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Aza-Wacker-Type Reaction between Electron-Deficient Olefins and *N*-Alkylsulfonamides

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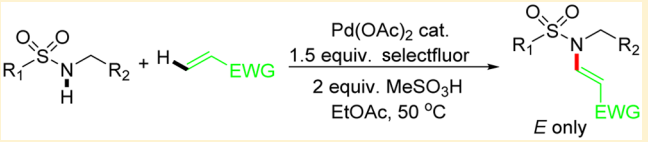
Supporting Information

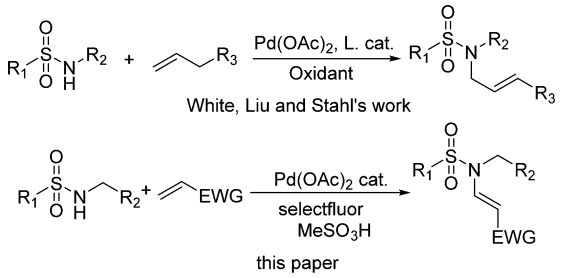
ABSTRACT: A palladium-catalyzed oxidative amination protocol of electron-deficient olefins by aza-Wacker-type reaction with *N*-alkylsulfonamides was developed. The presence of the stoichiometric amount of methanesulfonic acid was crucial for the success of this transformation. The reactions were conducted in green solvent under mild conditions and scalable with excellent *E*-type stereoselectivity. In addition, a Pd(II)/Pd(0) catalytic cycle with the existence of a very strong oxidant (Selectfluor) was proposed.



Many therapeutically important agents contain the structure of sulfonamides, for example, antibacterial sulfonamides and anticonvulsant sultiame.[1] Moreover, they are also important protected intermediates of primary and secondary amines with interesting biological activities.[2] On the other hand, Pd(II)-catalyzed oxidative amination of olefins, also called aza-Wacker reaction, has been the topic of intensive investigations.[3] Currently, the Pd(II)-catalyzed intermolecular aza-Wacker-type reactions are utilized to amines, amides, and nitrogen-containing heterocycles such as pyrroles, quinolines, and carbazoles.[4] In addition, the allylic amination of olefins with sulfonamides was reported by several groups.[5] Although significant progress of intramolecular aza-Wacker reaction has been achieved recently,[6] however, the same reaction with sulfonamides in an intermolecular way is less explored.[7] Therefore, the investigation of an efficient catalytic system for this reaction is highly desirable. As a follow-up of our reported methods,[8] we herein report a novel catalytic system for intermolecular aza-Wacker reaction between sulfonamides and electron-deficient olefins (Scheme 1).

In the preliminary study, *N*-benzyl-4-methylbenzenesulfonamide **1a** (0.20 mmol) and methyl acrylate **2a** (2.0 equiv) with palladium acetate (10%) as catalyst and 1,2-dichloroethane as solvent were chosen as our model system. As shown in Table 1, the yield of the proposed product **3aa** reached 29% using Selectfluor {1-chloromethyl-4-fluoro-1,4-diazoniabicyclo[2.2.2]octane bis(tetrafluoroborate), 1.5 equiv} as oxidant, which was superior than other oxidants (Table 1, entry 1 vs 2). The structure of **3aa** was confirmed by CCDC (see the Supporting Information).[9] When methanesulfonic acid (2.0 equiv) was added as an additive, the yield was increased to 66%. Other additives, however, were less efficient than methanesulfonic acid (entries 3−5). Regarding solvent and catalyst, methyl acetate and palladium acetate were found to be the most efficient for this transformation (entries 6−9). Noteworthy, when a lesser amount of methanesulfonic acid was added, the reaction time would be longer (entry 10, lower yield due to low conversion rate of **1a**). The optimal yield (89%) was achieved by using 5% palladium acetate as catalyst, 1.0 mL of methyl acetate as solvent, and heating under 50 °C for 10 h (Table 1, entry 14). Meanwhile, a little amount of **3ab** was formed through acid-catalyzed transesterification by using ethyl acetate as a solvent. Furthermore, under Elliott's reaction conditions,[7] the yield of **3aa** was only 42% (entry 15).

Scheme 1. Different Reaction Modes between Olefins and Sulfonamides



To explore the effect of different sulfonyl groups, an array of sulfonyl derivatives of benzylamine were reacted with **2b** (or **2a**) under standard conditions. As shown in Scheme 2, the electronic effect (electron-donating or electron-withdrawing) of sulfonyl groups had a significant effect on the yield of cross-coupling product. The *p*-toluenesulfonyl group was found most

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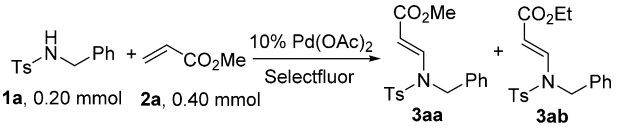
Table 1. Optimization of Reaction Conditions

