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Aluminum Chloride Promoted Hantzsch Reaction of *N*-Tosylhydrazones

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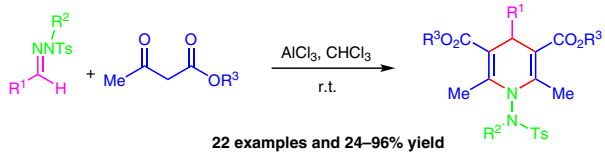

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Abstract An aluminum chloride promoted Hantzsch reaction of *N*-tosylhydrazones has been developed. The reaction is general for a wide range of *N*-tosylhydrazones, and a series of 1,4-dihydropyridines (1,4-DHPs) were prepared in moderate to excellent yields.

Key words synthetic method, aluminum chloride, Hantzsch reaction, *N*-tosylhydrazones, 1,4-dihydropyridines

Since Hantzsch's seminal report, the Hantzsch reaction, which incorporates two dicarbonyl compounds, an amine, and an aldehyde into a 1,4-dihydropyridine (1,4-DHP), has been used extensively in different settings.[1–5] 1,4-DHPs and their derivatives represent an important class of pharmacologically active compounds;[6,7] and some of them have been commercialized, such as nifedipine and felodipine, which are marketed drugs used as therapeutic for the treatment of cardiovascular diseases (Figure 1). 1,4-DHPs are also useful building blocks in organic chemistry and usually serve as selective reducing agents.[8–10]

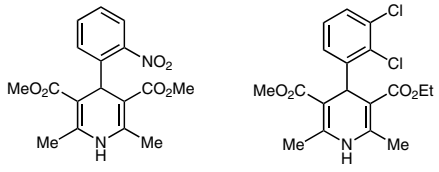
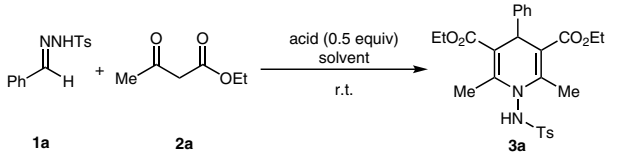


Figure 1 Some drugs containing 1,4-DHP structure

Literature survey revealed that inorganic ammonium salts, organic amines, imines, enamines, ureas, and thioureas have been employed as the source of nitrogen in the Hantzsch reaction.[11–14] But as a readily accessible and useful reagent,[15–17] *N*-tosylhydrazones have not been used in the Hantzsch reaction. Recently, Wu and Jiang et al. reported a copper-mediated [3+2] oxidative cyclization reaction of *N*-tosylhydrazones with β-keto esters to synthesize 2,3,5-trisubstituted furans.[18] In continuation of our ongoing interest in the synthesis of pyrazoles[19–22] and indazoles[23]

Table 1 Screening of the Reaction Conditions[a]



