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Solvent-free synthesis of *N*-sulfonyl imines using WCl_6 as a novel, highly efficient and reusable catalyst

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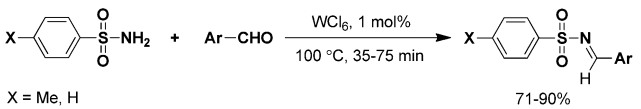
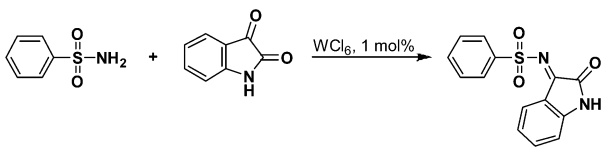
WCl_6 was used as a novel, efficient and reusable catalyst for the preparation of *N*-sulfonyl imines *via* the condensation of sulfonamides with aldehydes as well as isatin under solvent-free conditions. The turn-over frequency (TOF) value of the catalyst is several times higher than the previously reported catalysts. Clean reaction, simple purification, short reaction time and high yield are some other advantages of this work.

Imines bearing electron-withdrawing *N*-substituents are useful intermediates in organic synthesis.[1] Among them, *N*-sulfonyl imines are the center of attention for organic chemists because the sulfonyl moiety has proven to be a powerful activating group of the C=N bond in these compounds. As a consequence, *N*-sulfonyl imines have been widely used in organic transformations.[2] Furthermore, they are excellent substrates in nucleophilic additions,[3] reductions,[4] aza Diels–Alder reactions,[5] alternative aziridine synthesis involving nucleophilic addition across *N*-sulfonyl aldimines,[6] asymmetric synthesis of β-amino acid derivatives,[7] and oxaziridine synthesis,[8] as well as ene reactions.[9] Several kinds of synthetic routes toward *N*-sulfonyl imines have been developed namely *via* the Lewis and protic acid catalyzed reactions of sulfonamides with aldehyde precursors,[10–22] rearrangement of oxime *O*-sulfinates,[23] tellurium mediated reaction of aldehydes with chloramine T by utilization of *in situ* generated *N*,*N*′-ditosyltellurodiimide,[24] application of *N*-sulfinyl sulfonamides instead of sulfonamides to generate sulfonyl imines *in situ via* a [2 + 2] cycloaddition and extrusion of sulfur dioxide,[25] generation of sulfonamidosulfones and basic elimination,[26,27] and catalyzed isomerization or rearrangement of *N*-sulfonyl aziridines.[28] However, some of the reported methods suffer from drawbacks such as long reaction times, unsatisfactory yields, harsh conditions, the use of expensive reagents, the use of multiple steps and cumbersome procedures, and no agreement with green chemistry protocols. Therefore, the development of an efficient, one-step and environmentally friendly procedure for the preparation of *N*-sulfonyl imines is desirable.



Scheme 1 Synthesis of sulfonyl imines using WCl_6.



Scheme 2 Condensation of benzenesulfonamide with isatin using WCl_6.

Solvent-free reactions have been demonstrated to be an efficient technique for various organic transformations instead of using harmful organic solvents. Solvent-free conditions often lead to a remarkable decrease in reaction times, increased yields, easier workup, matches with green chemistry protocols, and may enhance the regioselectivity and stereoselectivity of reactions.[29–36]

Table 1 Effect of different amounts of the catalyst and temperature on the reaction of 4-methylbenzenesulfonamide (1 mmol) with 4-chlorobenzaldehyde (1 mmol)

Catalyst	Mol% of Catalyst	Temp. (°C)	Time (min)	Yield[a] (%)
WCl_6	1	100	45	87
WCl_6	2	100	45	87
WCl_6	3	100	45	87
WCl_6	1	60	90	71
WCl_6	1	80	60	80
WCl_6	1	110	45	87

[a] Isolated yield.

