

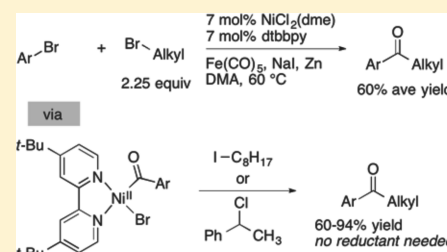
Stoichiometric Reactions of Acylnickel(II) Complexes with Electrophiles and the Catalytic Synthesis of Ketones

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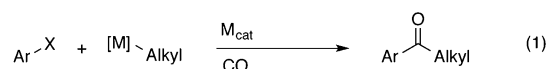
Supporting Information

ABSTRACT: Acylnickel(II) complexes feature prominently in cross-electrophile coupling (XEC) reactions that form ketones, yet their reactivity has not been systematically investigated. We present here our studies on the reactivity of acylnickel(II) complexes with a series of carbon electrophiles. Bromobenzene, α -chloroethylbenzene, bromooctane, and iodoctane were reacted with (dtbbpy)-Ni^{II}(C(O)C₅H₁₁)(Br) (**1b**) and (dtbbpy)Ni^{II}(C(O)tolyl)(Br) (**1c**) to form a variety of organic products. While reactions with bromobenzene formed complex mixtures of ketones, reactions with α -chloroethylbenzene were highly selective for the cross-ketone product. Reactions with iodoctane and bromooctane also produced the cross-ketone product, but in intermediate yield and selectivity. In most cases the presence or absence of a chemical reductant (zinc) had only a small effect on the selectivity of the reaction. The coupling of **1c** with iodoctane (60% yield) was translated into a catalytic reaction, the carbonylative coupling of bromoarenes with primary bromoalkanes (six examples, 60% average yield).



INTRODUCTION

The ketone is ubiquitous in organic synthesis because it is a synthetically useful functional group and a common motif in biologically active molecules. Among the many synthetic methods known, carbonylative cross-coupling of a carbon nucleophile with a carbon electrophile is attractive because it is convergent (eq 1).¹ A common challenge for all of these



carbonylative cross-coupling reactions is the availability and stability of the carbon nucleophile component, which has led to the development of alternative methods, such as C–H activation,^{1b} and milder organometallic reagents.²

An alternative strategy to avoid the challenges of nucleophilic carbon reagents is the coupling of two different carbon electrophiles (Figure 1). Cross-electrophile coupling (XEC) has been much less studied than the cross-coupling of electrophiles with nucleophiles, but recent reports have demonstrated the generality of this approach^{3–6} and have shed light on the origins of selectivity.⁷ Two different nickel-catalyzed XEC approaches to ketones have been developed: the coupling of acid chlorides with alkyl and benzyl halides⁴ and the carbonylative coupling of aryl halides with alkyl halides.⁶ The carbonylative coupling approach has only been demonstrated with electrochemical reduction (Ni/Fe sacrificial anode), and high yields were only obtained with aryl iodides and benzyl bromides.^{6f}

A common feature of many^{4d–f,6} of these approaches (A and B, Figure 1) is the intermediacy of an acylnickel(II) intermediate (**1**) that is proposed to react with a carbon

electrophile (R²X) to form the ketone product (R¹C(O)R²). Studies of the generation of acylnickel(II) intermediates from nickel(0) have clearly delineated its formation, but no such systematic studies on the reactivity of **1** with carbon electrophiles have been reported.

Despite our recent success in developing and understanding the mechanism of nickel-catalyzed cross-electrophile coupling of aryl halides with alkyl halides, we foresaw several challenges for the carbonylative reaction. First, the coupling of two electrophiles with a third component (CO) results in a large number of potential products in comparison to two-component couplings.⁸ Second, the reactivity of the proposed acylnickel intermediates is relatively unknown, limiting our ability to troubleshoot reactions.

We report here our progress toward understanding the reactivity of acylnickel(II) complexes toward aryl, alkyl, and benzylic electrophiles and a cross-selective carbonylative coupling of unactivated primary alkyl bromides with aryl halides to form aryl alkyl ketones.

BACKGROUND

Stoichiometric reactions with Ni(CO)₄ with electrophiles to form ketones are well-known to proceed via intermediate acylnickel(II) complexes (eq 2),⁹ but these reactions are not often used today due to toxicity concerns¹⁰ and limited availability.^{11,12} Catalytic versions of these stoichiometric reactions have proven to be difficult to develop.

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RESULTS AND DISCUSSION

Stoichiometric Studies. In order to study the key proposed bond-forming step, we synthesized the dark red (dtbbpy)Ni^{II}(C(O)C₅H₁₁)Br (**1b**) from the reaction of deep purple (dtbbpy)Ni⁰(cod)^{3g} (**3**) with hexanoyl bromide in THF, in analogy to several literature reports (Table 1).¹⁶ The

Table 1. Synthesis of (dtbbpy)Ni^{II}(COR¹)Br and Selected Characterization Data^a

entry ^b	[Ni]	yield (%) ^c	IR (cm ⁻¹) ^d	NMR (ppm) ^e	UV-vis (cm ⁻¹) (10 ³ M ⁻¹ cm ⁻¹) ^f
1	1b	74	1612	3.12 (t)	20325 (5)
2	1c	89	1617	N/A	20576 (7)

^adtbbpy = 4,4'-di-*tert*-butyl-2,2'-bipyridine. ^bSee the Supporting Information for full characterization data and procedures. ^c¹H NMR yield vs liberated cyclooctadiene; average of two runs. ^dC=O stretches reported that are characteristic of M-C(O)R complexes.^{15e} ^e¹H NMR chemical shift and multiplicity for α proton of M-C(O)CH₂R.^{15c} N/A = not applicable. ^fUV-vis absorbances reported as wavenumbers (ϵ values are given in parentheses).