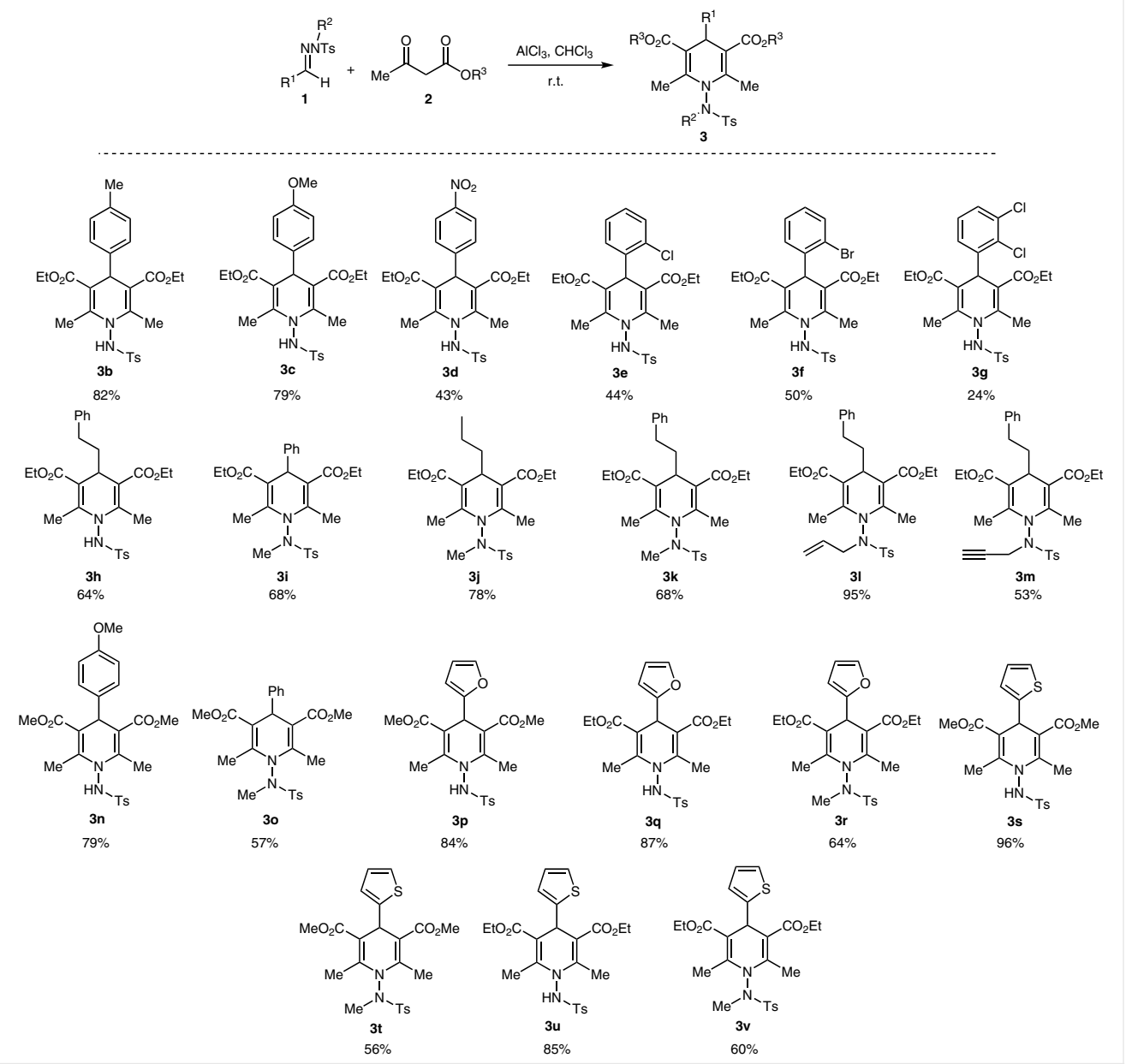
Entry	Acid	Solvent	Time (h)	Yield (%)[b]
1	none	$CHCl_3$	4	–
2	$AlCl_3$	$CHCl_3$	1.5	74
3	H_2SO_4	$CHCl_3$	4	–
4	HCl (concd)	$CHCl_3$	4	trace
5	$BF_3{\cdot}OEt_2$	$CHCl_3$	4	–
6	$ZnBr_2$	$CHCl_3$	4	–
7	$TiCl_4$	$CHCl_3$	4	–
8	PTS	$CHCl_3$	4	–
9	$AlCl_3$	DCE	4	63
10	$AlCl_3$	CH_2Cl_2	2	66
11	$AlCl_3$	CCl_4	8	60
12	$AlCl_3$	toluene	8	trace
13	$AlCl_3$	MeCN	8	trace
14	$AlCl_3$	THF	8	–

[a] Reactions were performed with *N*-tosylhydrazone **1a** (0.3 mmol), ethyl acetoacetate (**2a**; 0.75 mmol) in 3 mL of solvent.
[b] Isolated yields.

from *N*-tosylhydrazones, herein, we present the results of our investigations on the Hantzsch reaction of *N*-tosylhydrazones.

Initially, we conducted the reaction of the *N*-tosylhydrazone **1a** with ethyl acetoacetate (**2a**) in the presence of various Brønsted acids and Lewis acids in $CHCl_3$ at room temperature (Table 1, entries 2–8), but most of the acids gave disappointing results. Fortunately, the use of $AlCl_3$ resulted in a good yield of **3a** and the reaction could reach completion within 1.5 hours (entry 2). Of the solvents screened (entries 9–14), DCE, CH_2Cl_2, and CCl_4 gave moderate yields but the reactions required longer times (entries 9–11).

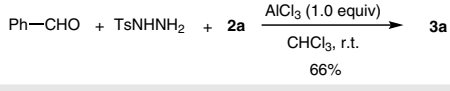
Under the above optimized conditions, we then attempted to synthesize a variety of 1,4-DHPs to test the generality and scope of the method (Scheme 1). First, the scope of the reaction was evaluated with regard to the structure of the substituent R^1. *N*-Tosylhydrazones derived from benzaldehyde featuring electron-donating (**3b** and **3c**) or electron-withdrawing (**3d**, **3e**, **3f**, and **3g**) substituents in aromatic ring all gave the corresponding 1,4-DHP derivatives. However, lower yields were observed with electron-



Scheme 1 Synthesis of 1,4-DHPs. *Reagents and conditions*: Reactions were performed with *N*-tosylhydrazone **1** (0.3 mmol), **2** (0.75 mmol), and $AlCl_3$ (0.15 mmol) in $CHCl_3$ (3 mL). Isolated yields are shown.