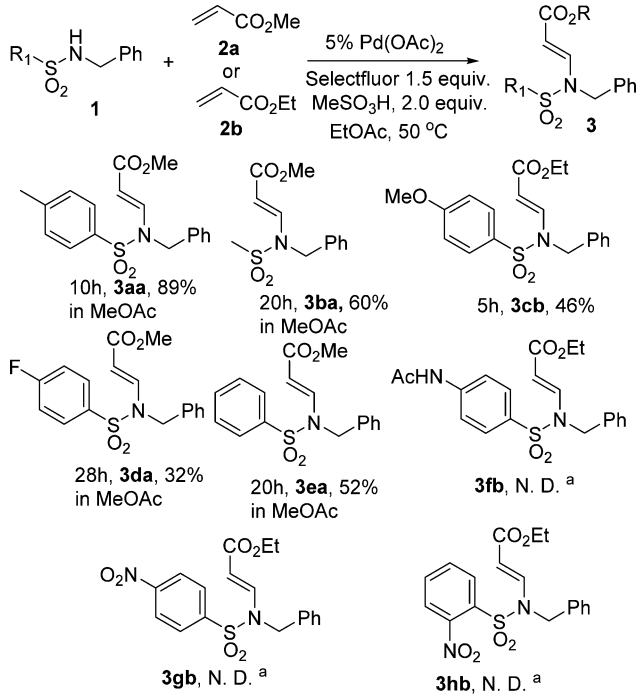


1a, 0.20 mmol 2a, 0.40 mmol

entry	additive, mmol	temp (°C)	time (h)	solvent	yield (%)[a]
1	TFA[b], 0.60	r.t.[c]	24	DCE[d]	29
2[e]	TFA, 0.60	r.t.−80	24	DCE	<10
3	$NaHCO_3$, 0.60	r.t.	24	DCE	0
4	$MeSO_3H$, 0.40	r.t.	24	DCE	66
5	other acids[f], 0.40	r.t.	24	DCE	0−41
6	$MeSO_3H$, 0.40	r.t.	10	DCE	41
7	$MeSO_3H$, 0.40	r.t.	10	EtOAc	70
8	$MeSO_3H$, 0.40	r.t.	10	other solvent[g]	21−55
9[h]	$MeSO_3H$, 0.40	r.t.	10	EtOAc	13−42
10	$MeSO_3H$, 0.04	r.t.	10	EtOAc	29
11	$MeSO_3H$, 0.20	r.t.	10	EtOAc	50
12	$MeSO_3H$, 1.0	r.t.	10	EtOAc	43
13[i]	$MeSO_3H$, 0.40	50	10	EtOAc	86
14[i]	**$MeSO_3H$, 0.40**	**50**	**10**	**MeOAc**	**89**
15[j]	no addition	40	24	DME[k]	42

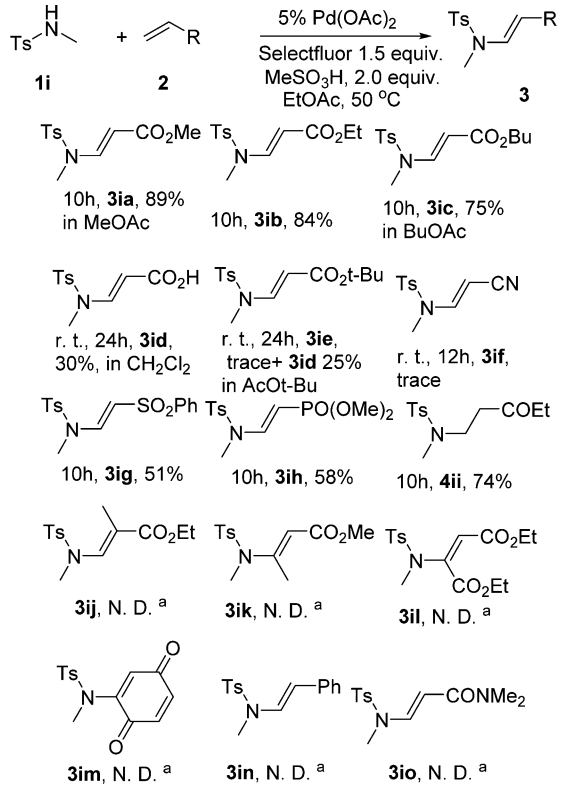
[a]Isolated yield. [b]2,2,2-Trifluoroacetic acid. [c]Room temperature. [d]1,2-Dichloroethane. [e]Other oxidants examined included copper oxide, silver oxide, sodium persulfate, and *N*-fluoro-*N*-(phenylsulfonyl)benzenesulfonamide. [f]Other acids examined included acetic acid, pivalic acid, trifluoromethanesulfonic acid, 4-methylbenzenesulfonic acid, 2,6-difluorobenzoic acid. [g]Other solvents include 1,2-dimethoxyethane, acetonitrile, dichloromethane, 1,4-dioxane, toluene, and dimethyl carbonate. [h]Other catalysts were applied, include palladium oxide, palladium chloride, and bis(2,2,2-trifluoroacetoxy)palladium. [i]5% palladium acetate was used. [j]Standard reaction condition of Elliott's work. [k]1,2-Dimethoxyethane.

Scheme 2. Effect of Sulfonyl Group



[a]N. D. = not detected.

Scheme 3. Scope of Olefins



[a]N. D. = not detected.

efficient for this transformation. Meanwhile, nitrobenzenesulfonyl and *p*-acetamino-benzenesulfonyl groups were ineffective (Scheme 2).

As regarding the substrate scope of electron-deficient olefins, a series of olefins coupled with **1i** were studied under standard conditions (Scheme 3). Acrylates gave good yields; however, its derivatives, such as acrylonitrile, etc., did not give the corresponding product or just gave a poor yield. Moreover, (vinylsulfonyl)benzene (**2g**) and dimethyl vinylphosphonate (**2h**) were able to form the corresponding product in moderate yields. Surprisingly, pent-1-en-3-one (**2i**) gave the Michael

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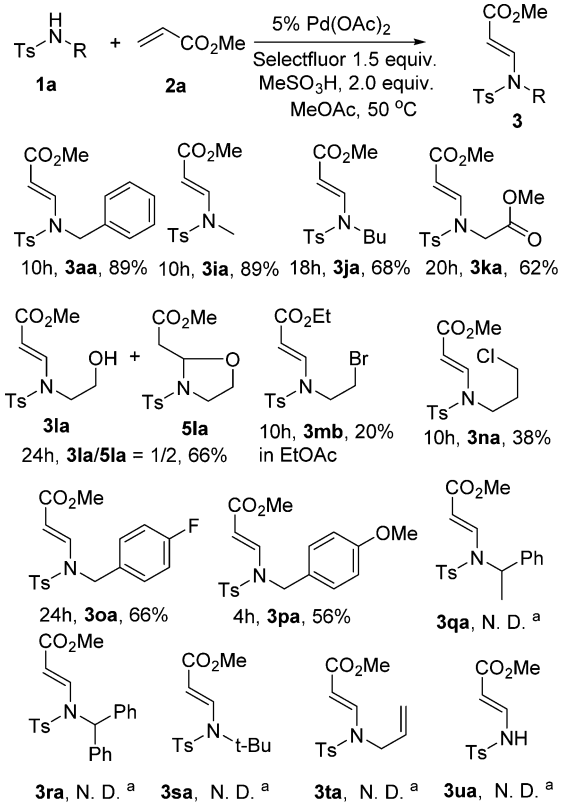
addition product **4ii** instead of the proposed cross-coupling product **3ii**. Furthermore, styrene failed to give any corresponding product under standard conditions.

