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AN EFFICIENT ONE-POT SYNTHESIS OF 2,5-DISUBSTITUTED 1,3,4-OXADIAZOLES FROM DI-THIOESTERS UNDER MILD CONDITION

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ABSTRACT

A wide range of functionalized di-substituted oxadiazoles (5a-5o) were formed by intramolecular cyclization of (Z)-N'-benzoylbenzohydrazonic hypoiodous thioanhydride, which was made possible by atom-efficient, environmentally friendly reactions that used the least amount of organic solvent. 2,5 disubstituted 1,3,4-oxadiazole (5a-5o) was prepared by the reaction of substituted di thioester with various aromatic benzo hydrazides in the presence of a mild base. Based on spectral and analytical data, the structures of all the substances have been determined.

Keywords: Benzo Hydrazides, Dithioester, Ethanol, Molecular Iodine, Oxadiazoles, Potassium Carbonate.
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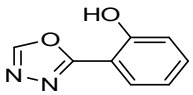
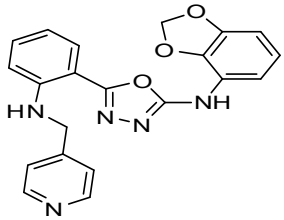
INTRODUCTION

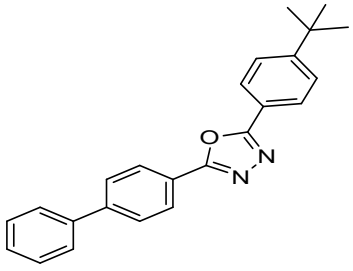
Oxadiazoles are captivating compounds in drug design, serving as robust substitutes for esters and amides with diverse biological impacts.[1] Their derivatives display potent antitumor effects in cancer research by inhibiting enzymes and growth factors.[2] These variants showcase traits such as HIV integrase inhibition, anti-inflammatory, and antibacterial properties.[3,4] Pharmaceuticals like Raltegravir for HIV and Zibotentan for cancer harness the power of the 1,3,4-oxadiazole motif, highlighting its pivotal role.[5] Additionally, among these compounds, Fenadiazole acts as a hypnotic, MK-0633 p-toluene sulfonate inhibits 5-lipoxygenase, Nesapidil serves as an antihypertensive, and ABT-751-oxadiazole and Furamizole function as antibiotics[653] (as shown in Fig.-1).



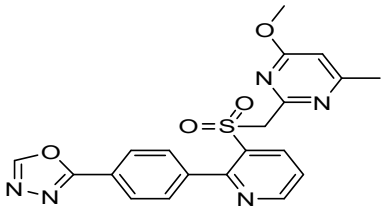
Fenadiazole



ABT-751-oxadiazole



electron-transport material (ETM)



anticancer agent

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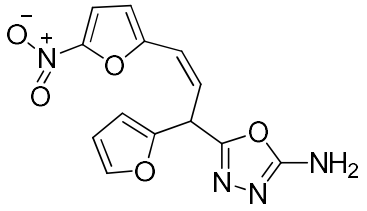
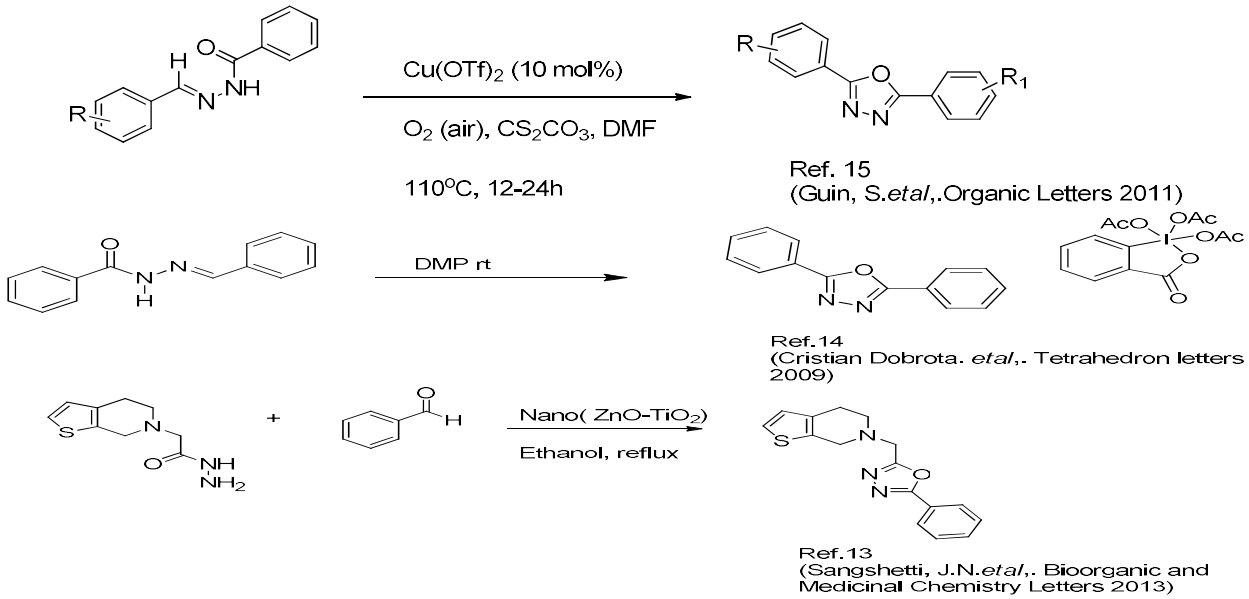