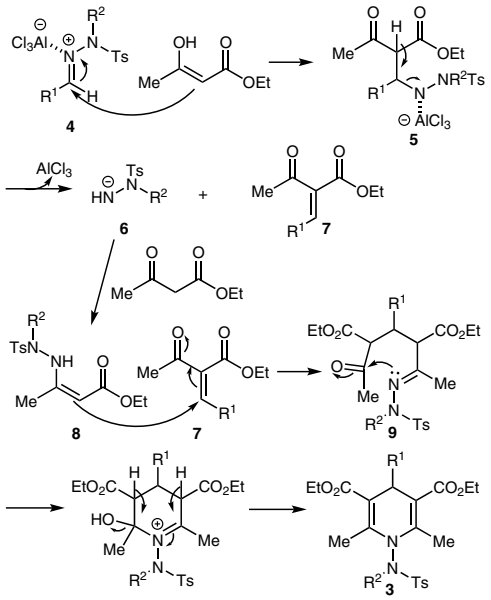
withdrawing substituents; *N*-tosylhydrazone derived from 2-nitrobenzaldehyde was also tested, but no product could be isolated. And the reaction was also general for aliphatic aldehyde tosylhydrazone **3h**. Additionally, some N-alkylated tosylhydrazones were employed in the reaction. As shown in Scheme 1, methyl (**3i**, **3j** and **3k**), allyl (**3l**), and propargyl (**3m**) were all suitable for R^2 and gave the corresponding 1,4-DHP derivatives in good to high yields. Other dicarbonyl compounds were also investigated. Methyl acetoacetate was suitable for the reaction (**3n** and **3o**), but ethyl benzoylacetate, 2,4-pentanedione, and diethyl malonate resulted in complex products. Furthermore, tosylhydrazones derived from 2-furaldehyde and 2-thiophenaldehyde were also appropriate for the reaction, and products **3p–v** were obtained in good yields.

We also tried to use benzaldehyde and *p*-toluenesulfonyl hydrazide instead of *N*-tosylhydrazone **1a** to carry out the Hantzsch reaction. However, to ensure the consumption of the in situ formed *N*-tosylhydrazone more than 1.0 equivalent of $AlCl_3$ was needed and the yield of **3a** was 66% (Scheme 2).



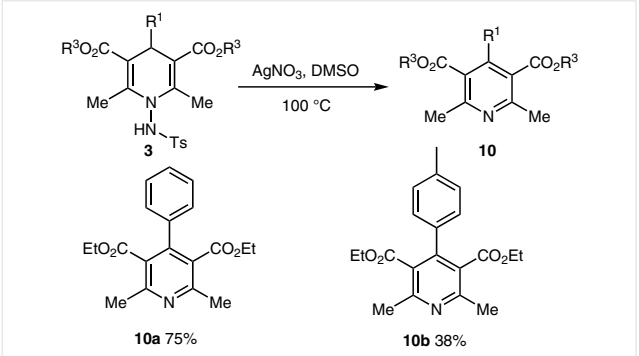
Scheme 2 Using benzaldehyde and *p*-toluenesulfonyl hydrazide instead of *N*-tosylhydrazone

According to the classical mechanism of the Hantzsch reaction, we propose a plausible pathway for the transformation. As shown in Scheme 3, the reaction is initiated by the nucleophilic addition of dicarbonyl compounds to tosylhydrazone iminium salt **4** resulting in intermediate **5**, and then a H-elimination gives *p*-toluenesulfonyl hydrazide anion **6** and α,β-unsaturated carbonyl compound **7**. Condensation of **6** with another equivalent of dicarbonyl compound affords **8**. Subsequently, the Michael addition of **8** to the α,β-unsaturated carbonyl compound **7** produces the intermediate **9**, which undergoes an intramolecular condensation and elimination to form 1,4-DHPs **3**.



Scheme 3 Proposed pathway for 1,4-DHPs formation

With the 1,4-DHPs **3** in hand, the N–N bond cleavage reactions and detosylations of these products were investigated to demonstrate their utility. 1,4-DHPs **3** could be transformed to pyridine derivatives **10** by N–N bond cleavage and aromatization with silver nitrate in DMSO;[24] thus products **10a** and **10b** were prepared in good yields (Scheme 4). Some common conditions for detosylation were then screened, such as TBAF in THF, $Mg(OMe)_2$ in MeOH, NaOEt in EtOH, and NaOH in EtOH, but no reactions were observed, even at higher temperature.



Scheme 4 N–N Bond cleavage reactions of 1,4-DHPs **3**

In summary, we have reported the $AlCl_3$-promoted Hantzsch reaction of *N*-tosylhydrazones. The protocol was applied to a wide range of *N*-tosylhydrazones and demonstrated excellent tolerance to a variety of substituents, and a series of 1,4-DHPs were prepared in moderate to excellent yields. A plausible pathway for the transformation was proposed.

For product purification by flash column chromatography, silica gel (200–300 mesh) and light petroleum ether (bp 30–60 °C) were used. ^1H and ^{13}C NMR spectra were recorded on a Varian Mercury 300 MHz or Bruker Avance III 400 MHz spectrometer. The HRMS data were determined on a Bruker Daltonics APEXII 47e FT-ICR spectrometer. Melting points are uncorrected.

N-Tosylhydrazones **1** were prepared according to our reported procedure.[20,25]

1,4-DHPs 3; General Procedure

Under an argon atmosphere, a mixture of *N*-tosylhydrazone **1** (0.3 mmol), dicarbonyl compound **2** (0.75 mmol), and $AlCl_3$ (0.15 mmol) in $CHCl_3$ (3 mL) was stirred at r.t. for 1–10 h. After quenching with H_2O, the product was extracted with EtOAc and the organic layer was

washed with sat. aq Na_2CO_3 and brine, dried (anhyd $MgSO_4$), filtered, and concentrated in vacuo. Purification by chromatography on silica gel using PE/EtOAc as eluent afforded the desired product **3**.

