Nickel-Catalyzed Electrochemical Arylation of Activated Olefins

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Nickel-catalyzed electrochemical conjugate additions of substituted aryl bromides to activated olefins under recently optimized reaction conditions are reported. Good to high yields were obtained, whatever the nature of substituents in the meta- and para-positions of the benzene ring. In the ortho-substituted series, yields were good with electron-donating substituents, but low with electron-withdrawing groups. The activation of aryl chlorides and the sequential functionalization of aryl dihalides were also investigated.

Introduction

Functionalized aryl rings occur both in natural substances and in biologically active molecules of pharmaceutical or agrochemical interest. Activation of aryl halides by the preparation of organometallic reagents or by metal transition catalysis are attractive routes for introduction of aryl moieties onto a substrate through coupling or addition reactions.

In conjugate addition reactions,[1] the use either of organocuprate reagents[2] or of organometallic reagents in the presence of copper salts[3] are the classic methods for regioselective 1,4-addition. These procedures require, as a preliminary step, the preparation of air- and/or moisture-sensitive organometallic reagents (such as organolithium or organomagnesium) and the reaction usually has to be carried out at controlled temperatures to ensure both the stability of the reagent and the regioselectivity of the addition. Moreover, the yields reported in the literature are often based on the addition step, without mention of the overall yields. There are also problems when the organometallic reagent derives from a precursor bearing sensitive functional groups such as ketone, ester, or nitrile. Recent studies have shown ways to circumvent the low functional group tolerance, either through the use of activated magnesium[4] at −78 °C (Rieke magnesium) or through the preparation of functionalized organometallic compounds by halogen/metal exchange[5,6] either at low (magnesium)[6] or at very low (lithium)[6] temperatures, eventually followed by transmetallation with ZnBr₂ or CuX (X = CN, I) prior to treatment[6,7] with an electrophile. One-step chemical or electrochemical procedures, then, remain of high interest.

Homogeneous catalysis involving transition metal complexes has already been proposed as a valuable alternative, the catalyst precursor being reduced in situ either by zinc[8–10] or electrochemically.[11] We recently reported that the electrochemical arylation of activated olefins can be efficiently performed with either nickel[12] or cobalt[13] catalysts in the presence of the cheap pyridine ligand, in combination with the sacrificial anode procedure.[14] In the nickel-catalyzed electrochemical arylation[12] of activated olefins (Scheme 1), the low-valent nickel is generated in situ by cathodic reduction of NiBr₂, in an undivided cell provided with an iron rod as the sacrificial anode.

Although the mechanism of this reaction remains to be clarified, it may be pointed out that pyridine, which is used as a co-solvent, probably interacts, along with the activated olefin, with the zero-valent nickel species generated at ca. −1 V/SCE, thus preventing precipitation of the metal (Scheme 2). The reaction thus most probably proceeds through an organonickel complex, which arises through oxidative addition of aryl halide (ArX) to the nickel catalyst, followed by an insertion reaction.

The fate (Scheme 3) of the resulting organonickel complex is still unclear. Iron ions released by the oxidation of the sacrificial anode may undergo a transmetallation reac-

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tion (path A). Alternatively, the species may be protonated in situ by residual water present in the solvent to afford the final product (path B). It is worth noting that completely anhydrous solvent is not required, and that the rate and the yield of the reaction are not affected by a quantity of added water (1 equiv. vs. ArX).

Scheme 3

This straightforward and versatile electrochemical method is characterized by mild reaction conditions, high regioselectivity, and high tolerance towards sensitive functional groups on the aromatic ring. In our first report,[12] however, the yields were moderate, and not optimized, and only a few aryl halides were studied.

Here we wish to report on the scope of the reaction. This includes a study devoted to the influence of the nature and the position of the substituents on the aromatic rings. The activation of aryl chlorides has also been examined, as has the extension of the procedure to the asymmetrical alkylation of aryl dihalides.

