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Unprecedented C–C Bond Formation *via* Ipso Nucleophilic Substitution of 2,4-Dinitrobenzene Sulfonic Acid with Active Methylene Compounds

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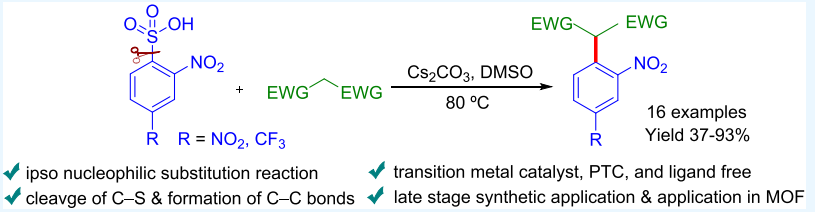

ABSTRACT: The sulfonic acid functionalization of sufficiently electron-deficient benzene sulfonic acids undergoes ipso nucleophilic substitution with various active methylene compounds, leading to new C−C bond formation. Good to excellent yields are obtained under mild conditions without transition-metal (Pd or Cu) catalyst, PTC, and ligand. No solid waste is generated. It is a highly effective strategy for incorporating various active methylene compounds into the *o*-nitro-substituted benzene ring. This method has been applied not only for synthesizing APIs but also in materials chemistry. It shows a novel route for creating heavily crowded all-carbon quaternary centers. Carbon−carbon bond formation by substituting a sulfonic acid group was unknown.

INTRODUCTION

Alkylation to an aromatic ring is a fundamental transformation in organic synthesis.[1] Although the Friedel−Crafts reaction (FCR) is the first route to achieve such alkylation,[2] it is not applicable for aromatic substrates with electron-withdrawing groups. However, multidirecting alkylation is a significant drawback of FCR. Many transition-metal-catalyzed alkylation or arylation are known where carbon−carbon or carbon−heteroatom (N, O, S) bonds form on aromatic halides.[3,4] Alternatively, "C" nucleophiles generated from active methylene compounds can be alkylated to an electron-deficient aromatic ring by ipso substitution.[5] In 1929, Hurtley first reported the C-alkylation of active methylene compounds such as malonic esters with ortho-substituted aromatic halides using a catalytic amount of copper acetate.[6] Later, Hurtley's reaction improved significantly.[7−10] Similar transformations are reported using other transition-metal catalysts such as Pd and Re.[11,12] Ipso substitution by active methylene compounds is also performed using PTC[13] or organo-catalyst under microwave irradiation.[14] However, using only halides as the leaving group, copper or toxic palladium as a reagent, and the need for chelating ligands limit the application scope of these transformations.

Previously, we have developed an efficient method for synthesizing arylamine from sulfonic acid analogues via ipso nucleophilic substitution of sulfonic acid by amine [Scheme 1i].[15] In this communication, we describe the new carbon−carbon bond formation via ipso nucleophilic substitution of sulfonic acid of 2-nitrobenzene sulfonic acid analogues by active methylene compounds [Scheme 1ii]. In this ipso nucleophilic substitution reaction, the sulfonic acid group acts as a leaving group. This is the first report on the ipso nucleophilic substitution of a sulfonic acid group by active methylene compounds. Also, in this method, neither a toxic transition-metal catalyst nor an expensive ligand is required (Schemes 2−5).

RESULTS AND DISCUSSION

Solvent optimization by reacting 2,4-dinitrobenzene sulfonic acid with diethyl malonate revealed DMSO to be the best [Table 1]. While no desired product was found with TEA and DIPEA in DCM, a 5% yield of the product was separated using K_2CO_3 as a base. However, Cs_2CO_3 performed better than K_2CO_3 (entry 14). Nitrogenous bases may substitute the sulfonic acid group.[15] Yield of this reaction increased with temperature till 80 °C (entries 14−18). Two equivalents of the base and dimethyl malonate were required for the highest efficiency. Adding more dimethyl malonate (3.0 and 4.0 equivalent) did not enhance the yield.

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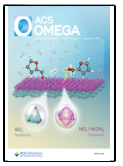

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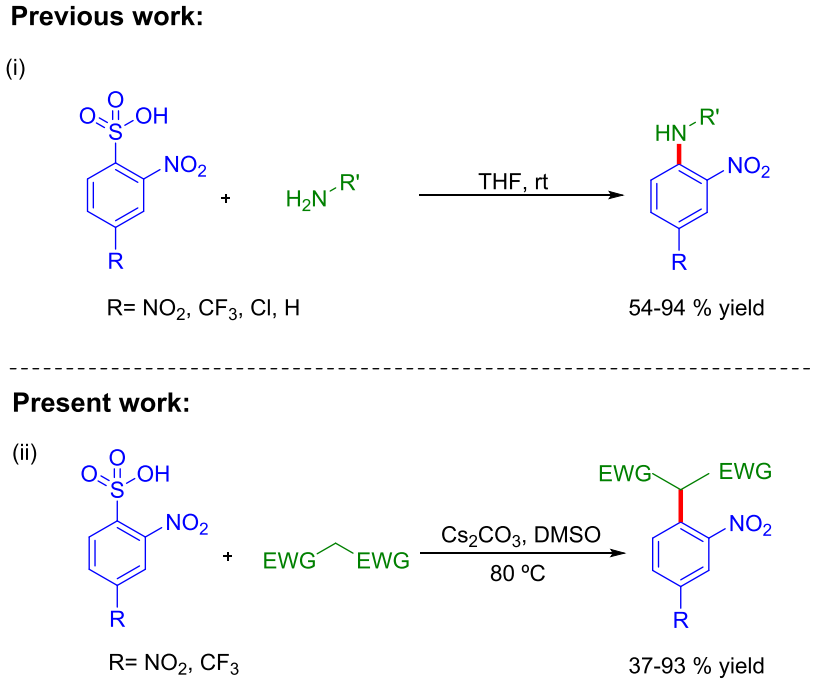
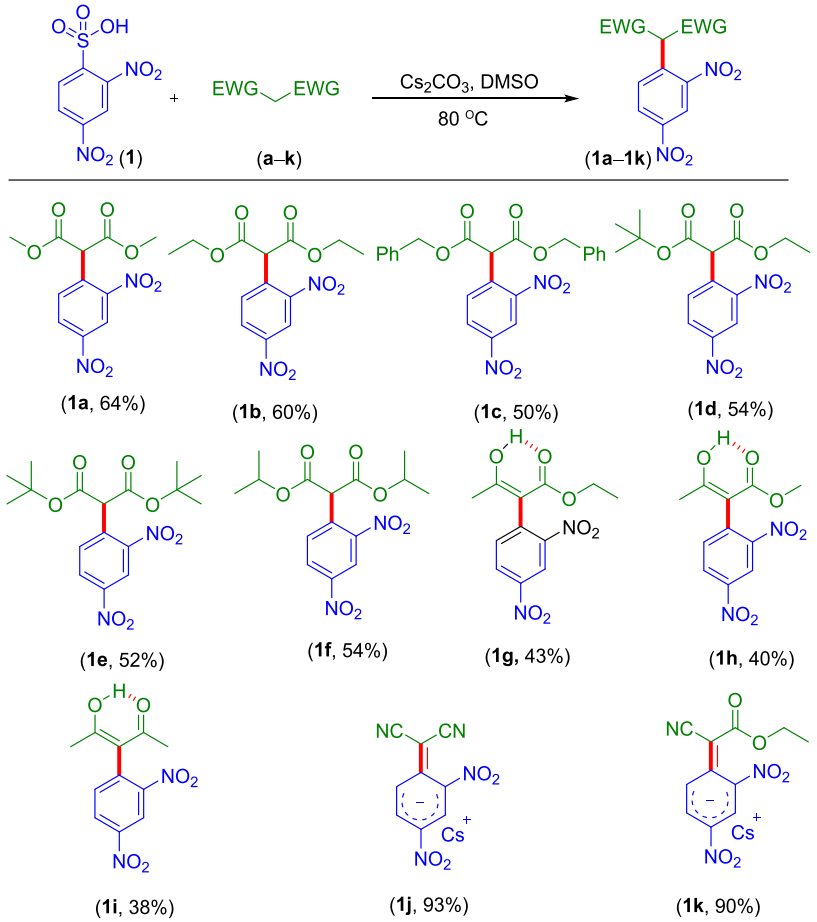
Scheme 1. Ipso Substitution on *o*-Nitrobenzene Sulfonic Acid Derivatives



