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Cleavage of Carboxylic Esters by Aluminum and Iodine

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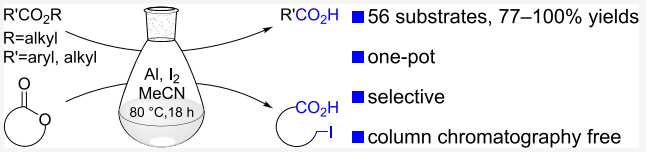
ABSTRACT: A one-pot procedure for deprotecting carboxylic esters under nonhydrolytic conditions is described. Typical alkyl carboxylates are readily deblocked to the carboxylic acids by the action of aluminum powder and iodine in anhydrous acetonitrile. Cleavage of lactones affords the corresponding ω-iodoalkylcarboxylic acids. Aryl acetylates undergo deacetylation with the participation of the neighboring group. This method enables the selective cleavage of alkyl carboxylic esters in the presence of aryl esters.



INTRODUCTION

Carboxylic acids and phenols are frequently masked as carboxylic esters in multistep organic syntheses.[1] Selective hydrolysis of esters is often crucial in complex synthetic sequences.[2] An array of methods has been established to unmask one out of two or more ester groups, such as the selective cleavage of methyl esters in the presence of bulkier alkyl esters by Me_3SnOH,[2] NaCN,[3] and $(Bu_3Sn)_2O$,[4] the selective cleavage of allyl esters in the presence of alkyl esters by $NaBH_4$,[5] the selective cleavage of *tert*-butyl esters by ytterbium triflate[6] and trifluoroacetic acid,[7] and the selective cleavage of prenyl esters by silica-supported $NaHSO_4$.[8] Notably, methods available for the selective cleavage of esters usually rupture the aryl ester preferentially in the presence of alkyl esters,[9] due to the good leaving-group nature of the phenolic moiety.[2] For example, methyl 4-acetoxybenzoate has been selectively deacetylated to afford methyl 4-hydroxybenzoate efficiently by AcCl−MeOH,[10] $AlCl_3·6H_2O$−KI,[11] Amberlyst-15,[12] NH_4Ac,[13] K_2CO_3,[9a] $NaBO_3$,[14] PhSNa,[15] toluene-4-sulfonic acid absorbed on silica,[16] and baker's yeast[17] (Scheme 1A). In sharp contrast, approaches for selective cracking of alkyl carboxylates in the presence of aryl esters remain scarce.[18]

Nonhydrolytic cleavage of esters by Lewis acids is an alternative approach to ester hydrolysis.[1] Sandhu and coworkers developed a procedure for cleaving esters using excess AlI_3 (2 equiv), a strong Lewis acid effective for cleaving various C−O bonds,[19] and noted the Fries rearrangement of phenyl benzoate under the conditions that afforded a mixture of *o*- and *p*-hydroxybenzophenone (Scheme 1B).[20] Our recent study on selective cleavage of acid-labile aryl alkyl ethers by AlI_3,[21] however, revealed a clean and exhaustive deprotection of eugenol acetate without any rearranged product.[21c,d] This discrepancy invoked a systematic study on the power of AlI_3 in cleaving carboxylic esters. Herein, we describe that (1) cleavage of typical alkyl esters could be effected by Al and substoichiometric amount of I_2 (0.75 equiv) in a one-pot manner; (2) phenyl benzoate is stable under the conditions; and (3) alkyl esters could be selectively deprotected without affecting aryl esters (Scheme 1C).

RESULTS AND DISCUSSION

Methyl benzoate (**1**) was selected as the model substrate for the optimization of ester cleaving conditions (Table 1). A slight excess of AlI_3 (1.1 equiv), prepared *in situ* from I_2 and Al, was applied to mediate the demethylation (entries 1−5) following our previous recipes for ether cleavages.[22] Thus, upon treating **1** with iodine (1.65 equiv) and excess Al in MeCN for 18 h at 80 °C, benzoic acid (**2**) was obtained in 99% yield (entry 1). Conducting the cleavage at a lower temperature (60 °C) was also successful (entry 2). However, the yield dropped to 85% when performed at rt (entry 3). It is worth noting that $AlCl_3$−NaI was also efficient for deprotecting alkyl benzoates in refluxing MeCN;[18] however, the reagent turned unreactive towards methyl benzoate moiety at rt.[23] When cyclohexane or CS_2 was used as the solvent, the yield decreased further to nearly negligible (entries 4 and 5). We also endeavored to minimize the amount of I_2 (entries 6 and 7) in anticipation of the full exploitation of all three iodine atoms of AlI_3. Pleasingly, acid **2** was obtained in 98% yield when less iodine (0.75 equiv) was used (entry 6). Further decreasing the amount of iodine, however, led to a markedly lower yield (entry 7). The yield of acid **2** remained essentially quantitative without adverse consequences when a large excess of iodine (3 equiv) was applied (entry 8).

With the optimum conditions in hand, we next explored the substrate scope and limitations (Table 2). Ten para-substituted

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Scheme 1. Cleavage of Esters

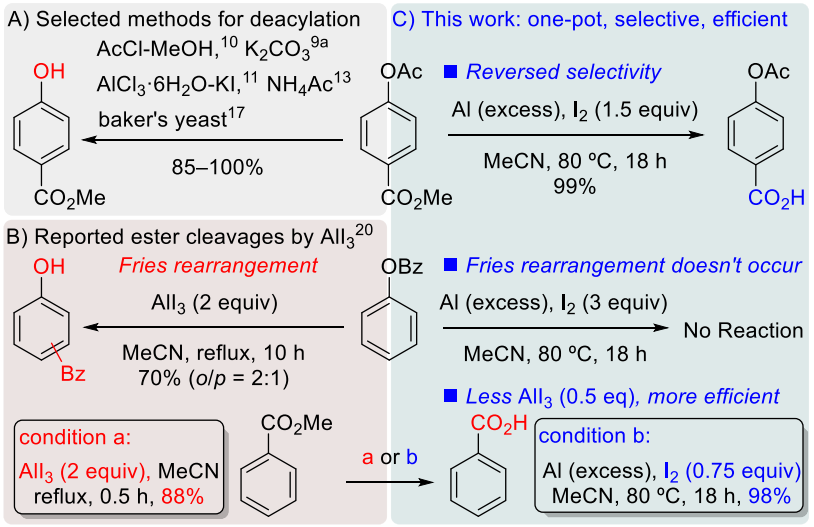
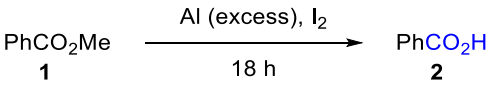
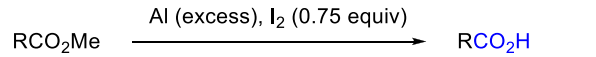


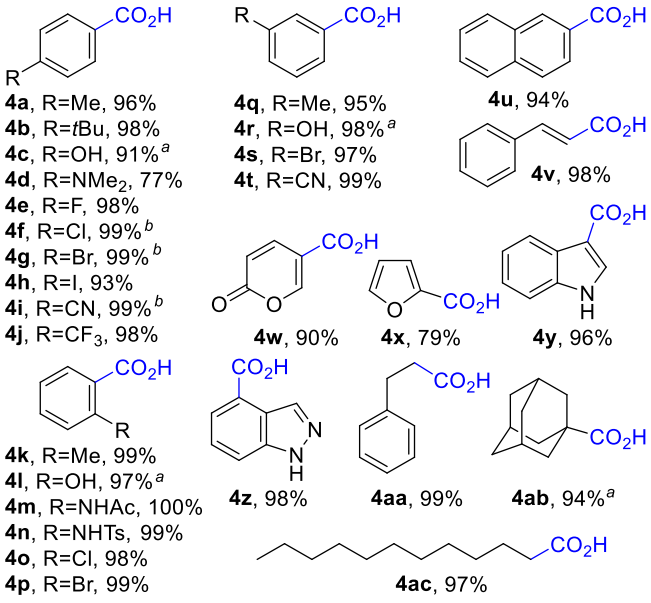
Table 1. Optimization of Ester Cleavage Conditions



entry	I_2 (equiv)	calcd AlI_3 (equiv)	solvent	T (°C)	yield **2** (%)
1	1.65	1.1	MeCN	80	99
2	1.65	1.1	MeCN	60	99
3	1.65	1.1	MeCN	rt	85
4	1.65	1.1	cyclohexane	70	18
5	1.65	1.1	CS_2	rt	7
6	0.75	0.5	MeCN	80	98
7	0.525	0.35	MeCN	80	88
8	3	2	MeCN	80	98