Compound 3a

Yellow oil; yield: 110.6 mg (74%).

^{1}H NMR (400 MHz, DMSO-d_6): δ = 1.16 (t, *J* = 7.2 Hz, 6 H), 2.05 (s, 6 H), 2.35 (s, 3 H), 4.01–4.13 (m, 4 H), 5.02 (s, 1 H), 7.22–7.26 (m, 7 H), 7.33–7.36 (m, 2 H), 10.92 (br s, 1 H).

^{13}C NMR (100 MHz, DMSO-d_6): δ = 14.0, 14.8, 20.9, 37.7, 59.8, 106.1, 126.4, 127.0, 128.0, 129.8, 135.6, 144.1, 144.6, 149.8, 166.5.

HRMS (ESI): *m*/*z* calcd for $C_{26}H_{31}N_2O_6S$ [M + H]$^+$: 499.1897; found: 499.1892.

Compound 3b

Yellow oil; yield: 126.0 mg (82%).

^{1}H NMR (400 MHz, DMSO-d_6): δ = 1.16 (t, *J* = 7.2 Hz, 6 H), 2.04 (s, 6 H), 2.29 (s, 3 H), 2.36 (s, 3 H), 4.00–4.10 (m, 4 H), 4.96 (s, 1 H), 7.14 (s, 4 H), 7.27–7.32 (m, 4 H), 10.87 (s, 1 H).

^{13}C NMR (100 MHz, DMSO-d_6): δ = 14.5, 15.3, 21.1, 21.5, 37.9, 60.3, 106.8, 127.5, 127.6, 129.1, 130.4, 135.9, 136.2, 142.2, 144.7, 150.0, 167.1.

HRMS (ESI): *m*/*z* calcd for $C_{27}H_{32}N_2O_6SNa$ [M + Na]$^+$: 535.1873; found: 535.1879.

Compound 3c

Yellow oil; yield: 125.2 mg (79%).

^{1}H NMR (400 MHz, $CDCl_3$): δ = 1.26 (t, *J* = 7.2 Hz, 6 H), 2.15 (s, 6 H), 2.37 (s, 3 H), 3.80 (s, 3 H), 4.13–4.19 (m, 4 H), 5.11 (s, 1 H), 6.88–6.90 (m, 2 H), 7.09 (d, *J* = 8.4 Hz, 2 H), 7.22–7.26 (m, 2 H), 7.29–7.33 (m, 3 H).

^{13}C NMR (100 MHz, $CDCl_3$): δ = 14.2, 15.1, 21.6, 37.2, 55.3, 60.3, 107.9, 113.5, 127.8, 128.5, 129.9, 134.6, 136.7, 144.8, 149.4, 158.3, 167.4.

HRMS (ESI): *m*/*z* calcd for $C_{27}H_{32}N_2O_7SNa$ [M + Na]$^+$: 551.1822; found: 551.1831.

Compound 3d

Yellow oil; yield: 70.1 mg (43%).

^{1}H NMR (400 MHz, $CDCl_3$): δ = 1.18 (t, *J* = 7.2 Hz, 6 H), 2.12 (s, 6 H), 2.30 (s, 3 H), 4.06–4.13 (m, 4 H), 5.13 (s, 1 H), 7.06 (d, *J* = 8.0 Hz, 2 H), 7.20–7.23 (m, 2 H), 7.54 (d, *J* = 8.8 Hz, 2 H), 7.82 (s, 1 H), 8.12 (d, *J* = 8.8 Hz, 2 H).

^{13}C NMR (100 MHz, $CDCl_3$): δ = 14.1, 15.2, 21.5, 38.6, 60.7, 106.5, 123.3, 127.4, 128.6, 130.0, 134.7, 145.2, 146.6, 150.7, 152.4, 166.8.

HRMS (ESI): *m*/*z* calcd for $C_{26}H_{29}N_3O_8SNa$ [M + Na]$^+$: 566.1568; found: 566.1595.

Compound 3e

Yellow oil; yield: 70.3 mg (44%).

^{1}H NMR (400 MHz, $CDCl_3$): δ = 1.23 (t, *J* = 7.2 Hz, 6 H), 2.11 (s, 6 H), 2.40 (s, 3 H), 4.05–4.19 (m, 4 H), 5.46 (s, 1 H), 7.13–7.17 (m, 1 H), 7.22–7.26 (m, 3 H), 7.29–7.33 (m, 2 H), 7.60 (d, *J* = 8.4 Hz, 2 H), 7.77 (dd, *J* = 8.0, 1.2 Hz, 1 H).

^{13}C NMR (100 MHz, $CDCl_3$): δ = 14.1, 15.1, 21.6, 36.7, 60.5, 108.2, 127.2, 127.7, 127.9, 129.4, 130.2, 130.5, 132.4, 135.2, 142.7, 145.1, 148.0, 167.4.