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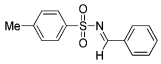
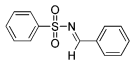
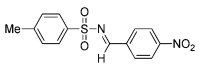
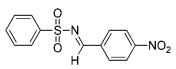
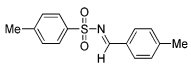
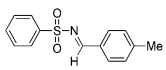
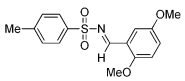
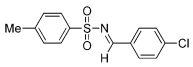
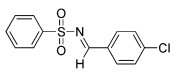
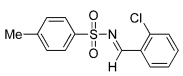
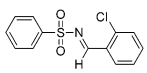
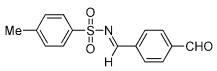
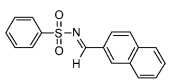
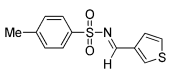
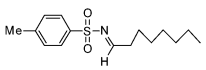
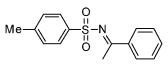
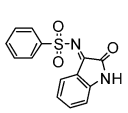
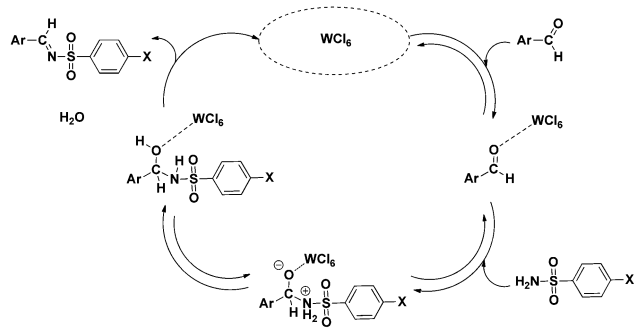
Table 2 Preparation of *N*-sulfonyl imines in the presence of WCl_6 at 100 °C

Entry	Product	Time (min)/Yield[a] (%)	M.p. (Lit.)[Ref.]
1		45/88	107–110 (108–109)[16]
2		40/86	75–77 (76–78)[16]
3		40/85	163–165 (164–166)[17]
4		40/90	159–162 (161–163)[16]
5		45/86	110–113 (112–114)[16]
6		45/83	114–116 (113–115)[17]
7		75/79	123–125 (124–126)[16]
8		45/87	169–172 (171–173)[16]
9		35/91	132–135 (131–133)[17]
10		55/84	127–129 (128–129)[16]
11		60/85	129–131 (129–130)[38]
12[b]		60/71	95–98 (98–100)[18,19]
13		40/85	164–167 (166–168)[19]
14		45/84	125–128 (127–129)[16]
15		60/55	135–136 (136–137)[21]
16		60/58	85–87 (84–86)[21]
17		50/80	142–144 (144–145)[22]

[a] Isolated pure product. [b] In this reaction, bis-*N*-sulfonyl imine was obtained in very low yield.



Scheme 3 Plausible mechanism for the synthesis of sulfonyl imines using WCl_6.

Considering the above facts, in continuation of our investigations on the application of WCl_6 in organic transformations,[37] we report here a highly efficient and simple method for the synthesis of *N*-sulfonyl imines *via* the reaction of sulfonamides with aromatic aldehydes, as well as isatin using WCl_6 as a catalyst under solvent-free conditions (Schemes 1 and 2).

To optimize the reaction conditions, as a model reaction, the solvent-free condensation of 4-methylbenzenesulfonamide with 4-chlorobenzaldehyde was examined in the presence of different amounts of WCl_6 in the range 60–110 °C. Higher yield and shorter reaction time were obtained when the reaction was carried out using 1 mol% of WCl_6 at 100 °C (Table 1).

Afterward, 4-methylbenzenesulfonamide and benzenesulfonamide were condensed with various aldehydes as well as with isatin, in order to assess the applicability and scope of the catalyst; the respective results are displayed in Table 2. As Table 2 indicates, all reactions proceeded efficiently in the presence of WCl_6 at 100 °C and the *N*-sulfonyl imines were produced in high to excellent and in relatively short reaction times.