To study the substrate scope of amines, *p*-toluenesulfonyl derivatives of different amines were coupled with **2a** under standard conditions (Scheme 4). As shown in Scheme 4,

Scheme 4. Scope of Amines

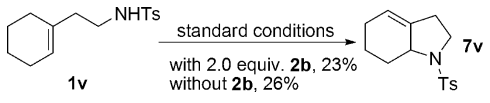


[a]N. D. = not detected.

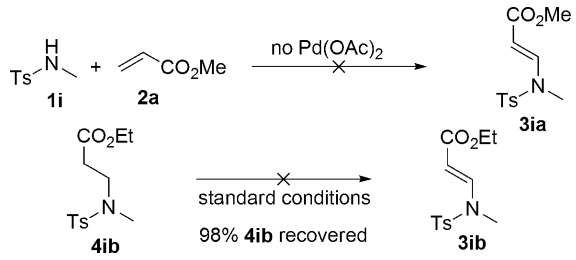
toluenesulfonyl derivatives of amines were reacted with **2a** and generated the corresponding cross-coupling product smoothly. Unfortunately, toluenesulfonamide (**1u**) and *N*-allyl-4-methylbenzenesulfonamide (**1t**) were unstable and easy to undergo decomposition under optimal reaction conditions. Moreover, highly hindered substrates (**1q**−**1s**) were unreactive and did not give any designed products. Furthermore, *N*-(2-hydroxyethyl)-4-methylbenzenesulfonamide (**1l**) gave the mixture of linear and cyclic isomers with the ratio of 1/2 based on the analysis of ^{1}H NMR. In addition, *N*-(2-(cyclohex-1-en-1-yl)ethyl)-4-methylbenzenesulfonamide (**1v**) only gave intramolecular allylic amination product (**7v**) with or without ethyl acrylate **2b** (Scheme 5). The structure of **7v** was confirmed by CCDC.[10]

To reveal the reaction mechanism, some control experiments were conducted (Scheme 6). No **3ia** was detected under standard reaction conditions in the absence of palladium acetate, indicating that the palladium catalyst is crucial for the

Scheme 5. Intramolecular Allylic Amination of 1v



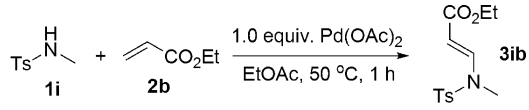
Scheme 6. Control Experiments



transformation. Meanwhile, the Michael addition product **4ib** was nearly fully recovered (98%) under standard reaction conditions, and no **3ib** was detected. These results ruled out the reaction pathway of Michael addition, followed by oxidative dehydrogenation.

To reveal the nature of the catalyst, experiments with stoichiometric palladium in the absence of oxidant were conducted (Scheme 7). Only 2% of **3ib** was detected by ^{1}H

Scheme 7. Equivalent Experiments



NMR, when the mixture of **1i**, **2b**, and palladium acetate (1.0 equiv) was heated at 50 °C for 1 h. However, under the same conditions, except adding 2.0 equiv of methanesulfonic acid as additive, 59% of **3ib** was detected after 1 h. These results suggested a Pd(II)/Pd(0) catalytic cycle mechanism and indicated that palladium methanesulfonate may be the real catalyst.

To understand the interaction between palladium and substrates, some reactions were conducted in NMR tubes using $CDCl_3$ as solvent. Even after mixed with palladium acetate at room temperature for 22 h, the ^{1}H NMR peaks of **1i** did not change much. However, these peaks changed immediately after 0.20 mmol of methanesulfonic acid was added (details in the Supporting Information). The ^{1}H NMR spectra of palladium acetate with methanesulfonic acid and palladium acetate with methyl acrylate are presented in the Supporting Information. Palladium acetate reacted with methanesulfonic acid to give a yellow precipitate (should be palladium methanesulfonate) and acetic acid, which is confirmed by ^{1}H NMR. In addition, no interaction between palladium acetate and methyl acrylate is observed by ^{1}H NMR. These results confirmed the interaction between the palladium salt and sulfonamide **1i** in the presence of methanesulfonic acid.

On the basis of results above, we proposed the reaction mechanism as shown in Scheme 8. First, palladium methanesulfonate (**8**) was formed by anion exchange (details in the Supporting Information), and then **8** reacted with **1** to form intermediate **9** through metallization. Then, **9** coordinated with **2** and further transformed to product (**3**) through insertion and *β*-hydrogen elimination and released [(methylsulfonyl)oxy]palladium(II) hydride (**11**). At last, the **11** or Pd(0) was oxidized to **8** by Selectfluor in the presence of methanesulfonic acid to finish the catalytic cycle.

