Esterification of Aryl/Alkyl Acids Catalysed by N-bromosuccinimide under Mild Reaction Conditions

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Abstract: N-halosuccinimides (NXSs) are well-known to be convenient, easily manipulable and low-priced halogenation reagents in organic synthesis. In the present work, N-bromosuccinimide (NBS) has been promoted as the most efficient and selective catalyst among the NXSs in the reaction of direct esterification of aryl and alkyl carboxylic acids. Comprehensive esterification of substituted benzoic acids, mono-, di- and tri-carboxy alkyl derivatives has been performed under neat reaction conditions. The method is metal-free, air- and moisture-tolerant, allowing for a simple synthetic and isolation procedure as well as the large-scale synthesis of aromatic and alkyl esters with yields up to 100%. Protocol for the recycling of the catalyst has been proposed.

Keywords: esterification; N-halosuccinimide; metal-free catalyst; aryl acids; alkyl acids

1. Introduction

Esterification reaction is one of the most important synthetic routes in organic synthesis due to the significance of its products. It is an irreplaceable reaction step during the synthesis of pharmaceuticals, cosmetics, plasticizers, perfumes, flavour chemicals, fine chemicals, electronic materials, solvents and chiral auxiliaries [1] and together with transesterification, it is a transformation of major significance in the biodiesel production [2–5]. Aside from being among the most prevalent final products and/or intermediates in the fields of science and industry, esters also play a significant role in biology, as the ester bonds are key linking groups in many primary lipid metabolites as well as secondary cyclodepsipeptide and polyketide metabolites [6]. As a result, a plethora of approaches have been reported for ester preparation, one of the most common being the reaction of direct esterification between carboxylic acids and alcohols (Fischer esterification) [7]. Conventionally, it is performed with excessive amounts of reagents/dehydrating agents or with activated carboxylic acid derivatives in the presence of a stoichiometric base, which results in significant amounts of by-products and waste at the end of the process as well as in energy-, time- and solvent-consuming purification [8]. Therefore, methods of catalytic direct condensation between carboxylic acids and alcohols, which lack these disadvantages, have recently become an attractive research subject, employing a broad spectra of different catalysts, such as Brønsted acids [9], metal catalysts [10,11], Lewis acids [12,13], solid-supported catalysts [14,15] and solid acids [16,17], ionic liquids [18,19], PPh3-based catalysts [20], enzymes [21,22], zeolites [23,24], etc. From the industrial and sustainability perspective, the ideal esterification method would include the use of easily manipulable, metal-free, low-cost, water-
and air-tolerant recyclable catalyst and mild solvent-free reaction conditions without the need for stoichiometric amounts of activators, large excesses of reagents and simultaneous removal of water. It should also be applicable to a broad substrate scope with high selectivity; it should be suitable for large-scale synthesis and allow a simple purification procedure, providing high product yields. The majority of known methods do not comply with at least one of the mentioned criteria; therefore, the field of sustainable design of esterification methods remains an attractive research challenge.

N-halosuccinimides (NXSs) belong to the class of N-halo reagents which are widely used in organic synthesis as halogenating, hydroxyhalogenating, oxidizing and condensing agents [25]. Their reactivity originates from the great lability of the N–X bond and various modes of its splitting [26]. Depending on the reaction conditions, different highly reactive species can be formed: N-radicals, N-cations, N-anions as well as their corresponding halogen counter particles, etc. [27]. Due to these convenient chemical properties, together with their metal-free character, low-cost, accessibility and higher stability relative to other N-halo reagents, NXSs have recently been attracting attention as mediators in substoichiometric amounts for different types of organic transformations [28–31]. The catalytic potential of N-bromosuccinimide (NBS) has recently been reviewed [32]; however, to the best of our knowledge, the use of N-bromosuccinimide as the only catalytic component in substoichiometric amounts for direct dehydrative esterification between alcohols and carboxylic acids has not been explored so far.

In our continuous pursuit of sustainable synthetic protocols [33–37], including those where NXSs are used as reagents [38–45], we now report and introduce the use of substoichiometric amounts of these compounds as mediators for efficient and selective comprehensive metal-free direct esterification of carboxyl functionality in organic molecules under neat reaction conditions (Scheme 1).

**Scheme 1.** Direct dehydrative esterification of carboxylic acids catalysed by substoichiometric amounts of NXSs.

### 2. Results and Discussion

Previously, some advantages of N-bromosuccinimide (NBS) as a catalyst in reactions of transesterification have been observed, but the reaction was limited to transesterification of α-keto esters [46] or acetylation of alcohols using acetic anhydride [47]. In addition, esterification of carboxylic acids with alcohols in the presence of triphenylphosphine (PPh₃) and N-bromo/iodosuccinimides has been reported as a method for ester preparation [48]. However, its significant drawback is posed by the by-product, phosphine oxide, formed in equimolar amounts, as it is difficult to remove during the purification step. Besides, the esterification was performed in halogenated solvent (dichloromethane) in the presence of equimolar amounts of base (pyridine) and NBS/NIS. Furthermore, molecular iodine has been presented as a convenient Lewis acid catalyst for direct dehydrative esterification, but attempts to prepare esters from corresponding aromatic acids have been found unsuccessful [49] or unselective [50,51]. Furthermore, bromine (Br₂)-mediated esterification of carbocyclic acids with methanol has been reported [52], though this methodology carries handling safety risks due to the potentially hazardous effects of Br₂/MeOH solution [53]. All the aforementioned provided us with an impetus to improve the reaction of direct esterification of aryl/alkyl acids. Since N-halosuccinimides have been widely used as more convenient and safer X₂ substitutes in halogenation reactions, the catalytic activity of corresponding N-halosuccinimide derivatives in the reaction of direct condensation between various structurally different carboxylic acid and alcohols has been investigated and presented herein.

Initially, benzoic acid (1) has been chosen as an aromatic acid model molecule to verify expectations and optimize reaction protocols. In the typical experimental procedure, 1 has
been refluxed with methanol (MeOH) in the presence of substoichiometric amounts of NXS: N-chlorosuccinimide (NCS), NBS, or N-iodosuccinimide (NIS). The results presented in Table 1 reveal that NBS seems to be the most promising catalyst in reactions of esterification, while without the presence of any of the NXSs, no conversion of starting material has been observed. In search of optimal reaction conditions, the effect of catalyst NBS loading has been examined by changing the amount of catalyst from 3 mol% to 15 mol% (Table 1). The amount below 7 mol% NBS furnished significantly lower conversion, while increasing the amount above 7 mol% did not significantly improve the yield of the corresponding ester. Therefore, further studies were carried out with 7 mol% of NBS. Moreover, the influence of temperature on the conversion of 1 to methyl benzoate (1a, Table 1) has been studied. The variation of temperature from 30 °C to 100 °C has been found to have a significant impact on the conversion of the acid to ester with the optimal temperature being 70 °C. Moreover, under dry reaction conditions (in the presence of Na2SO4) the efficiency of the esterification dropped considerably (entry 8). The promoting activities of NXSs, halogen mineral acids and molecular bromine were compared in the present esterification reaction. In the case of both aqueous HCl (entry 12) and molecular Br2 (entry 15), the conversions were comparable and their activity was similar to that of NBS (entry 6). On the other hand, the esterification efficiency in the case of both HBr and HI was considerably lower (entry 13 and 14) and resulted in the conversion yields of 84% and 68%, respectively. From the green-chemical point of view, NBS exhibited the highest catalytic activity among the examined catalysts.