Table 2. Demethylation of Carboxylic Esters





[a]Equimolar AlI_3, prepared *in situ* from iodine (1.5 equiv), was used. [b]Excess iodine (1.65 equiv) was used.

methyl benzoates (**3a**–**3j**) were successfully cleaved to afford the corresponding acids **4a**–**4j** in good to excellent yields despite the electronic character of the substituents. Ortho- and meta-substituted esters **3k**–**3t** were also cleaved efficiently, which provided acids **4k**–**4t** in excellent yields. 2-Naphthoic acid (**4u**) and cinnamic acid (**4v**) were obtained in a similar manner from carboxylates **3u** and **3v** in excellent yields. Four heteroaryl-containing carboxylates (**3w**–**3z**) were deprotected, which provided acids **4w**–**4z** in good to excellent yields. Cleavage of aliphatic acid esters was efficient as well, and three aliphatic carboxylic acids (**4aa**–**4ac**) were obtained in excellent yields from the corresponding carboxylic esters.

Deprotection of Bulky Esters. Next, the substrate scope was extended to bulky alkyl esters (Table 3). Seven alkyl carboxylic esters were efficiently cleaved to the corresponding carboxylic acids by the one-pot protocol. The cleavage of ethyl (**5a**–**5e**), isopropyl (**5f**), *tert*-butyl (**5g**), and benzyl (**5h**) carboxylates proceeded smoothly and afforded the related carboxylic acids (**2**, **4a**, and **6a**–**6d**) in very good to excellent yields.

Cleavage of Lactones. Lactones were also readily cleaved by aluminum and iodine. ε-Caprolactone (**7a**), ε-hexanolactone (**7b**), and ω-pentadecalactone (**7c**) were converted into the corresponding ω-iodoalkylcarboxylic acids (**8a**–**8c**) in essentially quantitative isolated yields. Treatment of γ-decalactone under the conditions, however, produced a mixture of unidentified by-products according to an NMR analysis.

Selective Ester Cleavages. Unexpectedly, Fries rearrangement was not observed when phenyl benzoate was subjected to current conditions. No reaction had proceeded when excess iodine (3 equiv) and aluminum powder were applied. An attempted repetition of the rearrangement using preprepared AlI_3 was also futile. This inert transformation suggested that alkyl benzoates might be preferentially cleaved in the presence of phenyl carboxylates. Thus, methyl 4-acetoxybenzoate (**9a**) and 3-acetoxybenzoate (**9b**) were tentatively subjected to the ester cleavage conditions (Table 4). As expected, 4- and 3-acetoxybenzoic acid (**10a** and **10b**) were obtained in excellent

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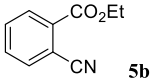
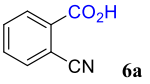
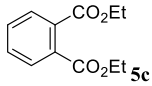
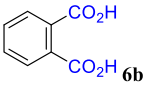
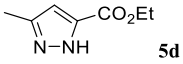
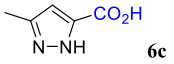
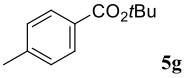
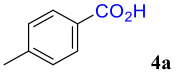
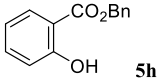
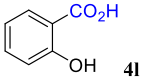
Table 3. Cleavage of Other Alkyl Carboxylates and Lactones[a]

Substrate	Product	Yield/%
$PhCO_2Et$ **5a**	$PhCO_2H$ **2**	87[b]
 **5b**	 **6a**	99
 **5c**	 **6b**	97
 **5d**	 **6c**	93[c]
$BnCH(CO_2Et)_2$ **5e**	$BnCH(CO_2H)_2$ **6d**	93
$PhCO_2iPr$ **5f**	$PhCO_2H$ **2**	99
 **5g**	 **4a**	96[c]
 **5h**	 **4l**	86
 **7a**, n=1 **7b**, n=2 **7c**, n=11	 **8a**, n=1 **8b**, n=2 **8c**, n=11	96[c] 99[c] 99[c]

[a]Conditions: ester (1 equiv), Al (excess), I_2 (1.5 equiv), MeCN, 80 °C, 18 h. [b]Excess iodine (1.65 equiv) was used. [c]Substoichiometric amount of AlI_3, prepared *in situ* from iodine (0.75 equiv), was used.

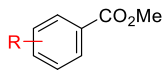
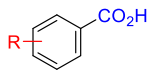
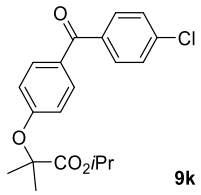
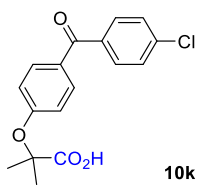
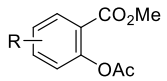
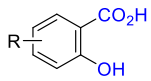
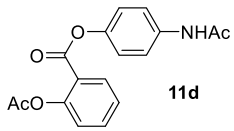
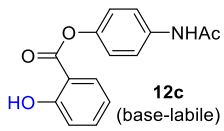
yields. Benzoyloxy, pivaloyloxy, and tosyloxy also remained intact during the demethylation of esters **9c−9f** that afforded the corresponding carboxylic acids **10c−10f** in excellent yields. Selective cleavage of methyl 4-(phenoxycarbonyl)benzoate (**9g**) afforded 4-(phenoxycarbonyl)benzoic acid (**10g**) in 99% yield. The ether linkages in esters **9h−9k** remained unaffected under these ester cleaving conditions, either.

Anchimeric Effect. Notably, the cleavage of esters is affected by adjacent groups. For example, deprotection of aspirin methyl ester (**11a**) afforded salicylic acid (**4l**) in 97% yield. To probe the progress of this conversion, a set of ^1H NMR experiments were performed in CD_3CN (Figure 1). Ester **11a** showed typical peaks of aryl, methoxy, and acetyl protons (Figure 1A). These peaks disappeared after stirring with Al and I_2 for 6 h at 80 °C (Figure 1B). A new peak appeared at 2.19 ppm, and was identified as MeI. After quenching with CF_3CO_2H and a few drops of D_2O, a peak at 2.01 ppm was observed, and was recognized as HOAc (Figure 1C).

The exhaustive deprotection of ester **11a** implied the participation of the adjacent ester group. In comparison, the isolated acetoxy groups in **11b** and **11c** remained intact during ester cleavages (Table 4). To demonstrate the involvement of anchimeric effect in ester cleavages, benorilate (**11d**), a nonsteroidal anti-inflammatory drug, was deacetylated to the base-labile[24] acetaminosalol (**12c**) in 99% yield under the conditions. The phenyl benzoate and acetamide moieties remained intact during deacetylation. Therefore, deacetylation can be effected by Al and I_2 with the facilitation of a neighboring group.

