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Lanthanum-catalyzed stereoselective synthesis of vinyl sulfides and selenides

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ABSTRACT

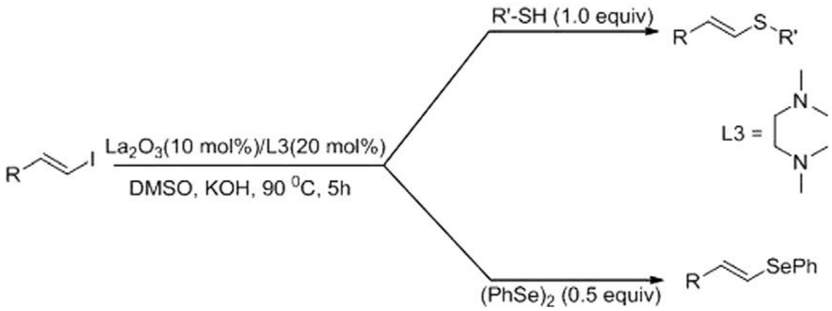
Lanthanum oxide/TMEDA-catalyzed cross-coupling of vinyl halides with thiols/diphenyl diselenide in anhydrous DMSO and KOH is reported. Utilizing this protocol various vinyl sulfides and selenides were synthesized in excellent yields with retention of the stereochemistry. The catalyst was recyclable.

Vinyl sulfides and selenides are valuable compounds found in many biologically active molecules with a broad range of applications in organic synthesis.[1] They can be used as equivalents of carbonyl compounds[2] and Michael acceptors,[3] and as key intermediates in the stereoselective synthesis of functionalized alkenes.[4]

Various processes have been reported for the synthesis of these vinyl sulfides and selenides. The most commonly employed strategy involves the reaction of vinyl halides with thiols or diphenyl diselenide,[5] and different protocols have been developed for the synthesis of vinyl sulfides and selenides.[6,7] Notable amongst them is the well defined catalytic systems such as, copper complex [Cu(phen)(PPh3)$_2$]NO$_3$ system,[5c] CuI/l-proline in ionic liquids,[5f] and CuI/ *cis*-1,2-cyclohexanediol in DMF.[5g] However, most of these metal-catalyzed reactions involve expensive and moisture-sensitive catalysts/co-catalysts causing major problems in purification of the product, separation of metal catalysts, and stereocontrol of double bond geometry. Thus, it is desirable to develop an inexpensive, environmentally benign, and recyclable catalytic system for an efficient access to such biologically important compounds.

For the past several years, transition metal catalysts such as palladium, nickel, and copper-based catalysts were explored for the synthesis of vinyl sulfides and selenides. However, until now there has been no report on lanthanum-catalyzed cross-coupling reactions. In continuation of our interest in the field of cross-coupling reactions,[8] we wish to report, herein, the synthesis of vinyl sulfides and selenides in a very efficient manner by the cross-coupling of vinyl halides with thiols or diphenyl diselenides in the presence of lanthanum oxide as a recyclable catalyst. To the best of our knowledge, this is the first lanthanum-catalyzed coupling of vinyl halides with thiols or diphenyl diselenide to form vinyl sulfides and selenides (Scheme 1). This novel method is economically attractive since the catalyst will be recyclable, inexpensive, and the reaction can be performed in the absence of co-catalyst.

In the first instance, the reaction conditions were optimized using trans-β-iodostyrene and benzene thiol as model substrates, to observe the effect of the base, solvent, ligand, and catalyst on this cross-coupling reaction. Initially, we examined the effect of different ligands L1–L5 with the combination of La(OTf)$_3$ in differ-



Scheme 1.

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Table 1
Optimized conditions for the synthesis of vinyl sulfides[a]

Entry	Catalyst	Ligands	Solvents	Base	Yield (%)
1	La(OTf)$_3$	L1	DMF	K_3PO_4	0
2	La(OTf)$_3$	L1	PhMe	KOH	0
3	La(OTf)$_3$	L2	DMSO	Cs_2O_3	Trace
4	La(OTf)$_3$	L3	DMSO	K_3PO_4	25
5	La(OTf)$_3$	L3	DMF	KOH	51
6	La(OTf)$_3$	L3	DMSO	KOH	79
7	La(OTf)$_3$	L3	DMSO	KOH	40[b]
8	La(OTf)$_3$	L3	DMSO	KOH	79[c]
9	La(OTf)$_3$	L3	DMSO	KOH	79[d]
10	La(OTf)$_3$	L4	DMSO	KOH	56
11	La(OTf)$_3$	L5	DMSO	KOH	49
12	La_2O_3	L1	DMSO	KOH	81
13	La_2O_3	L2	DMSO	KOH	67
14	La_2O_3	L3	DMSO	KOH	95
15	La_2O_3	L4	DMSO	KOH	51
16	La_2O_3	L5	DMSO	KOH	75
17	$InBr_3$	L3	DMSO	KOH	71
18	In(OTf)$_3$	L3	DMSO	KOH	78
19	In_2O_3	L3	DMSO	KOH	92[e]
20	In_2O_3	L3	DMSO	KOH	79
21	$FeCl_3$	L3	DMSO	KOH	69
22	Fe_2O_3	L3	DMSO	KOH	76
23	Fe_2O_3	L3	DMSO	KOH	93
24	--	L3	DMSO	KOH	10
25	La_2O_3	--	DMSO	KOH	51
26	La_2O_3	L3	DMSO	--	0