Scheme 2. Substrate Scope with 2,4-Dinitrobenzene Sulfonic Acid[a]



[a]Reaction conditions: Sulfonic acid (**1**, 0.5 mmol), active methylene compound (1.0 mmol), cesium carbonate (1.0 mmol) reaction time 4−8 h at 80 °C.

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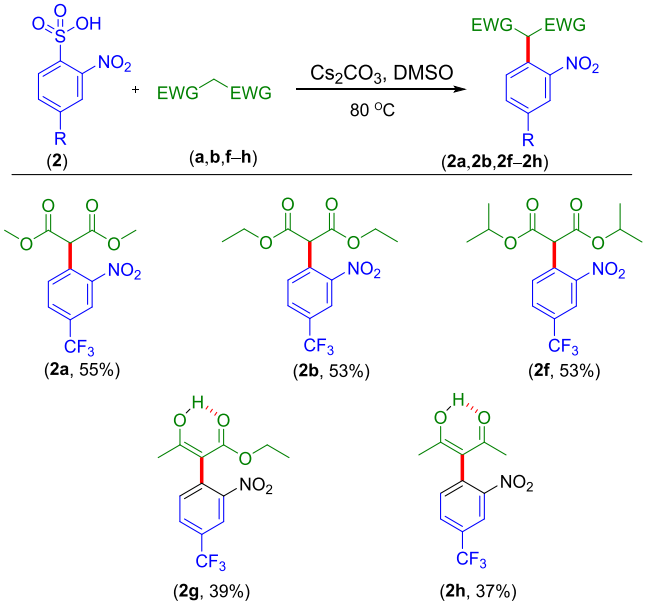
Scheme 3. Reaction Scope with 2-NBSA Analogues[a]



[a]Reaction conditions: Sulfonic acid (0.5 mmol), Dimethyl malonate (1.0 mmol), Cesium carbonate (1.0 mmol), 4–8 h at 80 °C.

The scope of the reaction between 2,4-dinitrobenzene sulfonic acid and different active methylene compounds was investigated under optimized conditions. Active methylene compounds with two ester groups (**1a**–**1f**) produced a higher yield. The products with ethyl acetoacetate (**1g**) and methyl acetoacetate (**1h**) are stable in enol form via the formation of a 6-member ring through H-bonding. Acetylacetone also behaved similarly (**1i**), but a comparatively lower yield was obtained due to the formation of a byproduct. Interestingly, with malononitrile (**1j**) and ethyl cyanoacetate (**1k**), a reddish solid precipitate, which was crystallized in methanol, was noted upon the addition of DCM after the reaction. These two compounds seem to be resonance-stabilized in the anionic form in the presence of metal. However, cyclic active methylene compounds and substituted active methylene compounds did not react even at an elevated temperature (Table S1, SI), probably for a steric reason.

Substrate scope using 2,4-dinitrobenzene sulfonic acid analogues produced expected products with sufficiently high yield. Substrates bearing an *o*-nitro group and an electron-withdrawing group at the para position, such as the $-CF_3$, also produced similar yields (**2a, 2b, 2f**–**2h**). However, sulfonic acids without or with one nitro group are not sufficiently electron deficient in reacting (Table S2, ESI).

The composition and the structure of compounds **1g** and **1j** were challenging to establish without the single-crystal X-ray diffraction analysis.

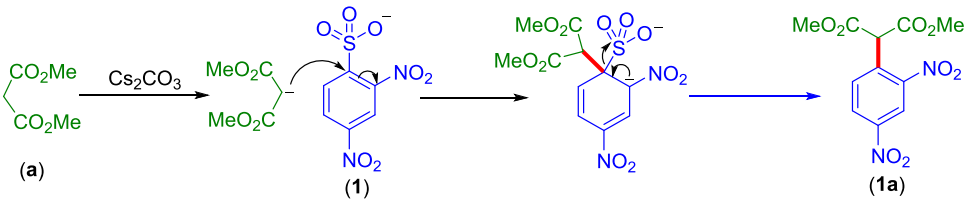
In the case of **1g**, the C–C bond lengths in the ring are comparable to the standard delocalized bonds in the benzene ring (1.40 Å; C_1–C_2 = 1.409 Å, C_2–C_3 = 1.382 Å, C_3–C_4 = 1.375 Å, C_4–C_5 = 1.376 Å, C_5–C_6 = 1.378 Å, C_6–C_1 = 1.397 Å). The exocyclic C_1-C_7 bond is slightly longer than the standard C_{sp2}–C_{sp2} bond length (1.455 Å) and close to the C–C single bond length. C_7–C_8 bond (1.454 Å) length corresponds to the C–C single bond, and C_7–C_{11} is 1.369 Å, much closer to the C–C double bond. C_{11}–O_5 is 1.331 Å and C_8–O_6 is 1.232 Å. This close observation of the bond lengths indicates that the first one represents a C–O single bond, and the latter represents a C–O double bond. The above critical analysis of the bond lengths indicates enolization occurs via rearrangement of the active methylene proton over the keto group.[16]