Selective Deacetylation. Although aryl acetates do not undergo substitution under the same conditions for cleaving alkyl benzoates by Al and I_2, deacetylation proceeds readily by the action of $AlBr_3$. For instance, treatment of **9a** with $AlBr_3$ in MeCN afforded methyl 4-hydroxybenzoate (**3c**) in 86% yield (Scheme 2). Phenol **3c** was also produced using Al and I_2 in

Table 4. Selective Cleavage of Esters[a,e]

Substrate	Product	Yield/%
		
R = 4-OAc, **9a**	**10a**	99,[b] 98[c]
3-OAc, **9b**	**10b**	95[b]
4-OBz, **9c**	**10c**	99
4-OPiv, **9d**	**10d**	98
4-OTs, **9e**	**10e**	98
2-OTs, **9f**	**10f**	96
4-CO_2Ph, **9g**	**10g**	99
4-OMe, **9h**	**10h**	90[d]
4-OEt, **9i**	**10i**	89[d]
4-O*i*Pr, **9j**	**10j**	90[d]
 **9k**	 **10k**	97
		
R = H, **11a**	**4l**	97
4-OAc, **11b**	**12a**	99
5-OAc, **11c**	**12b**	99
 **11d**	 **12c** (base-labile)	99[e]

[a]Conditions: ester (1 equiv), Al (excess), I_2 (1.5 equiv), MeCN, 80 °C, 18 h. [b]Substoichiometric amount of iodine (0.75 equiv) was used. [c]AlI_3 was prepared in advance. [d]The reaction was conducted at rt. [e]Excess iodine (3 equiv) was used.

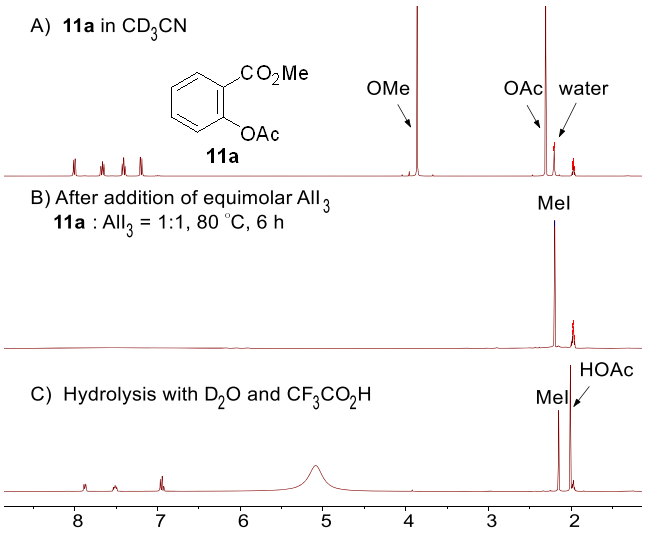


Figure 1. NMR experiments (400 MHz, CD_3CN): (A) ^1H NMR spectrum of **11a**; (B) deprotection by equimolar *in situ* generated AlI_3; and (C) hydrolysis of the mixture using D_2O and CF_3CO_2H.

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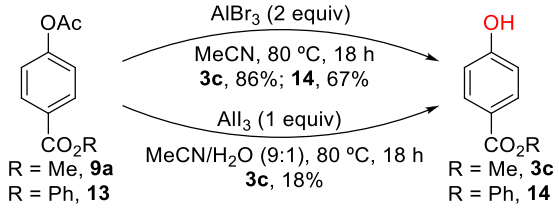
Scheme 2. Selective Deacetylation



wet MeCN, though in a poor yield of 18%. This was due to the *in situ* formed HI, which initiated the deacetylation.[11] Analogously, ester **13** was selectively deacetylated to phenol **14** in 67% yield. These results can be explained satisfactorily with Pearson's hard and soft acids and bases (HSAB) theory.[25] I^- ion as a soft base favors the methyl (soft acid), whereas Br^- ion prefers to attack the acetyl carbonyl (hard acid). Altogether, $AlBr_3$ has a different preference for cleaving esters from that of AlI_3, which makes the selectivity for cleaving carboxylic esters tunable.

***Z*/*E* Isomerization.** The influence of AlI_3 on *Z*-stilbene was also investigated. An unexpected *Z* to *E* double-bond isomerization had been observed during an attempted exhaustive demethylation of (*Z*)-3,4′,5-trimethoxystilbene.[26] To evaluate whether such isomerization would occur in AlI_3-mediated ester cleavages, dimethyl *cis*-stilbene-4,4-dicarboxylate (**15**) was selected as a probe (Figure 2). The partially

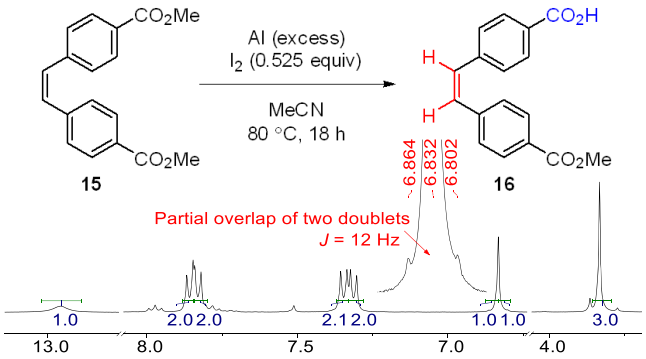
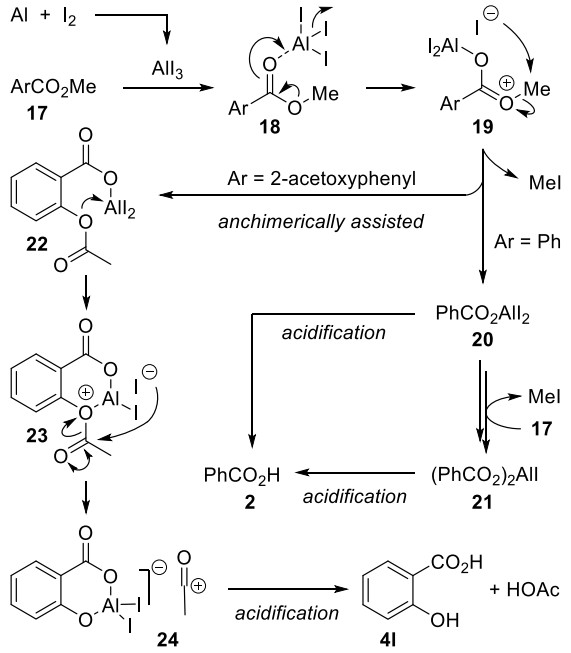


Figure 2. Expected *E*/*Z* geometric isomerization of stilbene C═C bond was not observed, suggesting that the isomerization is either substrate-specific, or untied to AlI_3.

cleaved product was characterized by ^1H and ^{13}C NMR, and the typical ^3J = 12 Hz for the vicinal olefinic hydrogens, highlighted in red, indicated the product to be *cis*-**16**. The absence of *trans*-**16** implies that stilbene isomerization is substitution-pattern-dependent. Besides, some other reagents, such as BBr_3 and $AlCl_3$,[27] were also effective for this *Z*/*E* isomerization.[26] Furthermore, the *in situ* generated phenoxide ions may also facilitate the transformation through resonance stabilization.[28] Therefore, AlI_3 is unlikely tied to the *Z*/*E* isomerization of olefins.