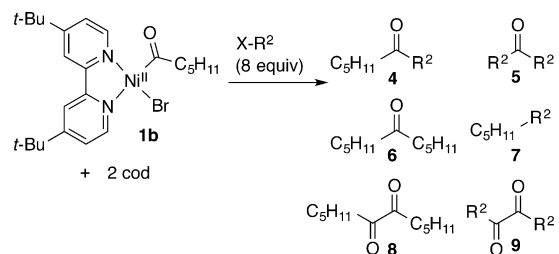
resulting acylnickel(II) intermediate proved difficult to isolate; therefore, it was characterized in solution by ¹H NMR, IR, and UV-vis. The yield was determined to be 74% by NMR (average of two runs).

The results compared well to those of Yamamoto.^{15c} Distinctive features were as follows: (1) the Ni-C(O)-CH₂CH₂CH₂CH₃ triplet (3.12 ppm) agrees well with the 3.19 ppm triplet reported for (bpy)Ni^{II}(C(O)Et)(Cl); (2) the IR spectrum revealed a CO stretch at 1612 cm⁻¹, in good agreement with (bpy)Ni^{II}(C(O)Et)(Cl) at 1655 cm⁻¹ and consistent with other acylnickel complexes (1600–1640 cm⁻¹);^{15b,d,e} (3) the UV-vis spectrum showed a strong MLCT at 20325 cm⁻¹, in good agreement with Yamamoto's report for (bpy)Ni^{II}(C(O)Et)(Cl) (19880 cm⁻¹).^{15c}

A similar reaction with 4-methylbenzoyl bromide afforded (dtbbpy)Ni^{II}(C(O)tolyl)Br (**1c**). This complex was similarly characterized in solution by ¹H NMR, IR, and UV-vis. ¹H NMR analysis clearly showed the formation of a single, new diamagnetic complex in 89% yield. The IR stretch was in good agreement with that reported for (dppe)Ni^{II}(C(O)Ph)Cl: 1617 vs 1630 cm⁻¹.^{16b}

Reactions of hexanoylnickel **1b** with four different organic halides (bromobenzene, α -chloroethylbenzene, bromooctane, and iodoctane) were performed, and the results are summarized in Table 2.¹⁷ Because **1b** decomposes over about 2 h in solution, we generated it fresh for each experiment in THF-*d*₈ and then diluted it with DMA to a 1/1 mixture for reactions with electrophiles. Finally, because it has been proposed that intermediate reduction of an acylnickel complex

Table 2. Reaction of (dtbbpy)Ni^{II}(COC₅H₁₁)Br with RX^a



entry	R ² -X	T (°C), t	products (% yield) ^b
1	PhBr	60 °C, 14 h	4 (12), 8 (11), 9 (11), 5 (8)
2	w/Zn	60 °C, 14 h	4 (22), 5 (13)
3	Ph-CH ₂ -Cl	21 °C, 5 min	4 (54)
4	w/Zn	21 °C, 5 min	4 (44)
5	H ₁₇ C ₈ Br	60 °C, 14 h	4 (17), 5 (12)
6	w/Zn	60 °C, 14 h	4 (31), 5 (20)
7	H ₁₇ C ₈ I	60 °C, 12 h	4 (33), 5 (18)

^aReactions run in a 1/1 THF-*d*₈/DMA mixture using freshly prepared **1b**. See the Supporting Information for full experimental details and tables with all products formed. ^bYields are uncorrected GC yields of products formed in >7% yield.

is needed before it can react with organic halides, we also ran reactions with an added reductant, zinc flake.

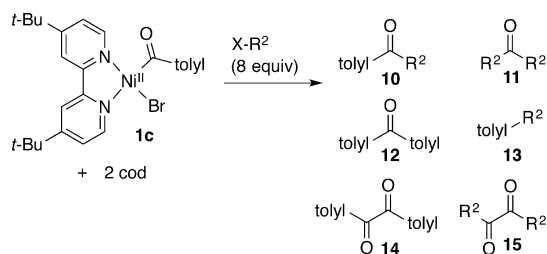
The reaction of **1b** with bromobenzene produced similar amounts of cross-ketone (**4**) and symmetric ketone or diketone products (**8** and **9**; Table 2, entry 1). The addition of zinc flake eliminated the symmetric diketone products (**8** and **9**), but the reaction remains only marginally selective (entry 2).

Hexanoyl complex **1b** reacts with α -chloroethylbenzene rapidly (under 5 min at room temperature) to exclusively form cross-ketone product **4** (Table 2, entry 3) in a yield that compares well with those reported for the XEC of acid chlorides with α -chloroethylbenzene (49–52% for similar conditions).^{4c,f} The addition of zinc flake did not improve the reaction yield or selectivity (entry 4), suggesting that reduction of **1b** is not required.