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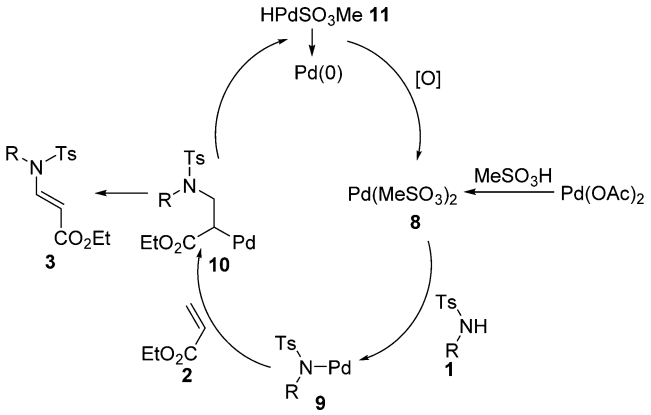
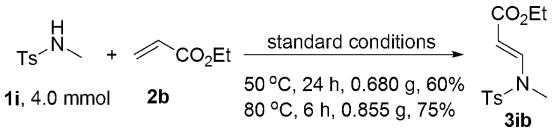
Scheme 8. Proposed Reaction Mechanism



To demonstrate the synthetic utility of this method, the reaction was performed on a 4 mmol scale, producing **3ib** in 60% yield (50 °C, 24 h, 0.680 g) and 75% yield (80 °C, 6 h, 0.855 g; Scheme 9).

Scheme 9. Gram-Scale Experiments



In summary, a palladium-catalyzed aza-Wacker reaction between *N*-alkylsulfonamides and electron-deficient olefins using green solvent was developed. The presence of the stoichiometric amount of methanesulfonic acid was crucial for the success of this transformation. Only the *E* isomer was formed, and a wide range of functional groups were tolerated in this reaction. In addition, a Pd(II)/Pd(0) catalytic cycle with the existence of a very strong oxidant (Selectfluor) was proposed. To conclude, the versatility of the sulfonamide moiety should render this protocol highly attractive for both synthetic and medicinal chemistry.

EXPERIMENTAL SECTION

General Methods. Unless otherwise noted, all commercial reagents and solvents were obtained from the commercial provider and used without further purification. ^{1}H NMR, ^{19}F NMR, ^{31}P NMR, and ^{13}C NMR spectra were recorded on 400 MHz spectrometers. Chemical shifts were reported relative to internal tetramethylsilane (δ 0.00 ppm) or $CDCl_3$ (δ 7.26 ppm) for ^{1}H NMR and $CDCl_3$ (δ 77.0 ppm) for ^{13}C NMR. Flash column chromatography was performed on 300−400 mesh silica gels. Analytical thin layer chromatography was performed with precoated glass baked plates (250 μ) and visualized by fluorescence. HRMS were recorded on a TOF-Q spectrometer. Substrates were synthesized according to the literature (**1a**−**1h**, **1j**, **1o**−**1t**, **1v**;[11] **1k**;[12] **1l**;[13] **1m**, **1n**[14]).

General Procedure for Oxidative Amination of Electron-Deficient Olefins with *N*-Alkylsulfonamides. *N*-Alkylsulfonamide (0.20 mmol), electron-deficient olefin (0.40 mmol), palladium acetate (2.2 mg, 0.01 mmol), methanesulfonic acid (26 μL, 0.40 mmol), Selectfluor (110 mg, 0.30 mmol), and 1.0 mL of ethyl acetate (or other solvent indicate in paper) were added to a reaction tube under air. Then, the mixture was stirred at 50 °C. The reaction was monitored by TLC. When the reaction finished, the mixture was cooled down to room temperature, poured into water, and extracted with $CHCl_3$ (10 mL × 3). The organic layers were combined and washed with saturated sodium bicarbonate and brine and dried with Na_2SO_4 and filtered. Then, the mixture was evaporated under vacuum and the crude mixture was purified by flash chromatography (silica gel, eluted by petroleum ether/ethyl acetate or petroleum ether/chloroform).

Procedure for the Equivalent Experiments. *N*,4-Dimethylbenzenesulfonamide (19 mg, 0.10 mmol), ethyl acrylate (21 μL, 0.20 mmol), palladium acetate or palladium oxide (0.10 mmol), and 0.50 mL of ethyl acetate with or without methanesulfonic acid (13 μL, 0.20 mmol) were added to a reaction tube under air. Then, the mixture was stirred at 50 °C for 1 h. Then, the mixture was cooled down to room temperature, poured into water, and extracted with $CHCl_3$ (10 mL × 3). The organic layers were combined and washed with saturated sodium bicarbonate and brine and dried with Na_2SO_4 and filtered. Then, the mixture was evaporated under vacuum. Then, the crude mixture was analyzed by ^{1}H NMR with *N*,*N*-dimethylacetamide (10.0 μL) as internal standard.

Procedure for the Gram-Scale Experiments. *N*,4-Dimethylbenzenesulfonamide (741 mg, 4.0 mmol), ethyl acrylate (0.87 mL, 8.0 mmol), palladium acetate (45 mg, 0.20 mmol), methanesulfonic acid (0.53 mL, 8.0 mmol), Selectfluor (2.17 g, 6.0 mmol), and 20 mL of ethyl acetate were added to a reaction tube under air. Then, the mixture was stirred at 50 °C for 24 h or at 80 °C for 6 h. Then, the mixture was cooled down to room temperature, poured into water, and extracted with $CHCl_3$ (30 mL × 3). The organic layers were combined and washed with saturated sodium bicarbonate and brine and dried with Na_2SO_4 and filtered. Then, the mixture was evaporated under vacuum and the crude mixture was purified by flash chromatography (silica gel, eluted by petroleum ether/ethyl acetate = 6/1).

Characteristic Data of New Compounds. *(E)-Methyl 3-(N-Benzylmethylsulfonamido)acrylate (**3ba**).* This compound was obtained as a white solid (32.3 mg, 60%) by following the general procedure: mp 89−91 °C; ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.01 (d, J = 14.0 Hz, 1H), 7.40−7.33 (m, 2H), 7.33−7.28 (m, 3H), 5.17 (d, J = 14.0 Hz, 1H), 4.79 (s, 2H), 3.69 (s, 3H), 2.97 (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 167.1, 141.6, 134.0, 129.0, 128.2, 127.0, 99.4, 51.4, 49.8, 41.0; IR (NaCl): 3029, 2951, 2930, 1705, 1627, 1456, 1362; HRMS (ESI): m/z calcd for $C_{12}H_{15}NO_4S$: 292.0614 $[M + Na]^+$, found: 292.0613.