[a] Reaction conditions: *trans*-iodostyrene (1.0 mmol), benzene thiol (1.0 mmol), catalyst (10 mol %), ligand (20 mol %), KOH (1.5 equiv), and DMSO (2.0 mL), 90 °C, 5 h.
[b] At 50 °C.
[c] At 90 °C.
[d] At 110 °C.
[e] After 9 h.

ent solvent and base combinations. Among the bases screened KOH has shown the best efficiency with DMSO as the solvent and 90 °C as the optimum temperature. L3 was found to be the efficient ligand giving the coupling product in 79% yield (Table 1, entry 8). Encouraged by these results, we have chosen moisture stable and inexpensive La_2O_3 to examine the effect with various ligands L1–L5 in DMSO with KOH as the base at 90 °C. Among the ligands, TMEDA (L3) was found to be the most effective for the synthesis of vinyl sulfides (Table 1, entry 14). Then we examined the reactivity of several metal catalysts with the combination of TMEDA (L3) as a ligand. Amongst these catalysts, La_2O_3 has shown better activity compared to other metal sources such as Fe_2O_3, In_2O_3, La(OTf)$_3$, $FeCl_3$, $InBr_3$, and In(OTf)$_3$ (Table 1). But Fe_2O_3, and In_2O_3 gave competitive yields after longer reaction times (Table 1, entries 19 and 23). Only a trace amount of the expected product was formed without the metal source, (Table 1, entry 24) and moderate yields were observed with La_2O_3 in the absence of ligand (Table 1, entry 25). The optimum reaction conditions for the synthesis of vinyl sulfides were, vinyl halide (1.0 equiv), thiol (1.0 equiv) La_2O_3 (0.1 equiv), TMEDA (0.2 equiv), KOH (1.5 equiv), and a reaction temperature of 90 °C for 5 h with DMSO as the solvent.[9,10]

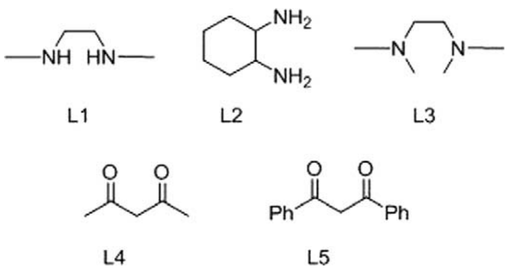
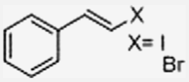
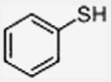
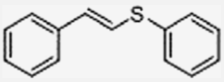
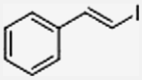
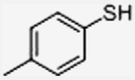
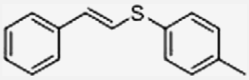
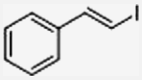
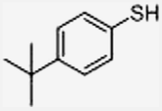
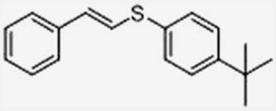
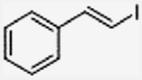
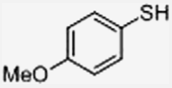
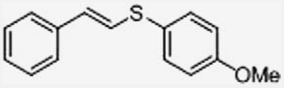
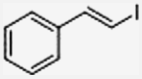
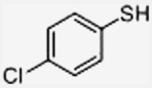
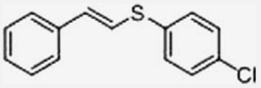
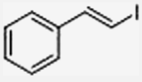
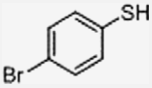
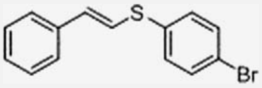
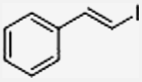
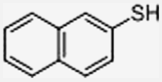
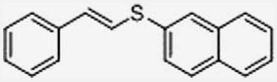
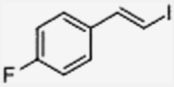
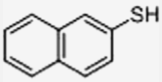
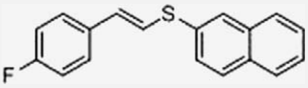