HRMS (ESI): *m*/*z* calcd for $C_{26}H_{29}ClN_2O_6SNa$ [M + Na]$^+$: 555.133; found: 555.134.

Compound 3f

Yellow oil; yield: 86.4 mg (50%).

^{1}H NMR (400 MHz, $CDCl_3$): δ = 1.23 (t, *J* = 7.2 Hz, 6 H), 2.09 (s, 6 H), 2.40 (s, 3 H), 4.08–4.19 (m, 4 H), 5.40 (s, 1 H), 7.06 (td, *J* = 7.2, 1.6 Hz, 1 H), 7.25–7.39 (m, 4 H), 7.48 (dd, *J* = 8.0, 1.2 Hz, 1 H), 7.66 (d, *J* = 8.4 Hz, 2 H), 7.81 (dd, *J* = 8.0, 1.6 Hz, 1 H).

^{13}C NMR (100 MHz, $CDCl_3$): δ = 14.3, 15.2, 21.6, 39.2, 60.5, 108.6, 122.6, 127.7, 128.0, 128.2, 130.2, 130.7, 132.8, 135.3, 144.8, 145.2, 147.5, 167.5.

HRMS (ESI): *m*/*z* calcd for $C_{26}H_{29}BrN_2O_6SNa$ [M + Na]$^+$: 599.0822; found: 599.0831.

Compound 3g

Yellow oil; yield: 61.5 mg (24%).

^{1}H NMR (300 MHz, DMSO-d_6): δ = 0.97 (t, *J* = 6.6 Hz, 6 H), 1.87 (s, 6 H), 2.24 (s, 3 H), 3.84–3.91 (m, 4 H), 5.25 (s, 1 H), 7.26–7.38 (m, 4 H), 7.49–7.53 (m, 3 H), 10.80 (br s, 1 H).

^{13}C NMR (75 MHz, DMSO-d_6): δ = 14.5, 15.5, 21.6, 37.9, 60.5, 106.9, 127.6, 128.9, 129.1, 129.5, 130.0, 130.7, 132.2, 136.7, 145.0, 146.4, 149.2, 167.0.

HRMS (ESI): *m*/*z* calcd for $C_{26}H_{28}Cl_2N_2O_6SNa$ [M + Na]$^+$: 589.0937; found: 589.0941.

Compound 3h

Yellow oil; yield: 101.0 mg (64%).

^{1}H NMR (400 MHz, DMSO-d_6): δ = 1.17 (t, *J* = 7.2 Hz, 6 H), 1.63–1.69 (m, 2 H), 2.02 (s, 6 H), 2.40 (s, 3 H), 2.47–2.51 (m, 2 H), 3.86 (t, *J* = 7.2 Hz, 1 H), 4.04–4.12 (m, 4 H), 7.17–7.21 (m, 3 H), 7.29–7.33 (m, 2 H), 7.38 (d, *J* = 8.0 Hz, 2 H), 7.59 (d, *J* = 8.4 Hz, 2 H), 10.95 (br s, 1 H).

^{13}C NMR (100 MHz, DMSO-d_6): δ = 14.5, 15.1, 21.5, 31.9, 32.9, 36.7, 60.2, 107.2, 126.1, 127.5, 128.4, 128.8, 130.4, 136.5, 142.5, 144.8, 150.0, 167.0.

HRMS (ESI): *m*/*z* calcd for $C_{28}H_{34}N_2O_6SNa$ [M + Na]$^+$: 549.2030; found: 549.2037.

Compound 3i

Yellow oil, yield: 104.5 mg (68%).

^{1}H NMR (400 MHz, $CDCl_3$): δ = 1.24 (t, *J* = 7.2 Hz, 6 H), 2.10 (s, 6 H), 2.39 (s, 3 H), 3.35 (s, 3 H), 4.13 (q, *J* = 7.2 Hz, 4 H), 5.02 (s, 1 H), 7.17–7.24 (m, 3 H), 7.32–7.40 (m, 4 H), 7.51 (d, *J* = 7.2 Hz, 2 H).

^{13}C NMR (100 MHz, $CDCl_3$): δ = 14.2, 15.2, 21.6, 38.6, 41.8, 60.2, 107.5, 126.4, 127.3, 128.0, 128.1, 130.1, 135.3, 144.5, 145.6, 149.3, 167.3.

HRMS (ESI): *m*/*z* calcd for $C_{27}H_{32}N_2O_6SNa$ [M + Na]$^+$: 535.1873; found: 535.1882.

Compound 3j

Yellow oil; yield: 111.9 mg (78%).

^{1}H NMR (400 MHz, $CDCl_3$): δ = 0.96 (t, *J* = 7.2 Hz, 3 H), 1.27–1.35 (m, 8 H), 1.50–1.56 (m, 2 H), 2.03 (s, 6 H), 2.45 (s, 3 H), 3.35 (s, 3 H), 3.81 (t, *J* = 7.2 Hz, 1 H), 4.11–4.24 (m, 4 H), 7.33 (d, *J* = 8.0 Hz, 2 H), 7.68 (d, *J* = 8.0 Hz, 2 H).