In structure **1j** (potassium metal–organic framework, Figure 1b), C_4–C_9 bond is strongly elongated, 1.424 Å. Similarly, C_4–C_5 is a longer, 1.420 Å. The remaining bonds in the benzene ring C_5–C_6 (1.384 Å), C_6–C_7 (1.376 Å), C_7–C_8 (1.382 Å), and C_8–C_9 (1.362 Å) are shorter than the standard delocalized bond in benzene ring (1.40 Å). These results indicate the absence of complete delocalization in the ring, and the −ve charge is distributed over C5–C6, C6–C7, C7–C8, and C8–C9 bonds.[17] C_2–C_4 is an exocyclic bond (1.421 Å), slightly smaller than the standard C_{sp2}–C_{sp2} single bond length (1.455 Å). C_1–C_2 (1.412 Å) and C_3–C_2 (1.410 Å) are longer than the standard C_{sp2}–C_{sp2} double bond length (1.34 Å), i.e., the partial double bond character exists. C_1–N_1 (1.140 Å) and C_3–N_2 (1.142 Å) bonds are comparable with standard CN triple bonds (1.13 Å). The structure of **1j** stabilized with cesium metal (Figure 1c) was similar to that of **1j** stabilized with potassium ion (Figure 1b).

According to established literature, a plausible reaction mechanism for the alkylation by active methylene compound on 2,4-dinitrobenzene sulfonic acid has been drawn.[18–20] This reaction undergoes via Meisenheimer adduct[21] formation, which is stabilized by resonance through the electron-withdrawing groups attached to the benzene ring. The ortho effect may stabilize the Meisenheimer adduct.[22] However, the possibility of nucleophilic replacement of hydrogen on the aromatic ring[23–25] cannot be obviated. However, so far in the present reaction conditions, no such side product formation could be noted.

The current method has great potential in biologically active compound synthesis. For example, 2-oxoindole and 1-methoxyindole structural frameworks are valuable synthetic building blocks for many natural products and biologically active molecules.[26] Indoline and Ziprasidone are 2-oxoindole core-based successful pharmaceutical agents. Indoline is used in treating cardiovascular diseases and ischemic chest pain, Ziprasidone is used in treating mental illnesses like schizophrenia. Neoxalline is an 1-methoxyindole-based compound that stimulates the central nervous system. The nitro-

Scheme 4. Plausible Mechanism for Alkylation on 2,4-Dinitrobenzene Sulfonic Acid



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Scheme 5. Representative Postsynthetic Application

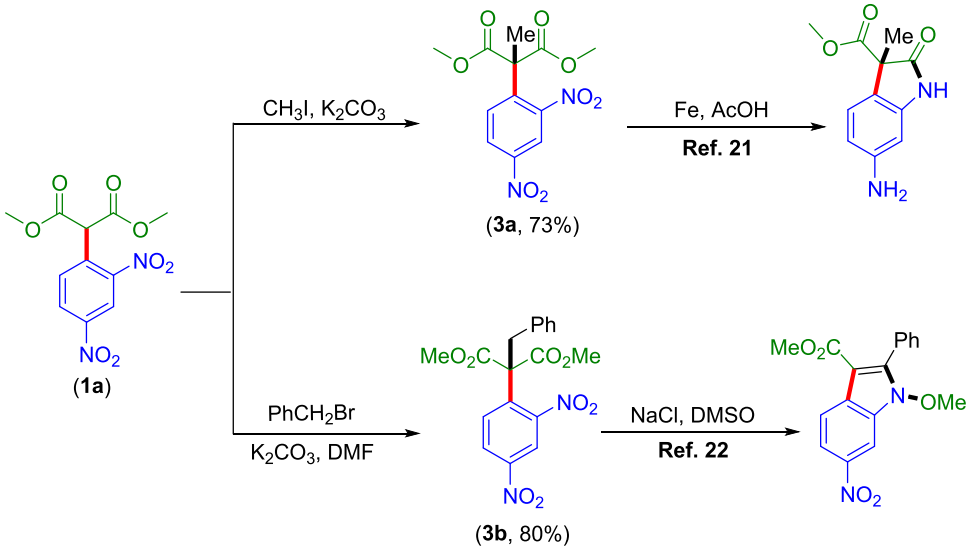
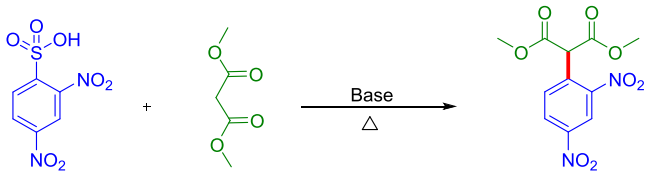


Table 1. Optimization of the Reaction Conditions[a]



entry	solvent	base	temperature	yield (%)[b]
1	DMF	K_2CO_3 2.0 equiv	80 °C	34
2	DMSO	”	”	49
3	CH_3CN	”	”	24
4	CH_3OH	”	”	27
5	THF	”	”	11
6	EtOAc	”	”	8
7	H_2O	”	”	n.r[c]
8	acetone	”	”	11
9	DCE	”	”	7
10	DCM	”	40 °C	5
11	DCM	DIPEA 2.0 equiv	”	n.r[c]
12	DCM	TEA 2.0 equiv	”	n.r[c]
13	DMSO	Na_2CO_3 2.0 equiv	80 °C	24
14	”	Cs_2CO_3 2.0 equiv	”	64
15	”	”	60 °C	42
16	”	”	25 °C	34
17	”	”	120 °C	62
18	”	”	140 °C	57

[a]Reaction conditions: sulfonic acid (0.5 mmol), dimethyl malonate (1.0 mmol), reaction time 4−8 h. [b]Isolated yield with respect to the sulfonic acid. [c]No reaction.

diesters (**3a** and **3b**), crucial for synthesizing the above active pharmaceutical ingredients, can be easily accessed using this method.[27]

Metal−organic framework (MOF) is an exciting topic in the present research. Metal ions or clusters are linked with multiple organic moieties in a repetitive pattern to form a MOF structure. Due to its ordered pore structures, facile functionalization, and large surface areas, MOF is highly applicable for gas separation, semiconductors, radioactive waste absorption, biological imaging, and sensing. Using this protocol, we have synthesized MOFs where potassium and cesium ions are linked with 2-(2,4-dinitrophenyl)malononitrile moiety (**1j**). The channel-like layer structure formation in solid-state stabilized through π-π stacking interaction between two benzene rings (centroid to centroid distance = 3.720 Å) and chelating interaction of potassium ion with ligand binding site such as two nitro as well as cyano group. (Figure 2) In this molecular structure, one potassium ion is bonded to nine donor atoms (six “O” and three “N”).