Table 2
La_2O_3-catalyzed stereoselective synthesis of vinyl sulfides[a]

Entry	Halides	Thiol	Product	Yield (%)
1 2				95 55
3				91
4				89
5				91
6				90
7				89
8				92
9				88

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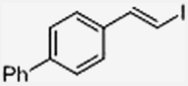
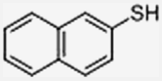
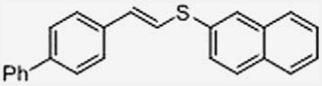
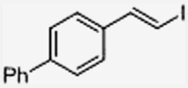
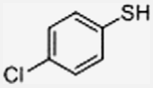
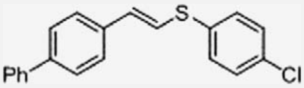
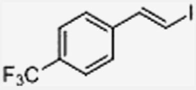
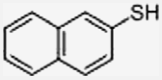
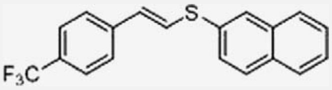
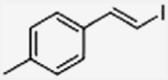
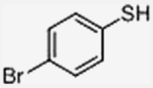
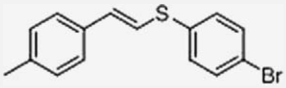
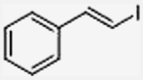
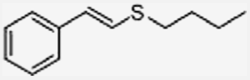
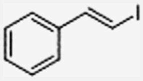
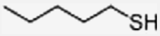
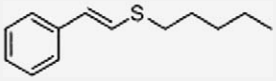
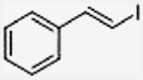
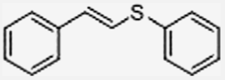
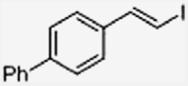
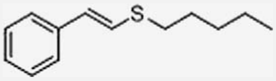
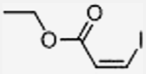
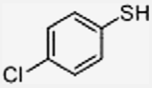
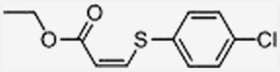
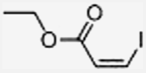
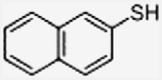
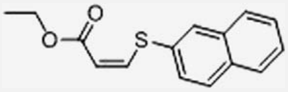
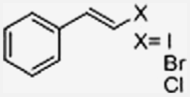
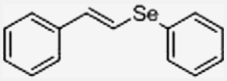
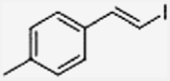
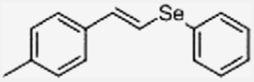
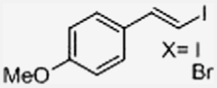
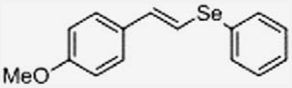
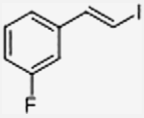
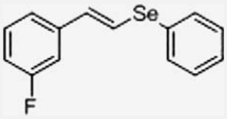
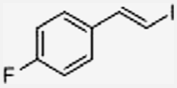
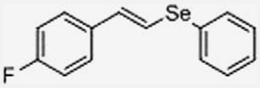
10				86
11				85
12				82
13				87
14				85
15				82
16				83
17				81
18				85
19				82

[a] Reaction conditions: *trans*-β-iodostyrenes (1.0 mmol), thiols (1.0 mmol), La_2O_3 (10 mol %), TMEDA (20 mol %), KOH (1.5 equiv), and DMSO (2.0 mL), at 90 °C.

To expand the scope of this novel transformation, we examined various vinyl halides with different thiols for cross-coupling (Table 2). This protocol efficiently cross-coupled *trans*-β-iodostyrene having electron-rich, electron-neutral, and electron-poor functionalities with various thiols such as aromatic, acyclic, and cyclic thiols under the optimized reaction conditions and generated the desired products in high yields (Table 2). Fortunately, aromatic thiols with both electron-donating and electron-withdrawing func-

Table 3

La_2O_3-catalyzed stereoselective synthesis of vinyl selenides[a]

Entry	Halides	Product	Yield (%)
1			96
2			51
3			Trace
4			92
5			89
6			41
7			83
8			88

[a] Reaction conditions: *trans*-β-iodostyrene (1.0 mmol), diphenyl diselenide (0.5 mmol), La_2O_3 (10 mol %), TMEDA (20 mol %), KOH (1.5 equiv), and DMSO (2.0 mL) at 90 °C.

