Synthesis K. A. Aravinda Kumar et al. Paper

A Metal-Free Approach to Carboxylic Acids by Oxidation of Alkyl, Aryl, or Heteroaryl Alkyl Ketones or Arylalkynes

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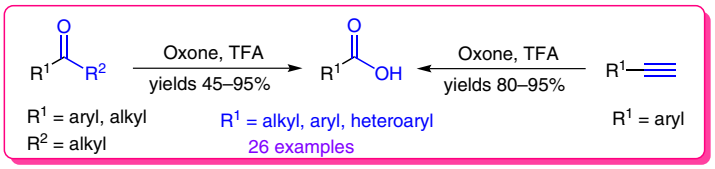

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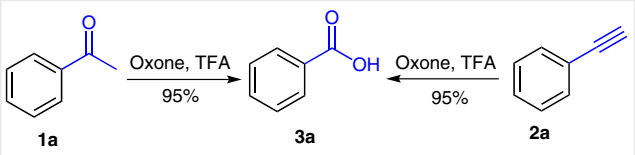
Abstract The metal-free oxidation of dialkyl, alkyl aryl, or alkyl heteroaryl ketones or arylalkynes to the corresponding carboxylic acids is achieved using an oxidative mixture of Oxone and trifluoroacetic acid. This green method is a simple and mild protocol to obtain carboxylic derivatives in excellent yields.

Key words ketones, alkynes, oxidation, carboxylic acids, green chemistry

The carboxylic acid moiety is an important functional group in organic chemistry or biology, and it plays an important role as a versatile building block in the synthesis of natural products, pharmaceuticals, agricultural chemicals, polymers, and dyes.[1] Many oxidation processes to prepare such carbonyl derivatives are known to produce undesired waste materials. In conventional oxidation procedures, nitric acid, sulfuric acid, hydrogen peroxide, hydrobromic acid, carbon tetrabromide–triphenylphosphine, and other oxidants are commonly used that have harsh conditions and it is sometimes difficult to perform the oxidation in a controlled manner.[2] Frequently, oxidation processes are problematic and many are unacceptable for practical synthetic use. The use of heavy metal oxidants produces toxic waste during the process. Therefore, an efficient oxidant/reagent/catalyst system and the correct choice of reaction conditions are important for the feasibility of an ideal oxidation procedure.

Several long-standing methods for the synthesis of carboxylic acids involve the ozonolysis[3] of olefins and alkynes or the two-step dihydroxylation and oxidative cleavage of diols with sodium periodate and oxidants.[4] These methods aside, there are many methods that have been reported for the conversion of acetophenones and terminal arylalkynes into the corresponding carboxylic acids by the direct conversion of alkynes and/or alkenes to carboxylic acids catalyzed by different metals such as osmium; the olefin oxidation is carried out with osmium tetroxide and a variety of co-oxidants [H_2O_2, TBHP, Oxone, PhI(OAc)$_2$, $NaIO_4$] are used.[5] Manganese and its oxides are also used for this type of conversion.[6] Ruthenium[4b,7] and other metals including lead,[8] gold,[9] rhenium,[10] and tungsten oxides,[11] and other metals or their oxides, have been used for the oxidation of various precursors to carbonyl derivatives. Many oxo acids have also been used for this type of oxidation reaction.[12] The development of novel metal-free methods for the preparation of carboxylic acids is an interesting target for organic chemists. Simple, inexpensive, and metal-free methods have great importance for this conversion; safer and cleaner oxidation procedures are still in demand and need to be developed.

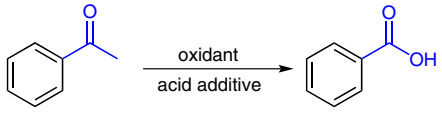
In continuation of our interest in the development of metal-free reactions,[13] we now report a simple and efficient method for the oxidation of dialkyl, alkyl aryl, or alkyl heteroaryl ketones or arylalkynes to the corresponding carboxylic acids. Excellent yields of carboxylic acids were obtained when the reaction was carried out with a mixture of trifluoroacetic acid and Oxone. Initially, acetophenone (**1a**) was chosen to optimize the reaction conditions. The reaction of acetophenone (**1a**) with trifluoroacetic acid and Oxone (1:1) in 1,4-dioxane at 101 °C gave the desired carboxylic acid **3a** in good yield (Scheme 1). Similarly, phenylacetylene (**2a**) was converted into benzoic acid (**3a**) in excellent yield (Scheme 1). The reaction with Oxone or trifluoroacetic acid alone did not give the product; this confirms that using trifluoroacetic acid alone had no effect. The proportional mixture of Oxone/trifluoroacetic acid (1:1; 2 equiv with respect to reactant) is required for the reaction to progress.