CONCLUSIONS

In summary, we have disclosed a method for the arylation of active methylene compounds by *o*-nitrobenzene sulfonic acid derivatives. This method is an example of a C−C bond formation reaction by ipso substitution of a sulfonic acid group. No toxic transition-metal catalyst, PTC, or ligand is required. Although this method works only for sufficiently electron-deficient aromatic sulfonic acids, the diverse derivatization possibilities make it an essential tool for API synthesis. Application possibilities in medicinal chemistry and material chemistry are demonstrated. This methodology opens up a novel route for accessing densely substituted quaternary carbon centers (**3a, 3b**).

EXPERIMENTAL SECTION

General Information. All reagents were purchased from commercial sources. NMR spectra were recorded on 400, 500, and 600 MHz spectrometers using $CDCl_3$ or DMSO-d_6 as solvent and tetramethylsilane (TMS) as an internal standard. Chemical shifts (δ) were reported in ppm, and spin−spin coupling constants (J) were given in Hz. Abbreviations to denote the multiplicity of a particular signal are s (singlet), d (doublet), t (triplet), q (quartet), dd (doublet of doublet), dq (doublet of quartet), and m (multiplet).$^{13}C\{^1H\}$ indicates the proton decoupled NMR experiment. Reactions were monitored using thin-layer chromatography with silica gel G254. The reaction products were purified by column chromatography using silica gel (60−120 mesh) using eluent EtOAc/hexane. Solvents were removed under reduced pressure using a Buchi rotary evaporator. Melting points were determined using

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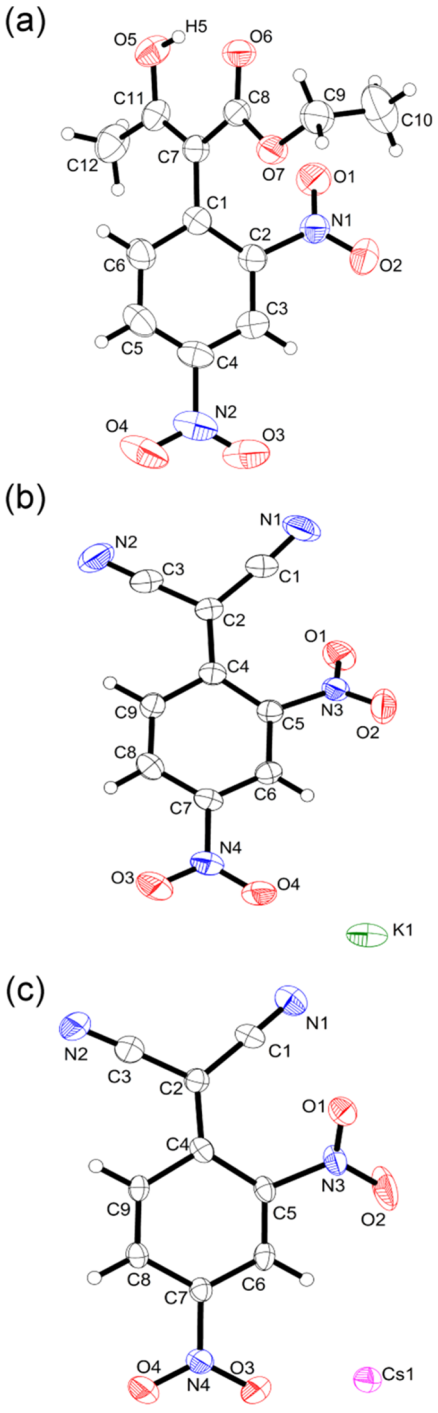

Figure 1. ORTEP Diagram with ellipsoid of 40% probability (a) **1g** (CCDC no. 2155058), (b) **1j** with potassium ion (CCDC no. 2155062), and (c) **1j** with cesium ion (CCDC no. 2166732).

a dedicated melting point measuring apparatus, and FT-IR spectra were recorded on an FT-IR spectrometer.

General Procedure for the Synthesis of Arylated Product. Active methylene compound (1.0 mmol) was taken in DMSO solvent (2 mL), and Cs_2CO_3 (1.0 mmol) was added to it. The mixture was stirred at room temperature for 10 min, and then sulfonic acid (0.5 mmol) was added. Then, the temperature was increased to 80 °C. The progress of the reaction was monitored by TLC. After completion of the reaction, the mixture was diluted with ethyl acetate (15 mL)

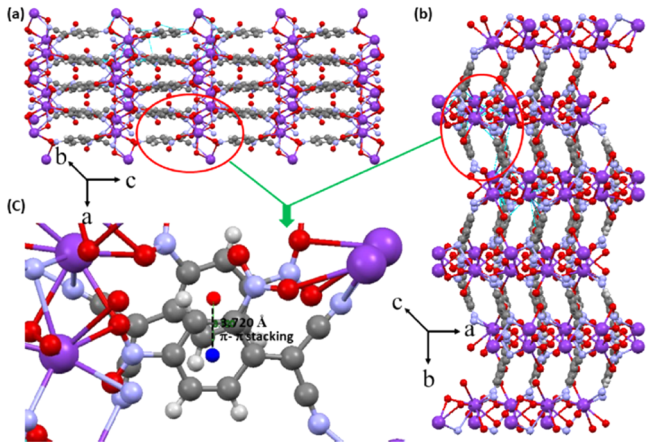

Figure 2. (a) Linear channel-like layer arrangement along *c*-axis, (b) helical channel-like layer architecture along the crystallographic b-axis in higher-order molecular packing, and (c) $\pi-\pi$ stacking interaction and Cs^+ ion binding interaction inside the channel of molecule 2-(2,4-dinitrophenyl)malononitrile.

and washed with ice-cold water. The accumulated organic layer was washed with 5% HCl (2 × 10 mL), 5% $NaHCO_3$ (2 × 10 mL), and saturated NaCl solution (2 × 10 mL) and dried over anhydrous Na_2SO_4. After that, the reaction mixture was concentrated using a rotary evaporator. The residue was purified by column chromatography using 10−15% EtOAc/hexane.