Table 4
Recycling of La_2O_3

Cycle	Catalyst recovery (%)	Yield (%)
1	98	95
2	95	91
3	91	89
4	91	84

tional groups, such as methyl and chloro groups, afforded the corresponding products in good yields (Table 2, entries 3, 4, 6, 7, 11, and 13). This protocol was applied for the cross-coupling of alkyl vinyl iodides with different thiols and the desired vinyl sulfides were also obtained in impressive yields (Table 2, entries 18 and 19). Encouraged by these results, we tested the coupling of *trans*-β-bromostyrenes with benzene thiol under the same conditions. The reaction of *trans*-β-bromostyrenes with benzene thiol proceeded smoothly to afford the desired product in reasonable yield (Table 2, entry 2). Unfortunately, the crosss-coupling of heteroaromatic thiols with *trans*-β-iodostyrene has failed.

The same catalytic system was applied for the C–Se bond formation via coupling of diphenyl diselenide with *trans*-β-iodostyrene under the optimized conditions. This protocol efficiently cross-coupled different substituted *trans*-β-iodostyrene with diphenyl diselenide and produced the vinyl selenides in high yields (Table 3). The reaction of *trans*-β-bromostyrenes with diphenyl diselenide proceeded smoothly to afford the desired product in reasonable yield (Table 3, entries 2 and 6). Furthermore, the stereochemistry of the vinyl sulfides and vinyl selenides was retained in all the cases as determined by ^{1}H NMR studies.

La_2O_3 was used directly in the next cycle. The catalyst was found to be recyclable without the loss of catalytic activity up to four cycles (Table 4). The structures of all the products were determined from their analytical and spectral (IR, ^{1}H NMR, and ^{13}C NMR) data and by direct comparison with authentic samples.

In conclusion, La_2O_3 acts as an active, moisture stable, inexpensive, and nontoxic catalyst for the stereo selective synthesis of vinyl sulfides and selenides under additive-free conditions in excellent yields. The catalyst can also be easily recovered and reused.

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9. *General procedure for the synthesis of vinyl sulfides*: To a stirred solution of *trans*-β-iodostyrene (1.0 mmol) and La_2O_3 (10 mol%) in DMSO (2.0 mL) was added benzenethiol (1.0 mmol) followed by TMEDA (20 mol%) and KOH (1.5 equiv) and stirred at 90 °C for 5 h. The progress of the reaction was monitored by TLC. The mixture was allowed to cool to room temperature, diethyl ether (5.0 mL) was added, and the organic phase was separated, dried over anhydrous Na_2SO_4, evaporated, and the crude product was purified by chromatography on silica gel (*n*-hexane as eluent) to afford the corresponding coupling product in 95% yield.

   General procedure for the synthesis of vinyl selenides: To a stirred solution of *trans*-β-iodostyrene (1.0 mmol) and La_2O_3 (10 mol %) in DMSO (2.0 mL) was added diphenyl diselenide (1.0 mmol) followed by TMEDA (20 mol %) and KOH (1.5 equiv). The reaction mixture was then stirred at 90 °C for 5 h. The progress of the reaction was monitored by TLC. The mixture was allowed to cool to room temperature. Diethyl ether (5.0 mL) was added, and the organic phase was separated, dried over anhydrous Na_2SO_4, evaporated, and the crude product was purified by chromatography on silica gel (*n*-hexane as eluent) to afford the corresponding coupling product in 96% yield.

   Recycling of the catalyst: After the reaction was complete, the reaction mixture was allowed to cool, and a 1:1 mixture of ethyl acetate/water (2.0 mL) was added and La_2O_3 was removed by centrifugation. After each cycle, the catalyst was recovered by simple centrifugation, washed with deionized water followed by acetone, and then dried in vacuo. The recovered La_2O_3 was used directly in the next cycle.
10. Data for the representative examples of synthesized compounds: (*E*)-phenyl(styryl)sulfane (Table 2, entries 1 and 2): Colorless oil; ^{1}H NMR (200 MHz, $CDCl_3$, TMS): $\delta = 7.39$ (d, 2H, $J = 7.62$ Hz), 7.34–7.18 (m, 8H), 6.88 (d, 1H, $J = 15.25$ Hz), 6.69 (d, 1H, $J = 15.25$ Hz); ^{13}C NMR (100 MHz, $CDCl_3$, TMS): $\delta = 135.1$, 132.5, 131.7, 129.7, 129.3, 129.1, 128.6, 127.6, 127.5, 127.3, 126.9, 126.0, 123.3, 119.3