Finally, the reaction of **1b** with bromooctane or iodoctane produced nearly equal amounts of cross-ketone product **4** and dioctyl ketone **5** (Table 2, entries 5–7). The addition of zinc flake improved the yield of ketone products (entry 6) but did not improve the selectivity for cross-ketone over symmetric ketone significantly (1.4/1 to 1.6/1). XEC of acid chlorides with alkyl halides is reported to be sensitive to the reductant and solvent, perhaps explaining the difference between these modest yields and those reported by Gong^{4d} and ourselves.^{4c}

The reactivity of acylnickel **1c** was examined in the same manner as for **1b**, and the results are shown in Table 3. Complex **1c** was more stable than **1b**, but we again prepared it fresh for each experiment.

Reaction of **1c** with bromobenzene again produced a mixture of ketone products (Table 3, entry 1). The addition of zinc as a reductant improved the total yield of all coupled products from **1c** (nearly quantitative from 70%) but also resulted in the formation of significant amounts of noncarbonylated cross-aryl product **7** (entry 2).

Table 3. Reaction of (dtbbpy)Ni^{II}(COC₆H₄CH₃)Br with RX^a

entry	R ² -X	t	products (% yield) ^b
1	PhBr	12 h	10 (25), 12 (23), 11 (21), 14 (8)
2	w/Zn	12 h	13 (35), 10 (25), 12 (30), 11 (26)
3		7.5 h	10 (94) ^c
4	w/Zn	≤12 h	10 (87)
5	H ₁₇ C ₈ I	1 h	10 (60), 11 (8)
6	w/Zn	5 min	10 (58), 11 (58)

^aReactions were run in a 1/1 mixture of THF-*d*₈/DMA using freshly prepared **1c**. See the Supporting Information for full experimental details and tables with all products formed. ^bYields are uncorrected GC yields of products formed in >7% yield. ^c76% ¹H NMR yield after workup and filtration through silica gel.

The reaction of aroynickel **1c** with α -chloroethylbenzene was again rapid and clean, affording a 94% GC yield of the cross-ketone product **10** (Table 3, entry 3). In this case, we filtered the product mixture and obtained a 76% NMR yield of the cross-ketone product. There are no reports of a catalytic version of this reaction, but Gong reported that benzyl bromide and methallyl chloride couple with benzoyl chloride in high yield (70 and 76%).^{4d} This result suggests that, as long as the aroyl activated ester reacts with nickel(0) first, such a cross-coupling will be high-yielding. Again, the addition of a reductant (zinc flake) did not improve the yield or selectivity (entry 4).

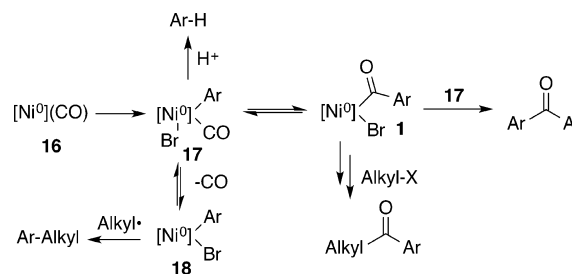
The reaction of iodoctane with aroynickel **1c** formed cross-ketone in 60% yield along with some dioctyl ketone **11** (Table 3, entry 5). If zinc flake was added, the amount of dioctyl ketone increased significantly (entry 6), suggesting decarbonylation of **1c**, loss of the tolyl group, and coupling with iodoctane. Dioctyl ketone is not a major side product in the carbonylative coupling of aryl bromides with alkyl bromides, but the isolated yields of cross-ketone **10** are similar between the two methods (vide infra; Table 4, entry 17). Here, the addition of zinc increased the rate of the reaction (entry 6) but not the selectivity.

A comparison of the reaction of hexaoylnickel **1b** with bromobenzene (Table 2, entries 1 and 2) and the reaction of aroynickel **1c** with iodoctane (Table 3, entries 5 and 6) strongly suggests that the carbonylative coupling of aryl halides with alkyl halides will work best if the aryl halide reacts first with the nickel catalyst. Our recent work on the reactivity of (dtbbpy)Ni⁰(cod) demonstrated that aryl halides do react more quickly than alkyl halides under similar conditions.^{7b}

Catalytic Studies. We started our catalytic studies by adding carbon monoxide sources to our published conditions for the coupling of aryl bromides with alkyl bromides.^{3d} Initial results with 20 mol % of Fe(CO)₅ were modest (26% yield).

Examination of several metal carbonyls (Mn₂CO₁₀, W(CO)₆, Mo(CO)₆, Cr(CO)₆) showed that iron carbonyl was best and that the reaction could be run in DMA instead of DMPU, but no significant improvements in yield were forthcoming.