Results and Discussion


The study was carried out with aryl bromides, with methyl vinyl ketone (MVK) as Michael acceptor. All the reactions were performed according to the general method previously described for the arylation of activated olefins. They were conducted in an undivided cell[14] provided with an iron rod as the anode, and a nickel grid as the cathode, under argon, in commercial solvents used without further purification. The ionic conductivity was ensured by Bu4NBr and Bu4NI added to the reaction mixture. An improvement on the previously reported procedure[12] for nickel-catalyzed alkenylation[15] of activated olefins was found in the form of a short pre-electrolysis at room temperature, involving the oxidation of the iron anode along with the reduction of 1,2-dibromoethane in N,N-dimethylformamide (DMF)/pyridine, prior to the electrolysis of the mixture of the reagents and the catalyst precursor. Afterward, the electrolysis of the solution containing the aryl bromide, MVK, and the catalyst precursor was run at 70 °C under a constant current intensity of 0.1 A, until full consumption of the aryl halide. The cathode potential throughout the electrolysis was between −0.9 and −1 V versus SCE. Results are reported in Table 1. High chemical yields were obtained from reagents with either electron-donating or electron-withdrawing substituents in the meta- or para-positions in the benzene ring after consumption of ca. 2.2 F per mol of aryl halide.

Activation of ortho-substituted derivatives was usually more critical. In this procedure, activation of ortho-substituted aryl bromides and their use in the conjugate addition reaction was feasible to some extent. Indeed, yields were good for substrates with electron-donating substituents (Table 1, Entries 1, 2), but very low with electron-withdrawing substituents (Table 1, Entries 3–6). This has already been observed in some catalyzed coupling reactions, and remains unexplained.[16] In addition, different behavior was observed in the latter series. o-Bromobenzonitrile was largely recovered after passage of a charge of 5.3 F per mol of ArX (Entry 3). This means that one step in the catalytic cycle was too slow, and a electrochemical side-reaction, such as the reduction of metallic salts released by oxidation of the iron rod, had occurred. On the other hand, with CO2Et, COCH3, or CF3 as the ring substituent, ArX was consumed (Entries 4–6) after passage of a charge of 4.3 F per mol of ArX. The main side reaction was the reduction of ArBr into ArH. With 2-bromoacetophenone (Scheme 4), 2-acetyl-3-methylindene (14)[17] was formed (26%, isolated yield) along with 15% of the desired product 12a (Table 1, Entry 5) and acetophenone. With ethyl 2-bromobenzoate

![Table 1. Comparative study of the influence of the nature and of the position of the substituent on the aryl bromide](image_url)

<table>
<thead>
<tr>
<th>Entry</th>
<th>R</th>
<th>Isolated yields (%)</th>
<th>ortho</th>
<th>meta</th>
<th>para</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>CH3</td>
<td>8a</td>
<td>62%</td>
<td>87</td>
<td>8c</td>
</tr>
<tr>
<td>2</td>
<td>OCH3</td>
<td>9a</td>
<td>67%</td>
<td>85</td>
<td>9e</td>
</tr>
<tr>
<td>3</td>
<td>CN</td>
<td>10a</td>
<td>&lt;10</td>
<td>79</td>
<td>10c</td>
</tr>
<tr>
<td>4</td>
<td>CO2Et</td>
<td>11a</td>
<td>&lt;5</td>
<td>89</td>
<td>11e</td>
</tr>
<tr>
<td>5</td>
<td>COCH3</td>
<td>12a</td>
<td>15</td>
<td>87</td>
<td>12c</td>
</tr>
<tr>
<td>6</td>
<td>CF3</td>
<td>13a</td>
<td>24</td>
<td>71</td>
<td>13e</td>
</tr>
</tbody>
</table>

[a] 50% of starting material recovered after a passage of 5.3 F per mol of ArX.
(Scheme 5), we obtained mainly the dehalogenated compound 15 along with traces of the cyclic diketone 16 (7% GC yield).

The nickel-catalyzed electrochemical procedure described here thus enables substituted aryl bromides to be activated and used synthetically without any need to protect sensitive functional groups. Even hydroxy groups are tolerated without any protection. Hence, the reaction between 3-bromo-phenol and MVK yielded 4-(3-hydroxyphenyl)propan-2-one in 75% yield.