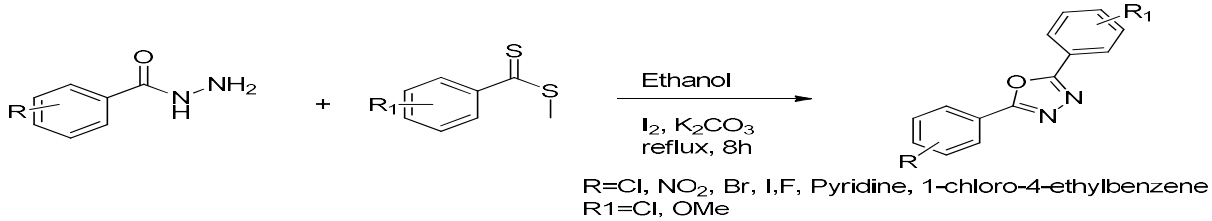
Fig.-1: Bioactive Molecules Containing 1,3,4-oxadiazole Ring

Numerous studies explore 1,3,4-oxadiazole synthesis. techniques include nanoscale zinc oxide and titanium oxide catalysis by Jaipraksh *et al.*[7] Dess-Martin reagent use by Dobrota *et al.*[8] copper-catalyzed oxidative coupling for 2,5 disubstituted variants, microwave synthesis by Bijju *et al.*[9] TBTU coupling by Stabile *et al.*[10] and HATU coupling followed by Burgess reagent addition by Dickson *et al.*[11] Challenges arise due to costly catalysts and low-temperature requirements for the Burgess reagent, posing hurdles for large-scale production despite high efficiency in formation. Building on prior work in synthesizing biologically active compounds[12–16] and creating versatile methods for heterocyclic compound preparation, we explored synthesizing 2,5-disubstituted 1,3,4-oxadiazoles. Leveraging our expertise in dithioesters[17–24] and the availability of diverse carboxylic acids, we aimed to conduct a cyclo-condensation reaction with benzo hydrazides, followed by de-sulfurization using catalytic iodine, all within a single pot (Scheme-1).

Previous work



Present work



Scheme-1

EXPERIMENTAL

Material and Methods

Experimental procedures for analytical thin layer chromatography (TLC) involved E. Merck silica gel 60F254 aluminum plates visualized using UV light. Various mobile phases, including chloroform, methanol, hexane, and ethyl acetate in different ratios, were used for TLC analysis. Characterization of

newly synthesized compounds employed instrumental techniques such as ^{1}H and ^{13}C NMR spectroscopy, as well as mass spectroscopy. ^{1}H and ^{13}C NMR spectra were obtained using Bruker-AV (500, 400, and 126,100 MHz) and Agilent WM (400 and 100 MHz) Fourier transform spectrophotometers in $CDCl_3$ or DMSO-d6 solutions, with tetramethyl silane (TMS) as the internal standard. Chemical shifts were recorded in parts per million (ppm) relatives to TMS. Mass and purity were determined using an LC-MSDTrap-XCT from Agilent Technologies Inc. Reagents and chemicals utilized were sourced from Sigma Aldrich chemicals.

General Procedure

A mixture of benzene-substituted esters (1mmol) and hydrazine hydrazide (1mmol) in Ethanol was added and refluxed for 6 h. After the reactant disappeared (as monitored by TLC), the crude product (benzo hydrazide) was carried to the next step.

General Procedure for the Synthesis of 5a-5o

A mixture of benzo hydrazide (1a) (1mmol) and dithioester (2a) (2mmol) derivative was allowed to stir in Ethanol solvent (3 ml) in the presence of molecular iodine (2 mmol) and K_2CO_3 (2 mmol) at reflux condition for 8 h. Then, the contents were poured into 30 ml, 10% aqueous solution of sodium thiosulphate, and extracted with 30 ml ethyl acetate. The ethyl acetate extract was separated, and dried over anhydrous sodium sulphate, and the solvent was removed under reduced pressure to afford the crude product, 2,5-diphenyl1,3,4-oxadiazole derivatives (5a-o). The thus obtained crude product was purified by column chromatography over silica gel using ethyl acetate in hexane as eluent to obtain pure 2,5-diphenyl 1,3,4-oxadiazole derivatives. (5a–5o).