The major reaction products were our desired aryl alkyl ketone, hydrodehalogenated aryl bromide, diaryl ketone, and noncarbonylated product. We envisioned that both the diaryl ketone and the aryl alkyl ketone product could arise from the aroyl nickel (**1**) formed by CO insertion into the aryl–nickel bond of **17** (Scheme 3). Aroylnickel(II) complexes are well-

Scheme 3. Proposed Source of Aryl Side Products

known to decompose into diaryl ketones by disproportionation upon heating.^{15,16} The noncarbonylated product presumably arose when not enough CO was available in solution, allowing for the formation of **18**.^{7b}

Consistent with these hypotheses, the addition of more alkyl bromide (2.25 equiv from 1 equiv) resulted in less diaryl ketone, although little effect was observed above 2.25 equiv (Table 4, entries 1–4). Increasing the amount of iron carbonyl eliminated noncarbonylated products, but too much iron carbonyl diminished yields (Table 4, entry 3 vs entries 5–7).

The addition of iodide was essential for reactivity. A reaction with no NaI gave no ketone product (Table 4, entry 8), but substitution of NaI with LiI and KI provided results similar to those for NaI (Table 4, entry 3 vs entries 9 and 10). Lowering the catalyst loading from 7 to 5 mol % resulted in a 14% lower yield (entry 11). A reaction run without added reductant produced a small amount of **22**. In this case, the Fe(CO)₅ likely served as the reductant (entry 15). Finally, 6/1 and 1/1 mixtures of DMA to THF formed products in 76% and 52% yields, respectively, but a 1/2 mixture did not consume most of the starting material (entries 16–18).

The highest yields were obtained when water was strictly excluded. For example, if starting materials were left on the bench for extended periods of time, the yield of product would drop (up to 20% difference in yield). Reactions also worked best when the mixtures were heated immediately after assembly. Stirring a reaction mixture at room temperature for 30 min before heating to 60 °C diminished the yield by about 10%.

In order to examine the scope of this reaction, several aryl bromides were coupled with primary alkyl bromides (Table 5). Yields were similar to those for the optimized reaction, but the coupling of an aryl bromide containing an electron-withdrawing group, –CF₃, resulted in a lower yield (Table 5, entries 1 and 5), due to competitive formation of both diaryl ketone and biaryl.¹⁸ Aryl chlorides were not reactive (entry 2), and both protected alcohols and fluorinated substrates were also well tolerated (entries 4–6). Although α -chloroethylbenzene formed high yields of ketone product from reactions with

Table 4. Optimization and Controls^a

$\text{EtO}-\text{C}(=\text{O})-\text{CH}_2-\text{CH}_2-\text{CH}_2-\text{Br}$ (19, Y equiv) + $\text{Ph}-\text{Br}$ (25) $\xrightarrow[7 \text{ mol\% dtbbpy}]{7 \text{ mol\% NiCl}_2(\text{dme})}$ $\text{EtO}-\text{C}(=\text{O})-\text{CH}_2-\text{CH}_2-\text{CH}_2-\text{C}(=\text{O})-\text{Ph}$ (22) + $\text{Ph}-\text{C}(=\text{O})-\text{Ph}$ (20) + $\text{Ph}-\text{H}$ (21)

Reagents: $\text{Fe}(\text{CO})_5$ (X equiv), NaI (0.25 equiv), Zn^0 (2 equiv), DMA, 60 °C

entry	notes	X	Y	22	20	21
1		0.35	2.50	69	5	4
2		0.35	2.25	72 (60)	6	6
3		0.35	2.0	56	7	8
4		0.35	1.5	50	9	15
5 ^b		0.40	2.0	51	7	8
6 ^c		0.45	2.0	42	3	5
7 ^c		0.50	2.0	32	3	4
8 ^d	no NaI	0.35	2.0	0	0	0
9	LiI for NaI	0.35	2.0	49	7	7
10	KI for NaI	0.35	2.0	48	4	8
11	5 mol % catalyst	0.35	2.0	42	6	9
12 ^e	no dtbbpy	0.35	2.25	0	0	2
13 ^{e,f}	no Ni or Zn	0.35	2.0	0	0	1
14 ^{e,g}	no Ni	0.35	2.0	<1	<1	0
15 ^{c,g}	no Zn	0.35	2.25	25	<1	4
16	6/1 DMA/THF	0.35	2.25	76	7	0
17	1/1 DMA/THF	0.35	2.25	52	7	3
18 ^{e,g}	1/2 DMA/THF	0.35	2.25	<1	0	1

^aReactions were run on a 0.75 mmol scale in 3 mL of DMA. Yields are uncorrected GC yields vs dodecane. The yield in parentheses is an isolated yield of purified product. ^bPhBr (8%) remained. ^cPhBr (27%–47%) remained. ^dStarting materials were unchanged after 40 h, except for a 13% yield of hydrodehalogenated **19**. ^ePhBr (75%) remained. ^fAlkyl-Br **19** not consumed. ^gDialkyl ketone (12–23%) was formed.

acylnickel complexes (Tables 2 and 3), the catalytic reactions were plagued by rapid dimerization of this reactive substrate.

CONCLUSIONS

In conclusion, our studies on acylnickel complexes have revealed differential reactivity with respect to electrophiles. Both aryl- and alkanoylnickel complexes react with secondary benzylic chlorides to form product without added reductant, but the arylnickel complex reacts with alkyl iodides to produce more cross-ketone than the alkanoylnickel complex. Neither complex reacts with bromobenzene to selectively produce cross-ketone product. The addition of an external reductant (zinc flake) did not improve the selectivity of reactions with alkyl or benzyl halides but did improve the rate in one case, suggesting that reduction of acylnickel(II) to acylnickel(I)^{4d–f} is not a necessary step in XEC ketone synthesis reactions and that zinc might facilitate a radical initiation step.⁷ Gong reported a reductant effect more dramatic than the effect we observed, but under significantly different conditions. Finally, the observed reactivity of **1c** with alkyl halides can be translated into the first carbonylative cross-coupling of bromoarenes with bromoalkanes. Further studies on the reactivity of acylnickel complexes and translation to new reactions is ongoing.