^{13}C NMR (100 MHz, $CDCl_3$): δ = 14.2, 14.8, 18.7, 21.6, 32.2, 39.2, 42.0, 60.0, 108.4, 127.2, 130.0, 135.5, 144.6, 149.1, 167.5.

HRMS (ESI): *m*/*z* calcd for $C_{24}H_{34}N_2O_6SNa$ [M + Na]$^+$: 501.2030; found: 501.2050.

Compound 3k

Yellow oil; yield: 110.2 mg (68%).

^{1}H NMR (400 MHz, $CDCl_3$): δ = 1.28 (t, *J* = 7.2 Hz, 6 H), 1.85–1.91 (m, 2 H), 2.07 (s, 6 H), 2.43 (s, 3 H), 2.62–2.68 (m, 2 H), 3.36 (s, 3 H), 3.91 (t, *J* = 7.2 Hz, 1 H), 4.13–4.21 (m, 4 H), 7.13–7.17 (m, 1 H), 7.26–7.30 (m, 6 H), 7.64 (d, *J* = 8.4 Hz, 2 H).

^{13}C NMR (100 MHz, $CDCl_3$): δ = 14.2, 14.9, 21.6, 31.9, 32.7, 38.0, 42.0, 60.1, 107.9, 125.4, 127.2, 128.1, 128.2, 130.1, 135.5, 142.8, 144.6, 149.4, 167.4.

HRMS (ESI): *m*/*z* calcd for $C_{29}H_{36}N_2O_6SNa$ [M + Na]$^+$: 563.2186; found: 563.2195.

Compound 3l

Yellow oil; yield: 161.3 mg (95%).

^{1}H NMR (400 MHz, DMSO-d_6): δ = 1.18 (t, *J* = 7.2 Hz, 6 H), 1.74–1.80 (m, 2 H), 2.01 (s, 6 H), 2.42 (s, 3 H), 2.53–2.57 (m, 2 H), 3.80 (t, *J* = 6.8 Hz, 1 H), 4.06–4.13 (m, 4 H), 4.41 (d, *J* = 6.8 Hz, 2 H), 5.29–5.32 (m, 1 H), 5.39–5.44 (m, 1 H), 5.98–6.08 (m, 1 H), 7.15–7.22 (m, 3 H), 7.27–7.31 (m, 2 H), 7.44 (d, *J* = 8.0 Hz, 2 H), 7.63 (d, *J* = 8.4 Hz, 2 H).

^{13}C NMR (100 MHz, DMSO-d_6): δ = 14.1, 15.5, 21.0, 31.2, 32.4, 38.2, 58.6, 59.7, 106.9, 120.9, 125.6, 127.1, 127.9, 128.3, 130.1, 132.2, 135.4, 142.1, 144.8, 149.0, 166.7.

HRMS (ESI): *m*/*z* calcd for $C_{31}H_{38}N_2O_6SNa$ [M + Na]$^+$: 589.2343; found: 589.2355.

Compound 3m

Yellow oil: yield: 89.7 mg (53%).

^{1}H NMR (400 MHz, DMSO-d_6): δ = 1.18 (t, *J* = 7.2 Hz, 6 H), 1.71–1.77 (m, 2 H), 2.04 (s, 6 H), 2.42 (s, 3 H), 2.51–2.56 (m, 2 H), 3.56 (t, *J* = 2.4 Hz, 1 H), 3.81 (t, *J* = 7.2 Hz, 1 H), 4.08–4.12 (m, 4 H), 4.75 (d, *J* = 2.0 Hz, 2 H), 7.16–7.22 (m, 3 H), 7.28–7.32 (m, 2 H), 7.41 (d, *J* = 8.4 Hz, 2 H), 7.69 (d, *J* = 8.4 Hz, 2 H).

^{13}C NMR (100 MHz, DMSO-d_6): δ = 14.1, 15.1, 21.0, 31.3, 32.4, 37.8, 45.0, 59.8, 77.3, 78.1, 107.0, 125.6, 127.3, 127.9, 128.3, 129.9, 135.1, 142.0, 145.1, 149.4, 166.7.

HRMS (ESI): *m*/*z* calcd for $C_{31}H_{36}N_2O_6SNa$ [M + Na]$^+$: 587.2186; found: 587.2198.

Compound 3n

Yellow oil: yield: 118.5 mg (79%).

^{1}H NMR (400 MHz, $CDCl_3$): δ = 2.16 (s, 6 H), 2.36 (s, 3 H), 3.72 (s, 6 H), 3.80 (s, 3 H), 5.11 (s, 1 H), 6.88–6.91 (m, 2 H), 7.07 (d, *J* = 8.0 Hz, 2 H), 7.17 (d, *J* = 8.4 Hz, 2 H), 7.26–7.30 (m, 2 H), 7.42 (s, 1 H).