*(E)-Ethyl 3-(N-Benzyl-4-methoxyphenylsulfonamido)acrylate (**3cb**).* This compound was obtained as a colorless sticky oil (34.5 mg, 46%) by following the general procedure; ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.19 (d, J = 14.0 Hz, 1H), 7.82−7.72 (m, 2H), 7.35−7.28 (m, 3H), 7.25−7.19 (m, 2H), 7.04−6.95 (m, 2H), 4.99 (d, J = 14.0 Hz, 1H), 4.63 (s, 2H), 4.14 (q, J = 7.1 Hz, 2H), 3.90 (s, 3H), 1.25 (t, J = 7.1 Hz, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 167.0, 163.8, 141.6, 134.1, 129.6, 129.4, 128.8, 127.8, 126.7, 114.8, 99.5, 60.1, 55.7, 49.7, 14.3; IR (NaCl): 3065, 2979, 1705, 1624, 1595, 1497, 1456, 1363; HRMS (ESI): m/z calcd for $C_{19}H_{21}NO_5S$: 398.3933 $[M + Na]^+$, found: 398.3938.

*(E)-Methyl 3-(N-Benzyl-4-fluorophenylsulfonamido)acrylate (**3da**).* This compound was obtained as a white solid (23.3 mg, 32%) by following the general procedure: mp 91−92 °C; ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.17 (d, J = 14.0 Hz, 1H), 7.89−7.80 (m, 2H), 7.32−7.26 (m, 3H), 7.23−7.16 (m, 4H), 5.06 (d, J = 14.0 Hz, 1H), 4.66 (s, 2H), 3.70 (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 167.1, 165.7 (J = 255.7), 141.4, 134.4 (J = 3.3), 133.6, 130.0 (J = 9.5), 128.9, 128.0, 126.7, 116.9 (J = 22.7), 100.0, 51.5, 49.9; ^{19}F NMR (376 MHz, $CDCl_3$) δ −102.79; IR (KBr): 3101, 3067, 2954, 2921, 2850, 1719, 1634, 1590, 1493, 1456, 1366; HRMS (ESI): m/z calcd for $C_{18}H_{18}FNO_4S$: 386.0833 $[M + Na]^+$, found: 386.0838.

*(E)-Methyl 3-(N-Benzylphenylsulfonamido)acrylate (**3ea**).* This compound was obtained as a white solid (34.5 mg, 52%) by following the general procedure: mp 121−123 °C; ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.18 (d, J = 14.0 Hz, 1H), 7.87−7.79 (m, 2H), 7.68−7.60 (m, 1H), 7.54 (dd, J = 8.5, 7.1 Hz, 2H), 7.32−7.27 (m, 2H), 7.24 (d, J = 7.2 Hz, 1H), 7.22−7.15 (m, 2H), 5.00 (d, J = 14.0 Hz, 1H), 4.63 (s, 2H), 3.66 (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 167.2, 141.7, 138.4, 133.79, 133.76, 129.6, 128.8, 127.9, 127.2, 126.7, 99.7, 51.4, 49.9; IR (NaCl): 3065, 2950, 2922, 1715, 1627, 1447, 1367; HRMS (ESI): m/z calcd for $C_{17}H_{17}NO_4S$: 354.0771 $[M + Na]^+$, found: 354.0779.

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*(E)-Methyl 3-(N,4-Dimethylphenylsulfonamido)acrylate (**3ia**).* This compound was obtained as a white solid (48.0 mg, 89%) by following the general procedure: mp 39−41 °C; ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.18 (d, J = 13.8 Hz, 1H), 7.70 (d, J = 8.0 Hz, 2H), 7.36 (d, J = 8.0 Hz, 2H), 5.05 (d, J = 13.8 Hz, 1H), 3.75 (s, 3H), 2.97 (s, 3H), 2.46 (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 167.4, 144.9, 142.9, 134.5, 130.2, 127.1, 98.2, 51.4, 32.2, 21.6; IR (NaCl): 3094, 2952, 1715, 1623, 1435, 1367; HRMS (ESI): m/z calcd for $C_{12}H_{15}NO_4S$: 292.0614 [M + Na]$^+$, found: 292.0620.

*(E)-Ethyl 3-(N,4-Dimethylphenylsulfonamido)acrylate (**3ib**).* This compound was obtained as a white solid (0.20 mmol, 47.6 mg, 84%; 4.0 mmol, 50 °C, 24 h, 0.680 g, 60%; 4.0 mmol, 80 °C, 6 h, 0.855 g, 75%) by following the general procedure: mp 73−75 °C; ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.15 (d, J = 13.8 Hz, 1H), 7.68 (d, J = 7.8 Hz, 2H), 7.34 (d, J = 7.9 Hz, 2H), 5.04 (d, J = 13.8 Hz, 1H), 4.19 (q, J = 7.1 Hz, 2H), 2.96 (s, 3H), 2.44 (s, 3H), 1.29 (t, J = 7.0 Hz, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 166.9, 144.8, 142.6, 134.5, 130.2, 127.1, 98.7, 60.1, 32.2, 21.6, 14.4; IR (NaCl): 3094, 2980, 2929, 1737, 1715, 1622, 1597, 1456, 1363; HRMS (ESI): m/z calcd for $C_{13}H_{17}NO_4S$: 306.0771 [M + Na]$^+$, found: 306.0777.

*(E)-Butyl 3-(N,4-Dimethylphenylsulfonamido)acrylate (**3ic**).* This compound was obtained as a colorless sticky oil (46.7 mg, 75%) by following the general procedure; ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.15 (d, J = 13.8 Hz, 1H), 7.69 (d, J = 7.9 Hz, 2H), 7.35 (d, J = 7.9 Hz, 2H), 5.05 (d, J = 13.8 Hz, 1H), 4.14 (t, J = 6.6 Hz, 2H), 2.96 (s, 3H), 2.45 (s, 3H), 1.70- 1.60 (m, 2H), 1.46- 135 (m, 2H), 0.95 (t, J = 7.3 Hz, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 167.0, 144.8, 142.6, 134.5, 130.2, 127.1, 98.7, 64.1, 32.2, 30.8, 21.6, 19.2, 13.8; IR (NaCl): 3094, 2960, 2874, 1714, 1626, 1597, 1457, 1367; HRMS (ESI): m/z calcd for $C_{15}H_{21}NO_4S$: 334.1084 [M + Na]$^+$, found: 334.1087.