Proposed Mechanism. Based on the above results and our previous observations,[22a] a mechanism was proposed (Scheme 3). AlI_3 was formed *in situ* after mixing Al and I_2 in anhydrous MeCN. Coordination of the carbonyl oxygen of ester **17** to AlI_3 afforded a transient complex (**18**), which would then provide the ion pair **19**. The I^- ion then served as the nucleophile, and effected the cleavage of the ester moiety. For typical alkyl benzoates such as methyl benzoate (**1**), attack of the alkyl by I^- ion may afford aluminum benzoate **20**, along

Scheme 3. Proposed Mechanism



with the release of alkyl iodide. The complete cleavage of methyl benzoate by the substoichiometric amount (0.5 equiv) of the *in situ* generated AlI_3 suggested that **20** might also serve as an ester cleaving agent, affording carboxylate **21** upon further reaction with ester **17**. Acidification of **20** and **21** afforded benzoic acid **2**. In the case of **11a**, the aryl acetate (**22**) was further attacked by the adjacent aluminum carboxylate moiety (**23**) to provide a six-membered intermediate **24** and AcI in their ionized form. Acidification of **24** afforded salicylic acid (**4l**) and HOAc.

CONCLUSIONS

In summary, a procedure for deprotecting alkyl carboxylic esters has been developed. Typical esters undergo dealkylation conveniently after stirring with iodine (0.75 equiv) and excess aluminum powder (about 2 equiv) in a one-pot manner in MeCN for 18 h at 80 °C; the corresponding acids were obtained in good to excellent yields. Lactones are transformed to the corresponding *ω*-iodoalkylcarboxylic acids under the conditions. For deacylation of aryl esters, the assistance of an adjacent group is needed. The markedly different reactivities of alkyl and aryl carboxylic esters toward AlI_3 permit selective cleavage of alkyl carboxylates in the presence of aryl esters. $AlBr_3$, on the contrary, cleaves aryl acetylates preferentially in MeCN without affecting the concurrent alkyl carboxylate moieties. These complementary actions of AlI_3 and $AlBr_3$ could be exploited for a tunable and selective nonhydrolytic cleavage of aryl and alkyl carboxylic esters.

EXPERIMENTAL SECTION

General Information. Unless specified, all reagents and solvents were purchased and used as received without further purification. Aluminum used was in a powder form (100−200 mesh), and iodine was in the form of granules. Acetonitrile was of HPLC grade with less than 500 ppm of water. NMR spectra were recorded using a Bruker Avance-400 FT NMR spectrometer with TMS as the internal standard. Melting points were uncorrected. EA denotes ethyl acetate and PE denotes petroleum ether (60−90 °C).

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Benzoic Acid (2) General Procedure. To a 100 mL round-bottom flask equipped with a magnetic bar (2 cm) and a refluxing condenser sealed with an empty balloon at the top (to prevent moisture) was added in sequence methyl benzoate (**1**, 0.681 g, 5 mmol), aluminum (0.162 g), iodine (0.951 g, 3.75 mmol, 0.75 equiv), and acetonitrile (40 mL). The mixture was stirred at 80 °C in an oil bath for 18 h. After cooling to rt, the mixture was quenched by dilute aqueous hydrochloric acid (2 M, 5 mL) and was extracted with EA (50 mL × 3). The organic phases were combined, washed with saturated aqueous $Na_2S_2O_3$, and dried over $MgSO_4$. After filtration, the organic solvents were removed by rotary evaporation to afford benzoic acid (**2**) as a white solid; yield: 0.600 g (98%); mp 121−122 °C (lit.:[29] 121−123 °C); R_f = 0.29 (PE/EA = 3:1). From ethyl benzoate (**5a**) using substoichiometric amount of iodine (0.75 equiv), yield: 0.533 g (87%). From isopropyl benzoate (**5f**) using excess iodine (1.65 equiv); yield: 0.607 g (99%). ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.20−8.08 (m, 2H), 7.68−7.57 (m, 1H), 7.55−7.42 (m, 2H).

*p-Toluic Acid (**4a**).* From methyl *p*-toluate (**3a**, 0.751 g, 5 mmol); off-white solid; yield: 0.658 g (96%); mp 181−182 °C (lit.:[30] 182 °C); R_f = 0.71 (PE/EA = 1:1). From *tert*-butyl *p*-toluate (**5g**, 0.961 g, 5 mmol); yield: 0.655 g (96%). ^{1}H NMR (400 MHz, DMSO-d_6) δ 12.80 (br s, 1H), 7.84 (d, J = 8.3 Hz, 2H), 7.29 (d, J = 7.8 Hz, 2H), 2.36 (s, 3H).

*4-tert-Butylbenzoic Acid (**4b**).* White solid; yield: 0.879 g (98%); mp 162−166 °C (lit.:[31] 162−165 °C); R_f = 0.22 (PE/EA = 10:1). ^{1}H NMR (400 MHz, DMSO-d_6) δ 12.81 (br s, 1H), 7.88 (d, J = 8.5 Hz, 2H), 7.51 (d, J = 8.5 Hz, 2H), 1.29 (s, 9H).

*4-Hydroxybenzoic Acid (**4c**).* Excess iodine (1.5 equiv) was used; white solid; yield: 0.634 g (91%); mp 214−217 °C (lit.:[29] 213−215 °C); R_f = 0.44 (PE/EA = 1:1). ^{1}H NMR (400 MHz, DMSO-d_6) δ 12.39 (br s, 1H), 10.27 (br s, 1H), 7.79 (d, J = 8.6 Hz, 2H), 6.83 (d, J = 8.7 Hz, 2H).

*4-Dimethylaminobenzoic Acid (**4d**).* From methyl 4-dimethylaminobenzoate (**3d**, 0.448 g, 2.5 mmol); yellow solid; yield: 0.321 g (77%); decomposed at above 234 °C (lit.:[31] 241−243 °C dec.); R_f = 0.37 (PE/EA = 3:1). ^{1}H NMR (400 MHz, DMSO-d_6) δ 12.06 (br s, 1H), 7.76 (d, J = 9.0 Hz, 2H), 6.70 (d, J = 9.0 Hz, 2H), 2.98 (s, 6H).

*4-Fluorobenzoic Acid (**4e**).* White solid; yield: 0.688 g (98%); mp 183−185 °C (lit.:[31] 182−184 °C); R_f = 0.39 (PE/EA = 3:1). ^{1}H NMR (400 MHz, DMSO-d_6) δ 13.09 (br s, 1H), 8.07−7.95 (m, 2H), 7.32 (td, J_1 = 8.9 Hz, J_2 = 1.5 Hz, 2H).

*4-Chlorobenzoic Acid (**4f**).* Excess iodine (1.65 equiv) was used; off-white solid; yield: 0.772 g (99%); mp 238−240 °C (lit.:[30] 242 °C); R_f = 0.48 (PE/EA = 3:1). ^{1}H NMR (400 MHz, DMSO-d_6) δ 13.20 (br s, 1H), 7.95 (d, J = 8.6 Hz, 2H), 7.58 (d, J = 8.6 Hz, 2H).

*4-Bromobenzoic Acid (**4g**).* Excess iodine (1.65 equiv) was used; off-white solid; yield: 1.001 g (99%); mp 254−258 °C (lit.:[29] 253−255 °C); R_f = 0.13 (PE/EA = 3:1). ^{1}H NMR (400 MHz, DMSO-d_6) δ 13.22 (br s, 1H), 7.87 (d, J = 8.5 Hz, 2H), 7.72 (d, J = 8.5 Hz, 2H).

*4-Iodobenzoic Acid (**4h**).* From methyl 4-iodobenzoate (**3h**, 0.524 g, 2 mmol); white solid; yield: 0.462 g (93%); mp 270−272 °C (lit.:[31] 270−273 °C); R_f = 0.09 (PE/EA = 3:1). ^{1}H NMR (400 MHz, DMSO-d_6) δ 13.16 (br s, 1H), 7.90 (d, J = 8.4 Hz, 2H), 7.69 (d, J = 8.4 Hz, 2H).