2,5-diphenyl-1,3,4-oxadiazole (5a): buff solid, yield: (96%); m. p = 132–135°C; ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.14 (d, *J* = 5.4 Hz, 4H), 7.55 (s, 6H).^{13}C NMR (100 MHz, $CDCl_3$) δ 164.65, 132.18, 131.83, 131.51, 129.56, 129.17, 128.97, 128.79, 127.13, 126.88, 123.96. LCMS (ESI): m/z Calcd for $C_{14}H_{10}N_2O$ $[M + H]^+$:222.0793; Found: 223.1203.

2-(4-chlorophenyl)-5-phenyl-1,3,4-oxadiazole (5b): white solid, yield: (85%); m. p = 168–172°C; ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.14 – 8.09 (m, 2H), 8.08 – 8.03 (m, 2H), 7.55 – 7.48 (m, 4H).^{13}C NMR (100 MHz, $CDCl_3$) δ 164.81 (s), 163.86 (s), 138.10 (s), 131.86 (s), 129.71 (s), 129.41 (d, *J* = 9.9 Hz), 129.08 (s), 128.27 (d, *J* = 5.7 Hz), 127.03 (d, *J* = 12.8 Hz), 123.75 (s), 122.42 (s). LCMS (ESI): m/z Calcd for $C_{14}H_9ClN_2O$ $[M + H]^+$:290.0014; Found: 291.0431.

2-(3-chlorophenyl)-5-phenyl-1,3,4-oxadiazole (5c): white solid, yield: (82%); m. p = 147–150°C; ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.12 (s, 1H), 8.10 (s, 1H), 7.98 (t, *J* = 7.4 Hz, 3H), 7.66 (d, *J* = 8.4 Hz, 2H), 7.53 (d, *J* = 7.2 Hz, 2H).^{13}C NMR (100 MHz, $CDCl_3$) δ 165.36 (s), 164.59 (s), 135.14 – 133.59 (m), 133.59 – 131.70 (m), 132.20 – 131.70 (m), 130.09 (s), 129.51 (s), 129.18 (s), 127.81 (dd, *J* = 90.3, 61.2 Hz), 127.48 (s), 127.36 (d, *J* = 23.7 Hz), 127.24 (s), 124.35 (s), 123.50 (s). LCMS (ESI): m/z Calcd for $C_{14}H_9ClN_2O$ $[M + H]^+$: 256.0403; Found: 257.0828.

2-(2,4-dichlorophenyl)-5-phenyl-1,3,4-oxadiazole (5d): buff solid, yield: (90%); m. p = 138–142°C; ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.13 (d, *J* = 6.4 Hz, 2H), 8.06 (d, *J* = 8.5 Hz, 1H), 7.61 – 7.50 (m, 4H), 7.41 (dd, *J* = 8.5, 1.9 Hz, 1H).^{13}C NMR (100 MHz, $CDCl_3$) δ 165.12 (s), 162.27 (s), 138.04 (s), 133.72 (s), 132.22 (s), 131.67 (t, *J* = 24.0 Hz), 131.30 – 131.17 (m), 130.91 (s), 129.34 (s), 128.84 (s), 127.83 (s), 127.72 – 127.60 (m), 127.19 (d, *J* = 30.4 Hz). LCMS (ESI): m/z Calcd for $C_{14}H_8Cl_2N_2O$ $[M + H]^+$:291.1321; Found: 291.0431.

2-(4-nitrophenyl)-5-phenyl-1,3,4-oxadiazole (5e): brown solid, yield: (75%); m. p = 125–127°C; ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.07 (s, 2H), 8.00 (d, *J* = 6.2 Hz, 2H), 7.61 – 7.36 (m, 5H). ^{13}C NMR (100 MHz, $CDCl_3$) δ 165.67 (s), 162.90 (s), 134.12 (s), 132.75 (s), 129.61 (d, *J* = 9.7 Hz), 129.07 (s), 127.93 (d, *J* = 5.6 Hz), 127.44 (d, *J* = 10.8 Hz), 127.07 (s), 124.55 (d, *J* = 4.7 Hz). LCMS (ESI): m/z Calcd for $C_{14}H_9N_3O_3[M + H]^+$: 267.0644; Found: 268.1063.