*(E)-3-((N,4-Dimethylphenyl)sulfonamido)acrylic acid (**3id**).* This compound was obtained as a white solid (15.3 mg, 30%) by following the general procedure: mp 133−135 °C; ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.26 (d, J = 13.7 Hz, 1H), 7.72 (d, J = 8.0 Hz, 2H), 7.37 (d, J = 7.9 Hz, 2H), 5.05 (d, J = 13.7 Hz, 1H), 3.00 (s, 3H), 2.47 (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 172.2, 145.0, 144.7, 134.4, 130.2, 127.2, 97.3, 32.2, 29.7; IR (NaCl): 3099, 2963, 1682, 1621, 1600, 1433, 1367, 1352; HRMS (ESI): m/z calcd for $C_{11}H_{13}NO_4S$: 278.0458 [M + Na]$^+$, found: 278.0458.

*(E)-N,4-Dimethyl-N-(2-(phenylsulfonyl)vinyl)benzenesulfonamide (**3ig**).* This compound was obtained as a white solid (35.8 mg, 51%) by following the general procedure: mp 147−149 °C; ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.18 (d, J = 13.4 Hz, 1H), 7.90 (d, J = 7.6 Hz, 2H), 7.72 (d, J = 8.2 Hz, 2H), 7.61 (t, J = 7.2 Hz, 1H), 7.54 (t, J = 7.5 Hz, 2H), 7.38 (d, J = 8.1 Hz, 2H), 5.52 (d, J = 13.4 Hz, 1H), 2.93 (s, 3H), 2.47 (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 145.4, 142.0, 141.7, 134.0, 133.0, 130.4, 129.3, 127.3, 127.1, 107.8, 32.5, 21.7; IR (NaCl): 3077, 2928, 1614, 1447, 1367; HRMS (ESI): m/z calcd for $C_{16}H_{17}NO_4S_2$: 374.0492 [M + Na]$^+$, found: 374.0493.

*(E)-Dimethyl (2-(N,4-Dimethylphenylsulfonamido)vinyl)phosphonate (**3ih**).* This compound was obtained as a colorless sticky oil (37.0 mg, 58%) by following the general procedure; ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.82 (dd, J = 16.5, 15.4 Hz, 1H), 7.69 (d, J = 8.2 Hz, 2H), 7.35 (d, J = 8.1 Hz, 2H), 4.57 (dd, J = 15.2, 11.4 Hz, 1H), 3.73 (d, J = 11.2 Hz, 6H), 2.95 (s, 3H), 2.44 (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 144.9, 144.8 (J = 19.5), 134.5, 130.2, 127.1, 89.7 (J = 202.7), 52.4 (J = 5.6), 31.7, 21.6; ^{31}P NMR ($CDCl_3$, 162 MHz) δ 23.8; IR (NaCl): 2953, 2871, 1614, 1457, 1362; HRMS (ESI): m/z calcd for $C_{12}H_{18}NO_5PS$: 342.0536 [M + Na]$^+$, found: 342.0547.

*N,4-Dimethyl-N-(3-oxopentyl)benzenesulfonamide (**4ii**).* This compound was obtained as a colorless sticky oil (39.9 mg, 74%) by following the general procedure; ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.68 (d, J = 8.2 Hz, 2H), 7.33 (d, J = 8.1 Hz, 2H), 3.27 (t, J = 7.0 Hz, 2H), 2.80- 2.73 (m, 5H), 2.48 (t, J = 7.3 Hz, 2H), 2.44 (s, 3H), 1.07 (t, J = 7.3 Hz, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 209.5, 143.5, 134.1, 129.8, 127.5, 45.4, 41.6, 36.3, 36.1, 21.5, 7.6; IR (NaCl): 2977, 2938, 1715, 1597, 1457, 1378, 1339; HRMS (ESI): m/z calcd for $C_{13}H_{19}NO_3S$: 292.0978 [M + Na]$^+$, found: 292.0986.

*Methyl (E)-3-((N-Butyl-4-methylphenyl)sulfonamido)acrylate (**3ja**).* This compound was obtained as a white solid (42.4 mg, 68%) by following the general procedure: mp 71−72 °C; ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.12 (d, J = 14.0 Hz, 1H), 7.71 (d, J = 8.0 Hz, 2H), 7.35 (d, J = 8.0 Hz, 2H), 5.08 (d, J = 14.0 Hz, 1H), 3.75 (s, 3H), 3.42−3.30 (m, 2H), 2.46 (s, 3H), 1.57 (t, J = 7.9 Hz, 2H), 1.40−1.24 (m, 2H), 0.92 (t, J = 7.4 Hz, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 167.6, 144.7, 142.0, 135.5, 130.1, 127.1, 97.4, 51.4, 46.0, 28.7, 21.6, 20.0, 13.6; IR (NaCl): 2958, 2875, 1715, 1622, 1457, 1367; HRMS (ESI): m/z calcd for $C_{15}H_{21}NO_4S$: 334.1084 [M + Na]$^+$, found: 334.1089.

*(E)-Methyl 3-(N-(2-Methoxy-2-oxoethyl)-4-methylphenylsulfonamido)acrylate (**3ka**).* This compound was obtained as a white solid (40.6 mg, 62%) by following the general procedure: mp 146−148 °C; ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.10 (d, J = 13.9 Hz, 1H), 7.76 (d, J = 8.0 Hz, 2H), 7.37 (d, J = 8.0 Hz, 2H), 4.95 (d, J = 14.0 Hz, 1H), 4.30 (s, 2H), 3.73 (s, 3H), 3.65 (s, 3H), 2.46 (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 167.0, 166.8, 145.2, 141.5, 135.0, 130.0, 127.6, 98.4, 52.7, 51.5, 46.7, 21.7; IR (KBr): 3104, 2953, 2849, 1753, 1717, 1630 1598, 1498, 1428, 1375, 1301; HRMS (ESI): m/z calcd for $C_{14}H_{17}NO_6S$: 350.0669 [M + Na]$^+$, found: 350.0678.