Table 1. Catalyst loading and temperature optimization studies 1.

| Entry | NXS  | Loading [mol%] | Temperature [°C] | Conversion of Benzoic Acid to Methyl Benzoate [%] 2 |
|-------|------|----------------|-----------------|--------------------------------------------------|
| 1     | /    | /              | 70              | 0                                                |
| 2     | NCS  | 15             | 70              | 17                                               |
| 3     | NBS  | 15             | 70              | 94                                               |
| 4     | NIS  | 15             | 70              | 30                                               |
| 5     | NBS  | 10             | 70              | 94                                               |
| 6     | NBS  | 7              | 70              | 94                                               |
| 7     | NBS  | 3              | 70              | 76                                               |
| 8 3   | NBS  | 7              | 70              | <10                                              |
| 9     | NBS  | 7              | 30              | 0                                                |
| 10    | NBS  | 7              | 50              | 75                                               |
| 11    | NBS  | 7              | 100             | 94                                               |
| 12    | HCl  | 7              | 70              | 93                                               |
| 13    | HBr  | 7              | 70              | 84                                               |
| 14    | HI   | 7              | 70              | 68                                               |
| 15    | Br2  | 7              | 70              | 94                                               |

1 Reaction conditions: 1 (1.0 mmol), MeOH (0.5 mL), NXS, HCl (37%), HBr (48%), HI (57%), Br2, T, 20 h. 2 Conversions were determined by 1H-NMR analysis of the crude reaction mixtures. 3 Freshly dried MeOH was used and the reaction performed over anhydrous Na2SO4.

The optimal reaction conditions presented above (entry 6, Table 1) have been applied to 1-octanoic acid (2) as an alkyl acid model compound. As expected, 1-octanoic acid has been quantitatively converted to the corresponding methyl octanoate (2a, Figure 1), while in the absence of NBS, no conversion of the starting material was observed.

To compare the reactivity of the aromatic and alkyl acids, the optimization of reaction time has been performed (Figure 1). Relative to benzoic acid, significantly higher activity of alkyl acid (2) has been observed, which was in accordance with our expectations. Due to resonance stabilization of
carboxyl group in aromatic acids, its lower activation resulted in longer reaction time and slightly lower conversion.

![Graph](image)

**Figure 1.** The effect of reaction time on the efficiency of esterification of benzoic (1) and octanoic acid (2) with methanol in the presence of 7 mol% of NBS at 70 °C.

Encouraged by these promising results, the scope of the alcohols, suitable for esterification with acids 1 and 2, has been studied (Table 2). It can be observed that almost in all cases, alkyl acid (2) is significantly more active than aromatic acid (1) and the conversions to the corresponding esters (2a–i) are higher. Since nucleophilic characters, as well as steric properties, have been envisioned to have a considerable impact on reaction kinetics, different alcohols have been tested (a–i, Table 2). 2-Fluoro-1-ethanol (FCH₂CH₂OH, b) is a significantly weaker nucleophile than MeOH, therefore the reaction time for esterification of 1 as well as of 2 had to be prolonged. The elongation of the alcohol alkyl chain (a, d, f) had a stronger impact on esterification efficiency of benzoic acid than on esterification efficiency of octanoic acid, resulting in higher yields of octanoate esters (2a, 2d, 2f) relative to benzoate esters (1a, 1d, 1f). Moreover, the effect of increased steric hindrance of the nucleophilic alcohol component was followed by varying the bulkiness of alcohol from primary to tertiary structure (a, c and g, e and i). Interestingly, the esterification of octanoic acid was considerably less affected by the structural change from primary (MeOH, 2a) to secondary alcohol (i-PrOH and cyclopentanol, 2c and 2g) than the transformation of benzoic acid, where low (i-PrOH, 1a) or no conversion (cyclopentanol, 1g) was detected. Unfortunately, the limitation of the method was observed in reactions with bulky tertiary alcohols t-BuOH (e) and adamantanol (i), where no product was detected. Similarly, when phenol (h) has been used as the nucleophile, no reaction products were noticed, which can be assigned to the low nucleophilicity originating from the relatively high acidity of phenol molecule.

Due to the commercial importance of certain methyl esters in biodiesel production (fatty acid methyl esters, FAME) and perfumery (methyl benzoate), esterification of different types of carbocyclic acids with MeOH under optimal reaction conditions has been furtherly investigated (Table 3). As can be noticed, electronic effects of substituents, as well as their position on the phenyl ring of the investigated aromatic acids have exhibited a significant influence on the conversion of acids (3–12) to their corresponding methyl esters.
Table 2. The effect of alcohol structure on esterification of benzoic (1) and octanoic acid (2)\(^{1,2,3}\).

| R\(_2\)OH   | R\(_1\) = Ph                      | R\(_1\) = Heptyl         |
|-------------|----------------------------------|--------------------------|
| MeOH (a)    | ![Image of 1a](image) 94% (90%)  | ![Image of 2a](image) 100% (97%) 6 |
| FCH\(_2\)CH\(_2\)OH (b) | ![Image of 1b](image) 99% (95%) 4 | ![Image of 2b](image) 96% (92%) 4 |
| i-PrOH (c)  | ![Image of 1c](image) 12% (7%)   | ![Image of 2c](image) 85% (80%) |
| n-BuOH (d)  | ![Image of 1d](image) 80% (75%)  | ![Image of 2d](image) 100% (95%) 6 |
| t-BuOH (e)  | ![Image of 1e](image) 0%         | ![Image of 2e](image) 0%    |
| n-Octanol (f) | ![Image of 1f](image) 60% (57%) | ![Image of 2f](image) 91% (87%) |
| Cyclopentanol (g) | ![Image of 1g](image) 0% | ![Image of 2g](image) 99% (94%) 6 |
| Phenol (h)  | ![Image of 1h](image) 0%         | ![Image of 2h](image) 0%    |
| OH (i)      | ![Image of 1i](image) 0%         | ![Image of 2i](image) 0%    |

1 Reaction conditions: carboxylic acid (1 mmol), alcohol (1 mmol, 2 mmol or 0.5 mL), NBS (0.07 mmol), 70 °C, 20 h.
2 Conversions were determined by \(^1\)H NMR spectroscopy.
3 The values in brackets stand for yields of isolated products.
4 Conversion (yield of isolated product) after 40 h.
5 Conversion (yield of isolated product) after 2 h.
6 Conversion (yield of isolated product) after 15 h.
Table 3. Esterification of substituted benzoic and different alkyl carboxylic acids with MeOH in the presence of NBS.\(^1\)

\[
\begin{array}{cccc}
\text{R} & \text{O} & \text{O} & \text{Me} \\
\text{3-12} & \text{3-12a} & \\
\end{array}
\]