2-(4-bromophenyl)-5-phenyl-1,3,4-oxadiazole (5f): yellow solid, yield: (80%); m. p = 167–170°C; ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.08 (d, *J* = 6.8 Hz, 2H), 8.05 (s, 1H), 7.98 (d, *J* = 7.4 Hz, 1H), 7.55 – 7.40 (m,

5H). ^{13}C NMR (100 MHz, $CDCl_3$) δ 164.94 (s), 163.47 (s), 135.29 (s), 132.35 (s), 132.12 (s), 131.85 (s), 131.23 (d, *J* = 82.0 Hz), 130.38 (s), 130.38 (s), 129.27 (d, *J* = 48.6 Hz), 127.21 (s), 126.89 – 124.27 (m), 124.85 – 124.59 (m), 124.85 – 124.27 (m). LCMS (ESI): m/z Calcd for $C_{14}H_9BrN_2O$ [M + H] $^+$: 299.9898; Found: 301.0294.

2-(3,4-dimethoxyphenyl)-5-phenyl-1,3,4-oxadiazole (5g): white solid, yield: (78%); m. p = 172–175°C; ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.42 (dd, *J* = 7.3, 2.3 Hz, 2H), 7.99 (d, *J* = 1.8 Hz, 1H), 7.97 (d, *J* = 1.8 Hz, 1H), 7.94 (d, *J* = 1.7 Hz, 1H), 7.82 (dd, *J* = 8.6, 3.1 Hz, 3H), 4.29 (s, 3H), 4.25 (s, 3H).^{13}C NMR (100 MHz, $CDCl_3$) δ 164.45, 164.21, 164.13, 162.97, 151.02, 150.73, 135.29, 130.66, 130.37, 129.20, 128.79, 127.09, 126.86, 126.67, 125.29, 125.04, 124.85, 123.89, 120.44, 120.15, 116.36, 111.02, 77.48, 77.16, 76.83, 56.24, 56.13, 56.00, 55.90. LCMS (ESI): m/z Calcd for $C_{16}H_{14}N_2O_3$[M + H] $^+$: 282.1004; Found: 283.1436.

2-(2-iodophenyl)-5-phenyl-1,3,4-oxadiazole (5h): buff solid, yield: (82%); m. p = 157–160°C; ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.28 (d, *J* = 8.5 Hz, 1H), 8.23 – 8.16 (m, 1H), 8.15 – 8.06 (m, 1H), 8.02 (d, *J* = 7.4 Hz, 1H), 7.69 – 7.51 (m, 4H), 7.44 – 7.29 (m, 1H).^{13}C NMR (100 MHz, $CDCl_3$) δ 165.16 (s), 164.22 (s), 141.51 (d, *J* = 5.5 Hz), 132.55 (s), 131.58 (s), 129.26 (d, *J* = 19.9 Hz), 128.41 (d, *J* = 25.1 Hz), 127.15 (d, *J* = 15.2 Hz), 123.81 (s), 94.00 (s).LCMS (ESI): m/z Calcd for $C_{14}H_9IN_2O$ [M + H] $^+$: 347.9760; Found: 349.0190.

2,5-bis(3-chlorophenyl)-1,3,4-oxadiazole (5i): white off solid, yield: (88%); m. p = 151–153°C; ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.07 (s, 2H), 8.00 (d, *J* = 6.7 Hz, 2H), 7.56 – 7.42 (m, 4H). ^{13}C NMR (100 MHz, $CDCl_3$) δ 164.82 (s), 164.04 (s), 133.01 – 132.98 (m), 133.01 – 131.12 (m), 131.62 – 131.12 (m), 129.52 (s), 128.94 (s), 128.60 (s), 127.23 (dd, *J* = 89.6, 63.7 Hz), 126.90 (s), 126.78 (d, *J* = 23.7 Hz), 126.66 (s), 123.74 (s), 122.92 (s). LCMS (ESI): m/z Calcd for $C_{14}H_8Cl_2N_2O$ [M + H] $^+$:290.0014; Found: 291.0501.

2-(3,4-dimethoxyphenyl)-5-(pyridin-4-yl)-1,3,4-oxadiazole (5j): buff solid, yield: (75%); m. p = 163–165°C; ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.82 (dd, *J* = 4.5, 1.6 Hz, 2H), 7.98 (dd, *J* = 4.5, 1.6 Hz, 2H), 7.71 (dd, *J* = 8.4, 2.0 Hz, 2H), 7.65 (d, *J* = 1.9 Hz, 1H), 4.00 (s, 3H), 3.97 (s, 3H). ^{13}C NMR (100 MHz, $CDCl_3$) δ 165.78 (s), 162.68 (s), 151.30 (s), 150.93 (s), 131.45 (s), 121.27 (s), 120.89 (s), 120.58 (d, *J* = 20.4 Hz), 116.10 (s), 111.53 (s), 110.05 (s), 109.62 (s), 56.62 (s), 56.39 (s). LCMS (ESI): m/z Calcd for $C_{15}H_{13}N_3O_3$ [M + H] $^+$:283.0957; Found: 283.1436.