General Procedure for the Synthesis of 1j and 1k. Active methylene compound (2.0 mmol) was taken in DMSO solvent (2 mL), and Cs_2CO_3 (2.0 mmol) was added to it. The mixture was stirred at room temperature for 10 min, and then sulfonic acid (1.0 mmol) was added. Stirring continued at 80 °C. The progress of the reaction was monitored by TLC. After completion of the reaction, DCM was added to the reaction mixture. A large amount of precipitate was formed. This precipitate was separated by filter paper and dried at room temperature. No column chromatography purification was required in this procedure.

General Procedure for the Synthesis of 3a and 3b. Dimethyl 2-(2,4-dinitrophenyl)malonate (0.5 mmol) was taken in 50 mL RB in a DMF medium. K_2CO_3 (0.5 mmol) was added to this mixture and stirred at room temperature for 10 min. Then, alkyl halide (0.6 mmol) was added to the above reaction mixture, and stirring was continued overnight. The progress of the reaction was monitored by TLC. After completion of the reaction, the mixture was diluted with ethyl acetate (15 mL) and washed with ice-cold water. The accumulated organic layer was washed with 5% HCl (2 × 10 mL), 5% $NaHCO_3$ (2 × 10 mL), and saturated NaCl solution (2 × 10 mL) and dried over anhydrous Na_2SO_4. After that, the reaction mixture was concentrated using a rotary evaporator. The obtained residue was purified by column chromatography using 10−15% EtOAc/hexane.

Procedure for Large-Scale Synthesis of Compound 1a. Dimethyl malonate (8.06 mmol) was taken in DMSO solvent (8 mL), and Cs_2CO_3 (8.06 mmol) was added to it. We stirred the mixture at room temperature for 10 min, and then 2,4-dinitrobenzene sulfonic acid (4.03 mmol) was added. Then, the reaction was stirred at 80 °C. The progress of the reaction was monitored by TLC. After completion of the reaction, the mixture was diluted with ethyl acetate (30 mL)

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and washed with ice-cold water. The accumulated organic layer was washed with 5% HCl (2 × 20 mL), 5% $NaHCO_3$ (2 × 20 mL), and saturated NaCl solution (2 × 20 mL) and dried over anhydrous Na_2SO_4. After that, the reaction mixture was concentrated using a rotary evaporator. The obtained residue was purified by column chromatography using 10−15% EtOAc/hexane. The pure product was a white crystalline solid (745 mg. 2.5 mmol, 62%).

Characterization Data. *Dimethyl 2-(2,4-dinitrophenyl)-malonate (**1a**).*[28] As a white solid (85 mg, 64% yield, mp 90−92 °C); purification over a column of silica gel (10−15% EtOAc in hexane); ^{1}H NMR ($CDCl_3$, 400 MHz): δ 8.89 (d, 1H, J = 2.4 Hz), 8.48 (dd, 1H, J_1 = 2.4 Hz, J_2 = 8.4 Hz), 7.82 (d, 1H, J = 8.8 Hz), 5.41 (s, 1H), 3.82 (s, 6H); ^{13}C{^{1}H} NMR ($CDCl_3$, 100 MHz): δ 166.7, 149.2, 147.9, 134.3, 133.5, 127.6, 120.8, 54.0, 53.8; IR (KBr, cm^{-1}): 3078, 2963, 2916, 2847, 1754, 1730, 1605, 1532, 1344, 1298, 1242, 1002, 837, 734; HRMS (ESI/Q-TOF) (m/z) calcd for $C_{11}H_{11}N_2O_8$ [M + H]$^+$ 299.0510; found 299.0507.

*Diethyl 2-(2,4-dinitrophenyl)malonate (**1b**).*[29] As a yellow liquid (98 mg, 60% yield); purification over a column of silica gel (10−15% EtOAc in hexane); ^{1}H NMR ($CDCl_3$, 400 MHz): δ 8.88 (d, 1H, J = 2.4 Hz), 8.47 (dd, 1H, J_1 = 2.4 Hz, J_2 = 8.4 Hz), 7.82 (d, 1H, J = 8.8 Hz), 5.36 (s, 1H), 4.29 (dq, 4H, J_1 = 2.6 Hz, J_2 = 7.0 Hz), 1.29 (t, 6H, J = 7.2 Hz); ^{13}C{^{1}H} NMR ($CDCl_3$, 100 MHz): δ 166.3, 149.3, 147.8, 134.6, 133.4, 127.5, 120.7, 63.0, 54.4, 14.1; IR (KBr, cm^{-1}): 3105, 2984, 2919, 2853, 1732, 1607, 1532, 1466, 1346, 1298, 1175, 1023, 835, 723; HRMS (ESI/Q-TOF) (m/z) calcd for $C_{13}H_{14}N_2O_8Na$ [M + Na]$^+$ 349.0642; found 349.0641.

*Dibenzyl 2-(2,4-dinitrophenyl)malonate (**1c**).* As a yellow solid (112 mg, 50% yield, mp 88−90 °C); purification over a column of silica gel (10−15% EtOAc in hexane); ^{1}H NMR ($CDCl_3$, 400 MHz): δ 8.88 (d, 1H, J = 2.4 Hz), 8.36 (dd, 1H, J_1 = 2.4 Hz, J_2 = 8.4 Hz), 7.63 (d, 1H, J = 8.8 Hz), 7.36−7.33 (m, 6H), 7.29−7.27 (m, 4H), 5.47 (s, 1H), 5.22 (s, 4H); ^{13}C{^{1}H} NMR ($CDCl_3$, 100 MHz): δ 166.1, 149.1, 147.8, 134.7, 134.3, 133.4, 128.99, 128.89, 128.7, 127.5, 120.8, 68.7, 54.5; IR (KBr, cm^{-1}): 3078, 2953, 2921, 2852, 1744, 1725, 1601, 1526, 1495, 1454, 1344, 1295, 1175, 1020, 979, 836, 731, 694; HRMS (ESI/Q-TOF) (m/z) calcd for $C_{23}H_{19}N_2O_8$ [M + H]$^+$ 451.1136; found 451.1144.