EXPERIMENTAL SECTION

Materials and Methods. $\text{NiCl}_2(1,2\text{-dimethoxyethane})$ ($\text{NiCl}_2(\text{dme})$) was purchased from Strem or synthesized according to the literature procedure.¹⁹ $\text{Ni}(\text{cod})_2$ was purchased from Strem. 4,4'-Di-*tert*-butyl-2,2'-bipyridine (dtbbpy) was purchased from Aldrich

Table 5. Scope of Reaction with Aryl-X^a

$\text{Alkyl}-\text{Br}$ (2.25 equiv) + $\text{Br}-\text{Ar}$ $\xrightarrow[7 \text{ mol\% dtbbpy}]{7 \text{ mol\% NiCl}_2(\text{dme})}$ $\text{Alkyl}-\text{C}(=\text{O})-\text{Ar}$ (22-27)

Reagents: $\text{Fe}(\text{CO})_5$ (0.35 equiv), NaI (0.25 equiv), Zn^0 (2 equiv), DMA, 60 °C

entry	product	yield (%) ^b
1		63
2		62
3		62
4		62
5		48
6 ^c		65

^aReactions were performed on a 0.75 mmol scale on the benchtop in 3 mL of DMA. ^bIsolated yield of purified product. ^cProduct contains an additional 3% of benzophenone.

or synthesized according to the literature procedures.^{20,21} Zinc flake (–325 mesh; Alfa) was used as received. Anhydrous *N,N*-dimethylacetamide (DMA; Aldrich) was stored over activated 4 Å molecular sieves. DMA used for stoichiometric reactions was sequentially dried over 4 Å MS, degassed, and then vacuum-transferred. The water content was routinely measured using Karl Fischer titration (Metrohm) and was less than 70 ppm. THF-*d*₈ was purchased from Cambridge Isotopes, dried sequentially over MS 4 Å, degassed, and then vacuum-transferred. Hexanoyl bromide and *p*-toluoyl bromide were synthesized using the literature procedures. 1-Iodoctane (Aldrich), 1-bromooctane (Aldrich), bromobenzene, and ethyl 4-bromobutanoate (Aldrich) were filtered through a dry, activated, basic alumina pad (1.5 cm) under nitrogen until they were colorless before use.

¹H and ¹³C NMR spectra were acquired on 500 or 400 MHz (proton) Bruker NMR instruments, and data analysis was performed using the iNMR software package (version 5.3.5, <http://www.inmr.net>). NMR chemical shifts are reported in ppm and referenced to the residual solvent peak as an internal standard (for CDCl_3 , δ 7.260 ppm (¹H), δ 77.160 ppm (¹³C); for THF-*d*₈, δ 1.720, 3.573 ppm (¹H)).

GC analyses were performed on an Agilent 7890A GC instrument equipped with dual DB-5 columns (20 m × 180 μm × 0.18 μm) and dual FID detectors and with hydrogen as the carrier gas. The analysis method used in all cases was a 1 μL injection of sample, an injection temperature of 300 °C, and a 100:1 split ratio; the initial inlet pressure was 20.3 psi but was varied as the column flow was held constant at 1.8

mL/min for the duration of the run. The initial oven temperature of 50 °C was held for 0.46 min, followed by a temperature ramp up to 300 °C at 65 °C/min; finally the temperature was held at 300 °C for 0.69 min. The total run time was ~5 min. The FID temperature was 325 °C. Dodecane (Aldrich) was used as an internal standard for GC analysis of catalytic reactions. Mesitylene (Aldrich) was used as an internal standard for GC analysis of stoichiometric reactions. GC analysis of reaction mixtures was accomplished by removal of a 25 μ L aliquot with a 100 μ L gastight syringe which was quenched with 50 μ L of 1 M aqueous NaHSO₄, diluted with ethyl ether or TBME (1 mL), and filtered through a short silica pad (2 cm) in a pipet packed with glass wool. The filtrate was analyzed by GC.

Thin-layer chromatography was performed on EMD Chemicals TLC silica gel 60 F254 plates. Visualization was accomplished with *p*-anisaldehyde stain after inspection under UV light. Flash chromatography was performed using EMD silica gel 60, particle size 0.040–0.063 mm, using standard flash techniques. Some compounds were purified using a Combiflash Rf 200 (Teledyne Isco) with Rediseq Rf Gold normal-phase silica columns.

4,4'-Di-*tert*-butyl-2,2'-bipyridine (dtbbpy). ¹H NMR (400 MHz; THF-*d*₈): δ 8.56 (s, 2H), 8.51 (d, *J* = 5.1 Hz, 2H), 7.31 (d, *J* = 5.1 Hz, 2H), 1.37 (s, 18 H).

Ni(cod)₂. ¹H NMR (400 MHz; THF-*d*₈): δ 4.30 (br s, 4H), 2.11 (br s, 8H).