Methyl Benzoates

\[
\begin{array}{cccc}
\text{O}_2\text{N} & \text{O} & \text{O}_2\text{N} & \text{O} \\
\text{3a, 99% (92%)\(^6\)} & \text{4a, 81% (78%)\(^6\)} & \text{5a, 76% (68%)\(^6\)} & \text{6a, 74% (70%)} \\
\text{Me} & \text{Me} & \text{Me} & \\
\text{7a, 90% (84%)\(^6\)} & \text{8a, 94% (90%)\(^6\)} & \text{9a, 0%} & \text{10a, 49% (45%)\(^6\)} \\
\end{array}
\]

Alkyl COOH + MeOH \[\xrightarrow{\text{NBS (7 mol\%), 70 °C, 20 h}}\] Alkyl COOMe

Methyl Alkyl Esters and Methyl Esters of Cholic Acid Derivatives

\[
\begin{array}{cccc}
\text{CH}_3\text{(CH}_2\text{)}_{15}\text{CH}_2 & \text{13a, 99% (95%)} \\
\text{CH}_3\text{(CH}_2\text{)}_7\text{(CH}_2\text{)}_7 & \text{14a, 99% (97%)\(^6\)} \\
\text{MeO} & \text{15a, 97% (94%)\(^6\)} \\
\text{OMe} & \text{16a, 98% (94%)\(^6\)} \\
\text{17a, 99% (96%)} & \\
\text{18a, 92% (89%)\(^4\)} & \text{19a, 91% (88%)\(^4\)} & \text{20a, 100% (97%)} \\
\text{21a, 100% (96%)} & \\
\text{22a, 100% (98%)} & \text{23a, 100% (99%)} \\
\end{array}
\]

\(^1\) Reaction conditions: carboxylic acid (1 mmol), MeOH (0.5 mL), NBS (0.07 mmol), 70 °C, 1–20 h. \(^2\) Conversions were determined by \(^1\)H-NMR spectroscopy. \(^3\) The values in brackets stand for yields of isolated products. \(^4\) Reaction conditions: carboxylic acid (0.25 mmol), MeOH (2 mL), NBS (0.018 mmol), 70 °C, 1 h; conversion (yield of isolated product) after 1 h. \(^5\) 1.5 mL of MeOH was used. \(^6\) 2 mL of MeOH was used.
Strong electron-withdrawing (4-NO$_2$, 3-NO$_2$), as well as weak electron-donating groups (4-Me, 3-Me) with only positive inductive (+I) and no mesomeric effect (M) have expressed moderate impact on the yield, while substituents with positive mesomeric (+M) and negative inductive (–I) effects (4-F, 3-F) have resulted in a decrease in the conversion. The strong electron-donating group at para position (–OMe, compound 9) has completely inhibited the reaction due to the strong resonance interaction between the lone electron pair of the substituent and carboxyl functional group, while m–positioned methoxy group which could not resonate with carboxyl moiety, resulted in fair yield of target benzoate 10a. On the other hand, in the case of aliphatic carboxylic acids, no scope limits have been observed and methyl stearate (13a), as well as methyl oleate (14a), methyl 2-cyanoacetate (20a), (S)-methyl 2-acetamido-3-phenylpropanoate (21a), methyl 2-(1H-indol-3-yl)acetate (22a) and methyl 4-(4-chlorophenyl)-4-oxobutanoate (23a) have been obtained almost quantitatively, while dimethyl oxalate (15a), trimethyl citrate (16a), and adamantane-1-carboxylic acid methyl ester (17a) have been gained in excellent yields.

Furthermore, the applicability of the method on more complex structural backbones has been demonstrated by performing the esterification of two significant steroidal carboxylic acids: cholic acid as one of the most common bile acids, formed as an end product of cholesterol metabolism in the liver [54], and its derivative dehydrocholic acid, which is the main component in many drugs against cholestatic liver disease and for dissolution of cholesterol gallstones [55]. In both cases, an excellent conversion of the starting material was achieved already after 1 h. Although in the crude reaction mixture obtained after esterification of dehydrocholic acid, partial conversion to ketal was observed, it was quantitatively converted into the corresponding ester during the isolation step by washing the mixture with 10% hCl (aq).

Moreover, to confirm the synthetic value of the presented methodology, synthesis of methyl benzoate (1a), methyl stearate (13a) and methyl citrate (16a) has been performed on 10–40 mmol scale with high to excellent yields (85–100%).

3. Materials and Methods

3.1. General Information

All reactions were performed in Mettler-Toledo Easymax 102 Advanced Synthesis Workstation using 25 mL reactor tubes. NMR spectra were recorded on Varian Inova 300 spectrometer (300 MHz $^1$H, 75 MHz $^{13}$C, 285 MHz $^{19}$F) at 25 °C. $^1$H-NMR spectra were obtained as solutions in CDCl$_3$ with TMS as the internal standard. $^{13}$C-NMR spectra were obtained as solutions in CDCl$_3$ with CFCl$_3$ as the internal standard. N-bromosuccinimide was freshly recrystallized before use. All other chemicals used for synthetic procedures were obtained from commercial sources and were of reagent grade purity or better (Merck, Sigma Aldrich, Carlo Erba, Fluka, Fisher Scientific, Apollo Scientific, etc.). Reactions were monitored by TLC with silica gel coated plates Silica gel/TLC cards, DC-Alufolien-Kieselgel with 60 Å medium pore diameter (Sigma Aldrich) and detection was conducted by UV absorption (254 nm). Purification of certain products was conducted on preparative silica gel glass plates PLC Kieselgel 60 F254 with 2 mm layer thickness. Succinimide, isolated at the end of the reaction, can easily be recycled back to N-bromosuccinimide according to the standard procedure by NaOH, as elaborated in other reports [56]. Copies of $^1$H-NMR, $^{13}$C-NMR and $^{19}$F-NMR spectra of isolated final products are available in Supplementary material file online.

3.2. Experimental Procedures

3.2.1. General Procedure for the Esterification between Carboxylic Acids and Alcohols

The mixture of carboxylic acid, alcohol and N-bromosuccinimide was stirred in a 25 mL reactor tube at 70 °C for 2–40 h. After the completion of the reaction, the mixture was cooled to room temperature and alcohol was evaporated under reduced pressure. The isolation procedure was as
follows, except where noted differently in Section 3.2.6. The residue was dissolved in ethyl acetate and consecutively washed with 10 mL of 10% Na$_2$S$_2$O$_3$(aq), 5 mL of saturated NaHCO$_3$(aq) and 10 mL of distilled water. The water phase was extracted with ethyl acetate (3 × 5 mL). The organic layers were combined, dried over Na$_2$SO$_4$ and the solvent was evaporated under reduced pressure.

3.2.2. Scale-Up Procedure for Preparation of Methyl Benzoate (1a) and Isolation of Succinimide

The mixture of benzoic acid (40 mmol, 4.88 g), MeOH (20 mL) and N-bromosuccinimide (2.80 mmol, 0.50 g) was stirred in a 25 mL reactor tube at 70 °C for 20 h. After the completion of the reaction, the mixture was cooled to room temperature and alcohol was evaporated under reduced pressure. The residue was washed with distilled water (20 mL) and the water phase was extracted with ethyl acetate (2 × 20 mL). The organic layers were combined and washed with the mixture of 10 mL of saturated NaHCO$_3$(aq), 10 mL of 10% Na$_2$S$_2$O$_3$(aq) and 15 mL of distilled water. The water layer was again extracted with ethyl acetate (2 × 20 mL). The organic layers were combined, dried over Na$_2$SO$_4$ and the solvent was evaporated under reduced pressure to furnish methyl benzoate as colourless oil. The water layer from the first washing of the crude reaction mixture was evaporated under the reduced pressure to give succinimide as a white solid.