Scheme 1 Formation of benzoic acid from acetophenone or phenylacetylene by oxidation using trifluoroacetic acid/Oxone mixture

Even though, the yields were found to be excellent in this reaction, we optimized the reaction conditions for the reaction of acetophenone (**1a**) by screening various oxidants, acid additives, and solvents (Table 1). The best conversion uses the Oxone and trifluoroacetic acid mixture (1:1; 2 equiv with respect to reactant) (entry 4). Among the solvents screened only tetrahydrofuran and 1,4-dioxane gave the desired product **3a** in 70% and 95% yields, respectively (entries 4 and 5); therefore, 1,4-dioxane was chosen to perform future reactions. The optimized conditions used for all further reactions are as shown in Table 1, entry 4.

Table 1 Optimization of Reaction Conditions for the Formation of Carboxylic Acids from Acetophenone Substrate



Entry	Solvent	Oxidant (equiv)	Acid additive (equiv)	Temp (°C)	Time (h)	Yield (%)
1	1,4-dioxane	Oxone (2)	TFA (2)	30	10	–
2	1,4-dioxane	Oxone (2)	TFA (2)	80	10	65
3	1,4-dioxane	Oxone (1)	TFA (1)	101	10	70
4	**1,4-dioxane**	**Oxone (2)**	**TFA (2)**	**101**	**10**	**95**
5	THF	Oxone (2)	TFA (2)	66	10	70
6	1,4-dioxane	Oxone (2)	$AlCl_3$ (2)	101	10	–
7	1,4-dioxane	Oxone (2)	$ZnCl_2$ (2)	101	10	–
8	1,4-dioxane	Oxone (2)	H_2SO_4 (2)	101	10	88
9	1,4-dioxane	Oxone (2)	AcOH (2)	101	10	30
10	1,4-dioxane	H_2O_2 (2)	TFA (2)	101	10	–
11	1,4-dioxane	TBHP (2)	TFA (2)	101	10	–
12	1,4-dioxane	MCPBA (2)	TFA (2)	101	10	–
13	1,4-dioxane	IBX (2)	TFA (2)	101	10	–
14	DMF	Oxone (2)	TFA (2)	154	10	–
15	H_2O	Oxone (2)	TFA (2)	100	10	–
16	MeOH	Oxone (2)	TFA (2)	65	10	–
17	1,4-dioxane	Oxone (2)	TCA (2)	101	10	–
18	1,4-dioxane	$K_2S_2O_8$ (2)	TFA (2)	101	10	–
19	1,4-dioxane	DTBP	TFA (2)	101	10	–
20	1,4-dioxane	$Na_2S_2O_8$ (2)	TFA (2)	101	10	–

To explore the possibility of varying the aryl substitution, alkyl substituted-aryl ketones were reacted with Oxone/trifluoroacetic acid under the optimized conditions (Table 1, entry 4). Various substituted-acetophenones **1a**–**n** were converted smoothly into the corresponding carboxylic acids **3a**–**n** (Table 2). Acetophenone substrates containing aryl groups substituted either with electron-withdrawing groups or electron-donating groups performed equally well and gave excellent yields of the corresponding carboxylic acid derivatives in 80–95% yields.

Table 2 Synthesis of Various Arenecarboxylic Acids from Alkyl Aryl Ketones under the Optimized Conditions

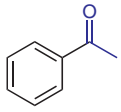
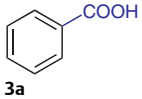
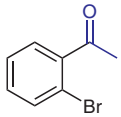
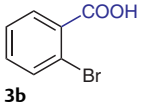
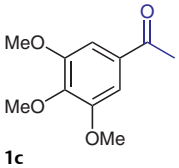
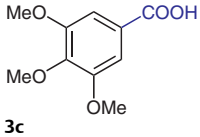
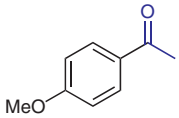
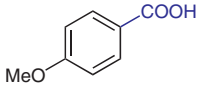
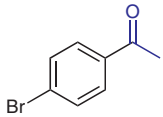
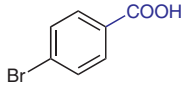
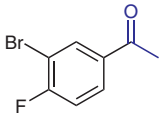
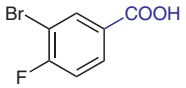
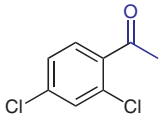
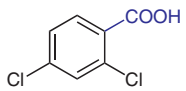
Entry	Substrate	Product	Yield (%)
1	 **1a**	 **3a**	95
2	 **1b**	 **3b**	88
3	 **1c**	 **3c**	95
4	 **1d**	 **3d**	90
5	 **1e**	 **3e**	85
6	 **1f**	 **3f**	88
7	 **1g**	 **3g**	80

