthio)-1,2,3-thiadiazol-4-yl)-ethan-1-one (4p): Yellow liquid; yield: 76%; ^{1}H NMR (400 MHz, $CDCl_3$, δ ppm): 3.11 (q, *J* = 7.5, 2H), 2.67 (s, 3H), 1.54 (t, *J* = 7.5, 3H); ^{13}C NMR (100 MHz, $CDCl_3$, δ ppm): 19.2.19, 167.06, 152.87, 30.50, 27.51, 14.25; IR (KBr, ν_{max}, cm^{-1}): 2974, 1638, 1386, 1211, 1017.

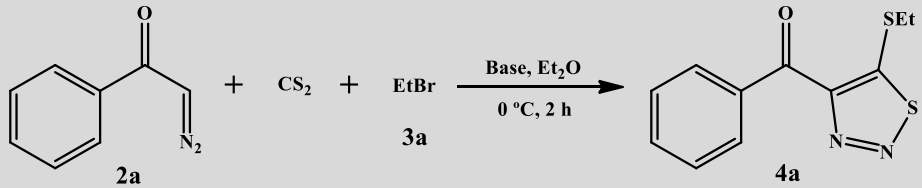
RESULTS AND DISCUSSION

Initially, α-diazoketones were synthesized *via* a modified Arndt-Eistert synthetic procedure [22]. This method allowed the efficient transformation of benzoyl chloride (**1a**) into diazoacetophenone (**2a**) using *N*-nitroso-*N*-methylurea as the diazomethane source, in the presence of KOH and CaO in diethyl ether at 0 ºC in an ice bath for 4 h. The resulting pale-yellow solid was dissolved in ether and used directly in subsequent reactions without extraction or further purification.

To evaluate the reactivity of the diazo group toward CS_2 as a nucleophile, studies were carried out using diazoacetophenone (**2a**) and ethyl bromide as the primary substrates, and a range of bases was screened during the initial optimization. The effect of solvents, different bases and temperature were examined and the corresponding results are enumerated in Table-1. During the reaction, the role of base is crucial. In the absence of base, there was no reaction in diethyl ether at 0 ºC and also at room temperature (Table-1, entries 1 and 2). Based on the above observations, the reaction was later carried out using KOH (1.0 equiv.) at 50 ºC (Table-1, entry 7). Due to exothermic nature of the reaction, required products were not formed, hence the reaction is carried at lower temperatures (Table-1, entries 12 to 16).

The yield of the desired 1,2,3-thiadiazole product **4a** was 87% at 0 ºC in 6 h (Table-1, entry **12**). From the above obtained results, the reaction was further carried out using commercially available common organic bases such as DBU, Et_3N, diisopropyl ethyl amine (DIPEA), Bu^tOK and inorganic bases like KOH and CsF at 0 ºC under solvent-free conditions and using solvents to improve the product yield. All the screened bases gave the required product in moderate yield. However,

TABLE-1
OPTIMIZATION OF REACTION CONDITIONS FOR CONVERSION OF DIAZO COMPOUND INTO 1,2,3-THIADIAZOLES



Entry	Base	Solvent	Temp. (°C)	Equivalency of CS_2	Time (h)	Yield[b] (%)
1	None	Et_2O	0	1.5	24 h	No reaction
2	None	Et_2O	25	1.5	24 h	No reaction
3	None	Et_2O	25	1.5	24 h	No reaction
4	KOH	Et_2O	0	1.5	24 h	No reaction
5	KOH	Et_2O	25	1.5	24 h	No reaction
6	KOH	Et_2O	25	2.0	24 h	No reaction
7	KOH	Et_2O	50	2.5	10 h	Trace
8	CSF	Et_2O	25	1.5	24 h	No reaction
9	Et_3N	Et_2O	25	1.5	24 h	Trace
10	Et_3N	Et_2O + DCM	25	1.5	24 h	Trace
11	KO^{t}Bu	Et_2O + THF	25	1.5	24 h	Trace
12	DBU	Et_2O + MeCN	0	2.2	6 h	87
13	DBU	Et_2O + MeCN	0	1.5	24 h	63
14	DBU	Et_2O + MeCN	0	2.0	24 h	67
15	DBU	Et_2O + MeCN	0	5.0	24 h	75
16	DIPEA	Et_2O + MeCN	0	1.5	24 h	35