*4-Cyanobenzoic Acid (**4i**).* Excess iodine (1.65 equiv) was used; white solid; yield: 0.731 g (99%); mp 217−221 °C (lit.:[31] 219−221 °C); R_f = 0.09 (PE/EA = 3:1). ^{1}H NMR (400 MHz, DMSO-d_6) δ 13.60 (br s, 1H), 8.09 (d, J = 8.5 Hz, 2H), 7.99 (d, J = 8.6 Hz, 2H).

*4-(Trifluoromethyl)benzoic Acid (**4j**).* Off-white solid; yield: 0.930 g (98%); mp 219−221 °C (lit.:[31] 219−220 °C); R_f = 0.21 (PE/EA = 3:1). ^{1}H NMR (400 MHz, DMSO-d_6) δ 13.53 (br s, 1H), 8.14 (d, J = 8.1 Hz, 2H), 7.88 (d, J = 8.0 Hz, 2H).

*o-Toluic Acid (**4k**).* From methyl 2-methylbenzoate (**3k**, 0.754 g, 5.02 mmol); off-white solid; yield: 0.681 g (99%); mp 103−106 °C (lit.:[29] 102−104 °C); R_f = 0.47 (PE/EA = 3:1). ^{1}H NMR (400 MHz, DMSO-d_6) δ 12.83 (br s, 1H), 7.82 (dd, J_1 = 7.8 Hz, J_2 = 1.5 Hz, 1H), 7.45 (td, J_1 = 7.5 Hz, J_2 = 1.5 Hz, 1H), 7.33−7.25 (m, 2H), 2.52 (s, 3H).

*Salicylic Acid (**4l**).* From methyl salicylate (**3l**) using excess iodine (1.5 equiv); white solid; yield: 0.678 g (97%); mp 157−159 °C (lit.:[29] 158−159 °C); R_f = 0.13 (PE/EA = 3:1). From benzyl salicylate (**5h**) using excess iodine (1.5 equiv); yield: 0.596 g (86%). From methyl 2-acetoxybenzoate (**11a**) using excess iodine (1.5 equiv); yield: 0.674 g (97%). ^{1}H NMR (400 MHz, DMSO-d_6) δ 13.79 (br s, 1H), 11.43 (br s, 1H), 7.80 (dd, J_1 = 7.8 Hz, J_2 = 1.8 Hz, 1H), 7.52 (ddd, J_1 = 8.6 Hz, J_2 = 7.2 Hz, J_3 = 1.8 Hz, 1H), 7.00−6.88 (m, 2H).

*o-Acetamidobenzoic Acid (**4m**).* Off-white solid; yield: 0.896 g (100%); mp 187−189 °C (lit.:[32] 184− 186 °C); R_f = 0.17 (PE/EA = 1:1). ^{1}H NMR (400 MHz, DMSO-d_6) δ 11.15 (br s, 1H), 8.47 (dd, J_1 = 8.4 Hz, J_2 = 1.2 Hz, 1H), 7.97 (dd, J_1 = 7.9 Hz, J_2 = 1.7 Hz, 1H), 7.56 (ddd, J_1 = 8.6 Hz, J_2 = 7.3 Hz, J_3 = 1.7 Hz, 1H), 7.13 (ddd, J_1 = 8.3 Hz, J_2 = 7.4 Hz, J_3 = 1.2 Hz, 1H), 2.13 (s, 3H).

*N-(p-Tosyl)anthranilic Acid (**4n**).* From methyl *N*-(*p*-tosyl)-anthranilate (**3n**, 0.611 g, 2 mmol); white solid; yield: 0.580 g (99%); mp 226−228 °C (lit.:[33] 225−226 °C); R_f = 0.31 (PE/EA = 1:1). ^{1}H NMR (400 MHz, DMSO-d_6) δ 11.12 (br s, 1H), 7.95−7.85 (m, 1H), 7.76−7.65 (m, 2H), 7.59−7.47 (m, 2H), 7.35 (d, J = 8.1 Hz, 2H), 7.11 (ddd, J_1 = 8.2 Hz, J_2 = 6.4 Hz, J_3 =2.2 Hz, 1H), 2.32 (s, 3H).

*2-Chlorobenzoic Acid (**4o**).* Light yellow solid; yield: 0.774 g (98%); mp 140−141 °C (lit.:[31] 138−140 °C); R_f = 0.10 (PE/EA = 3:1). ^{1}H NMR (400 MHz, DMSO-d_6) δ 13.47 (br s, 1H), 7.94−7.78 (m, 1H), 7.66−7.55 (m, 2H), 7.49 (ddd, J_1 = 7.7 Hz, J_2 = 5.8 Hz, J_3 =2.8 Hz, 1H).

*2-Bromobenzoic Acid (**4p**).* White solid; yield: 1.001 g (99%); mp 147−149 °C (lit.:[31] 147−150 °C); R_f = 0.09 (PE/EA = 3:1). ^{1}H NMR (400 MHz, DMSO-d_6) δ 13.42 (br s, 1H), 7.81−7.63 (m, 2H), 7.54−7.36 (m, 2H).

*3-Methylbenzoic Acid (**4q**).* Off-white solid; yield: 0.645 g (95%); mp 109−111 °C (lit.:[31] 108−111 °C); R_f = 0.44 (PE/EA = 3:1). ^{1}H NMR (400 MHz, DMSO-d_6) δ 12.89 (br s, 1H), 7.78 (s, 1H), 7.75 (d, J = 7.5 Hz, 1H), 7.44 (d, J = 7.6 Hz, 1H), 7.39 (t, J = 7.5 Hz, 1H), 2.37 (s, 3H).

*3-Hydroxybenzoic Acid (**4r**).* Excess iodine (1.5 equiv) was used; off-white solid; yield: 0.681 g (98%); mp 200−201 °C (lit.:[31] 200−203 °C); R_f = 0.26 (PE/EA = 1:1). ^{1}H NMR (400 MHz, DMSO-d_6) δ 12.81 (br s, 1H), 9.80 (br s, 1H), 7.38 (dt, J_1 = 7.6 Hz, J_2 = 1.3 Hz, 1H), 7.34 (dd, J_1 = 2.6 Hz, J_2 = 1.5 Hz, 1H), 7.29 (t, J = 7.8 Hz, 1H), 6.99 (ddd, J_1 = 8.0 Hz, J_2 = 2.6 Hz, J_3 = 1.1 Hz, 1H).

*3-Bromobenzoic Acid (**4s**).* From methyl 3-bromobenzoate (**3s**, 0.486 g, 2.3 mmol); white solid; yield: 0.441 g (97%); mp 156−158 °C (lit.:[30] 153 °C); R_f = 0.15 (PE/EA = 3:1). ^{1}H NMR (400 MHz, DMSO-d_6) δ 13.35 (br s, 1H), 8.04 (t, J = 1.8 Hz, 1H), 7.94 (dt, J_1 = 7.8 Hz, J_2 = 1.3 Hz, 1H), 7.84 (ddd, J_1 = 8.0 Hz, J_2 = 2.1 Hz, J_3 = 1.0 Hz, 1H), 7.49 (t, J = 7.9 Hz, 1H).

*3-Cyanobenzoic Acid (**4t**).* White solid; yield: 0.730 g (99%); mp 222−224 °C (lit.:[31] 220−224 °C); R_f = 0.11 (PE/EA = 3:1). ^{1}H NMR (400 MHz, DMSO-d_6) δ 13.57 (br s, 1H), 8.30 (t, J = 1.7 Hz, 1H), 8.24 (dt, J_1 = 7.9 Hz, J_2 = 1.5 Hz, 1H), 8.11 (dt, J_1 = 7.7 Hz, J_2 = 1.5 Hz, 1H), 7.74 (t, J = 7.8 Hz, 1H).