In this investigation, the influence of electron-withdrawing substituents, electron-releasing substituents and halogens on the aromatic ring of aldehydes upon the results of the reaction was studied. The results displayed that electron-withdrawing substituents and halogens increased the reaction yields (Table 2, entries 3 and 4 as well as 8–11); however, electron-releasing substituents slightly decreased the yields (Table 2, entries 5, 6 and 7). Moreover, the condensation of sulfonamides with dicarbonyl compounds as well as isatin can be powerfully carried out using WCl_6 as the catalyst (Scheme 2 and Table 2, entries 12 and 15).

In a plausible mechanism, which was supported by the literature,[11,37] WCl_6 could catalyze the synthesis of *N*-sulfonyl imines as a Lewis acid. Then the tungsten(VI) chloride was coordinated with the carbonyl group, which increased the electrophilicity of the aldehyde against the sulfonamide as a nucleophile. From the reaction of sulfonamide with activated aldehyde, one molecule of H_2O was removed and the sulfonyl imine was prepared (Scheme 3).

In another study, to compare the efficiency as well as the capacity of the solvent-free conditions with respect to solution conditions, the model reaction was examined in the presence of WCl_6 in several solvents (5 mL) under reflux conditions; the corresponding results are displayed in Table 3. As Table 3 indicates, the solvent-free condition is more efficient.

To compare the applicability and efficiency of WCl_6 with reported catalysts in the synthesis of *N*-sulfonyl imines, we have tabulated the turn-over frequency (TOF) of these catalysts in the condensation reaction of 4-methylbenzenesulfonamide with 4-chlorobenzaldehyde (Table 4). As shown in Table 4, WCl_6, relative to the previously reported catalysts, is superior in terms of TOF.

In another investigation, the reusability of the catalyst was examined upon the reaction of 4-methylbenzenesulfonamide (1 mmol) with 4-chlorobenzaldehyde (1 mmol). The reaction mixture was extracted with dichloromethane and separated from the catalyst. Afterward, the reused catalyst was employed for another reaction. We observed that the catalytic activity of the catalyst was restored within the limits of the experimental errors for four successive runs (Table 5).

Table 3 The condensation of 4-methylbenzenesulfonamide with 4-chlorobenzaldehyde using WCl_6 (1 mol%) in different solvents (5 mL) under reflux conditions

Entry	Solvent	Time (min)	Yield[a] (%)
1	EtOH	45	79
2	CH_3OH	50	78
3	CH_3CN	45	75
4	CH_2Cl_2	50	72
5	$CH_3COOC_2H_5$	45	81
6	—	45	87

[a] Isolated yield.

Table 4 The comparative condensation of 4-methylbenzenesulfonamide with 4-chlorobenzaldehyde using previously reported catalysts *versus* WCl_6

Catalyst	Catalyst amount (mol%)	Time (min)	Yield[a] (%)	TOF[b]	Ref.
WCl_6	1	45	87	1.93	—[c]
[Msim]Cl	200	20	95	0.023	22
$FeCl_3$	4	60	70	0.29	11
$InCl_3$	10	1440	91	0.0063	12
DMTrCl	12.5	50	80	0.128	18
$AlCl_3$	50	100	86	0.017	15
MgO	25	15	77	0.2	20

[a] Isolated pure product. [b] Turn-over frequency. [c] Our work.

Table 5 The reaction of 4-methylbenzenesulfonamide with 4-chlorobenzaldehyde in the presence of reused WCl_6 under solvent-free conditions at 90 °C

Entry	Cycle	Time (min)	Yield[a] (%)
1	1st run	45	87
2	2nd run	47	84
3	3rd run	50	81
4	4th run	60	79

[a] Isolated yield.