[a]Reaction conditions: Reaction were carried out using **2a** (1.0 mmol), EtBr **3a** (1.5 eq.), base (1.2 eq.), solvent (2 mL), reaction time 6 h, temperature 0 °C, sealed tube; [b]Isolated pure yield.

compared to DBU, the yield was not high (Table-1, entries 13-16).

The base DBU was found to be more effective than other inorganic and organic bases. The reaction was further investigated by screening different solvents, including Et_2O, CH_3CN and THF, to improve the yield; however, no significant improvement was observed (Table-1, entries 12–26). Finally, an optimized reaction condition (with yield 87%) was obtained by usage of CS_2 in 2.2 equiv. (entry 12), at 0 °C under *in situ* conditions using diethyl ether and acetonitrile mixture as solvent. There is no further increment in yield even by changing the equivalents of CS_2 to 5.0 (entry 15).

Further, the substrate scope of the optimized reaction was examined and the results are summarized in **Scheme-II**. Various alkyl bromides were employed and both *para*- and *ortho*- substituted aroyl halides (**4c-h**) were used and found that in all cases, the yields of the corresponding desired substituted thiadiazole product were moderate to high. Furthermore, to demonstrate the broad substrate scope, various aroyl chlorides were prepared and tested to produce the corresponding α-diazo carbonyl compounds, followed by the formation of substituted 1,2,3-thiadiazoles. The substrates proved highly suitable for the reaction, affording the products in good to excellent yields.

Compared to the established methods presented in **Scheme-I**, the current synthetic methodology provided higher yields of various substituted thiadiazoles under mild and green reaction conditions. As reported in previous studies [20-22], the reaction mechanism involves a standard deprotonation, followed by nucleophilic addition and cyclization, as illustrated in **Scheme-III**.

This conversion presents several noteworthy characteristics in demonstrating higher efficiency in bond formation, resulting in the formation of two new bonds and one new ring. This reaction occurs through a one pot reaction, initiated by the abstraction of a proton from α-diazomethane by DBU. Later, the addition of CS_2 and alkyl bromide to the reaction mixture leads to intramolecular S-cyclization, resulting a thiadiazole ring in excellent overall yields. The steric influence of *ortho*-substituents in aroyl halide is minimal and the electron withdrawing groups on the aromatic ring show a comparable reduction in reactivity during the synthesis of 1,2,3-thiadiazoles whereas the electron-donating groups yielded superior results in the synthesis of corresponding thiadiazoles. Moreover, polyaromatic rings and heteroaromatic rings also provided good yields of related 1,2,3-thiadiazoles.

Conclusion

In conclusion, a straightforward one-pot reaction method is established for synthesizing 4,5-disubstituted 1,2,3-thiadiazoles (**4a-q**) using α-diazo carbonyl compounds and CS_2 through nucleophilic addition followed by adding various alkyl halides. This approach serves as a viable method in comparison to conventional synthesis of 1,2,3-thiadiazoles, with C_1 building block (CS_2) under mild and green reaction conditions.