Yield (methyl benzoate): 4.60 g, 85%.
Yield (succinimide [57]): 272 mg, 98%.
$^1$H NMR (300 MHz, CDCl$_3$) $\delta$ 10.04 (s, 1H), 2.72 (s, 4H).
$^{13}$C NMR (76 MHz, CDCl$_3$) $\delta$ 178.8, 29.4.

3.2.3. Scale-Up Procedure for Preparation of Trimethyl Citrate (16a)

The mixture of citric acid (11 mmol, 2.11 g), MeOH (20 mL) and N-bromosuccinimide (0.77 mmol, 0.138 g) was stirred in a 25 mL reactor tube at 70 °C for 20 h. After the completion of the reaction, the mixture was cooled to room temperature and alcohol was evaporated under reduced pressure. The residue was dissolved in 50 mL of ethyl acetate, washed with the mixture of 10 mL of saturated NaHCO$_3$(aq), 10 mL of 10% Na$_2$S$_2$O$_3$(aq) and 25 mL of distilled water and the water phase was extracted with ethyl acetate (2 × 25 mL). The organic layers were combined, dried with Na$_2$SO$_4$ and the solvent was evaporated under reduced pressure to furnish methyl citrate as a white solid.

Yield: 2.55 g, 99%.

3.2.4. Scale-Up Procedure for Preparation of Methyl Stearate (13a)

The mixture of stearic acid (10 mmol, 2.85 g), MeOH (20 mL) and N-bromosuccinimide (0.70 mmol, 0.125 g) was stirred in a 25 mL reactor tube at 70 °C for 20 h. After the completion of the reaction, the mixture was cooled to room temperature and alcohol was evaporated under reduced pressure. The residue was dissolved in 50 mL of ethyl acetate, washed with the mixture of 10 mL of saturated NaHCO$_3$(aq), 10 mL of 10% Na$_2$S$_2$O$_3$(aq) and 15 mL of distilled water and the water phase was extracted with ethyl acetate (2 × 25 mL). The organic layers were combined, washed with distilled water (2 × 20 mL), dried with Na$_2$SO$_4$ and the solvent was evaporated under reduced pressure to furnish methyl stearate as a white solid.

Yield: 2.99 g, 100%.

3.2.5. Procedure for Recycling of N-bromosuccinimide (NBS) from Waste Succinimide

Succinimide (0.272 g, 2.75 mmol) was dissolved in a mixture of 1.36 g (3.29 mmol) NaOH, 0.5 g crushed ice and 1.5 mL of cold water. To this mixture, 0.156 mL (3.02 mmol, 0.483 g) of Br$_2$ was added while stirring. It was stirred for five minutes and then the product was filtered, washed with cold water and dried in a desiccator to isolate 0.348 g (71%) of NBS.
3.2.6. Detailed Procedures for the Preparation of Synthesized Compounds

*Methyl benzoate (1a)* [17]. Synthesized according to the general procedure. Reaction conditions: benzoic acid (1 mmol, 122.1 mg), MeOH (0.5 mL), NBS (0.070 mmol, 12.5 mg), 70 °C, 20 h. Purification: Not necessary. Yield: 122 mg of colourless oil (90%); 1H-NMR (300 MHz, CDCl3) δ 8.07–8.01 (m, 2H), 7.59–7.51 (m, 1H), 7.43 (ddd, J = 8.2, 6.8, 1.1 Hz, 2H), 3.91 (s, 3H); 13C-NMR (76 MHz, CDCl3) δ 174.5, 167.2, 133.0, 130.3, 129.7, 128.4, 52.2; hRMS (ESI) for C8H10O2: calculated m/z = 137.0603 (MH+); found m/z = 137.0606 (MH+).

*Methyl octanoate (2a)* [58]. Synthesized according to the general procedure. Reaction conditions: octanoic acid (1 mmol, 158.5 μL), MeOH (0.5 mL), NBS (0.070 mmol, 12.5 mg), 70 °C, 2 h. Purification: Not necessary. Yield: 167 mg of white solid (92%); 1H-NMR (300 MHz, CDCl3) δ 8.34–8.19 (m, 4H), 3.99 (s, 3H); hRMS (ESI) for C7H14O2: calculated m/z = 151.0759 (MH+): found m/z = 151.0755 (MH+).

*Methyl 3-methylbenzoate* (1b) [17]. Synthesized according to the general procedure. Reaction conditions: 3-methylbenzoic acid (1 mmol, 136.1 mg), MeOH (2 mL), NBS (0.070 mmol, 12.5 mg), 70 °C, 20 h. Purification: Not necessary. Yield: 136 mg of colourless oil (84%); 1H-NMR (300 MHz, CDCl3) δ 7.97–7.86 (m, 2H), 7.22 (d, J = 8.2 Hz, 2H), 3.88 (s, 3H), 2.39 (s, 3H); 13C-NMR (76 MHz, CDCl3) δ 166.2, 162.6 (d, J = 10.8 Hz, 2H), 160.9, 135.6, 130.8, 123.6, 77.2, 52.9.

*Methyl 4-fluorobenzoate* (4a) [59]. Synthesized according to the general procedure. Reaction conditions: 4-fluorobenzoic acid (1 mmol, 140.1 mg), MeOH (2 mL), NBS (0.070 mmol, 12.5 mg), 70 °C, 20 h. Purification: Not necessary. Yield: 122 mg of colourless oil (90%); 1H-NMR (300 MHz, CDCl3) δ 8.07–7.93 (m, 2H), 7.68 (t, J = 8.0 Hz, 1H), 4.00 (s, 3H); 13C-NMR (76 MHz, CDCl3) δ 165.0, 148.3, 135.3, 131.9, 129.7, 127.4, 124.6, 52.8; hRMS (ESI) for C7H6F2O2: calculated m/z = 182.0453 (MH+); found m/z = 182.0457 (MH+).

*Methyl 4-fluorobenzoate* (5a) [60]. Synthesized according to the general procedure. Reaction conditions: 4-fluorobenzoic acid (1 mmol, 140.1 mg), MeOH (2 mL), NBS (0.070 mmol, 12.5 mg), 70 °C, 20 h. Purification: Not necessary. Yield: 141 mg of yellow solid (78%); 1H-NMR (300 MHz, CDCl3) δ 8.87–8.80 (m, 2H), 7.71–7.63 (m, 2H), 7.64 (t, J = 8.0 Hz, 1H), 4.00 (s, 3H); 13C-NMR (76 MHz, CDCl3) δ 166.2, 165.8 (d, J = 12.2 Hz) 132.2 (d, J = 9.4 Hz), 126.5 (d, J = 3.0 Hz), 115.6 (d, J = 22.0 Hz), 52.2; 19F-NMR (285 MHz, CDCl3) δ -112.9 (d, J = 8.5, 5.4 Hz); hRMS (ESI) for C7H6F2O2: calculated m/z = 155.0508 (MH+); found m/z = 155.0505 (MH+).