2-(3-chlorophenyl)-5-(2-iodophenyl)-1,3,4-oxadiazole (5k): white solid, yield: (80%); m. p = 143–145°C; ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.15 (s, 1H), 8.07 (t, *J* = 8.0 Hz, 2H), 7.96 (d, *J* = 6.4 Hz, 1H), 7.50 (dd, *J* = 17.0, 10.0 Hz, 4H). ^{13}C NMR (100 MHz, $CDCl_3$) δ 164.43, 163.93, 141.57, 141.31, 135.24, 132.35, 131.99, 131.63, 131.44, 128.81, 127.12, 126.85, 125.33, 125.26, 125.02. LCMS (ESI): m/z Calcd for $C_{14}H_8ClIN_2O$ [M + H] $^+$:381.9370; Found: 382.9884.

2-(4-chlorobenzyl)-5-phenyl-1,3,4-oxadiazole (5l): white solid, yield: (89%); m. p = 140–143°C; ^{1}H NMR (400 MHz, $CDCl_3$) δ 9.03 (d, *J* = 30.1 Hz, 2H), 7.99 (d, *J* = 6.7 Hz, 1H), 7.79 (d, *J* = 8.4 Hz, 2H), 7.57 – 7.40 (m, 4H), 3.65 (s, 2H).^{13}C NMR (100 MHz, $CDCl_3$) δ 167.84 (s), 167.60 (s), 131.60 (d, *J* = 10.4 Hz), 131.05 (s), 130.85 (s), 130.30 (s), 129.51 (s), 129.23 (s), 128.55 (s), 127.63 (dd, *J* = 12.8, 11.4 Hz), 40.41 (s). LCMS (ESI): m/z Calcd for $C_{15}H_{11}ClN_2O$ [M + H] $^+$: 270.0560; Found: 271.0971.

2-phenyl-5-(pyridin-4-yl)-1,3,4-oxadiazole (5m): buff solid, yield: (83%); m. p = 153–155°C; ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.87 (dd, *J* = 4.5, 1.6 Hz, 2H), 8.18 (dd, *J* = 8.1, 1.5 Hz, 2H), 8.03 (dd, *J* = 4.5, 1.6 Hz, 2H), 7.63 – 7.56 (m, 3H). ^{13}C NMR (100 MHz, $CDCl_3$) δ 158.07 (s), 157.82 (s), 151.48 (s), 151.07 (s), 136.99 (s), 132.56 (s), 130.67 (s), 129.91 (s), 129.42 (s), 127.69 (d, *J* = 2.9 Hz), 120.99 (s), 120.57 (s). LCMS (ESI): m/z Calcd for $C_{13}H_9N_3O$ [M + H] $^+$:223.0746; Found: 224.1119.

2-(3,4-difluorophenyl)-5-phenyl-1,3,4-oxadiazole (5n): yellow solid, yield: (82%); m. p = 140–142°C; ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.13 (td, *J* = 8.0, 1.7 Hz, 2H), 8.00 – 7.88 (m, 2H), 7.59 – 7.50 (m, 3H), 7.34 (dd, *J* = 17.2, 9.0 Hz, 1H).^{13}C NMR (100 MHz, $CDCl_3$) δ 164.91 (d, *J* = 19.4 Hz), 163.07 (s), 132.50 (s), 132.11 (d, *J* = 16.8 Hz), 129.36 (dd, *J* = 44.1, 7.8 Hz), 128.95 – 127.92 (m), 127.20 (d, *J* = 15.1 Hz), 124.07 (s), 123.77 (s), 121.14 (s), 116.56 (s). LCMS (ESI): m/z Calcd for $C_{14}H_8F_2N_2O$ [M + H] $^+$:258.0605; Found: 259.1-16.

2-(3-chlorophenyl)-5-(4-chlorophenyl)-1,3,4-oxadiazole (5o): buff solid, yield: (94%); m. p = 158–160°C; ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.08 (d, *J* = 1.6 Hz, 1H), 8.07 (s, 1H), 8.04 (d, *J* = 5.0 Hz, 1H), 8.03 – 7.97 (m, 1H), 7.54 – 7.43 (m, 4H).^{13}C NMR (100 MHz, $CDCl_3$) δ 164.02 (s), 163.51 (s), 138.24 (s), 135.22 (s), 132.01 (s), 131.74 (s), 130.31 (s), 129.50 (d, *J* = 29.3 Hz), 129.28 – 129.26 (m), 128.21 (d, *J* = 6.0 Hz), 125.12 (d, *J* = 25.1 Hz), 122.02 (s).LCMS (ESI): m/z Calcd for $C_{14}H_8C_{l2}N_2O$ $[M + H]^+$:290.0014; Found: 291.0466