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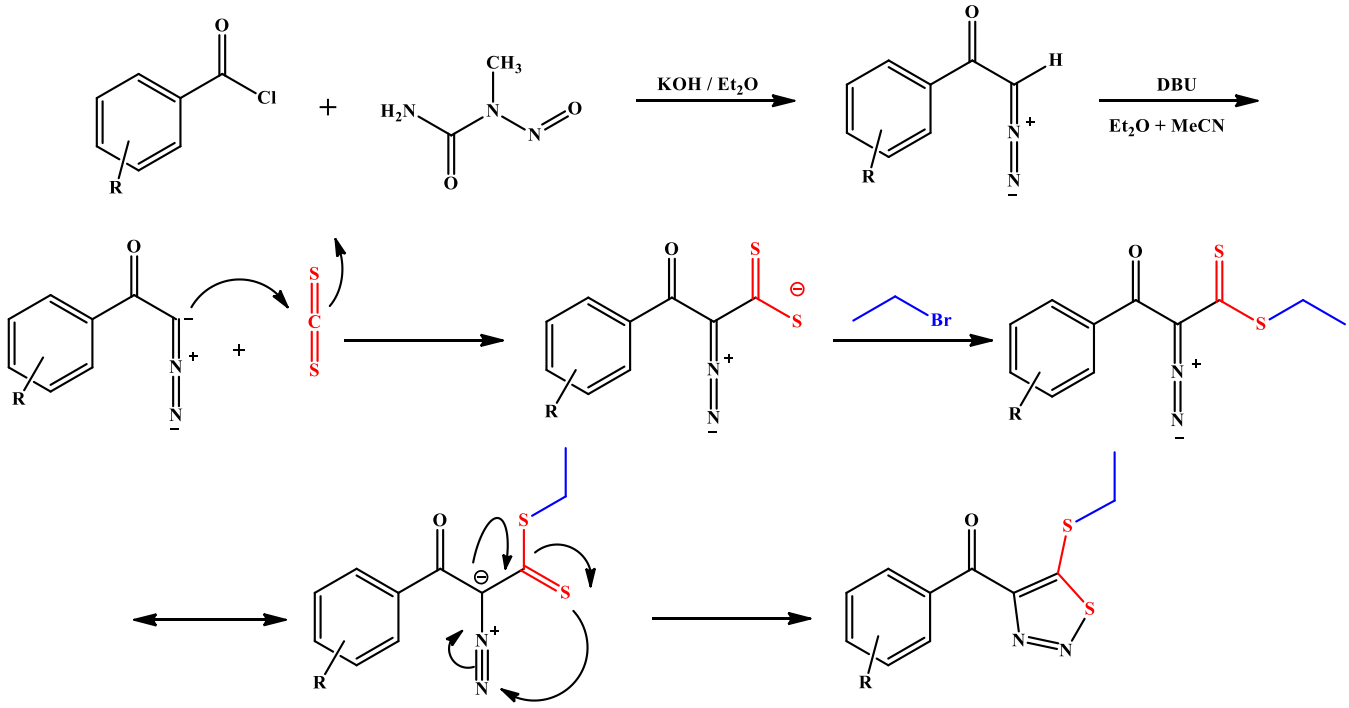

Scheme-III: Possible mechanism for the formation of 4,5-disubstituted 1,2,3-thiadiazoles (**4**)

CONFLICT OF INTEREST

The authors declare that there is no conflict of interests regarding the publication of this article.

DECLARATION OF AI-ASSISTED TECHNOLOGIES

During the preparation of this manuscript, the authors used an AI-assisted tool(s) to improve the language. The authors reviewed and edited the content and take full responsibility for the published work.