*1-(tert-Butyl)3-ethyl(R)-2-(2,4-dinitrophenyl)malonate (**1d**).* As a yellow liquid (95 mg, 54% yield); purification over a column of silica gel (10−15% EtOAc in hexane); ^{1}H NMR ($CDCl_3$, 400 MHz): δ 8.88 (d, 1H, J_1 = 2.4 Hz), 8.47 (dd, 1H, J_1 = 2.4 Hz, J_2 = 8.4 Hz), 7.81 (d, 1H, J = 8.8 Hz), 5.27 (s, 1H), 4.28 (dq, 2H, J_1 = 2.4 Hz, J_2 = 7.1 Hz), 1.48 (s, 9H), 1.30 (t, 3H, J = 7.2 Hz); ^{13}C{^{1}H} NMR ($CDCl_3$, 100 MHz): δ 166.7, 165.2, 149.3, 147.7, 135.1, 133.2, 127.4, 120.7, 84.4, 62.9, 55.5, 27.9, 14.2; IR (KBr, cm^{-1}): 3105, 2981, 2934, 2853, 1729, 1606, 1534, 1346, 1299, 1230, 1141, 1025, 835, 790, 727; HRMS (ESI/Q-TOF) (m/z) calcd for $C_{15}H_{18}N_2O_8K$ [M + K]$^+$ 393.0695; found 393.0684.

*Di-tert-Butyl 2-(2,4-dinitrophenyl)malonate (**1e**).* As a yellow solid (99 mg, 52% yield, mp 97−99 °C); purification over a column of silica gel (10−15% EtOAc in hexane); ^{1}H NMR ($CDCl_3$, 400 MHz): δ 8.86 (d, 1H, J = 2.4 Hz), 8.47 (dd, 1H, J_1 = 2.4 Hz, J_2 = 8.8 Hz), 7.83 (d, 1H, J = 8.8 Hz), 5.18 (s, 1H), 1.49 (s, 18H); ^{13}C{^{1}H} NMR ($CDCl_3$, 100 MHz): δ 165.6, 149.4, 147.5, 135.6, 133.0, 127.3, 120.6, 84.0, 56.4, 28.0; IR (KBr, cm^{-1}): 3105, 2979, 2930, 2850, 1728, 1606, 1535, 1346, 1249, 1136, 1066, 834, 748; HRMS (ESI/Q-TOF) (m/z) calcd for $C_{17}H_{23}N_2O_8$ [M + H]$^+$ 383.1449; found 383.1438.

*Diisopropyl 2-(2,4-dinitrophenyl)malonate (**1f**).* As a yellow solid (96 mg, 54% yield, mp 108−110 °C); purification over a column of silica gel (10−15% EtOAc in hexane); ^{1}H NMR ($CDCl_3$, 400 MHz): δ 8.86 (d, 1H, J = 2.4 Hz), 8.46 (dd, 1H, J_1 = 2.4 Hz, J_2 = 8.8 Hz), 7.79 (d, 1H, J = 8.8 Hz), 5.26−5.06 (m, 2H), 1.29−1.25 (m, 12H); ^{13}C{^{1}H} NMR ($CDCl_3$, 100 MHz): δ 165.8, 149.2, 147.7, 134.9, 133.2, 127.4, 120.6, 70.9, 54.9, 21.6; IR (KBr, cm^{-1}): 3104, 2984, 2939, 2875, 1728, 1606, 1534, 1467, 1346, 1263, 1168, 1096, 834, 725; HRMS (ESI/Q-TOF) (m/z) calcd for $C_{15}H_{19}N_2O_8$ [M + H]$^+$ 355.1136; found 355.1138.

*Ethyl (Z)-2-(2,4-dinitrophenyl)-3-hydroxybut-2-enoate (**1g**).*[16] As a yellow crystalline (64 mg, 43% yield, mp 93−95 °C); purification over a column of silica gel (10−15% EtOAc in hexane); ^{1}H NMR ($CDCl_3$, 400 MHz): δ 13.15 (s, 1H), 8.84 (d, 1H, J = 2.4 Hz), 8.43 (dd, 1H, J_1 = 2.4 Hz, J_2 = 8.4 Hz), 7.53 (d, 1H, J = 8.8 Hz), 4.24−4.19 (m, 1H), 4.07−4.02 (m, 1H), 1.92 (s, 3H), 1.12 (t, 3H, J = 7.2 Hz); ^{13}C{^{1}H} NMR ($CDCl_3$, 100 MHz): δ 174.5, 170.2, 149.9, 147.4, 136.8, 135.5, 126.9, 120.3, 100.0, 61.7, 20.3, 14.0; IR (KBr, cm^{-1}): 3075, 2963, 2921, 2852, 1729, 1640, 1603, 1531, 1467, 1344, 1218, 1098, 836, 729; ESI (m/z) calcd for $C_{12}H_{13}N_2O_7$ [M + H]$^+$ 297.0717; found 297.1045.

*Methyl (Z)-2-(2,4-dinitrophenyl)-3-hydroxybut-2-enoate (**1h**).*[30] As a yellow liquid (61 mg, 43% yield); purification over a column of silica gel (10−15% EtOAc in hexane); ^{1}H NMR ($CDCl_3$, 400 MHz): δ 12.98 (s, 1H), 8.82 (d, 1H, J = 2.4 Hz), 8.43 (dd, 1H, J_1 = 2.4 Hz, J_2 = 8.4 Hz), 7.55 (d, 1H, J = 8.4 Hz), 3.63 (s, 3H), 1.90 (s, 3H); ^{13}C{^{1}H} NMR ($CDCl_3$, 100 MHz): δ 174.5, 170.6, 149.6, 135.5, 127.0, 120.3, 99.6, 52.2, 20,1; IR (KBr, cm^{-1}): 3078, 2963, 2923, 2853, 1738, 1606, 1532, 1439, 1217, 1064, 835, 711; ESI (m/z) calcd for $C_{11}H_{10}N_2O_7Na$ [M + Na]$^+$ 305.0380; found 305.0494.