*Ethyl (E)-3-((N-(2-Bromoethyl)-4-methylphenyl)sulfonamido)-acrylate (**3mb**).* This compound was obtained as a white solid (15.0 mg, 20%) by following the general procedure: mp 68−70 °C; ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.04 (d, J = 14.1 Hz, 1H), 7.70 (d, J = 8.3 Hz, 2H), 7.35 (d, J = 8.0 Hz, 2H), 5.14 (d, J = 14.1 Hz, 1H), 4.19 (d, J = 7.1 Hz, 2H), 3.70 (dd, J = 9.2, 7.1 Hz, 2H), 3.39 (dd, J = 9.1, 7.1 Hz, 2H), 2.44 (s, 3H), 1.28 (t, J = 7.1 Hz, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 166.7, 145.3, 140.9, 134.8, 130.4, 127.2, 98.4, 60.4, 47.0, 25.5, 21.6, 14.4; IR(KBr): 3072, 2984, 2939, 1723, 1631, 1597, 1451, 1374; HRMS (ESI): m/z calcd for $C_{14}H_{18}BrNO_4S$: 398.0033 [M + Na]$^+$, found: 398.0042.

*(E)-Methyl 3-(N-(4-Fluorobenzyl)-4-methylphenylsulfonamido)-acrylate (**3oa**).* This compound was obtained as a white solid (48.0 mg, 66%) by following the general procedure: mp 93−94 °C; ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.18 (d, J = 13.9 Hz, 1H), 7.73 (d, J = 7.9 Hz, 2H), 7.36 (d, J = 7.9 Hz, 2H), 7.22 (dd, J = 8.3, 5.2 Hz, 2H), 7.01 (t, J = 8.5 Hz, 2H), 4.97 (d, J = 14.0 Hz, 1H), 4.58 (s, 2H), 3.69 (s, 3H), 2.47 (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 167.2, 162.3 (J = 245.2), 145.1, 141.6, 135.2, 130.2, 129.6 (J = 3.2), 128.5 (J = 8.1), 127.2, 115.8 (J = 21.6), 99.4, 51.4, 49.1, 21.7; ^{19}F NMR (376 MHz, $CDCl_3$) δ −114.24; IR (KBr): 3010, 3069, 2947, 2851, 1706, 1622, 1509, 1434, 1362; HRMS (ESI): m/z calcd for $C_{18}H_{18}FNO_4S$: 386.0833 [M + Na]$^+$, found: 386.0840.

*1-Tosyl-2,3,5,6,7,7a-hexahydro-1H-indole (**7v**).* This compound was obtained as a white solid (12.8 mg, 23%) by following the general procedure: mp 78−80 °C; ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.75 (d, J = 8.2 Hz, 2H), 7.34 (d, J = 7.9 Hz, 2H), 5.51 (t, J = 3.1 Hz, 1H), 3.60−3.50 (m, 1H), 3.43−3.35 (m, 1H), 3.34−3.26 (m, 1H), 2.57−2.48 (m, 1H), 2.45 (s, 3H), 2.30−2.20 (m, 1H), 2.10−1.96 (m, 3H), 1.89−1.80 (m, 1H), 1.55−1.30 (m, 2H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 143.3, 137.4, 134.6, 129.6, 127.6, 121.1, 58.7, 58.7, 47.6, 29.9, 24.3, 21.5, 20.2; IR (KBr): 3028, 2927, 1598, 1494, 1478, 1455, 1401, 1337; HRMS (ESI): m/z calcd for $C_{15}H_{19}NO_2S$: 300.1029 [M + Na]$^+$, found: 300.1034.

■ ASSOCIATED CONTENT

Supporting Information

The experimental procedure and ^{1}H NMR spectra for revealing the interaction between catalyst and substrates, NMR spectra for all new compounds, ^{1}H NMR spectra for known compounds, X-ray structures and CIF files of **3aa** and **7v**. This material is available free of charge via the Internet at http://pubs.acs.org.

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Notes

The authors declare no competing financial interest.

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■ REFERENCES

(1) (a) Kalgutkar, A.; Jones, R.; Sawant, A. In *Metabolism Pharmacokinetics and Toxicity of Functional Groups*; Smith, D. A., Ed.; RSC Drug Discovery Series No. 1; RSC: Cambridge, U.K., 2010; Chapter 5. (b) Chen, X.; Hussain, S.; Parveen, S.; Zhang, S.; Yang, Y.; Zhu, C. *Curr. Med. Chem.* **2012**, *19*, 3578−3604.

(2) Wuts, P. G. M.; Greene, T. W. In *Greene's Protective Groups in Organic Synthesis*, 4th ed.; John Wiley & Sons Inc: Hoboken, NJ, 2007; Chapter 7.

(3) For recent progress in aza-wacker reaction, see reviews: (a) Mu, X.; Liu, G. *RSC Catal. Ser.* **2013**, *11*, 363−408. (b) Kotov, V.; Scarborough, C. C.; Stahl, S. S. *Inorg. Chem.* **2007**, *46*, 1910−1923. (c) Minatti, A.; Muñiz, K. *Chem. Soc. Rev.* **2007**, *36*, 1142−1152. (d) Stahl, S. S. *Angew. Chem., Int. Ed.* **2004**, *43*, 3400−3420.