Table 2 (continued)

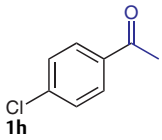
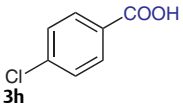
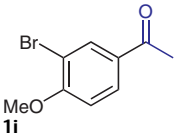
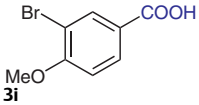
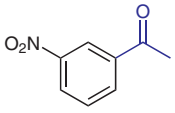
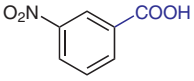
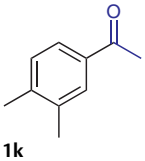
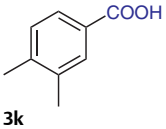
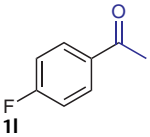
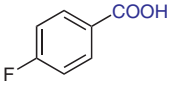
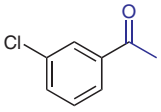
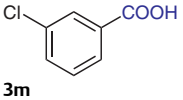
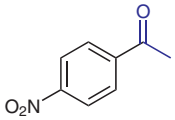
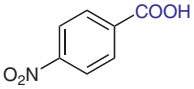
Entry	Substrate	Product	Yield (%)
8	 **1h**	 **3h**	85
9	 **1i**	 **3i**	87
10	 **1j**	 **3j**	81
11	 **1k**	 **3k**	86
12	 **1l**	 **3l**	88
13	 **1m**	 **3m**	84
14	 **1n**	 **3n**	82

Table 3 Synthesis of Various Alkane or Heteroarenecarboxylic Acids from Dialkyl or Alkyl Heteroaryl Ketones under the Optimized Conditions

Entry	Substrate	Product	Yield (%)
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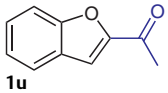
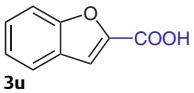
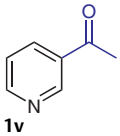
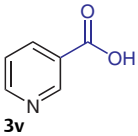
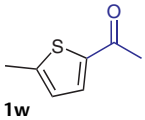
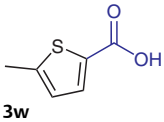
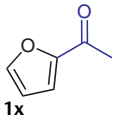
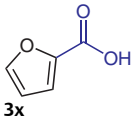
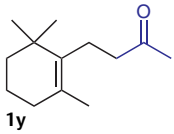
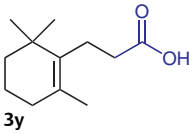
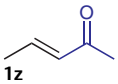
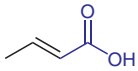
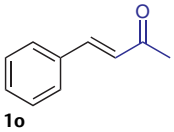
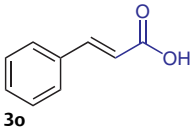
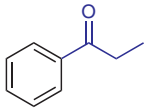
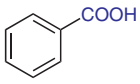
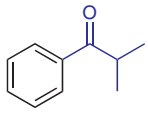
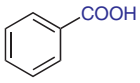
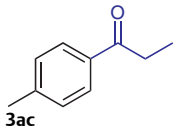
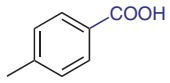
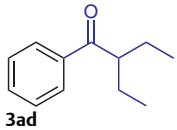
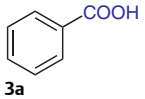
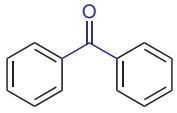
1	 **1u**	 **3u**	80
2	 **1v**	 **3v**	90
3	 **1w**	 **3w**	70
4	 **1x**	 **3x**	67
Alkyl			
5	 **1y**	 **3y**	60
6	 **1z**	 **3z**	58
7	 **1o**	 **3o**	68

Furthermore, this reaction was expanded to the use of alkyl heteroaryl and dialkyl ketones. The reaction with 2-acetylbenzofuran (**1u**) was performed and gave benzofuran-2-carboxylic acid (**3u**) in 80% yield (Table 3, entry 1). A few other heteroaryl substrates **1v**–**x** were explored (Table 3), which also gave respective products **3v**–**x** in good yields (entries 2–4). The use of the alkyl substrates **1o**,**y**,**z** was examined (entries 5–7) and gave the corresponding products **3o**,**y**,**z** in lower yields. Dihydro-β-ionone **1y** was converted into β-ionic acid **3y** in 60% yield, while α,β-unsaturated substrates pent-3-en-2-one (**1z**) and benzylideneacetone (**1o**) were converted into but-2-enoic acid (**3z**) and cinnamic acid (**3o**) in 58% and 68% yields, respectively.