*2-Naphthoic Acid (**4u**).* From methyl 2-naphthoate (**3u**, 0.374 g, 2 mmol); white solid; yield: 0.326 g (94%); mp 185−186 °C (lit.:[31] 185−187 °C); R_f = 0.29 (PE/EA = 3:1). ^{1}H NMR (400 MHz, DMSO-d_6) δ 13.10 (br s, 1H), 8.62 (d, J = 1.4 Hz, 1H), 8.12 (dd, J_1 = 8.1 Hz, J_2 = 1.4 Hz, 1H), 8.06−7.93 (m, 3H), 7.66 (ddd, J_1 = 8.2 Hz, J_2 = 6.8 Hz, J_3 = 1.5 Hz, 1H), 7.61 (ddd, J_1 = 8.2 Hz, J_2 = 6.8 Hz, J_3 = 1.4 Hz, 1H).

*Cinnamic Acid (**4v**).* White solid; yield: 0.731 g (98%); mp 134−135 °C (lit.:[31] 132−135 °C); R_f = 0.28 (PE/EA = 3:1). ^{1}H NMR (400 MHz, $CDCl_3$) δ 9.09 (br s, 1H), 7.80 (d, J = 16.0 Hz, 1H), 7.60−7.51 (m, 2H), 7.45−7.34 (m, 3H), 6.47 (d, J = 16.0 Hz, 1H).

*Coumalic Acid (**4w**).* Yellow solid; yield: 0.634 g (90%); turned dark at above 201 °C and decomposed at 204−206 °C (lit.:[31] 203−205 °C dec.); R_f = 0.16 (EA). ^{1}H NMR (400 MHz, DMSO-d_6) δ 13.31 (br s, 1H), 8.52 (dd, J_1 = 2.7 Hz, J_2 = 1.1 Hz, 1H), 7.81 (dd, J_1 = 9.8 Hz, J_2 = 2.6 Hz, 1H), 6.41 (dd, J_1 = 9.8 Hz, J_2 = 1.1 Hz, 1H).

*2-Furoic Acid (**4x**).* Off-white solid; yield: 0.508 g (79%); mp 130.5−131.5 °C (lit.:[31] 128−132 °C); R_f = 0.19 (EA). ^{1}H NMR (400

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MHz, DMSO-d_6) δ 13.08 (br s, 1H), 7.91 (dd, J_1 = 1.9 Hz, J_2 = 0.9 Hz, 1H), 7.21 (dd, J_1 = 3.5 Hz, J_2 = 0.9 Hz, 1H), 6.65 (dd, J_1 = 3.5 Hz, J_2 = 1.8 Hz, 1H).

*Indole-3-carboxylic Acid (**4y**).* From methyl indole-3-carboxylate (**3y**, 0.438 g, 2.5 mmol); light yellow solid; yield: 0.390 g (96%); decomposed at above 213 °C (lit.:[31] 232−234 °C dec.); R_f = 0.67 (PE/EA = 3:1). ^{1}H NMR (400 MHz, DMSO-d_6) δ 11.93 (br s, 1H), 11.82 (s, 1H), 8.10−7.92 (m, 2H), 7.53−7.38 (m, 1H), 7.21−7.17 (m, 1H), 7.17−7.13 (m, 1H). ^{13}C{^{1}H} NMR (101 MHz, DMSO-d_6) δ 166.4, 136.9, 132.7, 126.5, 122.6, 121.4, 121.0, 112.7, 107.8.

*1H-Indazole-4-carboxylic Acid (**4z**).* From methyl 1*H*-indazole-4-carboxylate (**3z**, 0.440 g, 2.5 mmol); off-white solid; yield: 0.400 g (98%); R_f = 0.61 (EA). ^{1}H NMR (400 MHz, DMSO-d_6) δ 13.29 (br s, 2H), 8.40 (d, J = 1.0 Hz, 1H), 7.82 (dd, J_1 = 12.1 Hz, J_2 = 7.8 Hz, 2H), 7.47 (dd, J_1 = 8.3 Hz, J_2 = 7.2 Hz, 1H). ^{13}C{^{1}H} NMR (101 MHz, DMSO-d_6) δ 167.8, 140.9, 134.2, 125.9, 124.2, 123.4, 121.7, 115.8.

*3-Phenylpropanoic Acid (**4aa**).* White solid; yield: 0.746 g (99%); mp 47−49 °C (lit.:[31] 45−48 °C); R_f = 0.40 (PE/EA = 3:1). ^{1}H NMR (400 MHz, $CDCl_3$) δ 10.26 (br s, 1H), 7.37−7.26 (m, 2H), 7.22 (t, J = 6.3 Hz, 3H), 2.96 (t, J = 7.8 Hz, 2H), 2.68 (t, J = 7.8 Hz, 2H).

*Adamantane-1-carboxylic Acid (**4ab**).* From methyl adamantane-1-carboxylate (**3ab**, 0.409 g, 2.1 mmol) using iodine (0.799 g, 3.15 mmol, 1.5 equiv) and excess aluminum; white solid; yield: 0.359 g (94%); mp 172−174 °C (lit.:[31] 172−174 °C); R_f = 0.50 (PE/EA = 10:1). ^{1}H NMR (400 MHz, DMSO-d_6) δ 11.97 (br s, 1H), 1.97−1.91 (m, 3H), 1.78 (d, J = 3.0 Hz, 6H), 1.72−1.56 (m, 6H). ^{13}C{^{1}H} NMR (101 MHz, DMSO-d_6) δ 178.9, 40.0, 39.0, 36.5, 27.9.

*Lauric Acid (**4ac**).* White solid; yield: 0.979 g (97%); mp 44−46 °C (lit.:[31] 44−46 °C); R_f = 0.41 (PE/EA = 3:1). ^{1}H NMR (400 MHz, $CDCl_3$) δ 2.35 (t, J = 7.5 Hz, 2H), 1.63 (p, J = 7.5 Hz, 2H), 1.43−1.14 (m, 18H), 0.88 (t, J = 6.8 Hz, 3H).

*2-Cyanobenzoic Acid (**6a**).* From ethyl 2-cyanobenzoate (**5b**); off-white solid; yield: 0.731 g (99%); mp 211−213 °C (lit.:[31] 212 °C); R_f = 0.03 (PE/EA = 3:1). ^{1}H NMR (400 MHz, DMSO-d_6) δ 13.88 (br s, 1H), 8.16−8.08 (m, 1H), 8.03−7.95 (m, 1H), 7.88−7.76 (m, 2H).

*Phthalic Acid (**6b**).* From ethyl phthalate (**5c**); white solid; yield: 0.799 g (97%); mp 198−200 °C (lit.:[30] 208−209 °C); R_f = 0.05 (EA). ^{1}H NMR (400 MHz, DMSO-d_6) δ 13.10 (br s, 2H), 7.70−7.65 (m, 2H), 7.63−7.53 (m, 2H).

*5-Methyl-2H-pyrazole-3-carboxylic Acid (**6c**).* From ethyl 5-methylpyrazole-3-carboxylate (**5d**, 0.385 g, 2.5 mmol) using substoichiometric amount of iodine (0.476 g, 1.875 mmol, 0.75 equiv); off-white solid; yield: 0.295 g (93%); mp 236−238 °C (lit.:[34] 235−237 °C); R_f = 0.03 (EA). ^{1}H NMR (400 MHz, DMSO-d_6) δ 12.91 (br s, 2H), 6.45 (s, 1H), 2.23 (s, 3H).