REFERENCES

1. P. Awasthi, A. Mittal, Swati, M. Singh and S. Sharma, *Curr. Top. Med. Chem.*, **26** (2026); https://doi.org/10.2174/0115680266394288251007083351
2. A. Irfan, S. Ullah, A. Anum, N. Jabeen, A.F. Zahoor, H. Kanwal, K. Kotwica-Mojzych and M. Mojzych, *Appl. Sci.*, **11**, 5742 (2021); https://doi.org/10.3390/app11125742
3. F. Hayat, A. Salahuddin, J. Zargan and A. Azam, *Eur. J. Med. Chem.*, **45**, 6127 (2010); https://doi.org/10.1016/j.ejmech.2010.09.066
4. Z. Li, Z. Wu and F. Luo, *J. Agric. Food Chem.*, **53**, 3872 (2005); https://doi.org/10.1021/jf0501746
5. P. Zhan, X. Liu, Y. Cao, Y. Wang, C. Pannecouque and E. De Clercq, *Bioorg. Med. Chem. Lett.*, **18**, 5368 (2008); https://doi.org/10.1016/j.bmcl.2008.09.055
6. W.L. Dong, Z.X. Liu, X.H. Liu, Z.M. Li and W.G. Zhao, *Eur. J. Med. Chem.*, **45**, 1919 (2010); https://doi.org/10.1016/j.ejmech.2010.01.032
7. M. Wu, Q. Sun, C. Yang, D. Chen, J. Ding, Y. Chen, L. Lin and Y. Xie, *Bioorg. Med. Chem. Lett.*, **17**, 869 (2007); https://doi.org/10.1016/j.bmcl.2006.11.060
8. I. Cikotiene, E. Kazlauskas, J. Matuliene, V. Michailoviene, J. Torresan, J. Jachno and D. Matulis, *Bioorg. Med. Chem. Lett.*, **19**, 1089 (2009); https://doi.org/10.1016/j.bmcl.2009.01.003
9. P. Frąckowiak, U. Gawlik-Dziki, P. Sanchez-Bel and A. Obrępalska-Stęplowska, *J. Agric. Food Chem.*, **71**, 12958 (2023); https://doi.org/10.1021/acs.jafc.3c03876
10. D. Quiroga, D. Rodríguez and E. Coy-Barrera, *Molecules*, **30**, 4373 (2025); https://doi.org/10.3390/molecules30224373
11. D. Kumar, N. Aggarwal, V. Kumar, H. Chopra, R.K. Marwaha and R. Sharma, *Future Med. Chem.*, **16**, 563 (2024); https://doi.org/10.4155/fmc-2023-0203
12. T. Lei, Y. Zhou, Ch. Cheng, Y. Cao, Y. Peng, J. Bian and J. Pei, *Org. Lett.*, **13**, 2642 (2011); https://doi.org/10.1021/ol200748c
13. M. Marinelli, A. Candini, F. Monti, A. Boschi, M. Zangoli, E. Salatelli, F. Pierini, M. Lanzi, A. Zanelli, M. Gazzano and F. Di Maria, *J. Mater. Chem. C Mater. Opt. Electron. Devices*, **9**, 11216 (2021); https://doi.org/10.1039/D1TC02641K
14. H. Pechmann and A. Nold, *Ber. Dtsch. Chem. Ges.*, **29**, 2588 (1896); https://doi.org/10.1002/cber.18960290336
15. C.D. Hurd and R.I. Mori, *J. Am. Chem. Soc.*, **77**, 5359 (1955); https://doi.org/10.1021/ja01625a047
16. L. Zhang, B. Sun, Q. Liu and F. Mo, *J. Org. Chem.*, **83**, 4275 (2018); https://doi.org/10.1021/acs.joc.8b00383
17. M.S. Singh, A. Nagaraju, G.K. Verma, G. Shukla, R.K. Verma, A. Srivastava and K. Raghuvanshi, *Green Chem.*, **15**, 954 (2013); https://doi.org/10.1039/c3gc37047j
18. L. Wolff, Justus Liebigs Ann. Chem., **333**, 1 (1904); https://doi.org/10.1002/jlac.19043330102
19. Q. Liu, M. Li, R. Xiong and F. Mo, *Org. Lett.*, **19**, 6756 (2017); https://doi.org/10.1021/acs.orglett.7b03573
20. C. Schmitt and T. Murai, Carbon Disulfide. Encyclopedia of Reagents for Organic Synthesis; John Wiley & Sons, Ltd., (2001).
21. Y. Tominaga, *J. Heterocycl. Chem.*, **26**, 1167 (1989); https://doi.org/10.1002/jhet.5570260501
22. T. Aoyama, Y. Iwamoto and T. Shioiri, *Heterocycles*, **24**, 589 (1986); https://doi.org/10.3987/R-1986-03-0589