In the runs above, the amount of NiBr$_2$·3H$_2$O was set to 10 mol% vs. ArBr without optimization. Regarding the optimum amount of NiBr$_2$·3H$_2$O required, it is first important to point out that the cathodic reaction is the reduction of Ni$^{II}$ and Ni$I$ into Ni$^{0}$, which enters the catalytic cycle through the oxidative addition with ArX. This means that the overall reaction rate is current-dependent as long as the concentration of the precursors of Ni$^{0}$ is high enough, for a given current density. This is actually ensured with at least 5% of NiBr$_2$ vs. ArBr for the reaction between 4-bromoacetophenone and MVK when conducted at $I = 0.1$ A. Thus, chemical and Faradaic yields were 90% (isolated) and ca. 80%, respectively, with 5% of nickel salt. At below 2.5% of NiBr$_2$ and still at 0.1 A, a reasonable 83% chemical yield could still be reached but after over-electrolysis corresponding to a 66% Faradaic yield.

The above reaction conditions are also suitable for efficiently performing the arylation of other activated olefins, such as ethyl acrylate (Table 2, Entries 3–5) or acrylonitrile (Table 2, Entry 6). However, alkyl substituents on the double bond of the activated olefin tended to slow down the rate of the reaction to a rather large extent, and low yields of ca. 25% were obtained with methyl crotonate, methyl methacrylate, and also with cyclohexenone. A second carboxy group on the carbon–carbon double bond was favorable, as observed with dimethyl maleate (Table 2, Entry 7). Another solvent combination, DMF/acetonitrile (AN) (1:1) already used in the previously studied alkenylation and also mediated by nickel catalysis, could be applied to the arylation reaction. The reported comparative results (Table 2) showed that DMF/AN was a good alternative to DMF/pyridine, and even more favorable for the reaction between 4-bromoacetoephene and acrylonitrile (Table 2, Entry 6).

2. Nickel-Catalyzed Conjugate Addition Reaction of Aryl Chlorides to Methyl Vinyl Ketone

Because of their low cost compared to aryl bromides, aryl chlorides are of considerable interest, and recent papers refer to their use in palladium- or nickel-catalyzed coupling reactions.$^{[23,24–27]}$ Aryl chlorides were found to be poorly reactive under the optimized reaction conditions described above. Attempts to activate them were thus carried out by a study of the reaction between methyl 4-chlorobenzoate and MVK. The results are reported in Table 3. We first found that raising the reaction temperature to 100 °C (Table 3, Entry 4) favored the oxidative addition of aryl chlorides to Ni$^{0}$, and thus promoted the catalytic cycle, whereas most of the starting material was recovered at 70 °C (Table 3, Entries 1–2). A solvent effect was also observed. Indeed, the reaction was fully completed only in DMF/pyridine (Table 3, Entries 5 and 7). We also found that the Bu$_4$NBr/Bu$_4$NI as supporting electrolyte can be advantageously replaced by the cheaper salt NaBr (Table 3,

![Scheme 5](image-url)

Table 2. Nickel-catalyzed electrochemical arylation of activated olefins under optimized reaction conditions

<table>
<thead>
<tr>
<th>Entry</th>
<th>Aryl bromide</th>
<th>Activated olefins</th>
<th>Product</th>
<th>Isolated yields$^{[a]}$ (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td></td>
<td></td>
<td></td>
<td></td>
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<tr>
<td>2</td>
<td></td>
<td></td>
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<td>3</td>
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<td>4</td>
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<tr>
<td>6</td>
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<td></td>
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<tr>
<td>7</td>
<td></td>
<td></td>
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<td></td>
</tr>
</tbody>
</table>

$^{[a]}$ Reactions were conducted with aryl bromide (7.5 mmol), activated olefin (2.5 equiv.), and NiBr$_2$·3H$_2$O (0.1 equiv.) in DMF/pyridine (9:1) at 70 °C at constant current density (0.3 A/dm$^2$).$^{[8]}$ DMF/pyridine (9:1) replaced by DMF/AN (1:1).