*(Z)-3-(2,4-Dinitrophenyl)-4-hydroxypent-3-en-2-one (**1i**).*[31] As a yellow liquid (53 mg, 40% yield); purification over a column of silica gel (10−15% EtOAc in hexane); ^{1}H NMR ($CDCl_3$, 500 MHz): δ 16.58 (s, 1H), 8.79 (d, 1H, J = 3.0 Hz), 8.50 (dd, 1H, J_1 = 2.5 Hz, J_2 = 8.5 Hz), 7.62 (d, 1H, J = 8.5 Hz), 1.86 (s, 6H); ^{13}C{^{1}H} NMR ($CDCl_3$, 125 MHz): δ 189.9, 150.7, 148.0, 137.7, 135.7, 127.4, 120.2, 108.9, 24.3; IR (KBr, cm^{-1}): 3109, 2955, 2917, 2850, 1739, 1597, 1526, 1349, 1261, 1186, 1015, 905, 834, 798; ESI (m/z) calcd for $C_{11}H_{11}N_2O_6$ [M + H]$^+$ 267.0612; found 267.1738.

*2-(2,4-Dinitrocyclohexylidene)malononitrile (**1j**)*[17a] *[in Reported Compound Cation is Triethylammonium Ion].* As a reddish crystalline (169 mg, 93% yield, mp 267−269 °C); ^{1}H NMR (DMSO-d_6, 600 MHz): δ 8.37 (d, 1H, J = 2.4 Hz), 7.97 (dd, 1H, J_1 = 1.5 Hz, J_2 = 9.9 Hz), 7.18 (d, 1H, J = 9.0 Hz).; ^{13}C{^{1}H} NMR (DMSO-d_6, 150 MHz): δ 142.1, 138.2, 135.8, 130.8, 125.7, 122.7, 122.7, 118.4; IR (KBr, cm^{-1}): 3114, 2974, 2919, 2853, 2201, 2173, 1738, 1563, 1480, 1287, 832.

*Ethyl (Z)-2-cyano-2-(2,4-dinitrocyclohexylidene)acetate (**1k**)*[17a] *[in Reported Compound, Cation is Triethylammonium Ion].* As a reddish crystalline (185 mg, 90% yield, mp 258−260 °C); ^{1}H NMR (DMSO-d_6, 600 MHz): δ 8.29 (d, 1H, J = 2.4 Hz), 7.97 (dd, 1H, J_1 = 3.3 Hz, J_2 = 9.3 Hz), 7.59 (d, 1H, J = 9.6 Hz), 3.96 (q, 2H, J = 7.2 Hz), 1.14 (t, 3H, J = 7.2 Hz); ^{13}C{^{1}H} NMR (DMSO-d_6, 150 MHz): δ 166.3, 142.9, 140.5, 135.9, 125.3, 124.9, 122.8, 122.2, 58.2, 14.8; IR (KBr, cm^{-1}): 3344, 3098, 2977, 2950, 2183, 2155, 1516, 1566, 1299, 1089, 827.

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*Dimethyl 2-(2-nitro-4-(trifluoromethyl)phenyl)malonate (**2a**).*[32] As a yellow liquid (88 mg, 55% yield); purification over a column of silica gel (10−15% EtOAc in hexane); ^{1}H NMR ($CDCl_3$, 400 MHz): δ 8.33 (d, 1H, J = 2.0 Hz), 7.92 (dd, 1H, J_1 = 2.0 Hz, J_2 = 8.0 Hz), 7.73 (d, 1H, J = 8.4 Hz), 5.39 (s, 1H), 3.82 (s, 6H); ^{13}C{^{1}H} NMR ($CDCl_3$, 100 MHz): δ 167.1, 149.0, 132.9, 131.8, 130.1 (q, J = 3.2 Hz), 124.1, 122.7 (q, J = 3.8 Hz), 121.4, 54.0, 53.6; ^{19}F NMR ($CDCl_3$): δ −63.1 (s); IR (KBr, cm^{-1}): 3105, 2962, 2916, 2851, 1760, 1732, 1634, 1539, 1440, 1329, 1242, 1128, 1088, 1009, 911, 700; ESI (m/z) calcd for $C_{12}H_{11}F_3NO_6$ [M + H]$^+$ 322.0533; found 322.0681.

*Diethyl 2-(2-nitro-4-(trifluoromethyl)phenyl)malonate (**2b**).*[33] As a yellow liquid (92 mg, 53% yield); purification over a column of silica gel (10−15% EtOAc in hexane); ^{1}H NMR ($CDCl_3$, 400 MHz): δ 8.32 (d, 1H, J = 2.0 Hz), 7.89 (dd, 1H, J_1 = 2.0 Hz, J_2 = 8.0 Hz), 7.73 (d, 1H, J = 8.4 Hz), 5.34 (s, 1H), 4.28 (dq, 4H, J_1 = 2.0 Hz, J_2 = 7.2 Hz), 1.29 (t, 6H, J = 7.2 Hz); ^{13}C{^{1}H} NMR ($CDCl_3$, 100 MHz): δ 167.8, 149.1, 132.8, 132.1, 130.0 (q, J = 3.5 Hz), 124.1, 122.7 (q, J = 3.9 Hz), 121.5, 62.9, 54.4, 14.2; ^{19}F NMR ($CDCl_3$): δ −63.1 (s); IR (KBr, cm^{-1}): 3105, 2993, 2924, 2858, 1735, 1633, 1542, 1465, 1325, 1227, 1132, 1088, 1025, 862, 788; HRMS (ESI/Q-TOF) (m/z) calcd for $C_{14}H_{15}F_3NO_6$ [M + H]$^+$ 350.0846; found 350.0846.

*Diisopropyl 2-(2-nitro-4-(trifluoromethyl)phenyl)-malonate (**2f**).*[34] As a yellow liquid (100 mg, 53% yield); purification over a column of silica gel (10−15% EtOAc in hexane); ^{1}H NMR ($CDCl_3$, 400 MHz): δ 8.30 (d, 1H, J = 2.0 Hz), 7.88 (dd, 1H, J_1 = 2.0 Hz, J_2 = 8.4 Hz), 7.72 (d, 1H, J = 8.0 Hz), 5.25 (s, 1H), 5.16−5.07 (m, 2H), 1.29−1.25 (m, 12H); ^{13}C{^{1}H} NMR ($CDCl_3$, 100 MHz): δ 166.3, 149.2, 132.6, 132.1, 129.9 (q, J = 3.3 Hz), 124.2, 122.6 (q, J = 4.0 Hz), 121.5, 70.7, 54.9, 21.7; ^{19}F NMR ($CDCl_3$): δ −63.1 (s); IR (KBr, cm^{-1}): 3114, 2985, 2939, 2883, 1730, 1632, 1542, 1325, 1230, 1134, 1088, 904, 830, 787; HRMS (ESI/Q-TOF) (m/z) calcd for $C_{16}H_{19}F_3NO_6$ [M + H]$^+$ 378.1159; found 378.1162.