Similarly, the use of various α-substituted alkyl aryl ketones **3aa**–**3ae** was examined (Table 4) to examine the possibilities of this reaction. The reaction of propiophenone (**3aa**) with trifluoroacetic acid/Oxone gave benzoic acid (**3a**) in 62% yield (entry 1). Other reactions with α-alkyl-substituted alkyl aryl ketones **3ab**–**ad** gave the products corresponding products **3a** and **3p** (entries 2–4), but benzophenone (**3ae**) was not converted into the carboxylic acid product (entry 5). The reason for the failure to react with benzophenone (**3ae**) could be its electronic nature, which is less reactive and in this case, it is difficult to cleave the C–C bond between phenyl ring and carbonyl carbon.

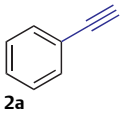
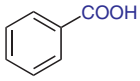
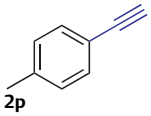
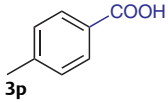
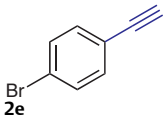
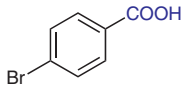
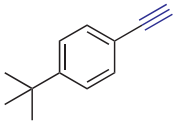
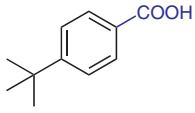
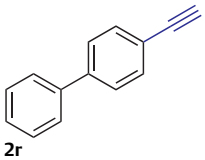
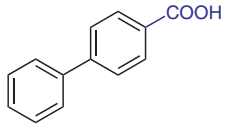
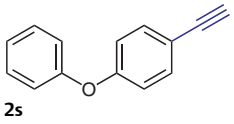
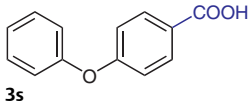
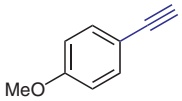
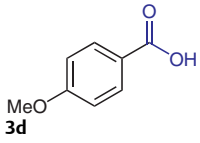
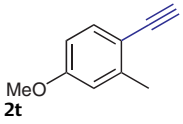
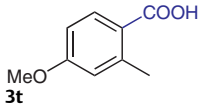
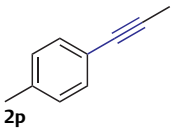
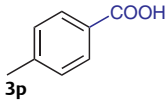
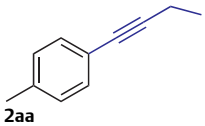
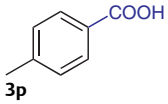
Table 4 Synthesis of Carboxylic Acids from Various α-Substituted Alkyl Aryl Ketones under the Optimized Conditions

Entry	Substrate	Product	Yield (%)
1	 **3aa**	 **3a**	62
2	 **3ab**	 **3a**	47
3	 **3ac**	 **3p**	60
4	 **3ad**	 **3a**	45
5	 **3ae**	–	–

The oxidative cleavage of alkynes to carboxylic acids is a fundamental reaction in organic chemistry. Many methods are known for this conversion and the use of Ozone, potassium permanganate, molybdenum, tungsten, or ruthenium reagents, and hydrogen peroxide mediated oxidation reaction are well reported.[14] The Oxone–trifluoroacetic acid procedure utilized for the oxidation of alkyl aryl ketones was also applied to substituted arylacetylenes **2**. The required substituted benzoic acids **3** were obtained in good to excellent yields for all substrates; various substitutions such as electron-donating and electron-withdrawing groups on the aryl group were acceptable (Table 5).

In summary, we have developed a mild and efficient procedure for the oxidation of dialkyl ketones, alkyl aryl ketones, or alkyl heteroaryl ketones or arylalkynes to the corresponding carboxylic acids in the presence of Oxone/trifluoroacetic acid. The present protocol is simple and can be effectively implemented in organic synthesis for various applications.