Table 3. Influence of temperature and solvents in nickel(0)-catalyzed conjugate addition of methyl 4-chlorobenzoate to MVK

<table>
<thead>
<tr>
<th>Entry</th>
<th>Temperature</th>
<th>Solvent$^{[a]}$</th>
<th>Supporting electrolyte</th>
<th>Isolated yields %</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>70°C</td>
<td>DMF/pyridine</td>
<td>NaBu$_4$Br/NaBu$_4$NI</td>
<td>&lt; 20</td>
</tr>
<tr>
<td>2</td>
<td>70°C</td>
<td>DMF/AN</td>
<td>NaBu$_4$Br/NaBu$_4$NI</td>
<td>&lt; 20</td>
</tr>
<tr>
<td>3</td>
<td>70°C</td>
<td>DMF/pyridine</td>
<td>NaBr</td>
<td>20</td>
</tr>
<tr>
<td>4</td>
<td>100°C</td>
<td>DMF/pyridine</td>
<td>NaBr</td>
<td>60</td>
</tr>
<tr>
<td>5</td>
<td>100°C</td>
<td>DMF/pyridine</td>
<td>NaBr</td>
<td>70</td>
</tr>
<tr>
<td>6</td>
<td>100°C</td>
<td>DMF/pyridine</td>
<td>LiBr</td>
<td>67</td>
</tr>
<tr>
<td>7</td>
<td>100°C</td>
<td>DMF/AN</td>
<td>NaBr</td>
<td>&lt; 15</td>
</tr>
</tbody>
</table>

$^{[a]}$ DMF/pyridine (9:1) and DMF/AN (1:1) were used.
Table 4. Scope of aryl chlorides in the conjugate addition reaction to methyl vinyl ketone

Unlike in the aryl bromide series, a striking influence of the substituent on the aromatic ring was observed. Whereas yields were good with the electron-poor aryl chlorides (Table 4, Entries 3–6) and the courses of the reaction were similar to those observed for aryl bromides, medium yields were obtained and significant amounts of the unreactive aryl chloride were recovered (36% of chloroanisole, 44% of chlorotoluene) with electron-rich aryl chlorides (Table 4, Entries 1, 2).

3. Extension of the Procedure to the Dialkylation Reaction

This study was extended to dibromobenzene, with the goal of achieving sequential additions. Results are reported in Table 5. The feasibility of dialkylation of dibromobenzene was first carried out with MVK as sole substrate. 1,3-Dibromobenzene and 1,4-dibromobenzene (Table 5, Entries 1, 2) showed approximately the same reactivity, and satisfying yields of the expected dialkylated product were obtained. 1,2-Dibromobenzene gave 4-(2-bromophenyl)butan-2-one (35% isolated yield) as the main product when treated under the same reaction conditions as for 1,3- and 1,4-dibromobenzene. Most of the 1,2-dibromobenzene was consumed and only traces of 2-(3-oxobutylphenyl)butan-2-one were detected by GC.

For unsymmetrical dialkylation of dibromobenzene, the second olefin used was ethyl acrylate, which is also a good Michael acceptor in the arylation process (Table 2, Entries 3–5). The reaction was conducted in one-pot fashion, and the two olefins were added sequentially to limit the amount of symmetrical dialkylated products, the second one being introduced into the cell after most of the dibromobenzene had been converted into its monobromo derivative and while the amount of symmetrical dialkylated compound was less than 10% (GC analysis). Obtained yields of the desired product were moderate, due to the inevitable formation of the two symmetrically dialkylated compounds. The yield of the reaction was not influenced by the order of introduction (Table 5, Entries 3, 4) of the two olefins. In order to limit the amount of symmetrical dialkylated com-

Table 5. Polyfunctionalization of aryl dihalides by sequential conjugate addition

Entries 4 and 5), which is worth considering in an industrial process. Table 4 reports the results obtained with various aryl chlorides.

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pounds, the second olefin was introduced in excess with respect to the first one (Table 5, Entries 4, 5). Thus, sequential treatment of 1,3-dibromobenzene with ethyl acrylate and MVK afforded the disymmetrical dialkylated compound 30 as the main product (Table 5, Entry 5), along with the two symmetrical dioxo and diester compounds (in 12 and 6% isolated yield, respectively). For comparative purposes, the preparation of ethyl 3-[3-(3-oxobutyl)phenyl]propanoate (30) in two steps afforded a 57% isolated yield of ethyl 3-(3-bromomethyl)propanoate in the first step and, after subsequent treatment with MVK, 80% of 30 in an overall 45% yield.