RESULTS AND DISCUSSION

The starting material, benzo hydrazide, was isolated after 8 hours of refluxing hydrazine hydrate and ethyl benzoate in ethanol. As a first instance, to achieve 2,5-disubstituted 1,3,4-oxadiazole, we stirred benzo hydrazide (1 mmol) and dithioester (1 mmol) at room temperature in an ethanol solvent for 24 hours; no desired results were obtained (Table-1 entry 1). We tried again with a K_2CO_3 base for the same protocol, but no results were found (Table-1, entry 2). The reaction was then modulated for 8 hours at 60°C by stirring with both starting materials (1a) and (2a) in 1 mmol, K_2CO_3 in 1 mmol, and I_2 in a catalytic amount (1 mmol) in an ethanol solvent. Surprisingly, we observed some changes in TLC and isolated the product with a 40% yield (Table-1, entry 3). Mass spectral analysis matches the expected mass, which boosted our work to further optimize for a good yield. Additionally, we modulated the equivalence of catalyst in 1.2, 1.5, and 2 equivalences of K_2CO_3, yielding 56%, 60%, and 96%, respectively (Table-1, entries 4-6). Based on these findings, 2 eq of I_2 and 1 eq of K_2CO_3 were found to be adequate for a good yield (Table-1, entry 6). No appreciable yield was found by modulating inorganic and organic bases (Table-1, entries 8-12). Modulating the catalyst amounts (2.2eq) of I_2 and (2 eq) of K_2CO_3 didn't improve the yield (Table-1, entry 7). Extending the reaction time with (2 eq) of K_2CO_3 didn't improve the yield (Table-1, entry 8). Finally, we screened the effect of solvent on yield (Table-1, entries 13-18) among the solvents used; only ethanol yielded about 96%. Hence, (Table-1, entry 4) found the best optimizing condition to obtain 2,5-diphenyl-1,3,4-oxadiazoles. Following the creation of the optimal reaction conditions, we conducted a substrate scope to examine the impact of various functional groups contained in the substrates (Table-2, 5a-5o). the yield of 2,5-diphenyl 1,3,4-oxadizole was unaffected by an electron-donating and withdrawing group of dithioesters. Based on Table 1, we may infer from the optimization reaction condition that we can get a yield of up to 96% by treating 1 mmol of each reactant, dithioester, and benzo hydrazide derivatives, in 2 mmol of K_2CO_3 and I_2 catalyst in the presence of ethanol at reflux.

Table-1: Optimization of the Reaction Conditions[a]

Entry	Solvent	Base	Catalyst (I_2)	(Base) Equivalence	Temp (°C)	Time (h)	Yield (%)
1	Ethanol	-	-	-	RT	24h	NR
2	Ethanol	K_2CO3	-	1	RT	24h	NR
3	Ethanol	K_2CO_3	1	1	60°C	8h	40%
4	Ethanol	K_2CO_3	1.2	2	reflux	8h	56%
5	Ethanol	K_2CO_3	1.5	2	reflux	8h	60%
6	Ethanol	K_2CO_3	2	2	reflux	8h	96%
7	Ethanol	K_2CO_3	2.2	2	reflux	8h	64%
8	Ethanol	K_2CO_3	2	2	reflux	10h	91%
9	Ethanol	Na_2CO_3	2	2	reflux	8h	68%
10	Ethanol	KOH	2	2	reflux	8h	48%
11	Ethanol	NaOH	2	2	reflux	8h	48%
12	Ethanol	LiOH	2	2	reflux	8h	38%
13	Ethanol	Et_3N	2	2	reflux	8h	52%
14	MeOH	K_2CO_3	2	2	reflux	8h	10%
15	MeCN	K_2CO_3	2	2	reflux	8h	15%
16	Toluene	K_2CO_3	2	2	reflux	8h	NR
17	Water	K_2CO_3	2	2	reflux	16h	NR
18	DMF	K_2CO_3	2	2	reflux	8h	NR
19	DMSO	K_2CO_3	2	2	reflux	8h	NR

[a] Reaction conditions: Reactions were carried out with 1a (1.0 mmol) and 2a (1.0 mmol) in the presence of K_2CO_3 (2 mmol), I_2 (2 mmol), and ethanol at reflux for 8 h.

Plausible Mechanism for the Synthesis of Compound 3

A plausible mechanism for the cyclization reaction leading to 2,5-disubstituted 1,3,4-oxadizole is displayed in Fig.-2. The lone pair of electrons from benzo hydrazide attack the electrophilic site of dithioester, giving 1a, followed by iodination at sulphur in the presence of potassium carbonate to generate intermediate 4a. subsequent iodination again at sulphur takes place to form an intermediate 4a, by abstracting proton by potassium carbonate promoted cyclization, giving the desired product 5a. and potassium iodide, potassium bicarbonate, and sulphur diiodide.