Table 5 Synthesis of Various Arenecarboxylic Acids from Arylalkynes under the Optimized Conditions

Entry	Substrate	Product	Yield (%)
1	 **2a**	 **3a**	95
2	 **2p**	 **3p**	90
3	 **2e**	 **3e**	89
4	 **2q**	 **3q**	87
5	 **2r**	 **3r**	87
6	 **2s**	 **3s**	83
7	 **2d**	 **3d**	91
8	 **2t**	 **3t**	90
9	 **2p**	 **3p**	83
10	 **2aa**	 **3p**	80

Analytical TLC was performed using TLC pre-coated silica gel 60 F_{254} Merck (20 × 20 cm). TLC plates were visualized by exposure to UV light or I_2 vapor, or immersion in an acidic staining solution of *p*-anisaldehyde followed by heating on hot plate. Organic solvents were removed by rotary evaporation on Buchi-Switzerland R-120 rotary evaporator and vacuum pump V-710. Purification of compounds was by column chromatography using Merck silica gel 230–400 mesh size. ^{1}H or ^{13}C NMR spectra were recorded with Bruker 400 or 500 MHz NMR instruments referenced to the residual proton in the NMR solvent ($CDCl_3$: δ = 7.26, or other solvents as mentioned). All NMR spectra were processed with either MestReNova or Bruker software. Mass spectra were recorded with an Agilent mass spectrometer.

Benzoic Acid (3a);[15a] Typical Procedure from Acetophenone or Phenylacetylene

To a mixture of acetophenone (100 mg, 1 equiv) or phenylacetylene (1 equiv) in dioxane (5 mL), Oxone (2 equiv) and TFA (2 equiv) were added. The mixture was then heated to reflux for 10 h and then cooled to r.t. H_2O (10 mL) was added and the mixture was extracted with EtOAc (2 × 20 mL). The combined organic layers were treated with sat. $NaHCO_3$ solution and the aqueous layer was poured onto crushed ice and treated with 2 M HCl; a colorless solid precipitated out. The precipitate was filtered off and dried in vacuo to give benzoic acid (3a)[15a] after column chromatography (silica gel; EtOAc–hexane, 1:9) as a white crystalline solid; yield: 0.096 g (95%) from 1a; mp 122–123 °C.

^{1}H NMR (400 MHz, CD_3OD): δ = 8.03 (d, *J* = 7.6 Hz, 2 H), 7.54 (t, *J* = 7.3 Hz, 1 H), 7.43 (t, *J* = 7.6 Hz, 2 H).

^{13}C NMR (100 MHz, CD_3OD): δ = 170.0, 134.1, 131.8, 130.8, 129.5.

MS (ESI): *m*/*z* = 123.3.

2-Bromobenzoic Acid (3b)[15a]

White solid; yield: 0.089 g (88%); mp 148–150 °C.

^{1}H NMR (400 MHz, CD_3OD): δ = 7.70–7.67 (m, 1 H), 7.58 (d, *J* = 8.0 Hz, 1 H), 7.33–7.25 (m, 2 H).

^{13}C NMR (126 MHz, CD_3OD): δ = 169.7, 135.3, 134.6, 133.6, 132.2, 128.5, 122.0.

MS (ESI, –): *m*/*z* = 199.2 [M^+ – 1].

3,4,5-Trimethoxybenzoic Acid (3c)[15d]

White crystalline solid; yield: 0.096 g (95%); mp 167–170 °C.

^{1}H NMR (400 MHz, $CDCl_3$): δ = 7.38 (s, 2 H), 3.94 (s, 3 H), 3.93 (s, 6 H).

^{13}C NMR (126 MHz, $CDCl_3$): δ = 171.4, 152.9, 142.9, 124.1, 107.4, 60.9, 56.2.

MS (ESI, –): *m*/*z* = 211.2 [M^+ – 1].

4-Methoxybenzoic Acid (3d)[15a]

White solid; yield: 0.091 g (90%); mp 183 °C.

^{1}H NMR (500 MHz, CD_3OD): δ = 7.87 (d, *J* = 8.9 Hz, 2 H), 6.87 (d, *J* = 8.9 Hz, 2 H), 3.75 (s, 3 H).

^{13}C NMR (126 MHz, CD_3OD): δ = 169.8, 165.1, 132.9, 124.0, 114.7, 55.9.

MS (ESI, –): *m*/*z* = 151.2 [M^+ – 1].

4-Bromobenzoic Acid (3e)[15a]

White solid; yield: 0.086 g (85%); mp 253 °C.

^{1}H NMR (400 MHz, CD_3OD): δ = 7.82 (d, *J* = 8.5 Hz, 2 H), 7.55 (d, *J* = 8.5 Hz, 2 H).

^{13}C NMR (126 MHz, CD_3OD): δ = 168.8, 132.8, 132.5, 131.1, 128.8.

MS (ESI, –): *m*/*z* = 199.2 [M^+ – 1].