    (E)-(2-(Biphenyl-4-yl)vinyl)(4-chlorophenyl)sulfane (Table 2, *entry 11*): white solid, mp 132–133 °C; IR (KBr): ν 3053, 2985, 1621, 1503, 1453, 1274, 943, 756 cm^{-1}; ^{1}H NMR (300 MHz, $CDCl_3$, TMS): $\delta = 7.58$–7.52 (m, 4H), 7.44–7.27 (m, 9H), 6.85 (d, 1H, $J = 15.38$ Hz), 6.76 (d, 1H, $J = 15.38$ Hz) ^{13}C NMR (100 MHz, $CDCl_3$, TMS): $\delta = 140.5$, 140.4, 135.2, 133.8, 132.9, 132.1, 130.9, 129.2, 128.7, 127.3, 126.8, 126.4, 122.5; Mass (ESI): *m*/*z* 345 [M+Na]; Anal. Calcd for $C_{20}H_{15}ClS$: C, 74.40; H, 4.68; S, 9.93. Found: C, 74.31; H, 4.59; S, 9.86.

    (*E*)*-Cyclohexyl(styryl)sulfane* (Table 2, *entry 16*): Colorless oil; ^{1}H NMR (300 MHz, $CDCl_3$, TMS): $\delta = 7.24$–7.20 (m, 4H), 7.19–7.09 (m, 1H), 6.66 (d, 1H, $J = 15.86$), 6.44 (d, 1H, $J = 15.86$ Hz), 2.98–2.87 (m, 1H), 2.06–2.02 (m, 2H), 1.82–1.79 (m, 2H), 1.65–1.61(m, 1H), 1.49–1.25 (m, 5H); ^{13}C NMR (100 MHz, $CDCl_3$, TMS): $\delta = 137.1$, 128.5, 126.8, 125.5, 124.0, 33.5, 29.6, 25.9, 25.6.

    (*Z*)*-Ethyl 3-(4-chlorophenylthio)acrylate* (Table 2, *entry 18*): Light yellow solid, mp 64–65 °C; IR (KBr): ν 3056, 2925, 1702, 1577, 1214, 959, 744 cm^{-1}; ^{1}H NMR (200 MHz, $CDCl_3$, TMS): $\delta = 7.39$ (d, 2H, $J = 8.49$ Hz), 7.31 (d, 2H, $J = 8.49$ Hz), 7.11 (d, 1H, $J = 10.00$ Hz), 5.89 (d, 1H, $J = 10.00$ Hz), 4.21 (q, 2H, $J = 6.98$ Hz), 1.33 (t, 3H, $J = 7.17$ Hz); ^{13}C NMR (100 MHz, $CDCl_3$, TMS): $\delta = 166.3$, 148.8, 134.5, 134.4, 132.2, 129.4, 113.7, 60.3, 14.2; Mass (ESI): *m*/*z* 265 [M+Na]; Anal. Calcd for $C_{11}H_{11}ClO_2S$: C, 54.43; H, 4.57; S, 13.21. Found: C, 54.37; H, 4.49; S, 13.15.

    (*E*)*-Phenyl(styryl)selane* (Table 3, *entries 1–3*): yellowish oil; ^{1}H NMR (200 MHz, $CDCl_3$, TMS): $\delta = 7.54$–7.49 (m, 2H), 7.31–7.18 (m, 8H), 7.13 (d, 1H, $J = 15.8$ Hz), 6.85 (d, 1H, $J = 15.8$ Hz); ^{13}C NMR (100 MHz, $CDCl_3$, TMS): $\delta = 136.9$, 135.0, 132.4, 130.0, 129.2, 128.6, 127.5, 127.3, 126.0, 119.3.

    (*E*)*-(4-Fluorostyryl)(phenyl)selane* (Table 3, *entry 8*): yellowish oil; ^{1}H NMR (200 MHz, $CDCl_3$, TMS): $\delta = 7.52$–7.50 (m, 2H), 7.32–7.26 (m, 5H), 7.05 (d, 1H, $J = 16.11$ Hz), 6.97 (t, 2H, $J = 8.0$ Hz), 6.76 (d, 1H, $J = 16.11$ Hz); ^{13}C NMR (100 MHz, $CDCl_3$, TMS): $\delta = 164.6$, 132.9, 132.7, 130.0, 129.9, 129.3, 127.6, 121.7, 114.3, 114.0; Mass (ESI): *m*/*z* 300 [M+Na]; Anal. Calcd for $C_{14}H_{11}FS$: C, 60.66; H, 4.0. Found: C, 60.59; H, 3.96.