We also tried to achieve better control in the selectivity of the sequential addition by performing the reaction with 1-bromo-4-chlorobenzene (31) (Scheme 6). The bromide substituent was replaced selectively on treatment with ethyl acrylate at 60 °C in DMF/pyridine media, and ethyl 3-(4-chlorophenyl)propanoate (32) was isolated in 74% yield. Attempts to induce it to react further with MVK under the reaction conditions described above for the activation of aryl chlorides, however, were unsuccessful.

![Scheme 6](image)

Recently, we described another procedure for electro-reductive coupling of aryl halides with activated olefins with [bis(2-pyridyl)amine]nickel complexes. These complexes enable bromides to be activated at room temperature in ethanol, a safe and inexpensive solvent. When the reaction between ethyl 3-(4-chlorophenyl)propanoate (32) and MVK was conducted under these conditions, however, either at room temperature or at 60 °C, only a small amount of desired product 33 was obtained (20% GC yield). When the electrolysis was conducted until full consumption of the starting reagents, mostly the dehalogenated compound was formed.

Conclusions

Activation of functionalized aryl halides by nickel catalysis under mild reaction conditions thus results in the formation of functionalized aryl nickel intermediates, which add regioselectively to activated olefins. Under the optimized reaction conditions, neither homocoupling of the aryl halide, nor the Heck reaction are observed. The main side-product is the dehalogenated (reduced) aryl compound. No protection of sensitive functional groups is required. Furthermore, the significant results obtained (Table 1) with the aryl bromide series demonstrate that the reaction is not confined to aryl bromides possessing electron-withdrawing groups, but is also quite efficient with electron-rich reagents. Aryl chlorides can also be activated at a higher temperature, but their use is restricted to the electron-poor aryl chlorides. Most importantly, this conjugate addition reaction is a one-step procedure that can be used advantageously for the preparation of biologically active substances from commercially available starting materials. Thus, 4-(4-methoxyphenyl)butan-2-one (9c) is the insect attractant for the scarabaeid subfamily Rutelinae, while 4-(2-methoxyphenyl)butan-2-one (9a) is a key intermediate en route to the bronchospasmytotically active [(arylalkyl)amino]hydroxyphenylethanols. Arylsuccinates are intermediates for the preparation of building blocks involved in the synthesis of anti-inflammatory agents, and 4-(6-methoxy-2-naphthyl)butan-2-one (18) (Nabumeton) is a nonsteroidal anti-inflammatory drug usually prepared in four steps in about 40% yield.

The arylation reactions described above were routinely performed in small undivided cells (volume 40 mL) charged with 7–15 mmol of the aryl halide and 2.5 equiv. of the activated olefin. The reaction can also be carried out quite efficiently in an electrochemical flow cell. In a typical run, the reaction between 4-bromoanisole (170 mmol) and butyl acrylate (420 mmol) in DMF/picoline (9:1) at 80 °C yielded 28 g (70% yield) of the addition product in a 90% Faradaic yield. A detailed study of the various parameters related to further scaling-up is underway in collaboration with Électricité de France.

Experimental Section

All solvents and reagents were purchased from commercial sources and used as received. DMF and AN were stored under argon. GC analysis was carried out on a 25-m DB-1 capillary column. Column chromatography was performed on silica gel, 70–230 mesh. H1, 13C, and 19F NMR spectra were recorded with a Bruker AC 200 MHz spectrometer. Mass spectra were obtained with a GCQ Thermoquest spectrometer coupled to a chromatograph fitted with a 25-m CPSIL5 CB capillary column. Elemental analyses were carried out by the Service Central de Microanalyses (CNRS, Lyon). The electrochemical cell has been described previously. IR spectra were measured with a Perkin Elmer 283B spectrophotometer; neat for liquid compounds and in CHCl3 for solid compounds.