3-Bromo-4-fluorobenzoic Acid (3f)[15e]

White solid; yield: 0.088 g (88%); mp 138–140 °C.

^{1}H NMR (400 MHz, $CDCl_3$): δ = 8.34 (m, 1 H), 8.07 (m, 1 H), 7.23 (m, 1 H).

^{19}F NMR (376 MHz, $CDCl_3$): δ = –98.11 (td, *J* = 7.2, 5.2 Hz).

^{13}C NMR (101 MHz, $CDCl_3$): δ = 170.2, 162.7 (d, *J* = 256.2 Hz), 136.1 (d, *J* = 1.7 Hz), 131.5 (d, *J* = 8.8 Hz), 126.7 (d, *J* = 3.5 Hz), 116.7 (d, *J* = 23.1 Hz), 109.5 (d, *J* = 21.8 Hz).

MS (ESI, –): *m*/*z* = 216.8 [M^+ – 1].

2,4-Dichlorobenzoic Acid (3g)[15b]

White solid; yield: 0.081 g (80%); mp 157–160 °C.

^{1}H NMR(400 MHz, $CDCl_3$): δ = 7.99 (d, *J* = 8.5 Hz, 1 H), 7.53 (d, *J* = 1.9 Hz, 1 H), 7.35 (dd, *J* = 8.5, 2.0 Hz, 1 H).

^{13}C NMR (101 MHz, $CDCl_3$): δ = 169.3, 139.6, 136.1, 133.5, 131.45, 127.2, 126.6.

MS (ESI, –): *m*/*z* = 189.2 [M^+ – 1].

4-Chlorobenzoic Acid (3h)[15b]

White solid; yield: 0.086 g (85%); mp 238–240 °C.

^{1}H NMR (400 MHz, CD_3OD): δ = 7.89 (d, *J* = 8.6 Hz, 2 H), 7.38 (d, *J* = 8.6 Hz, 2 H).

^{13}C NMR (101 MHz, CD_3OD): δ = 168.8, 140.2, 132.3, 129.7.

MS (ESI, –): *m*/*z* = 155.2 [M^+ – 1].

3-Bromo-4-methoxybenzoic Acid (3i)[15i]

White solid; yield: 0.087 g (87%); mp 220–221 °C.

^{1}H NMR (400 MHz, CD_3OD): δ = 8.05 (d, *J* = 2.1 Hz, 1 H), 7.90 (dd, *J* = 8.6, 2.1 Hz, 1 H), 7.01 (d, *J* = 8.7 Hz, 1 H), 3.85 (s, 3 H).

^{13}C NMR (126 MHz, CD_3OD): δ = 168.4, 161.0, 135.7, 132.0, 125.4, 112.5, 112.2, 57.0.

MS (ESI, –): *m*/*z* = 228.9 [M^+ – 1].

3-Nitrobenzoic Acid (3j)[15a]

Pale yellow solid; yield: 0.082 g (81%); mp 139–140 °C.

^{1}H NMR (400 MHz, CD_3OD): δ = 8.65 (d, *J* = 1.7 Hz, 1 H), 8.36–8.31 (m, 1 H), 8.26 (d, *J* = 7.7 Hz, 1 H), 7.63 (t, *J* = 8.0 Hz, 1 H).

^{13}C NMR (126 MHz, CD_3OD): δ = 165.9, 148.2, 135.0, 132.4, 129.6, 126.8, 123.8.

MS (ESI, –): *m*/*z* = 166.1 [M^+ – 1].

3,4-Dimethylbenzoic Acid (3k)[15c]

White solid; yield: 0.087 g (86%); mp 164 °C.

^{1}H NMR (400 MHz, $CDCl_3$): δ = 7.93–7.81 (m, 2 H), 7.28–7.18 (m, 1 H), 2.33 (d, *J* = 4.5 Hz, 6 H).

^{13}C NMR (101 MHz, $CDCl_3$): δ = 172.7, 143.3, 136.8, 131.2, 129.8, 127.8, 126.9, 20.1, 19.6.

MS (ESI, –): *m*/*z* = 148.8 [M^+ – 1].

4-Fluorobenzoic Acid (3l)[15b]

White crystalline solid; yield: 0.089 g (88%); mp 184 °C.

^{1}H NMR (400 MHz, $CDCl_3$): δ = 8.16–8.13 (m, 2 H), 7.15 (t, *J* = 8.0 Hz, 2 H).

^{13}C NMR (126 MHz, $CDCl_3$): δ = 168.7, 168.4, 165.9, 138.5, 133.4, 128.4, 116.5.

MS (ESI, –): *m*/*z* = 139.0 [M$^+$ – 1].