1,5-Cyclooctadiene (cod). ¹H NMR (400 MHz; THF-*d*₈): δ 5.49 (s, 4H), 2.32 (s, 8H).

(dtbbpy)Ni⁰(cod) (2). In a nitrogen-filled glovebox, an oven-dried 1 dram vial was charged with Ni(cod)₂ (10.0 mg, 0.0364 mmol), 4,4'-di-*tert*-butyl-2,2'-bipyridine (9.8 mg, 0.036 mmol), and dry, degassed THF-*d*₈ (0.75 mL). The resulting mixture was swirled by hand to give a deep purple solution. The mixture was then quantitatively transferred (2 \times 0.125 mL of THF-*d*₈ wash) to a screw-capped NMR tube with a PTFE-coated septum and sealed. The NMR tube was shaken until the mixture was homogeneous and was allowed to sit overnight at 22 °C (room temperature). The solution of (dtbbpy)Ni⁰(cod) and free cod was characterized by ¹H NMR, paramagnetic ¹H NMR, and ¹³C NMR. Data for the complex matched those in our previous literature report.^{7b}

(dtbbpy)Ni^{II}(C(O)R)Br. The NMR tube was returned to the glovebox, and a carboxylic acid bromide (0.0382 mmol, 1.05 equiv) was added. The color immediately changed to deep red in both cases, and the resulting mixture was characterized by ¹H NMR, paramagnetic ¹H NMR, IR, and UV–vis spectroscopy.²²

(dtbbpy)Ni(C(O)C₅H₁₁)(Br) (1b). The general procedure was followed with hexanoyl bromide²³ (6.8 mg, 0.038 mmol). The yield was determined by ¹H NMR: 72% (vs mesitylene, average of two runs), 74% (vs cyclooctadiene, average of two runs). ¹H NMR (400 MHz; THF-*d*₈): δ 9.09 (d, *J* = 4.1 Hz, 1H), 8.11 (m, 3H), 7.53–7.49 (m, 2H), 3.12 (t, *J* = 7.3 Hz, 2H), 1.64 (dt, *J* = 13.0, 6.3 Hz, 2H), 1.38 (s, 18H), 1.29–1.25 (m, 10H), 0.84 (t, *J* = 6.7 Hz, 3H). IR (cm⁻¹): 1612 (C=O). UV–vis (THF) 1/ λ (ϵ): 20325 cm⁻¹ (5 \times 10³).

(dtbbpy)Ni(C(O)C₆H₄Me)(Br) (1c). The general procedure was followed using 4-methylbenzoyl bromide²⁴ (7.6 mg, 0.038 mmol). The yield was determined by ¹H NMR: 95% (vs mesitylene, average of two runs), 89% (vs cyclooctadiene, average of two runs). The product mixture contained 7 mol % of toluoyl bromide, as evidenced by the characteristic doublets at 7.95 and 7.37 ppm. ¹H NMR (400 MHz; THF-*d*₈): δ 9.14 (d, *J* = 5.7 Hz, 1H), 8.37 (d, *J* = 8.0 Hz, 2H), 8.17 (d, *J* = 7.3 Hz, 2H), 7.74 (d, *J* = 6.0 Hz, 1H), 7.58 (d, *J* = 5.3 Hz, 1H), 7.29 (d, *J* = 4.3 Hz, 1H), 7.12 (d, *J* = 7.8 Hz, 2H), 2.32 (s, 3H), 1.41 (s, 9H), 1.34 (s, 9H). IR (cm⁻¹): 1617 (C=O). UV–vis (THF) 1/ λ (ϵ): 20576 cm⁻¹ (7 \times 10³).

Reactivity Studies (Tables 2 and 3). The NMR tube was returned to the glovebox, and dry, degassed DMA (1 mL, <16 ppm of H₂O by KF titration) was added to the red solution, resulting in a small change to dark red-orange. The appropriate electrophile (0.291 mmol, 8 equiv) was added, and the NMR tube was again sealed, removed from the glovebox, and heated to 60 °C (oil bath). The reaction was judged complete when the vivid red-orange color of the nickel acyl halide complex had disappeared. The resulting reaction was

quenched with diethyl ether (1 mL) and aqueous NaHSO₄ (1 M, 0.5 μ L), and the resulting mixture was filtered through a pad of silica gel before being analyzed by GC, GC/MS, and/or ¹H NMR. See the Supporting Information for tables of all products produced in these reactions. Attempts to visualize the nickel products of these reactions were unsuccessful, and in some cases precipitation of unknown products occurred.