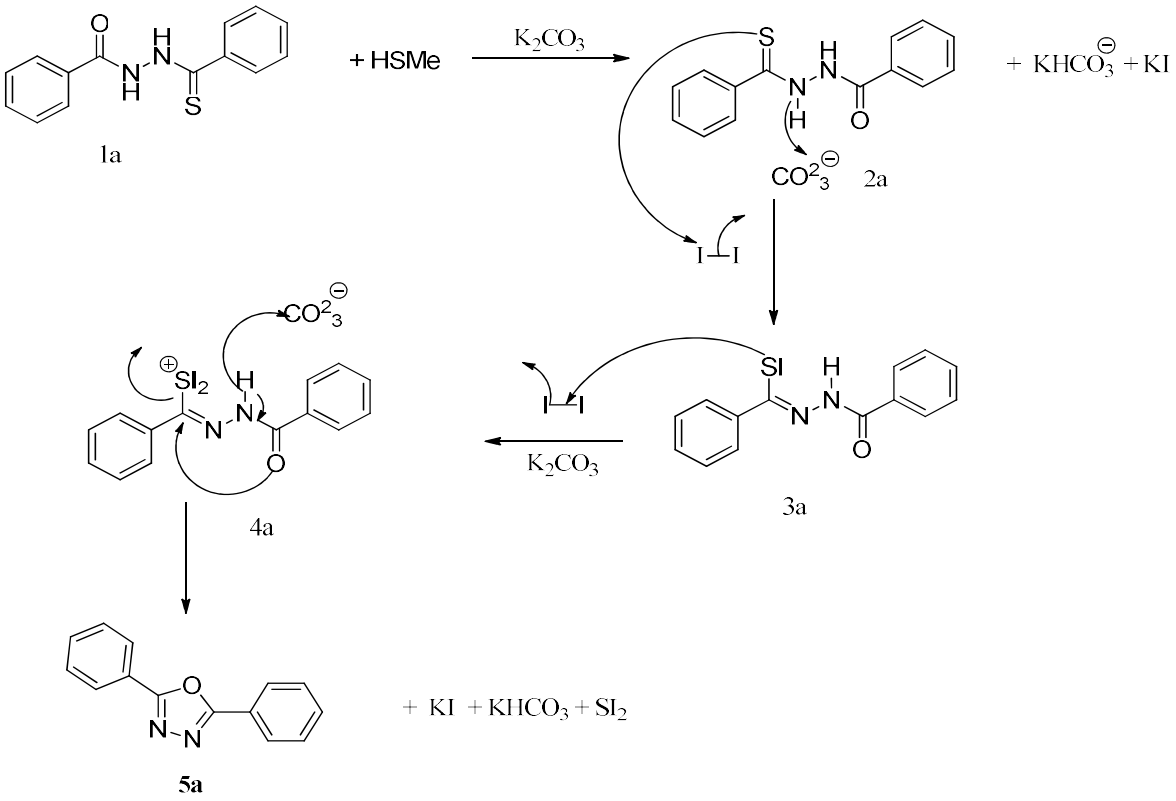
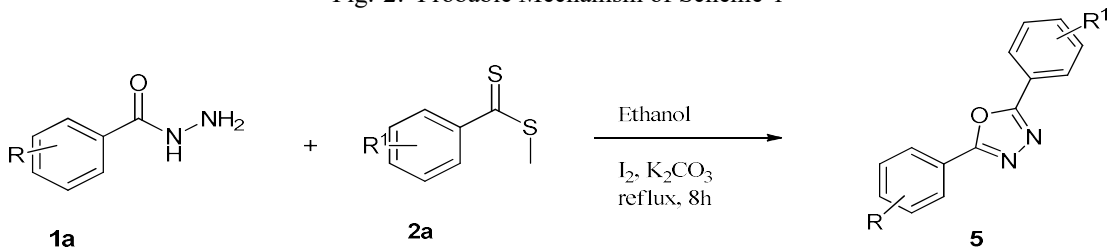
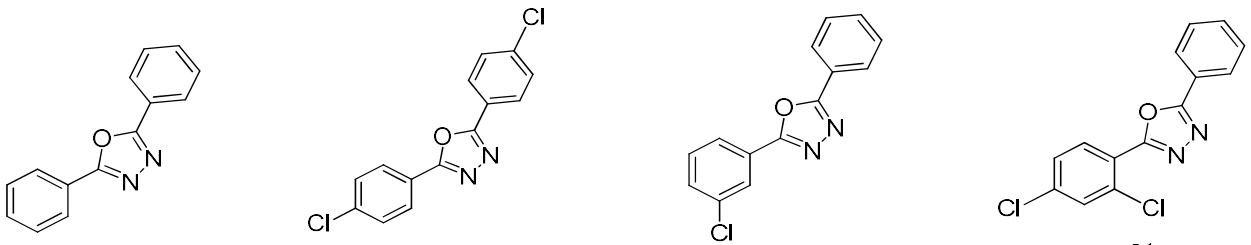