3-Chlorobenzoic Acid (3m)[15b]

White crystalline solid; yield: 0.085 g (84%); mp 167–170 °C.

^{1}H NMR (400 MHz, $CDCl_3$): δ = 8.09 (s, 1 H), 8.00 (d, *J* = 7.7 Hz, 1 H), 7.59 (d, *J* = 8.0 Hz, 1 H), 7.42 (t, *J* = 7.9 Hz, 1 H).

^{13}C NMR (101 MHz, CD_3OD): δ = 168.4, 135.5, 133.9, 131.2, 130.5, 129.0.

4-Nitrobenzoic Acid (3n)[15a]

Pale yellow solid; yield: 0.083 g (82%); mp 238 °C.

^{1}H NMR (400 MHz, CD_3OD): δ = 8.23 (d, *J* = 8.8 Hz, 2 H), 8.13 (d, *J* = 8.8 Hz, 2 H).

^{13}C NMR (126 MHz, CD_3OD): δ = 167.6, 151.9, 137.6, 131.9, 124.5.

MS (ESI, –): *m*/*z* = 166.2 [M$^+$ – 1].

Cinnamic Acid (3o)[15l]

White crystalline solid; yield: 0.069 g (68%); mp 130 °C.

^{1}H NMR (500 MHz, $CDCl_3$): δ = 7.81 (d, *J* = 16.0 Hz, 1 H), 7.57–7.55 (m, 2 H), 7.44–7.38 (m, 3 H), 6.47 (d, *J* = 16.0 Hz, 1 H).

^{13}C NMR (126 MHz, $CDCl_3$): δ = 172.8, 147.2, 134.0, 130.8, 129.0, 128.4, 117.3.

MS (ESI, +): *m*/*z* = 147.3 [M$^+$ + 1].

4-Methylbenzoic Acid (3p)[15a,c]

White solid; yield: 0.105 g (90%); mp 274 °C.

^{1}H NMR (400 MHz, $CDCl_3$): δ = 8.03 (d, *J* = 8.1 Hz, 2 H), 7.27 (t, *J* = 8.1 Hz, 2 H), 2.46 (s, 3 H).

^{13}C NMR (101 MHz, CD_3OD): δ = 170.1, 145.0, 130.8, 130.1, 129.1, 21.6.

MS (ESI, +): *m*/*z* = 137.4 [M$^+$ + 1].

4-*tert*-Butylbenzoic Acid (3q)[15a]

Colorless solid; yield: 0.088 g (87%); mp 162–164 °C.

^{1}H NMR (400 MHz, $CDCl_3$): δ = 8.04 (d, *J* = 8.5 Hz, 2 H), 7.49 (d, *J* = 8.5 Hz, 2 H), 1.35 (s, 9 H).

^{13}C NMR (126 MHz, $CDCl_3$): δ = 172.4, 150.2, 130.1, 129.1, 125.6, 40.6, 31.3.

MS (ESI, –): *m*/*z* = 177.2 [M$^+$ – 1].

4-Phenylbenzoic Acid (3r)[15c]

White solid; yield: 0.088 g (87%); mp 223–224 °C.

^{1}H NMR (500 MHz, CD_3OD): δ = 7.99 (dt, *J* = 8.4, 1.8 Hz, 2 H), 7.65–7.60 (m, 2 H), 7.59–7.55 (m, 2 H), 7.38–7.35 (m, 2 H), 7.31–7.26 (m, 1 H).

^{13}C NMR (126 MHz, CD_3OD): δ = 169.7, 147.0, 141.3, 131.4, 130.6, 130.1, 129.3, 128.2, 128.0.

MS (ESI, –): *m*/*z* = 197.3 [M$^+$ – 1].

4-Phenoxybenzoic Acid (3s)[15i]

White solid; yield: 0.084 g (83%); mp 165 °C.

^{1}H NMR (400 MHz, $CDCl_3$): δ = 8.08 (d, *J* = 8.8 Hz, 2 H), 7.41 (t, *J* = 7.9 Hz, 2 H), 7.21 (t, *J* = 7.4 Hz, 1 H), 7.09 (d, *J* = 7.7 Hz, 2 H), 7.01 (d, *J* = 8.8 Hz, 2 H).

^{13}C NMR (126 MHz, CD_3OD): δ = 169.3, 163.4, 157.09, 133.0, 131.2, 126.1, 125.7, 121.2, 118.2.

4-Methoxy-2-methylbenzoic Acid (3t)[15i]

White solid; yield: 0.102 g (90%); mp 178 °C.