Conclusions

In summary, we have introduced tungsten(VI) chloride (WCl_6), as a novel, efficient and reusable catalyst for the efficient synthesis of *N*-sulfonyl imines *via* the condensation of sulfonamides with aldehydes, as well as isatin, under solvent-free conditions.[39]

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38 K. Y. Lee, C. G. Lee and J. N. Kim, *Tetrahedron Lett.*, 2003, **44**, 1231.
39 General procedure for the synthesis of *N*-sulfonyl imines and recycling of WCl_6: to a mixture of compounds consisting of sulfonamide (1 mmol) and carbonyl compound (1 mmol) in a 25 mL round-bottomed flask was added WCl_6 (3.9 mg, 0.01 mmol, 1 mol%) as a catalyst. The resulting mixture was stirred at 100 °C for the appropriate time (Table 2). After completion of the reaction, as monitored by TLC, the reaction mixture was extracted with dichloromethane (2 × 10 mL) and filtered to separate the catalyst. The solvent was evaporated and the crude product was dissolved in warm ethyl acetate (4 mL), treated with n-hexane (12–15 mL), and was allowed to stand at room temperature for 5–6 h. During this time, crystals of product formed which were collected by filtration, washed with n-hexane and dried. Afterward, the remaining WCl_6 was dried and used for the next run under identical reaction conditions. (*E*)-*N*-Benzylidenebenzenesulfonamide (Table 2, entry 2). White solid; m.p. 75–77 °C (Lit. [16] m.p. 76–78 °C); ^{1}H NMR ($CDCl_3$): δ 7.61 (m, 6H), 8.02 (m, 4H), 9.05 (s, 1H); ^{13}C NMR ($CDCl_3$): δ 127.1, 128.3, 129.5, 130.3, 131.7, 132.8, 134.0, 136.1.0, 171.2. (*E*)-*N*-(4-Methylbenzylidene)-4-methylbenzenesulfonamide (Table 2, entry 5). White powder; m.p. 110–113 °C (Lit. [16] m.p. 112–114 °C); ^{1}H-NMR ($CDCl_3$): δ 2.42 (s, 6H), 7.26 (d, J = 7.5 Hz, 2H), 7.34 (d, J = 7.8 Hz, 2H), 7.82 (d, J = 7.5 Hz, 2H), 7.90 (d, J = 7.5 Hz, 2H), 8.96 (s, 1H). ^{13}C NMR($CDCl_3$): δ 22.0, 126.8, 128.4, 129.9, 130.2, 130.3, 131.8, 135.7, 144.9, 170.4. (*E*)-*N*-(4-Chlorobenzylidene)-4-methylbenzenesulfonamide (Table 2, entry 8). White needles; m.p. 169–172 °C (Lit. [16] m.p. 171–

173 °C); ^{1}H NMR ($CDCl_3$): δ 2.46 (s, 3H), 7.15 (d, J = 9.1 Hz, 2H), 7.38 (d, J = 9.0 Hz, 2H), 7.86 (d, J = 8.9 Hz, 4H), 9.01 (s, 1H). ^{13}C NMR ($CDCl_3$): δ 22.0, 128.5, 129.9, 130.2, 131.2, 132.7, 135.3, 141.8, 145.2, 169.0. (*E*)-*N*-(2-Oxoindolin-3-ylidene)benzenesulfonamide (Table 2, entry 15). Orange solid; m.p. 142–144 °C (Lit. [22] m.p. 144–145 °C); ^{1}H NMR (DMSO-d_6): δ 6.89 (m, 1H), 7.05 (m, 1H), 7.34 (m, 2H), 7.48 (m, 1H), 7.56 (m, 2H), 7.84 (m, 2H), 11.00 (s, 1H); ^{13}C NMR (DMSO-d_6): δ 112.2, 117.8, 122.7, 124.6, 125.5, 128.8, 131.7, 138.3, 144.1, 150.7, 159.3, 184.3.