*Benzylmalonic Acid (**6d**).* From diethyl benzylmalonate (**5e**, 0.626 g, 2.5 mmol) and iodine (0.951 g, 3.75 mmol, 1.5 equiv); light yellow solid; yield: 0.450 g (93%); mp 115−117 °C (lit.:[31] 117−120 °C); R_f = 0.10 (PE/EA = 1:1). ^{1}H NMR (400 MHz, DMSO-d_6) δ 12.76 (br s, 2H), 7.31−7.16 (m, 5H), 3.56 (t, ^{13}C{^{1}H} NMR (101 MHz, DMSO-d_6) δ 170.8, 139.0, 129.2, 128.7, 126.8, 53.8, 34.6.

*5-Iodopentanoic Acid (**8a**).* Yellow solid; yield: 1.097 g (96%); mp 59.5−61.5 °C (lit.[35] 58 °C); R_f = 0.77 (PE/EA = 1:1). ^{1}H NMR (400 MHz, DMSO-d_6) δ 12.06 (br s, 1H), 3.27 (t, J = 6.8 Hz, 2H), 2.24 (t, J = 7.4 Hz, 2H), 1.77 (qui, J = 7.0 Hz, 2H), 1.57 (qui, J = 7.6 Hz, 2H).

*6-Iodohexanoic Acid (**8b**).* Yellow solid; yield: 1.203 g (99%); mp 48−50 °C (lit.:[35] 41 °C); R_f = 0.77 (PE/EA = 1:1). ^{1}H NMR (400 MHz, $CDCl_3$) δ 10.47 (br s, 1H), 3.19 (t, J = 7.0 Hz, 2H), 2.38 (t, J = 7.5 Hz, 2H), 1.85 (qui, J = 7.0 Hz, 2H), 1.66 (qui, J = 7.5 Hz, 2H), 1.50−1.42 (m, 2H). ^{13}C{^{1}H} NMR (101 MHz, $CDCl_3$) δ 180.1, 33.9, 33.1, 29.9, 23.6, 6.5.

*15-Iodopentadecanoic Acid (**8c**).* Yellow solid; yield: 1.841 g (99%); mp 76−78 °C (lit.:[36] 78 °C); R_f = 0.78 (PE/EA = 3:1). ^{1}H NMR (400 MHz, DMSO-d_6) δ 11.95 (br s, 1H), 3.26 (t, J = 6.9 Hz, 2H), 2.18 (t, J = 7.4 Hz, 2H), 1.74 (qui, J = 6.9 Hz, 2H), 1.48 (qui, J = 7.0 Hz, 2H), 1.39−1.15 (m, 20H).

*4-Acetoxybenzoic Acid (**10a**).* White solid; yield: 0.892 g (99%); mp 192−193 °C (lit.:[31] 190−194 °C); R_f = 0.55 (PE/EA = 1:1). ^{1}H NMR (400 MHz, DMSO-d_6) δ 13.02 (br s, 1H), 8.00 (d, J = 8.7 Hz, 2H), 7.26 (d, J = 8.7 Hz, 2H), 2.29 (s, 3H).

*3-Acetoxybenzoic Acid (**10b**).* From methyl 3-acetoxybenzoate (**9b**, 0.893 g, 4.6 mmol); white solid; yield: 0.789 g (95%); mp 127−129 °C (lit.:[31] 131−134 °C); R_f = 0.15 (PE/EA = 3:1). ^{1}H NMR (400 MHz, DMSO-d_6) δ 13.22 (br s, 1H), 7.84 (dt, J_1 = 7.8 Hz, J_2 = 1.3 Hz, 1H), 7.67 (dd, J_1 = 2.4 Hz, J_2 = 1.5 Hz, 1H), 7.56 (t, J = 7.9 Hz, 1H), 7.40 (ddd, J_1 = 8.1 Hz, J_2 = 2.4 Hz, J_3 = 1.1 Hz, 1H), 2.30 (s, 3H).

*4-(Benzoyloxy)benzoic Acid (**10c**).* From methyl 4-(benzoyloxy)-benzoate (**9c**, 0.176 g, 0.69 mmol); white solid; yield: 0.165 g (99%); mp 224−226 °C (lit.:[18] 220−222 °C); R_f = 0.75 (PE/EA = 1:1). ^{1}H NMR (400 MHz, DMSO-d_6) δ 13.08 (br s, 1H), 8.16 (dd, J_1 = 8.4 Hz, J_2 = 1.3 Hz, 2H), 8.06 (d, J = 8.8 Hz, 2H), 7.78 (tt, J_1 = 7.6 Hz, J_2 = 1.2 Hz, 1H), 7.63 (t, J = 7.6 Hz, 2H), 7.44 (d, J = 8.8 Hz, 2H). ^{13}C{^{1}H} NMR (101 MHz, DMSO-d_6) δ 167.1, 164.7, 154.5, 134.7, 131.4, 130.4, 129.5, 129.1, 129.1, 122.7.

*4-(Pivaloyloxy)benzoic Acid (**10d**).* From methyl 4-(pivaloyloxy)-benzoate (**9d**, 0.520 g, 2.2 mmol); white crystalline solid; yield: 0.482 g (98%); mp 187−189 °C; R_f = 0.18 (PE/EA = 3:1). ^{1}H NMR (400 MHz, DMSO-d_6) δ 13.04 (br s, 1H), 8.00 (d, J = 8.6 Hz, 2H), 7.24 (d, J = 8.7 Hz, 2H), 1.31 (s, 9H).

*4-(Tosyloxy)benzoic Acid (**10e**).* From methyl 4-(tosyloxy)-benzoate (**9e**, 0.476 g, 1.55 mmol); off-white solid; yield: 0.448 g (98%); mp 170−172 °C (lit.:[37] 170−171.5 °C); R_f = 0.07 (PE/EA = 3:1). ^{1}H NMR (400 MHz, DMSO-d_6) δ 7.94 (d, J = 8.7 Hz, 2H), 7.76 (d, J = 8.4 Hz, 2H), 7.48 (d, J = 8.2 Hz, 2H), 7.16 (d, J = 8.7 Hz, 2H), 2.42 (s, 3H).

*2-(Tosyloxy)benzoic Acid (**10f**).* From methyl 2-(tosyloxy)-benzoate (**9f**, 0.306 g, 1 mmol); white solid; yield: 0.282 g (96%); mp 165−167 °C (lit.:[38] 165−171 °C); R_f = 0.21 (PE/EA = 1:1). ^{1}H NMR (400 MHz, DMSO-d_6) δ 13.16 (br s, 1H), 7.81 (dd, J_1 = 7.7 Hz, J_2 = 1.8 Hz, 1H), 7.70 (d, J = 8.4 Hz, 2H), 7.57 (ddd, J_1 = 8.2 Hz, J_2 = 7.5 Hz, J_3 = 1.8 Hz, 1H), 7.46 (d, 8.4 Hz, 2H), 7.42 (dt, J_1 = 7.6 Hz, J_2 = 1.2 Hz, 1H), 7.01 (dd, J_1 = 8.2 Hz, J_2 = 1.1 Hz, 1H), 2.43 (s, 3H). ^{13}C{^{1}H} NMR (101 MHz, DMSO-d_6) δ 165.9, 147.4, 146.2, 133.8, 132.1, 132.1, 130.6, 128.7, 128.0, 127.0, 123.9, 21.7.

*4-(Phenoxycarbonyl)benzoic Acid (**10g**).* From methyl 4-(phenoxycarbonyl)benzoate (**9g**, 0.686 g, 2.68 mmol); white solid; yield: 0.648 g (99%); mp 227−229 °C (lit.:[39] 230−235 °C); R_f = 0.58 (PE/EA = 1:1). ^{1}H NMR (400 MHz, DMSO-d_6) δ 13.47 (br s, 1H), 8.25 (d, J = 8.6 Hz, 2H), 8.15 (d, J = 8.6 Hz, 2H), 7.56−7.44 (m, 2H), 7.39−7.27 (m, 3H). ^{13}C{^{1}H} NMR (101 MHz, DMSO-d_6) δ 167.0, 164.5, 151.0, 135.9, 133.0, 130.5, 130.2, 130.1, 126.6, 122.3.