^{13}C NMR (100 MHz, $CDCl_3$): δ = 15.0, 21.6, 36.8, 51.6, 55.3, 107.5, 113.6, 127.7, 128.3, 129.9, 134.4, 136.3, 144.9, 150.1, 158.4, 167.8.

HRMS (ESI): *m*/*z* calcd for $C_{25}H_{28}N_2O_7SNa$ [M + Na]$^+$: 523.1509; found: 523.1518.

Compound 3o

Yellow oil; yield: 82.8 mg (57%).

^{1}H NMR (400 MHz, $CDCl_3$): δ = 2.10 (s, 6 H), 2.37 (s, 3 H), 3.35 (s, 3 H), 3.68 (s, 6 H), 5.05 (s, 1 H), 7.15 (d, *J* = 8.0 Hz, 2 H), 7.21–7.26 (m, 1 H), 7.30–7.36 (m, 4 H), 7.47 (d, *J* = 7.2 Hz, 2 H).

^{13}C NMR (100 MHz, $CDCl_3$): δ = 15.2, 21.5, 38.1, 41.9, 51.4, 107.1, 126.5, 127.3, 127.7, 128.1, 130.0, 135.2, 144.5, 145.2, 149.8, 167.7.

HRMS (ESI): *m*/*z* calcd for $C_{25}H_{28}N_2O_6SNa$ [M + Na]$^+$: 507.1560, found: 507.1570.

Compound 3p

Yellow oil; yield: 115.9 mg (84%).

^{1}H NMR (400 MHz, $CDCl_3$): δ = 2.15 (s, 6 H), 2.39 (s, 3 H), 3.75 (s, 6 H), 5.27 (s, 1 H), 6.14 (d, *J* = 3.2 Hz, 1 H), 6.36 (dd, *J* = 3.2, 2.0 Hz, 1 H), 7.13 (d, *J* = 8.0 Hz, 2 H), 7.27–7.31 (m, 2 H), 7.40 (s, 1 H), 7.64 (s, 1 H).

^{13}C NMR (100 MHz, $CDCl_3$): δ = 14.9, 21.6, 32.8, 51.7, 104.5, 105.4, 110.2, 127.8, 129.9, 134.3, 141.4, 145.0, 151.2, 156.3, 167.3.

HRMS (ESI): *m*/*z* calcd for $C_{22}H_{24}N_2O_7SNa$ [M + Na]$^+$: 483.1196; found: 483.1208.

Compound 3q

Yellow oil; yield: 127.4 mg (87%).

^{1}H NMR (400 MHz, $CDCl_3$): δ = 1.28 (t, *J* = 7.2 Hz, 6 H), 2.14 (s, 6 H), 2.40 (s, 3 H), 4.17–4.25 (m, 4 H), 5.29 (s, 1 H), 6.15 (d, *J* = 3.2 Hz, 1 H), 6.36 (dd, *J* = 3.2, 2.0 Hz, 1 H), 7.14 (d, *J* = 8.0 Hz, 2 H), 7.22 (s, 1 H), 7.33 (d, *J* = 8.4 Hz, 2 H), 7.40 (s, 1 H).

^{13}C NMR (100 MHz, $CDCl_3$): δ = 14.2, 15.0, 21.6, 33.0, 60.4, 105.0, 105.3, 110.2, 127.9, 129.9, 134.4, 141.2, 144.9, 150.6, 156.5, 166.9.

HRMS (ESI): *m*/*z* calcd for $C_{24}H_{28}N_2O_7SNa$ [M + Na]$^+$: 511.1509; found: 511.1518.

Compound 3r

Yellow oil; yield: 96.4 mg (64%).

^{1}H NMR (400 MHz, $CDCl_3$): δ = 1.27 (t, *J* = 7.2 Hz, 6 H), 2.07 (s, 6 H), 2.40 (s, 3 H), 3.36 (s, 3 H), 4.15–4.23 (m, 4 H), 5.19 (s, 1 H), 6.22 (dd, *J* = 2.4, 0.8 Hz, 1 H), 6.35 (dd, *J* = 3.2, 1.6 Hz, 1 H), 7.19 (d, *J* = 8.4 Hz, 2 H), 7.38–7.42 (m, 3 H).

^{13}C NMR (100 MHz, $CDCl_3$): δ = 14.2, 15.0, 21.6, 32.8, 42.2, 60.3, 104.7, 105.5, 110.3, 127.4, 130.0, 135.2, 141.0, 144.5, 150.5, 157.4, 166.9.

HRMS (ESI): *m*/*z* calcd for $C_{25}H_{30}N_2O_7SNa$ [M + Na]$^+$: 525.1666; found: 525.1678.

Compound 3s

Yellow oil; yield: 137.1 mg (96%).

^{1}H NMR (400 MHz, $CDCl_3$): δ = 2.17 (s, 6 H), 2.37 (s, 3 H), 3.76 (m, 6 H), 5.34 (s, 1 H), 6.94–6.95 (m, 1 H), 6.98–7.00 (m, 1 H), 7.08 (q, *J* = 17.2, 8.2 Hz, 4 H), 7.23–7.24 (m, 1 H), 7.45 (s, 1 H).