Fig.-2: Probable Mechanism of Scheme-1





5a (96%) 8h | 5b (85%) 12h | 5c (82%) 10h | 5d (90%) 11h

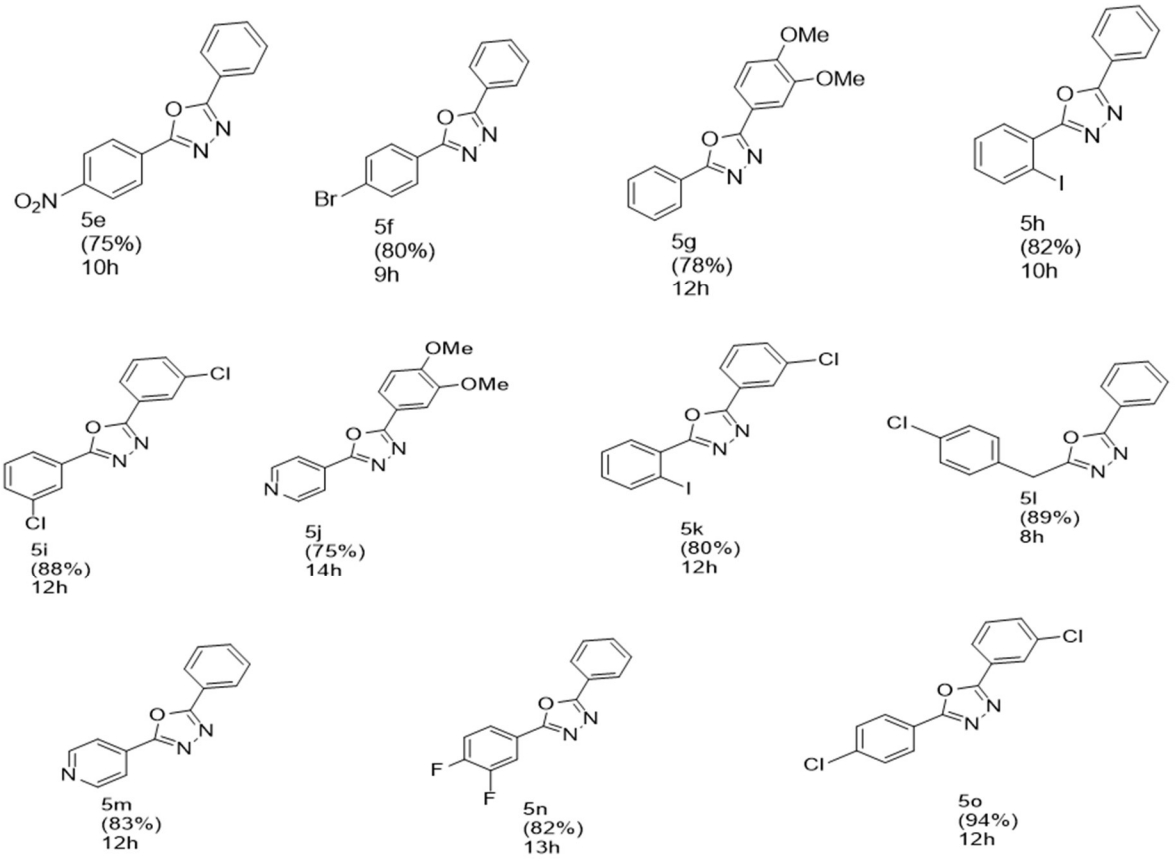


Fig.-2: Scheme and Substrate Scope of Reaction

CONCLUSION

We have developed a mild and efficient simple protocol by utilizing benzo hydrazides and dithioester for the synthesis of 2,5-diphenyl1,3,4-oxadizoles. It is non-toxic, easy to purify, has functional group tolerance, and is commercially available; it employs ethanol as a solvent and a cost-effective catalyst, I_2, as a desulfurizing agent. This method is simple and has a wide range of applications in the field of pharmaceuticals.

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CONFLICT OF INTERESTS

The authors declare that there is no conflict of interest.

AUTHOR CONTRIBUTIONS

All the authors contributed significantly to this manuscript, participated in reviewing/editing, and approved the final draft for publication. The research profile of the authors can be verified from their ORCID IDs, given below:

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