General Procedure for the Arylation of Electron-Deficient Olefins: Under argon, in an undivided cell equipped with a nickel grid (area 30 cm²) as the cathode and an iron rod as the anode, tetraethylammonium bromide (0.34 mmol) and tetrabutylammonium iodide (0.21 mmol) or NaBr (1.50 mmol) as supporting electrolytes were dissolved in a mixture of DMF (27 mL) and pyridine (3 mL). A short electrolysis was conducted in the presence of 1,2-dibromoethane (0.90 mmol) at constant current density (0.3 A dm⁻²) and at room temperature over 30 min to generate a small amount of iron ions. The current was then turned off. NiBr2·3H2O (0.75 mmol, 164 mg) and the activated olefin (18.75 mmol) was added, and the mixture was heated at 70 °C (when aryl bromide was used) or 100 °C (when aryl chloride was used) after the addition of the aryl halide (7.5 mmol). The electrosynthesis was run at constant current density (0.3 A dm⁻²). The reaction was monitored by GC and stopped after the aryl bromide was consumed. An average charge
of 2.5 F mol⁻¹ was used in most reactions described in Tables 1–4. The mixture was then hydrolyzed with hydrochloric acid (1 M, 30 mL) and diluted with diethyl ether (50 mL). The aqueous layer was extracted with diethyl ether (2 × 50 mL) and the combined organic layers were washed with water and saturated NaCl solution, then dried with MgSO₄. The oil thus obtained was purified by column chromatography to give desired compound.

**General Procedure for the Sequential Addition Reaction from Aryl Dihalides:** Under argon, in an undivided cell equipped with a nickel grid (area 30 cm²) as the cathode and an iron rod as the anode, tetraethylammonium bromide (0.34 mmol) and tetraethylammonium iodide (0.21 mmol) as supporting electrolytes were dissolved in a mixture of DMF (27 mL) and pyridine (3 mL). 1,2-Dibromoethane (0.90 mmol) was introduced. After a short electrolysis run at constant current density (0.3 A dm⁻²) and at room temperature for 30 min, the current was turned off and NiBr₂·3H₂O (0.37 mmol, 149 mg) and the first activated olefin (1.5 to 2.5 equiv.) were added. The mixture was then hydrolyzed with hydrochloric acid (1 M) at constant current density (0.3 A dm⁻²) and at room temperature for 1 h. The organic layers were washed with water and saturated NaCl solution, and the solvent was evaporated. The crude product thus obtained was purified by column chromatography.

**4-(3-Methylphenyl)butan-2-one (12b):** 1H NMR (200 MHz, CDCl₃): δ = 2.07 (s, 3 H, CH₃), 2.50 (s, 3 H, CH₃), 2.67 (t, J = 7.00 Hz, 2 H, CH₂), 7.21 (d, J = 7.18 Hz, 2 H, 7.81 (d, J = 7.18 Hz, 2 H, 1H NMR (200 MHz, CDCl₃): δ = 26.2, 29.3, 29.4, 44.1, 128.3 (2C), 83.0, 197, 206.8. MS; m/z (%): 191 (100), 190, 175, 147, 77. IR: ν = 3020, 1730, 1650, 1590, 1490, 1400, 800 cm⁻¹.

**4-(4-Acetophenyl)butan-2-one (12c):** 1H NMR (200 MHz, CDCl₃): δ = 2.06 (s, 3 H, CH₃), 2.50 (s, 3 H, CH₃), 2.67 (t, J = 7.00 Hz, 2 H, CH₂), 7.21 (d, J = 7.18 Hz, 2 H, 7.81 (d, J = 7.18 Hz, 2 H, 1H NMR (200 MHz, CDCl₃): δ = 26.2, 29.3, 29.4, 44.1, 128.3 (2C), 127.4, 146.7, 197.3, 206.8. MS; m/z (%): 191 (100), 190, 175, 147. IR: ν = 3080, 1730, 1690, 1610 cm⁻¹. C,H₄0F: calcd. C 75.76, H 7.42; found C 75.98, H 7.46.

**4-(3-Trifluoromethylphenyl)butan-2-one (13a):** 1H NMR (200 MHz, CDCl₃): δ = 2.04 (s, 3 H, CH₃), 2.64 (t, J = 7.00 Hz, 2 H, CH₂), 2.96 (t, J = 7.70 Hz, 2 H, CH₂), 7.14–7.52 (m, 5 H). 19F NMR (CDCl₃): δ = −59.60. MS; m/z (%): 216, 197, 196, 195 (100). IR: ν = 3020, 1730, 1610, 1590, 1450, 770 cm⁻¹. C₉H₇F₀: calcd. C 75.10, H 5.12; found C 75.06, H 5.23; F, 25.78.