^{13}C NMR (100 MHz, $CDCl_3$): δ = 14.9, 21.6, 33.9, 51.6, 106.8, 123.9, 124.1, 126.3, 127.7, 129.9, 134.1, 144.9, 148.0, 151.1, 167.2.

HRMS (ESI): *m*/*z* calcd for $C_{22}H_{24}N_2O_6S_2Na$ [M + Na]$^+$: 499.0968; found: 499.0977.

Compound 3t

Yellow oil; yield: 99.2 mg (56%).

^{1}H NMRd (400 MHz, $CDCl_3$): δ = 2.10 (s, 6 H), 2.37 (s, 3 H), 3.36 (s, 3 H), 3.74 (s, 6 H), 5.26 (s, 1 H), 6.97–7.03 (m, 2 H), 7.12 (d, *J* = 8.4 Hz, 2 H), 7.20–7.27 (m, 3 H).

^{13}C NMR (100 MHz, $CDCl_3$): δ = 15.0, 21.5, 33.7, 42.1, 51.5, 106.5, 124.0, 124.2, 126.4, 127.3, 130.0, 135.0, 144.5, 148.8, 150.8, 167.1.

HRMS (ESI): *m*/*z* calcd for $C_{23}H_{26}N_2O_6S_2Na$ [M + Na]$^+$: 513.1124; found: 513.1135.

Compound 3u

Yellow oil; yield: 128.5 mg (85%).

^{1}H NMR (400 MHz, $CDCl_3$): δ = 1.29 (t, *J* = 7.2 Hz, 6 H), 2.16 (s, 6 H), 2.37 (s, 3 H), 4.18–4.27 (m, 4 H), 5.36 (s, 1 H), 6.95–6.96 (m, 1 H), 6.98–7.00 (m, 1 H), 7.05–7.07 (m, 2 H), 7.11–7.13 (m, 2 H), 7.23 (dd, *J* = 4.8, 0.8 Hz, 1 H), 7.42 (s, 1 H).

^{13}C NMR (100 MHz, $CDCl_3$): δ = 14.2, 15.0, 21.6, 33.9, 60.5, 107.1, 123.8, 123.9, 126.2, 127.7, 130.0, 134.2, 144.8, 148.2, 150.7, 166.8.

HRMS (ESI): *m*/*z* calcd for $C_{24}H_{28}N_2O_6S_2Na$ [M + Na]$^+$: 527.1281; found: 527.1292.

Compound 3v

Yellow oil; yield: 93.3 mg (60%).

^{1}H NMR (400 MHz, $CDCl_3$): δ = 1.29 (t, *J* = 7.2 Hz, 6 H), 2.10 (s, 6 H), 2.38 (s, 3 H), 3.02 (s, 3 H), 4.16–4.24 (m, 4 H), 5.27 (s, 1 H), 6.96–6.98 (m, 1 H), 7.04–7.06 (m, 1 H), 7.13 (d, *J* = 8.0 Hz, 2 H), 7.20 (dd, *J* = 4.8, 1.2 Hz, 1 H), 7.24 (d, *J* = 8.4 Hz, 2 H).

^{13}C NMR (100 MHz, $CDCl_3$): δ = 14.2, 15.1, 21.6, 33.9, 42.1, 60.4, 107.0, 123.8, 124.3, 126.3, 127.3, 130.0, 135.1, 144.5, 149.0, 150.3, 166.8.

HRMS (ESI): *m*/*z* calcd for $C_{25}H_{30}N_2O_6S_2Na$ [M + Na]$^+$: 541.1437; found: 541.1447.

Pyridines 10; General Procedure

A mixture of 1,4-DHP **3** (0.1 mmol) and $AgNO_3$ (17 mg, 0.1 mmol) in DMSO (1.5 mL) was stirred at 100 °C for 3 h. After quenching with H_2O, the product was extracted with EtOAc and the organic layer was washed with brine, dried (anhyd $MgSO_4$), filtered, and concentrated in vacuo. Purification by chromatography on silica gel using PE/EtOAc as eluent afforded the desired product **10**.

The spectral data for compounds **10a** and **10b** are in agreement with the literature values.[26]

Compound 10a

Yellow oil; yield: 24.5 mg (75%).

^{1}H NMR (300 MHz, $CDCl_3$): δ = 0.90 (t, *J* = 9.0 Hz, 6 H), 2.61 (s, 6 H), 4.00 (q, *J* = 9.0 Hz, 4 H), 7.23–7.27 (m, 2 H), 7.34–7.37 (m, 3 H).

Compound 10b

Yellow oil; yield: 13.0 mg (38%).

^{1}H NMR (300 MHz, $CDCl_3$): δ = 0.95 (t, *J* = 9.0 Hz, 6 H), 2.36 (s, 3 H), 2.60 (s, 6 H), 4.03 (q, *J* = 9.0 Hz, 4 H), 7.16 (d, *J* = 3.0 Hz, 4 H).

Supporting Information

Supporting information for this article is available online at https://doi.org/10.1055/s-0036-1588496.

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