General Procedure for Aryl Bromides. A flame-dried 10 mL round-bottom flask (14/20 joint) containing a Teflon-coated magnetic stir bar was charged with NiCl₂(dme) (11.5 mg, 0.053 mmol), 4,4'-di-*tert*-butyl-2,2'-bipyridine (14.5 mg, 0.054 mmol), anhydrous NaI (28.1 mg, 0.1875 mmol), and zinc flake (98.0 mg, 2 equiv). The round-bottom flask was then fitted with a septum (14/20) and sealed tightly with a double strand of 20 gauge copper wire. The round-bottom flask was purged with nitrogen (1 min), and 2 mL of anhydrous DMA (<70 ppm of H₂O by KF titration) was added by syringe. The resulting mixture was stirred for 1 h at room temperature (~21 °C) until the supernatant had turned dark gray. Alkyl bromide (1.69 mmol, 2.25 equiv), a solution of aryl halide (0.75 mmol in 1 mL of anhydrous DMA), and Fe(CO)₅ (35 μ L, 52 mg, 0.27 mmol) were added sequentially by syringe. The reaction mixture was stirred (1000 rpm) at 60 °C (oil bath) until judged complete by GC analysis (less than 1% aryl bromide remaining, 17–36 h). The resulting mixture was filtered through a 1 cm silica gel pad and the pad rinsed with diethyl ether (~100 mL). The collected organic layer was then washed with 60 mL of water, and the aqueous layer was extracted with diethyl ether (3 \times 15 mL). The combined organic extracts were dried over MgSO₄, filtered, and concentrated in vacuo. The resulting residue was purified by flash chromatography (SiO₂) to yield the desired ketone products.

Ethyl 5-(Phenyl)-5-oxopentanoate (22) [73172-56-2].²⁵ The general procedure was followed with bromobenzene (80 μ L, 0.75 mmol) and ethyl 4-bromobutyrate (240 μ L, 1.69 mmol). The reaction was judged complete after 18 h. Following chromatography (1/10 ethyl acetate/hexanes, *R*_f = 0.25, UV and *p*-anisaldehyde visualization), the product was isolated as a light yellow oil (103.6 mg, 63% yield). ¹H NMR (400 MHz; CDCl₃): δ 7.97–7.95 (m, 2H), 7.55 (t, *J* = 7.4, 1.6 Hz, 1H), 7.47–7.43 (m, 2H), 4.13 (q, *J* = 7.1 Hz, 2H), 3.05 (t, *J* = 7.2 Hz, 2H), 2.43 (t, *J* = 7.2 Hz, 2H), 2.07 (quintet, *J* = 7.2 Hz, 2H), 1.25 (t, *J* = 7.1 Hz, 3H). ¹³C NMR (101 MHz; CDCl₃): δ 199.6, 173.4, 136.9, 133.2, 128.7, 128.2, 60.5, 37.6, 33.5, 19.5, 14.4. IR (cm⁻¹): 1728 (s, C=O, ester), 1682 (s, C=O, aryl ketone). EIMS (70 eV): *m/z* 220 (M⁺).

Ethyl 5-(4-Chlorophenyl)-5-oxopentanoate (23) [54029-03-7].²⁶ The general procedure was followed using 4-chlorobromobenzene (143.6 mg, 0.75 mmol) and ethyl 4-bromobutyrate (240 μ L, 1.68 mmol). The reaction was judged complete after 17 h. Following chromatography (6/1 hexanes/ethyl acetate, *R*_f = 0.42, stained purple with *p*-anisaldehyde stain), the product was isolated as a white crystalline solid (118.3 mg, 62%). Mp: 52–55 °C (lit.²⁶ mp 34–36 °C). ¹H NMR (500 MHz; CDCl₃): δ 7.90 (d, *J* = 8.6 Hz, 2H), 7.43 (d, *J* = 8.5 Hz, 2H), 4.14 (q, *J* = 7.1 Hz, 2H), 3.02 (t, *J* = 7.2 Hz, 2H), 2.43 (t, *J* = 7.1 Hz, 2H), 2.09–2.03 (m, 2H), 1.25 (t, *J* = 7.1 Hz, 3H). ¹³C NMR (126 MHz; CDCl₃): δ 198.4, 173.3, 139.7, 135.3, 129.6, 129.1, 60.6, 37.6, 33.4, 19.5, 14.4. IR (cm⁻¹): 1724 (s, C=O, ester), 1686 (s, C=O, aryl ketone). EIMS (70 eV): *m/z* 254 (M⁺).

Ethyl 5-(3,5-Dimethoxyphenyl)-5-oxopentanoate (24) [898758-62-8]. The general procedure was followed using 1-bromo-3,5-dimethoxybenzene (162.8 mg, 0.75 mmol) and ethyl 4-bromobutyrate (240 μ L, 1.68 mmol). The reaction was judged complete after 36 h. Following chromatography (23% ethyl acetate in hexanes, *R*_f = 0.40, stained purple with *p*-anisaldehyde stain), the product was isolated as a light pink amorphous solid (130.8 mg, 62%). Mp: 40.5–45 °C. ¹H NMR (400 MHz; CDCl₃): δ 7.09 (d, *J* = 2.3 Hz, 2H), 6.64 (t, *J* = 2.2 Hz, 1H), 4.14 (q, *J* = 7.1 Hz, 2H), 3.83 (s, 6H), 3.00 (t, *J* = 7.2 Hz, 2H), 2.42 (t, *J* = 7.2 Hz, 2H), 2.05 (quintet, *J* = 7.2 Hz, 2H), 1.25 (t, *J* = 7.1 Hz, 3H). ¹³C NMR (101 MHz; CDCl₃): δ 198.5, 172.8, 160.5, 138.5, 105.8, 105.3, 60.6, 55.8, 38.0, 33.8, 20.0, 14.7. IR (cm⁻¹): 1728 (s, C=O, ester), 1670 (s, C=O, aryl ketone). EIMS (70 eV): *m/z* 280 (M⁺).