*Methyl 3-fluorobenzoate* (6a) [61]. Synthesized according to the general procedure. Reaction conditions: 3-fluorobenzoic acid (1 mmol, 140.1 mg), MeOH (0.5 mL), NBS (0.070 mmol, 12.5 mg), 70 °C, 20 h. Purification: Not necessary. Yield: 108 mg of colourless oil (70%); 1H-NMR (300 MHz, CDCl3) δ 7.83 (dt, J = 7.7, 1.2 Hz, 1H), 7.71 (ddd, J = 9.4, 2.6, 1.5 Hz, 1H), 7.41 (td, J = 8.0, 5.6 Hz, 1H), 7.25 (td, J = 8.3, 2.5, 1.0 Hz, 1H), 3.92 (s, 3H); 13C-NMR (76 MHz, CDCl3) δ 166.0, 162.6 (d, J = 246.6 Hz), 132.4 (d, J = 7.6 Hz), 130.1 (d, J = 7.6 Hz), 125.4 (d, J = 2.9 Hz), 120.1 (d, J = 21.4 Hz), 116.6 (d, J = 23.0 Hz), 52.4; 19F-NMR (285 MHz, CDCl3) δ -112.42 (d, J = 9.4, 8.4, 5.6 Hz); hRMS (ESI) for C7H6F2O2: calculated m/z = 155.0508 (MH+); found m/z = 155.0511 (MH+).

*Methyl 4-methylbenzoate* (7a) [60]. Synthesized according to the general procedure. Reaction conditions: 4-methylbenzoic acid (1 mmol, 136.1 mg), MeOH (2 mL), NBS (0.070 mmol, 12.5 mg), 70 °C, 20 h. Purification: Not necessary. Yield: 126 mg of colourless oil (84%); 1H-NMR (300 MHz, CDCl3) δ 7.97–7.86 (m, 2H), 7.22 (d, J = 8.2 Hz, 2H), 3.88 (s, 3H), 2.39 (s, 3H); 13C-NMR (76 MHz, CDCl3) δ 167.2, 143.6, 129.6, 129.1, 127.5, 52.0, 21.7; hRMS (ESI) for C9H10O2: calculated m/z = 151.0759 (MH+); found m/z = 151.0755 (MH+).

*Methyl 3-methylbenzoate* (8a) [60]. Synthesized according to the general procedure. Reaction conditions: 3-methylbenzoic acid (1 mmol, 136.1 mg), MeOH (2 mL), NBS (0.070 mmol, 12.5 mg), 70 °C, 20 h. Purification: Not necessary. Yield: 136 mg of colourless oil (90%); 1H-NMR (300 MHz, CDCl3) δ
Trimethyl citrate

\[ \text{C}_9\text{H}_{16}\text{O}_7 \]

calculated: \( m/z = 151.0759 \) (MH\(^+\)); found \( m/z = 151.0762 \) (MH\(^+\)).

**Methyl 3-methoxybenzoate (10a)** [62]. Synthesized according to the general procedure. Reaction conditions: 3-methoxybenzoic acid (1 mmol, 152.1 mg), MeOH (2 mL), NBS (0.070 mmol, 12.5 mg), 70 °C, 20 h. Purification: Not necessary. Yield: 75 mg of yellow oil (45%); \(^{13}\)C-NMR (76 MHz, CDCl\(_3\)) \( \delta 167.3, 138.2, 133.7, 130.2, 128.3, 126.8, 52.1, 21.3 \); hRMS (ESI) for \( \text{C}_9\text{H}_{10}\text{O}_2 \): calculated \( m/z = 167.0708 \) (MH\(^+\)); found \( m/z = 167.0717 \) (MH\(^+\)).

**Methyl 4-ocetylbenzoate (11a)** [63]. Synthesized according to the general procedure. Reaction conditions: 4-ocetylbenzoic acid (1 mmol, 234.3 mg), MeOH (2 mL), NBS (0.070 mmol, 12.5 mg), 70 °C, 20 h. Purification: Not necessary. Yield: 194 mg of yellow oil, (78%); \(^1\)H-NMR (300 MHz, CDCl\(_3\)) \( \delta 8.02-7.87 \) (m, 2H), 7.31-7.16 (m, 2H), 3.89 (s, 3H), 2.73-2.57 (m, 2H), 1.69-1.54 (m, 2H), 1.43-1.19 (m, 10H), 0.87 (t, \( J = 6.7 \) Hz, 3H); \(^{13}\)C-NMR (76 MHz, CDCl\(_3\)) \( \delta 167.3, 148.6, 129.7, 128.5, 127.7, 52.0, 36.1, 32.0, 31.2, 29.5, 29.4, 29.3, 22.8, 14.2 \); hRMS (ESI) for \( \text{C}_{16}\text{H}_{24}\text{O}_2 \): calculated \( m/z = 249.1855 \) (MH\(^+\)); found \( m/z = 249.1853 \) (MH\(^+\)).

**Methyl 2-iodobenzoate (12a)** [64]. Synthesized according to the general procedure. Reaction conditions: 2-iodobenzoic acid (1 mmol, 248.0 mg), MeOH (0.5 mL), NBS (0.070 mmol, 12.5 mg), 70 °C, 20 h. Purification: Not necessary. Yield: 144 mg of colourless oil (55%); \(^1\)H-NMR (300 MHz, CDCl\(_3\)) \( \delta 7.95 \) (dd, \( J = 7.9, 1.1 \) Hz, 1H), 7.76 (dd, \( J = 7.8, 1.7 \) Hz, 1H), 7.36 (td, \( J = 7.6, 1.1 \) Hz, 1H), 7.11 (td, \( J = 7.7, 1.7 \) Hz, 1H), 3.90 (s, 3H); \(^{13}\)C-NMR (76 MHz, CDCl\(_3\)) \( \delta 166.9, 141.3, 135.1, 132.7, 130.9, 127.9, 94.1, 52.5 \); hRMS (ESI) for \( \text{C}_8\text{H}_{16}\text{O}_2 \): calculated \( m/z = 262.9569 \) (MH\(^+\)); found \( m/z = 262.9563 \) (MH\(^+\)).

**Methyl stearate (13a)** [14]. Synthesized according to the general procedure. Reaction conditions: stearic acid (1 mmol, 284.5 mg), MeOH (0.5 mL), NBS (0.070 mmol, 12.5 mg), 70 °C, 20 h. Purification: Not necessary. Yield: 285 mg of white solid (95%); \(^1\)H-NMR (300 MHz, CDCl\(_3\)) \( \delta 3.67 \) (s, 3H), 2.30 (t, \( J = 7.5 \) Hz, 2H), 1.69-1.55 (m, 2H), 1.37-1.20 (m, 28H), 0.88 (t, \( J = 7.0 \) Hz, 3H); \(^{13}\)C-NMR (76 MHz, CDCl\(_3\)) \( \delta 174.5, 51.6, 34.3, 32.1, 29.8, 29.8, 29.8, 29.8, 29.8, 29.8, 29.8, 29.8, 29.6, 29.5, 29.4, 29.3, 25.1, 22.8, 14.3 \); hRMS (ESI) for \( \text{C}_{18}\text{H}_{36}\text{O}_2 \): calculated \( m/z = 299.2950 \) (MH\(^+\)); found \( m/z = 299.2957 \) (MH\(^+\)).