**4-(4-Trifluoromethylphenyl)butan-2-one (13c):** 1H NMR (200 MHz, CDCl₃): δ = 2.20 (s, 3 H, CH₃), 2.84 (m, 2 H, CH₂), 3.01 (m, 2 H, CH₂), 7.36 (d, J = 8.00 Hz, 2 H), 7.58 (d, J = 8.00 Hz, 2 H). 19F NMR (CDCl₃): δ = −62.24. MS; m/z (%): 197, 196, 195, 194, 133 (100). IR: ν = 3020, 1730, 1610, 1590, 1450, 770 cm⁻¹. C₉H₇F₀: calcd. C 78.64, H 5.12; found C 78.59, H 5.23; F, 25.78.

**Ethyl 3-(3-Oxobutyl)benzoate (11c):** 1H NMR (200 MHz, CDCl₃): δ = 1.31 (t, J = 7.10 Hz, 3 H, CH₃), 2.08 (s, 3 H, CH₃), 2.70 (m, 2 H, CH₂), 2.88 (s, 2 H, CH₂), 4.29 (q, J = 7.10 Hz, 2 H, CH₂), 7.18 (d, J = 8.20 Hz, 2 H, 7.88 (d, J = 8.20 Hz, 2 H). 13C NMR (50.321 MHz, CDCl₃): δ = 14.1, 1.91, 29.5, 30.0, 53.1, 109.4, 128.0, 129.0, 135.4, 137.0, 141.1, 166.8, 206.8. MS; m/z (%): 220, 205, 174 (100), 149, 131, 105. IR: ν = 3020, 1730, 1650, 1450, 750 cm⁻¹.

**Ethyl 4-(3-Oxobutyl)benzoate (11e):** 1H NMR (200 MHz, CDCl₃): δ = 1.31 (t, J = 7.10 Hz, 3 H, CH₃), 2.08 (s, 3 H, CH₃), 2.70 (m, 2 H, CH₂), 2.88 (s, 2 H, CH₂), 4.29 (q, J = 7.10 Hz, 2 H, CH₂), 7.18 (d, J = 8.20 Hz, 2 H, 7.88 (d, J = 8.20 Hz, 2 H). 13C NMR (50.321 MHz, CDCl₃): δ = 14.1, 1.91, 29.5, 30.0, 53.1, 109.4, 128.0, 129.0, 135.4, 137.0, 141.1, 166.8, 206.8. MS; m/z (%): 220, 205, 174 (100), 149, 131, 105. IR: ν = 3020, 1730, 1650, 1450, 750 cm⁻¹.

**Ethyl 4-(3-Oxobutyl)propanoate (29):** 1H NMR (200 MHz, CDCl₃): δ = 1.15 (t, J = 7.13 Hz, 3 H, CH₃), 2.05 (s, 3 H, CH₃), 2.51 (t, J = 7.73 Hz, 2 H, CH₂), 2.61–2.87 (m, 6 H, 3 × CH₂), 4.04 (q, J = 7.13 Hz, 2 H, 2H), 7.03 (s, 4 H). 13C NMR (50.321 MHz, CDCl₃): δ = 207.4, 172.5, 138.6, 138.0, 128.4 (4 C).
Ethyl 3-(3-Oxobutyl)phenylpropanoate (30): 1H NMR (200 MHz, CDCl3): δ = 1.09 (t, J = 7.15 Hz, 3 H, CH3), 2.52 (t, J = 7.61 Hz, 2 H, CH2), 4.04 (q, J = 7.15 Hz, 2 H, CH2), 7.03–7.20 (m, 4 H). 13C NMR (50.321 MHz, CDCl3): δ = 13.9, 29.9, 35.4, 60.1, 128.2, 129.4, 131.7, 138.8, 172.2. MS; m/z (%): 249, 230, 203, 184, 174, 155 (100). IR: ν = 1740, 1720, 800 cm⁻¹. C11H13ClO2: calcd. C 62.12, H 6.16, Cl 16.67; found C 62.06, H 6.14, Cl 16.71.

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