(4) (a) Timokhin, V. I.; Anastasi, N. R.; Stahl, S. S. *J. Am. Chem. Soc.* **2003**, *125*, 12996−12997. (b) Brice, J. L.; Harang, J. E.; Timokhin, V. I.; Anastasi, N. R.; Stahl, S. S. *J. Am. Chem. Soc.* **2005**, *127*, 2868−2869. (c) Timokhin, V. I.; Stahl, S. S. *J. Am. Chem. Soc.* **2005**, *127*, 17888−17893. (d) Rogers, M. M.; Kotov, V.; Chatwichien, J.; Stahl, S. S. *Org. Lett.* **2007**, *9*, 4331−4334. (e) Liu, X.; Hii, K. K. *Eur. J. Org. Chem.* **2010**, 5181−5189. (f) Panda, N.; Jena, A. K.; Raghavender, M. *ACS Catal.* **2012**, *2*, 539−543. (g) Takeda, D.; Hirano, K.; Satoh, T.; Miura, M. *Org. Lett.* **2013**, *15*, 1242−1245. (h) Mizuta, Y.; Yasuda, K.; Obora, Y. *J. Org. Chem.* **2013**, *78*, 6332−6337. (i) Hosokawa, T.; Takano, M.; Kuroki, Y.; Murahashi, S. *Tetrahedron Lett.* **1992**, *33*, 6643−6646. (j) Lee, J. M.; Ahn, D.; Jung, D. Y.; Lee, J.; Do, Y.; Kim, S. K.; Chang, S. *J. Am. Chem. Soc.* **2006**, *128*, 12954−12962.

(5) (a) Reed, S. A.; White, M. C. *J. Am. Chem. Soc.* **2008**, *130*, 3316−3318. (b) Wu, L.; Qiu, S.; Liu, G. *Org. Lett.* **2009**, *11*, 2707−2710. (c) Liu, G.; Yin, G.; Wu, L. *Angew. Chem., Int. Ed.* **2008**, *47*, 4733−4736. (d) Scarborough, C. C.; Stahl, S. S. *Org. Lett.* **2006**, *8*, 3251−3254. (e) Reed, S. A.; Mazzotti, A. R.; White, M. C. *J. Am. Chem. Soc.* **2009**, *131*, 11701−11706. (f) Rajabi, J.; Lorion, M. M.; Ly, V. L.; Liron, F.; Oble, J.; Prestat, G.; Poli, G. *Chem.—Eur. J.* **2014**, *20*, 1539−1546.

(6) (a) Larock, R. C.; Hightower, T. R.; Hasvold, L. A.; Peterson, K. P. *J. Org. Chem.* **1996**, *61*, 3584−3585. (b) Fix, S. R.; Brice, J. L.; Stahl, S. S. *Angew. Chem., Int. Ed.* **2002**, *41*, 164−166. (c) Liu, G.; Stahl, S. S. *J. Am. Chem. Soc.* **2007**, *129*, 6328−6335. (d) Fraunhoffer, K. J.; White, M. C. *J. Am. Chem. Soc.* **2007**, *129*, 7274−7276. (e) Rice, G. T.; White, M. C. *J. Am. Chem. Soc.* **2009**, *131*, 11707−11711. (f) Qi, X.; Rice, G. T.; Lall, M. S.; Plummer, M. S.; White, M. C. *Tetrahedron* **2010**, *66*, 4816−4826. (g) Jiang, F.; Wu, Z.; Zhang, W. *Tetrahedron Lett.* **2010**, *51*, 5124−5126. (h) Ye, X.; Liu, G.; Popp, B. V.; Stahl, S. S. *J. Org. Chem.* **2011**, *76*, 1031−1044. (i) White, P. B.; Stahl, S. S. *J. Am. Chem. Soc.* **2011**, *133*, 18594−18597. (j) Paradine, S. M.; White, M. C. *J. Am. Chem. Soc.* **2012**, *134*, 2036−2039. (k) Jiang, C.; Covell, D. J.; Stepan, A. F.; Plummer, M. S.; White, M. C. *Org. Lett.* **2012**, *14*, 1386−1389. (l) Weinstein, A. B.; Stahl, S. S. *Angew. Chem., Int. Ed.* **2012**, *51*, 11505−11509. (m) Mazgarova1, G. G.; Skladchikov, D. A.; Nikolaev, V. P.; Gataullin, R. R. *Chem. Heterocycl. Compd.* **2013**, *49*, 739−747. (n) McDonald, R. I.; White, P. B.; Weinstein, A. B.; Tam, C. P.; Stahl, S. S. *J. Org. Chem.* **2013**, *78*, 2083−2090.

(7) Elliott, L. D.; Wrigglesworth, J. W.; Cox, B.; Lloyd-Jones, G. C.; Booker-Milburn, K. I. *Org. Lett.* **2011**, *13*, 728−731.

(8) (a) Hu, H.; Liu, Y.; Zhong, H.; Zhu, Y.; Wang, C.; Ji, M. *Chem.—Asian J.* **2012**, *7*, 884−888. (b) Hu, H.; Liu, Y.; Xu, J.; Kan, Y.; Wang, C.; Ji, M. *RSC Adv.* **2014**, *4*, 24389−24393.

(9) CCDC 1017862 (**3aa**) can be obtained from http://www.ccdc.cam.ac.uk/data_request/cif.ed.

(10) CCDC 1032578 (**7v**) can be obtained from http://www.ccdc.cam.ac.uk/data_request/cif.ed.

(11) Heffernan, S. J.; Beddoes, J. M.; Mahon, M. F.; Hennessy, A. J.; Carbery, D. R. *Chem. Commun.* **2013**, *49*, 2314−2316.

(12) Zhang, W.; Xu, H.; Xu, H.; Tang, W. *J. Am. Chem. Soc.* **2009**, *131*, 3832−3833.

(13) Fukudome, Y.; Naito, H.; Hata, T.; Urabe, H. *J. Am. Chem. Soc.* **2008**, *130*, 1820−1821.

(14) Schirrmacher, R.; Mathiasch, B.; Schirrmacher, E.; Radnic, D.; Rösch, F. *J. Labelled Compd. Radiopharm.* **2003**, *46*, 959−977.

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