Ethyl 5-(2-Methoxy-5-fluorophenyl)-5-oxopentanoate (25) [951889-85-3]. The general procedure was followed using 2-bromo-5-fluoroanisole (97 μ L, 0.75 mmol) and ethyl 4-bromobutyrate (240 μ L, 1.68 mmol). The reaction was judged complete after 22 h. Following chromatography (8/1 hexanes/ethyl acetate, R_f = 0.20, stained purple with *p*-anisaldehyde stain), the product was isolated as a white amorphous solid (132.1 mg, 62%). Mp: 30–33 °C. ^1H NMR (400 MHz; CDCl_3): δ 7.40 (dd, J = 7.1, 2.6 Hz, 1H), 7.14 (ddd, J = 7.2, 5.9, 2.6 Hz, 1H), 6.90 (dd, J = 7.3, 3.2 Hz, 1H), 4.12 (q, J = 5.7 Hz, 2H), 3.87 (s, 3H), 3.02 (t, J = 5.7 Hz, 2H), 2.37 (t, J = 5.9 Hz, 2H), 2.00 (quintet, J = 5.8 Hz, 2H), 1.23 (t, J = 5.7 Hz, 3H). ^{13}C NMR (126 MHz; CDCl_3): δ 200.3, 173.3, 156.9 (d, J = 240 Hz), 154.9 (d, J = 2.3 Hz), 129.2 (d, J = 5.7 Hz), 119.7 (d, J = 23.6 Hz), 116.4 (d, J = 23.8 Hz), 113.1 (d, J = 7.1 Hz), 60.3, 56.2, 42.7, 33.6, 19.6, 14.3. ^{19}F NMR (376 MHz; CDCl_3): δ -60.66. IR (cm^{-1}): 1728 (s, C=O, ester), 1674 (s, C=O, aryl ketone). EIMS (70 eV): m/z 268 (M^+).

Ethyl 5-(4-Trifluoromethylphenyl)-5-oxopentanoate (26) [898777-81-6].²⁷ The general procedure was followed using 4-bromobenzotrifluoride (105 μ L, 0.75 mmol) and ethyl 4-bromobutyrate (240 μ L, 1.68 mmol). The reaction was judged complete after 24 h. Following chromatography (15% ethyl acetate in hexanes, R_f = 0.40, stained purple with *p*-anisaldehyde stain), the product was isolated as a white amorphous solid (102.9 mg, 48%). Mp: 29–32.5 °C. ^1H NMR (500 MHz; CDCl_3): δ 8.07 (d, J = 8.0 Hz, 2H), 7.73 (d, J = 8.1 Hz, 2H), 4.14 (q, J = 7.1 Hz, 2H), 3.08 (t, J = 7.1 Hz, 2H), 2.44 (t, J = 7.1 Hz, 2H), 2.08 (quintet, J = 7.1 Hz, 2H), 1.26 (t, J = 7.1 Hz, 4H). ^{13}C NMR (126 MHz; CDCl_3): δ 198.5, 173.3, 139.5, 134.5 (q, J = 32.7 Hz), 128.5, 125.8 (q, J = 3.7 Hz), 123.7 (q, J = 273 Hz), 60.6, 37.9, 33.3, 19.3, 14.3. ^{19}F NMR (376 MHz; CDCl_3): δ -0.38. IR (cm^{-1}): 1728 (s, C=O, ester), 1674 (s, C=O, aryl ketone). EIMS (70 eV): m/z 288 (M^+).

1-Phenyl-4-(tert-butylidimethylsilyloxy)-1-butanone (27) [143878-47-1]. The general procedure was followed using bromobenzene (80 μ L, 0.75 mmol) and 3-(tert-butylidimethylsilyloxy)-1-bromopropane (427 mg, 1.68 mmol). The reaction was judged complete after 18 h. Following chromatography (4% diethyl ether in pentane, R_f = 0.22, stained yellow with *p*-anisaldehyde stain), the product was isolated with 3% benzophenone impurity as a clear, colorless oil (135.7 mg, 65%). ^1H NMR (500 MHz; CDCl_3): δ 7.96 (d, J = 7.7 Hz, 2H), 7.54 (t, J = 7.4 Hz, 1H), 7.44 (t, J = 7.7 Hz, 2H), 3.70 (t, J = 6.0 Hz, 2H), 3.05 (t, J = 7.2 Hz, 2H), 1.95 (quintet, J = 6.7 Hz, 2H), 0.88 (s, 9H), 0.03 (s, 6H). ^{13}C NMR (126 MHz; CDCl_3): δ 200.4, 137.3, 133.0, 128.7, 128.2, 62.4, 35.0, 27.6, 26.1, 18.5, -5.2. IR (cm^{-1}): 1686 (C=O aryl ketone). EIMS (70 eV): m/z 221 ($\text{M}^+ - t\text{-Bu}$).

■ ASSOCIATED CONTENT

Supporting Information

Tables S1 and S2, giving the full product distribution for Tables 2 and 3, respectively, pictures of the the reaction of **1c** with electrophiles, and figures giving NMR spectra for **1b,c**, **3**, and **22–27**. This material is available free of charge via the Internet at <http://pubs.acs.org>.

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Notes

The authors declare no competing financial interest.

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