**Methyl oleate (14a)** [14]. Synthesized according to the general procedure. Reaction conditions: oleic acid (1 mmol, 315.6 \( \mu \)L), MeOH (2 mL), NBS (0.070 mmol, 12.5 mg), 70 °C, 15 h. Purification: Not necessary. Yield: 289 mg of white solid (97%); \(^1\)H-NMR (300 MHz, CDCl\(_3\)) \( \delta 5.34 \) (ddd, \( J = 5.6, 3.5, 2.1 \) Hz, 2H), 3.66 (s, 3H), 2.30 (t, \( J = 7.5 \) Hz, 2H), 2.10-1.91 (m, 4H), 1.71-1.54 (m, 2H), 1.42-1.17 (m, 18H), 0.88 (t, \( J = 6.7 \) Hz, 3H); \(^{13}\)C-NMR (76 MHz, CDCl\(_3\)) \( \delta 174.4, 130.1, 129.9, 51.5, 34.2, 32.0, 29.9, 29.8, 29.7, 29.5, 29.4, 29.3, 29.3, 29.2, 27.3, 27.3, 25.1, 22.8, 14.2 \); hRMS (ESI) for \( \text{C}_{19}\text{H}_{36}\text{O}_2 \): calculated \( m/z = 297.2974 \) (MH\(^+\)); found \( m/z = 297.2978 \) (MH\(^+\)).

**Dimethyl oxalate (15a)** [65]. Synthesized according to the general procedure. Reaction conditions: oxalic acid (1 mmol, 90.0 mg), MeOH (2 mL), NBS (0.070 mmol, 12.5 mg), 70 °C, 15 h. Purification: Not necessary. Yield: 110 mg of white solid (93%); \(^1\)H-NMR (300 MHz, CDCl\(_3\)) \( \delta 3.92 \) (s, 6H); \(^{13}\)C-NMR (76 MHz, CDCl\(_3\)) \( \delta 157.8, 53.5 \); hRMS (ESI) for \( \text{C}_3\text{H}_4\text{O}_4 \): calculated \( m/z = 119.0344 \) (MH\(^+\)); found \( m/z = 119.0342 \) (MH\(^+\)).

**Trimethyl citrate (16a)** [66]. Synthesized according to the general procedure. Reaction conditions: citric acid (1 mmol, 210.1 mg), MeOH (2 mL), NBS (0.070 mmol, 12.5 mg), 70 °C, 20 h. Purification: Not necessary. Yield: 220 mg of white solid (94%); \(^1\)H-NMR (300 MHz, CDCl\(_3\)) \( \delta 4.10 \) (s, 1H), 3.81 (s, 3H), 3.67 (s, 6H), 2.89 (d, \( J = 15.6 \) Hz, 2H), 2.79 (d, \( J = 15.6 \) Hz, 2H); \(^{13}\)C-NMR (76 MHz, CDCl\(_3\)) \( \delta 173.8, 170.2, 73.3, 53.2, 52.0, 43.1 \); hRMS (ESI) for \( \text{C}_9\text{H}_{14}\text{O}_7 \): calculated \( m/z = 235.0818 \) (MH\(^+\)); found \( m/z = 235.0815 \) (MH\(^+\)).
Adamantane-1-carboxylic acid methyl ester (17a) [61]. Synthesized according to the general procedure. Reaction conditions: 1-adamantanecarboxylic acid (1 mmol, 180.2 mg), MeOH (0.5 mL), NBS (0.070 mmol, 12.5 mg), 70 °C, 20 h. Purification: Not necessary. Yield: 186 mg of white solid (96%); 1H-NMR (300 MHz, CDCl3) δ 3.60 (s, 3H), 2.01–1.92 (m, 3H), 1.88–1.80 (m, 6H), 1.74–1.59 (m, 3H); 13C-NMR (76 MHz, CDCl3) δ 178.08, 51.44, 40.64, 38.81, 36.46, 27.91; hRMS (ESI) for C12H18O2: calculated m/z = 195.1385 (MH⁺); found m/z = 195.1382 (MH⁺).

Methyl 3,7,12-trioxo-5β-cholan-24-oate (18a) [67]. The mixture of dehydrocholic acid (0.25 mmol, 101.6 mg), MeOH (2 mL) and N-bromosuccinimide (0.018 mmol, 3.1 mg) was stirred in a 25 mL reactor tube at 70 °C for 1 h. After the completion of the reaction, the mixture was cooled to room temperature and MeOH was evaporated under the reduced pressure. The residue was dissolved in ethyl acetate and first washed with the mixture of 10 mL of 10% Na2SO4(aq), 5 mL of saturated NaHCO3(aq) and 10 mL of distilled water and then with 10 mL of 10% hCl(aq). The water phase was extracted with ethyl acetate (3 × 5 mL). The organic layers were combined, dried with Na2SO4 and the solvent was evaporated under the reduced pressure. Purification: Not necessary. Yield: 93 mg of white solid (97%); 1H-NMR (300 MHz, CDCl3) δ 3.76 (s, 3H), 3.46 (s, 2H); 13C-NMR (76 MHz, CDCl3) δ 163.6, 113.2, 53.5, 24.4; hRMS (ESI) for C25H44O6: calculated m/z = 423.3110 (MH⁺); found m/z = 423.3128 (MH⁺).

Methyl 3α,7α,12α-trihydroxy-5β-cholan-24-oate (19a) [68]. The mixture of cholic acid (0.25 mmol, 102.1 mg), MeOH (2 mL) and N-bromosuccinimide (0.018 mmol, 3.1 mg) was stirred in a 25 mL reactor tube at 70 °C for 1 h. After the completion of the reaction, the mixture was cooled to room temperature and MeOH was evaporated under the reduced pressure. The residue was dissolved in ethyl acetate and washed with the mixture of 10 mL of 10% Na2SO4(aq), 5 mL of saturated NaHCO3(aq) and 10 mL of distilled water. The water phase was extracted with ethyl acetate (3 × 5 mL). The organic layers were combined, dried with Na2SO4 and the solvent was evaporated under the reduced pressure. Purification: Not necessary. Yield: 93 mg of white solid (96%); 1H-NMR (300 MHz, CDCl3) δ 3.95 (s, 1H), 3.83 (s, 1H), 3.66 (s, 3H), 3.55 (s, 3H), 3.49–3.32 (m, 1H), 2.48–1.07 (m, 24H), 0.98 (d, J = 5.8 Hz, 3H), 0.88 (s, 3H); 13C-NMR (76 MHz, CDCl3) δ 174.7, 72.9, 71.7, 68.3, 51.3, 46.8, 46.2, 41.4, 41.4, 39.3, 39.3, 35.2, 35.2, 34.6, 34.6, 31.0, 30.8, 30.2, 28.0, 27.4, 26.1, 23.1, 22.3, 17.2, 12.3; hRMS (ESI) for C25H42O5: calculated m/z = 423.3110 (MH⁺); found m/z = 423.3128 (MH⁺).