^{1}H NMR (400 MHz, DMSO): δ = 7.84 (d, *J* = 8.3 Hz, 1 H), 6.84 (s, 1 H), 6.82 (d, *J* = 2.4 Hz, 1 H), 3.79 (s, 3 H), 2.52 (s, 3 H).

^{13}C NMR (126 MHz, DMSO): δ = 168.0, 161.7, 142.1, 132.7, 122.0, 116.6, 111.1, 55.2, 21.8.

MS (ESI, +): *m*/*z* = 163.3 [M$^+$ + 1].

Benzofuran-2-carboxylic Acid (3u)[15j]

Light yellow solid; yield: 0.081 g (80%); mp 175–176 °C.

^{1}H NMR (500 MHz, CD_3OD): δ = 7.72 (d, *J* = 7.9 Hz, 1 H), 7.57 (t, *J* = 4.2 Hz, 2 H), 7.48–7.44 (m, 1 H), 7.31 (t, *J* = 7.5 Hz, 1 H).

^{13}C NMR (126 MHz, CD_3OD): δ = 161.0, 155.7, 146.0, 127.3, 127.1, 123.5, 122.6, 113.4, 111.5.

MS (ESI): *m*/*z* = 163.2 [M$^+$ + H].

Nicotinic Acid (3v)[15f]

White solid; yield: 0.091 g (90%); mp 236–239 °C.

^{1}H NMR (400 MHz, CD_3OD): δ = 9.02 (s, 1 H), 8.64 (d, *J* = 3.6 Hz, 1 H), 8.33–8.31 (m, 1 H), 7.49–7.46 (m, 1 H).

^{13}C NMR (101 MHz, CD_3OD): δ = 167.7, 153.6, 151.2, 139.3, 128.7, 125.3.

MS (ESI, +): *m*/*z* = 124.2 [M$^+$ + 1].

5-Methylthiophene-2-carboxylic Acid (3w)[15h]

Light yellow solid; yield: 0.071 g (70%); mp 139 °C.

^{1}H NMR (500 MHz, $CDCl_3$): δ = 7.71 (d, *J* = 2.6 Hz, 1 H), 6.81 (s, 1 H), 2.55 (s, 3 H).

^{13}C NMR (126 MHz, $CDCl_3$): δ = 165.6, 147.7, 133.4, 128.0, 124.6, 13.7.

MS (ESI, –): *m*/*z* = 143.0 [M$^+$ – 1].

2-Furoic acid (3x)[15g]

White color solid; yield: 0.068 g (67%); mp 128–132 °C.

^{1}H NMR (500 MHz, $CDCl_3$): δ = 10.92 (s, 1 H), 7.65 (d, *J* = 21.1 Hz, 1 H), 7.34 (dd, *J* = 22.5, 3.4 Hz, 1 H), 6.59–6.54 (m, 1 H).

^{13}C NMR (126 MHz, $CDCl_3$): δ = 163.8, 147.5, 143.8, 120.2, 112.3.

MS (ESI, +): *m*/*z* = 113.2 [M$^+$ + 1].

3-(2,6,6-Trimethylcyclohex-1-enyl)propanoic Acid (Dihydro-β-ionic Acid, 3y)[15m]

Colorless liquid; yield: 0.061 g (60%).

^{1}H NMR (400 MHz, $CDCl_3$): δ = 2.43–2.39 (m, 2 H), 2.37–2.34 (m, 2 H), 1.93–1.89 (t, *J* = 6.2 Hz, 2 H), 1.61 (s, 3 H), 1.61–1.55 (m, 2 H), 1.44–1.41 (m, 2 H), 1.00 (s, 6 H).

^{13}C NMR (101 MHz, $CDCl_3$): δ = 180.3, 135.4, 128.5, 39.7, 34.9, 34.7, 32.7, 28.3, 23.5, 19.65, 19.4.

HRMS (ESI, +): *m*/*z* [M$^+$] calcd for $C_{12}H_{20}O_2$: 196.1458; found: [M + H$^+$] 197.1530

Crotonic Acid (3z)[15k]

White color solid; yield: 0.059 g (58%); mp 181 °C.

^{1}H NMR (500 MHz, $CDCl_3$): δ = 12.34 (s, 1 H), 7.17–7.01 (m, 1 H), 5.91–5.79 (m, 1 H), 1.98–1.76 (m, 3 H).

^{13}C NMR (126 MHz, $CDCl_3$): δ = 172.3, 147.6, 122.2, 18.0.

MS (ESI, +): *m*/*z* = 87.2 [M$^+$ + 1].

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