*p-Anisic Acid (**10h**).* White solid; yield: 0.691 g (90%); mp 183−185 °C (lit.:[31] 182−185 °C); R_f = 0.24 (PE/EA = 3:1). ^{1}H NMR (400 MHz, DMSO-d_6) δ 11.83 (br s, 1H), 7.91 (d, J = 8.4 Hz, 2H), 7.00 (d, J = 8.4 Hz, 2H), 3.82 (s, 3H).

*p-Ethoxybenzoic Acid (**10i**).* White solid; yield: 0.802 g (89%); mp 197−198 °C (lit.:[31] 197−199 °C); R_f = 0.29 (PE/EA = 3:1).^{1}H NMR (400 MHz, DMSO-d_6) δ 12.61 (br s, 1H), 7.88 (d, J = 8.9 Hz, 2H), 7.00 (d, J = 8.9 Hz, 2H), 4.10 (q, J = 7.0 Hz, 2H), 1.34 (t, J = 7.0 Hz, 3H).

*4-Isopropoxybenzoic Acid (**10j**).* White solid; yield: 0.410 g (90%); mp 163−165 °C (lit.:[31] 164−167 °C); R_f = 0.32 (PE/EA = 3:1). ^{1}H NMR (400 MHz, DMSO-d_6) δ 12.59 (br s, 1H), 7.87 (d, J = 8.8 Hz, 2H), 6.98 (d, J = 8.7 Hz, 2H), 4.71 (hept, J = 5.8 Hz, 1H), 1.29 (d, J = 6.0 Hz, 6H).

*2-(4-(4-Chlorobenzoyl)phenoxy)-2-methylpropanoic Acid (**10k**).* From fenofibrate (**9k**, 0.722 g, 2 mmol); white solid; yield: 0.622 g (97%); mp 180−182 °C (lit.:[40] 179−180 °C); R_f = 0.43 (PE/EA = 1:1). ^{1}H NMR (400 MHz, DMSO-d_6) δ 13.17 (br s, 1H), 7.72 (d, J = 8.9 Hz, 2H), 7.71 (d, J = 8.6 Hz, 2H), 7.62 (d, J = 8.6 Hz, 2H), 6.93 (d, J = 8.9 Hz, 2H), 1.60 (s, 6H).

*4-Acetoxysalicylic Acid (**12a**).* From methyl 2,4-diacetoxybenzoate (**11b**, 0.767 g, 3.04 mmol); yellow solid; yield: 0.591 g (99%); mp 147−149 °C (lit.:[41] 150 °C); R_f = 0.1 (PE/EA = 3:1). ^{1}H NMR (400 MHz, DMSO-d_6) δ 7.82 (d, J = 8.6 Hz, 1H), 6.75 (d, J = 2.2 Hz, 1H), 6.70 (dd, J_1 = 8.6 Hz, J_2 = 2.3 Hz, 1H), 2.27 (s, 3H).

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*5-Acetoxysalicylic Acid (**12b**).* From methyl 2,5-diacetoxybenzoate (**11c**, 0.756 g, 3 mmol); light yellow solid; yield: 0.586 g (99%); mp 128−130 °C (lit.:[42] 130 °C); R_f = 0.04 (PE/EA = 3:1). ^{1}H NMR (400 MHz, DMSO-d_6) δ 7.51 (d, J = 2.9 Hz, 1H), 7.29 (dd, J_1 = 8.9 Hz, J_2 = 3.0 Hz, 1H), 6.99 (d, J = 8.9 Hz, 1H), 2.25 (s, 3H).

*Acetaminosalol (**12c**).* From benorilate (**11d**, 0.783 g, 2.5 mmol), using excess AlI_3 (2 equiv) prepared[43] *in situ* from aluminum (0.210 g) and iodine (0.952 g, 3.75 mmol, 1.5 equiv); off-white solid; yield: 0.677 g (99%); mp 187−189 °C (lit.:[44] 187 °C); R_f = 0.79 (PE/EA = 1:1). ^{1}H NMR (400 MHz, DMSO-d_6) δ 10.32 (br s, 1H), 10.07 (s, 1H), 7.99 (dd, J_1 = 7.9 Hz, J_2 = 1.8 Hz, 1H), 7.66 (d, J = 9.0 Hz, 2H), 7.59 (ddd, J_1 = 8.7 Hz, J_2 = 7.2 Hz, J_3 = 1.8 Hz, 1H), 7.23 (d, J = 8.9 Hz, 2H), 7.04 (dt, J_1 = 8 Hz, J_2 = 0.8 Hz, 1H), 7.02 (dt, J_1 = 7.2 Hz, J_2 = 0.8 Hz, 1H), 2.07 (s, 3H).

*Methyl 4-Hydroxybenzoate (**3c**).* A mixture of methyl 4-acetoxybenzoate (**9a**, 0.212 g, 1.09 mmol) and $AlBr_3$ (0.582 g, 2.18 mmol, 2 equiv) in acetonitrile (20 mL) was stirred at 80 °C for 18 h in an oil bath. The mixture was quenched with water (10 mL) and extracted with EA (50 mL × 3). The organic phases were combined and dried over $MgSO_4$. After filtration, the organic solvents were removed by rotary evaporation, and the residue was purified via flash column chromatography (eluent: PE/EA = 9:1, V/V) to afford methyl 4-hydroxybenzoate (**3c**) as a white solid; yield: 0.143 g (86%); mp 128−130 °C (lit.:[31] 125−128 °C); R_f = 0.44 (PE/EA = 3:1). From **9a** (0.388 g, 2 mmol), excess aluminum powder (0.265 g) and iodine (0.761 g, 3 mmol, 1.5 equiv); conducted in an aqueous acetonitrile solution (1:9, V/V) at 80 °C for 18 h; yield: 0.065 g (18%). ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.95 (d, J = 8.7 Hz, 2H), 6.88 (d, J = 8.8 Hz, 2H), 6.43 (br s, 1H), 3.90 (s, 3H).

*Phenyl 4-Hydroxybenzoate (**14**).* A mixture of phenyl 4-acetoxybenzoate (**13**, 0.548 g, 2.14 mmol) and $AlBr_3$ (1.140 g, 4.27 mmol, 2 equiv) in acetonitrile (20 mL) was stirred at 80 °C for 18 h in an oil bath. The mixture was quenched with water (10 mL) and extracted with EA (50 mL × 3). The organic phases were combined and dried over $MgSO_4$. After filtration, the organic solvents were removed by rotary evaporation, and the residue was purified via flash column chromatography (eluent: PE/EA = 4:1−1:1, V/V). White solid; yield: 0.309 g (67%); mp 177−179 °C (lit.:[45] 180 °C); R_f = 0.71 (PE/EA = 1:1). ^{1}H NMR (400 MHz, DMSO-d_6) δ 7.97 (d, J = 8.7 Hz, 2H), 7.46 (t, J = 7.9 Hz, 2H), 7.29 (t, J = 7.4 Hz, 1H), 7.23 (d, J = 7.4 Hz, 2H), 6.91 (d, J = 8.8 Hz, 2H). ^{13}C{^{1}H} NMR (101 MHz, DMSO-d_6) δ 164.9, 163.8, 151.3, 132.7, 130.0, 126.2, 122.5, 119.3, 116.2.

■ ASSOCIATED CONTENT

Supporting Information

The Supporting Information is available free of charge at https://pubs.acs.org/doi/10.1021/acs.joc.1c00034.

^{1}H and ^{13}C{1H} NMR spectra of compounds (PDF)

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Notes

The authors declare no competing financial interest.

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