Methyl 2-cyanoacetate (20a) [69]. Synthesized according to the general procedure. Reaction conditions: Cyanoacetic acid (1 mmol, 85.1 mg), MeOH (0.5 mL), NBS (0.070 mmol, 12.5 mg), 70 °C, 20 h. Purification: Not necessary. Yield: 96 mg of colourless oil (97%); 1H-NMR (300 MHz, CDCl3) δ 3.76 (s, 3H), 3.46 (s, 2H); 13C-NMR (76 MHz, CDCl3) δ 163.6, 113.2, 53.5, 24.4; hRMS (ESI) for C3H5NO2: calculated m/z = 100.0399 (MH⁺); found m/z = 100.0398 (MH⁺).

(S)-Methyl 2-acetamido-3-phenylpropanoate (21a) [70]. Synthesized according to the general procedure. Reaction conditions: N-Acetyl-L-phenylalanine (1 mmol, 207.2 mg), MeOH (0.5 mL), NBS (0.070 mmol, 12.5 mg), 70 °C, 20 h. Purification: Not necessary. Yield: 208 mg of white solid (91%); 1H-NMR (300 MHz, CDCl3) δ 7.33–7.18 (m, 3H), 7.18–7.05 (m, 2H), 6.38 (d, J = 7.5 Hz, 1H), 4.95–4.77 (m, 1H), 3.69 (s, 3H), 3.21–2.93 (m, 2H), 1.95 (s, 3H); 13C-NMR (76 MHz, CDCl3) δ 172.2, 169.8, 136.0, 129.2, 128.5, 127.0, 53.2, 52.2, 37.8, 22.9; hRMS (ESI) for C12H15NO3: calculated m/z = 222.1130 (MH⁺); found m/z = 222.1135 (MH⁺).

Methyl 2-((3H-indol-3-yl)acetate (22a) [71]. Synthesized according to the general procedure. Reaction conditions: heteroauxin (1 mmol, 175.2 mg), MeOH (0.5 mL), NBS (0.070 mmol, 12.5 mg), 70 °C, 20 h. Purification: Not necessary. Yield: 185 mg of brown oil (98%); 1H-NMR (300 MHz, CDCl3) δ 8.16 (s, 1H), 7.56 (dd, J = 6.7, 1.6 Hz, 2H), 7.24–6.98 (m, 3H), 6.84 (d, J = 2.4 Hz, 1H), 3.72 (s, 2H), 3.63 (s, 3H); 13C-NMR (76 MHz, CDCl3) δ 173.0, 136.1, 127.1, 123.4, 122.0, 119.5, 118.6, 111.4, 107.8, 52.0, 31.1; hRMS (ESI) for C11H11NO2: calculated m/z = 190.0868 (MH⁺); found m/z = 190.0865 (MH⁺).
Methyl 4-(4-chlorophenyl)-4-oxobutanoate (23a) [72]. Synthesized according to the general procedure. Reaction conditions: 3-(4-Chlorobenzoyl)propionic acid (1 mmol, 212.6 mg), MeOH (0.5 mL), NBS (0.070 mmol, 12.5 mg), 70 °C, 20 h. Purification: Not necessary. Yield: 224 mg of white solid (99%); 
1H-NMR (300 MHz, CDCl3) δ 7.90–7.81 (m, 2H), 7.41–7.33 (m, 2H), 3.64 (s, 3H), 3.22 (t, J = 6.6 Hz, 2H), 2.70 (t, J = 6.6 Hz, 2H); 13C-NMR (76 MHz, CDCl3) δ 196.8, 173.2, 139.6, 134.8, 129.4, 128.9, 51.8, 33.3, 27.9; hRMS (ESI) for C12H15O2: calculated m/z = 249.0294 (MNa+); found m/z = 249.0297 (MNa+).

2-Fluoroethyl benzoate (1b) [73]. Synthesized according to the general procedure. Reaction conditions: benzoic acid (1 mmol, 122.1 mg), 2-fluoroethanol (0.5 mL), NBS (0.07 mmol, 12.5 mg), 70 °C, 40 h. Purification: Preparative TLC (CH2Cl2/MeOH = 200:1). Yield: 160 mg of colourless oil (95%); 1H-NMR (300 MHz, CDCl3) δ 8.20–7.86 (m, 2H), 7.60–7.52 (m, 1H), 7.49–7.37 (m, 2H), 4.85–4.44 (m, 4H); 13C-NMR (76 MHz, CDCl3) δ 166.4, 133.3, 129.8, 128.5, 81.5 (d, J = 170.6 Hz), 63.9 (d, J = 20.2 Hz); 19F NMR (285 MHz, CDCl3) δ 5.03 (tt, J = 47.4, 28.6 Hz); hRMS (ESI) for C9H9FO2: calculated m/z = 169.0665 (MH+); found m/z = 169.0668 (MH+).

Isopropyl benzoate (1c) [74]. Synthesized according to the general procedure. Reaction conditions: benzoic acid (1 mmol, 122.1 mg), isopropanol (0.5 mL), NBS (0.07 mmol, 12.5 mg), 70 °C, 20 h. Purification: Not necessary. Yield: 12 mg of colourless oil (7%); 1H-NMR (300 MHz, CDCl3) δ 8.09–7.99 (m, 2H), 7.59–7.50 (m, 1H), 7.47–7.38 (m, 2H), 5.26 (hept, J = 6.3 Hz, 1H), 1.37 (d, J = 6.3 Hz, 6H); 13C-NMR (76 MHz, CDCl3) δ 166.3, 132.8, 131.1, 129.6, 128.4, 68.5, 22.1.

2-Fluoroethyl octanoate (2b) [75]. Synthesized according to the general procedure. Reaction conditions: octanoic acid (1 mmol, 158.5 µL), 2-fluoroethanol (0.5 mL), NBS (0.07 mmol, 12.5 mg), 70 °C, 20 h. Purification: Not necessary. Yield: 175 mg of yellow oil (92%); 1H-NMR (300 MHz, CDCl3) δ 4.73–4.20 (m, 4H), 2.36 (s, J = 7.5 Hz, 2H), 1.71–1.57 (m, 2H), 1.42–1.19 (m, 8H), 0.88 (t, J = 7.1 Hz, 3H); 13C-NMR (76 MHz, CDCl3) δ 173.7, 81.5 (d, J = 170.3 Hz), 63.2 (d, J = 20.1 Hz), 34.2, 31.7, 29.1, 29.0, 25.0, 22.7, 14.1; 19F-NMR (285 MHz, CDCl3) δ 4.86 (tt, J = 47.4, 28.7 Hz); hRMS (ESI) for C10H19O2: calculated m/z = 191.1447 (MH+); found m/z = 191.1446 (MH+).