*Ethyl (Z)-3-hydroxy-2-(2-nitro-4-(trifluoromethyl)phenyl) but-2-enoate (**2g**).*[35] As a yellow liquid (62 mg, 39% yield); purification over a column of silica gel (10−15% EtOAc in hexane); ^{1}H NMR ($CDCl_3$, 500 MHz): δ 13.06 (s, 1H), 8.24 (d, 1H, J = 2.0 Hz), 7.83 (dd, 1H, J_1 = 2.0 Hz, J_2 = 8.0 Hz), 7.47 (d, J = 8.0 Hz, 1H), 4.23−4.17 (m, 1H), 4.06−3.99 (m, 1H), 1.87 (s, 3H), 1.10 (t, J = 7.0 Hz, 3H); ^{13}C{^{1}H} NMR ($CDCl_3$, 125 MHz): δ 174.1, 170.6, 149.9, 135.2, 134.1, 131.4, 131.1, 129.3 (q, J = 3.4 Hz), 124.1, 121.9 (q, J = 4.0, Hz), 100.3, 61.4, 20.0, 13.9; ^{19}F NMR ($CDCl_3$): δ −62.9 (s); IR (KBr, cm^{-1}): 3026, 2974, 2924, 2861, 1737, 1605, 1537, 1319, 1130, 1078, 709; HRMS (ESI/Q-TOF) (m/z) calcd for $C_{13}H_{13}F_3NO_5$ [M + H]$^+$ 320.0740; found 320.0737.

*(Z)-4-Hydroxy-3-(2-nitro-4-(trifluoromethyl)phenyl)pent-3-en-2-one (**2h**).*[36] As a yellow liquid (54 mg, 37% yield); purification over a column of silica gel (10−15% EtOAc in hexane); ^{1}H NMR ($CDCl_3$, 400 MHz): δ 16.54 (s, 1H), 8.21 (d, 1H, J = 2.0 Hz), 7.91 (dd, 1H, J_1 = 1.6 Hz, J_2 = 8.0 Hz), 7.55 (d, 1H, J = 8.0 Hz), 1.85 (s, 6H); ^{13}C{^{1}H} NMR ($CDCl_3$, 100 MHz): δ 190.1, 150.7, 135.2, 132.5, 132.2, 129.8 (q, J = 3.4 Hz), 124.2, 122.0 (q, J = 3.6 Hz), 109.4, 24.2; ^{19}F NMR ($CDCl_3$): δ −62.9 (s); IR (KBr, cm^{-1}): 3103, 2970, 2916, 2853, 1737, 1605, 1537, 1319, 1257, 1175, 1130, 1078, 847, 789; HRMS (ESI/Q-TOF) (m/z) calcd for $C_{12}H_{11}F_3NO_4$ [M + H]$^+$ 290.0635; found 290.0627.

*Dimethyl 2-(2,4-dinitrophenyl)-2-methylmalonate (**3a**).* As a yellow liquid (114 mg, 73% yield); purification over a column of silica gel (10−15% EtOAc in hexane); ^{1}H NMR ($CDCl_3$, 400 MHz): δ 8.88 (d, 1H, J = 2.4 Hz), 8.44 (dd, 1H, J_1 = 2.4 Hz, J_2 = 8.8 Hz), 7.62 (d, 1H, J = 8.8 Hz), 3.76 (s, 6H), 2.06 (s, 3H); ^{13}C{^{1}H} NMR ($CDCl_3$, 100 MHz): δ 169.4, 149.3, 147.4, 140.9, 130.9, 127.4, 121.5, 59.4, 53.7, 23.8; IR (KBr, cm^{-1}): 3136, 3095, 2955, 2923, 2853, 1730, 1711, 1603, 1531, 1435, 1347, 1245, 1123, 1068, 972, 810, 782, 721; HRMS (ESI/Q-TOF) (m/z) calcd for $C_{12}H_{13}N_2O_8$ [M + H]$^+$ 313.0666; found 313.0723.

*Dimethyl 2-benzyl-2-(2,4-dinitrophenyl)malonate (**3b**).* As a yellow liquid (155 mg, 80% yield); purification over a column of silica gel (10−15% EtOAc in hexane); ^{1}H NMR ($CDCl_3$, 400 MHz): δ 8.73 (d, 1H, J = 2.4 Hz), 7.99 (dd, 1H, J_1 = 2.4 Hz, J_2 = 8.8 Hz),7.12−7.05 (m, 3H), 6.96 (d, 2H, J = 8.0 Hz), 6.78 (d, 1H, J = 8.8 Hz), 4.01 (s, 2H), 3.78 (s, 6H); ^{13}C{^{1}H} NMR ($CDCl_3$, 100 MHz): δ 168.5,138.2, 135.7, 134.4, 130.8, 128.4, 127.5, 125.2, 120.5, 65.6, 53.8, 40.8; IR (KBr, cm^{-1}): 3092, 3034, 2955, 2924, 2850, 1738, 1604, 1531, 1496, 1434, 1384, 1258, 1209, 1168, 1059, 907, 858, 725; HRMS (ESI/Q-TOF) (m/z) calcd for $C_{18}H_{17}N_2O_8$ [M + H]$^+$ 389.0979; found 389.0979.

■ ASSOCIATED CONTENT

Supporting Information

The Supporting Information is available free of charge at https://pubs.acs.org/doi/10.1021/acsomega.2c06865.

List of unsuccessful reactions and characterization data of the compounds (PDF)

FAIR Data, including the primary NMR FID files for compounds: [**1a−k, 2a, 2b, 2f−h, 3a, and 3b**] (CIF)

1j-Cesium (CIF)

1j-Potasium (CIF)

FID for publication (ZIP)

Accession Codes

CCDC 2155058, 2155062, and 2166732 contain supplementary crystallographic data for this paper. This data can be obtained free of charge via www.ccdc.cam.ac.uk-requst/cif, by emailing data-request@ccdc.cam.ac.uk, or by contacting The Cambridge Crystallographic Data Centre, 12 Union Road, Cambridge CB2 1EZ, UK; fax: +44 1223 336033.

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Author Contributions

S.M. performed the experiments and analyzed data; G.D. helped in crystallographic analyses. B.M. conceived and supervised the project, managed funding, and analyzed data.

All authors contributed to writing the manuscript and have approved the final version of the manuscript.

Notes

The authors declare no competing financial interest.

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