Isopropyl octanoate (2c) [76]. Synthesized according to the general procedure. Reaction conditions: octanoic acid (1 mmol, 158.5 µL), isopropanol (0.5 mL), NBS (0.07 mmol, 12.5 mg), 70 °C, 20 h. Purification: Not necessary. Yield: 149 mg of colourless oil (80%); 1H-NMR (300 MHz, CDCl3) δ 5.00 (hept, J = 6.3 Hz, 1H), 2.25 (s, J = 7.5 Hz, 2H), 1.67–1.55 (m, 2H), 1.35–1.25 (m, 8H), 1.23 (d, J = 6.3 Hz, 6H), 0.88 (t, J = 7.0 Hz, 3H); 13C-NMR (76 MHz, CDCl3) δ 173.4, 67.3, 34.8, 31.7, 29.2, 29.0, 25.1, 22.7, 21.9, 14.1; hRMS (ESI) for C11H22O2: calculated m/z = 187.1698 (MH+); found m/z = 187.1703 (MH+).

n-Butyl benzoate (1d) [77]. Synthesized according to the general procedure. Reaction conditions: benzoic acid (1 mmol, 122.1 mg), n-butanol (0.5 mL), NBS (0.07 mmol, 12.5 mg), 70 °C, 20 h. Purification: Preparative TLC (CH2Cl2/MeOH = 200:1). Yield: 134 mg of colourless oil (75%); 1H-NMR (300 MHz, CDCl3) δ 8.10–7.99 (m, 2H), 7.58–7.49 (m, 1H), 7.42 (t, J = 7.5 Hz, 2H), 4.32 (t, J = 6.6 Hz, 2H), 1.84–1.66 (m, 2H), 1.56–1.39 (m, 2H), 0.98 (t, J = 7.4 Hz, 3H); 13C-NMR (76 MHz, CDCl3) δ 166.7, 132.8, 130.6, 129.6, 128.4, 64.9, 30.9, 19.4, 13.8; hRMS (ESI) for C12H14O2: calculated m/z = 179.1072 (MH+); found m/z = 179.1070 (MH+).

n-Butyl octanoate (2d) [4]. Synthesized according to the general procedure. Reaction conditions: octanoic acid (1 mmol, 158.5 µL), n-butanol (1 mmol, 92 µL), NBS (0.07 mmol, 12.5 mg), 70 °C, 15 h. Purification: Not necessary. Yield: 190 mg of colourless oil (95%); 1H-NMR (300 MHz, CDCl3) δ 4.07 (t, J = 6.6 Hz, 2H), 2.29 (t, J = 7.5 Hz, 2H), 1.70–1.52 (m, 4H), 1.47–1.21 (m, 10H), 0.94 (t, J = 7.3 Hz, 3H), 0.87 (t, J = 6.9 Hz, 3H); 13C-NMR (76 MHz, CDCl3) δ 174.0, 64.1, 34.4, 31.8, 30.8, 29.2, 29.0, 25.1, 22.7, 19.2, 14.1, 13.7; hRMS (ESI) for C12H23O2: calculated m/z = 201.1855 (MH+); found m/z = 201.1857 (MH+).

n-Octyl benzoate (1f) [58]. Synthesized according to the general procedure. Reaction conditions: benzoic acid (1 mmol, 122.1 mg), n-octanol (1 mmol, 158 µL), NBS (0.07 mmol, 12.5 mg), 70 °C, 20 h. Purification: Preparative TLC (CH2Cl2/Hexane = 1:1). Yield: 134 mg of white solid (57%); 1H-NMR (300 MHz,
CDCl$_3$) $\delta$ 8.10–8.00 (m, 2H), 7.59–7.51 (m, 1H), 7.47–7.39 (m, 2H), 4.31 (t, $J = 6.7$ Hz, 2H), 1.83–1.70 (m, 2H), 1.51–1.21 (m, 10H), 0.88 (t, $J = 6.6$ Hz, 3H); $^{13}$C-NMR (76 MHz, CDCl$_3$) $\delta$ 166.8, 132.9, 130.7, 129.7, 128.4, 65.3, 31.9, 29.4, 29.3, 28.9, 26.2, 14.2; hRMS (ESI) for C$_{15}$H$_{22}$O$_2$: calculated $m/z = 235.1698$ (MH$^+$); found $m/z = 235.1697$ (MH$^+$).

n-Octyl octanoate (2f) [78]. Synthesized according to the general procedure. Reaction conditions: octanoic acid (1 mmol, 158.5 µL), n-octanol (1 mmol, 158 µL), NBS (0.07 mmol, 12.5 mg), 70 °C, 20 h. Purification: Preparative TLC (CH$_2$Cl$_2$/MeOH = 200:1). Yield: 223 mg of colourless oil (87%); $^1$H-NMR (300 MHz, CDCl$_3$) $\delta$ 4.06 (t, $J = 6.7$ Hz, 2H), 2.28 (t, $J = 7.5$ Hz, 2H), 1.68–1.54 (m, 4H), 1.39–1.19 (m, 18H), 0.88 (t, $J = 6.3$ Hz, 6H); $^{13}$C-NMR (76 MHz, CDCl$_3$) $\delta$ 173.9, 64.4, 34.4, 31.9, 31.8, 29.3, 29.2, 29.0, 28.8, 26.0, 25.1, 22.7, 22.7, 14.1, 14.1; hRMS (ESI) for C$_{16}$H$_{32}$O$_2$: calculated $m/z = 257.2481$ (MH$^+$); found $m/z = 257.2486$ (MH$^+$).

Cyclopentyl octanoate (2g) [79]. Synthesized according to the general procedure. Reaction conditions: octanoic acid (1 mmol, 158.5 µL), cyclopentanol (1 mmol, 91 µL), NBS (0.07 mmol, 12.5 mg), 70 °C, 15 h. Purification: Not necessary. Yield: 200 mg of colourless oil (94%); $^1$H-NMR (300 MHz, CDCl$_3$) $\delta$ 5.16 (tt, $J = 5.9$, 2.6 Hz, 1H), 2.25 (t, $J = 7.5$ Hz, 2H), 1.95–1.47 (m, 10H), 1.41–1.20 (m, 8H), 0.88 (d, $J = 7.0$ Hz, 3H); $^{13}$C-NMR (76 MHz, CDCl$_3$) $\delta$ 173.8, 76.8, 34.8, 32.8, 31.8, 29.2, 29.0, 25.2, 23.8, 22.7, 14.1; hRMS (ESI) for C$_{13}$H$_{24}$O$_2$: calculated $m/z = 213.1855$ (MH$^+$); found $m/z = 213.1860$ (MH$^+$).

4. Conclusions

In conclusion, a convenient and selective metal-free method for direct dehydrative esterification of free aromatic and aliphatic acids with different alcohols has been developed, using inexpensive and easy-to-handle N-bromosuccinimide as a moisture- and air-tolerant recyclable catalyst. The synthesis has been performed under neat reaction conditions without the need for simultaneous removal of water and excess reagents. In spite of some scope limitations, the method provides good to excellent product yields and in the majority of cases, enables simple isolation procedure only by extraction. Even in the case of di- and tri-carboxy aliphatic acids, esterification has been successfully accomplished with the same amount of NBS catalyst as in the case of mono-carboxy alkyl acids. The applicability of the method has been successfully demonstrated also on steroidal carboxylic acids. The large-scale synthesis of methyl benzoate, methyl stearate and trimethyl citrate as examples of commercially significant esters has been performed with high to excellent yields (85–100%).

Supplementary Materials: The following are available online, $^1$H-NMR, $^{13}$C-NMR and $^{19}$F-NMR spectra of isolated final products.

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**Sample Availability:** Samples of the compounds are not available from the authors.

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