

Nickel-Mediated Decarbonylation of Simple Unstrained Ketones through the Cleavage of Carbon–Carbon Bonds

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S Supporting Information

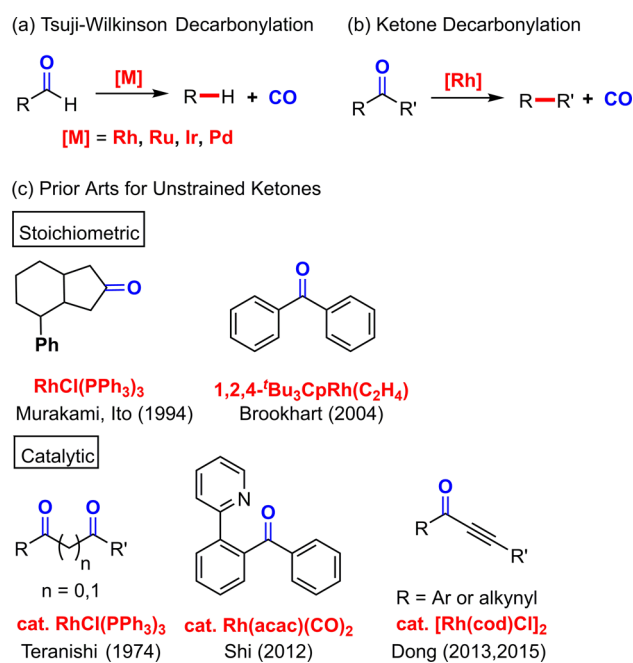
ABSTRACT: Despite advances in methods for the decarbonylation of aldehydes, the decarbonylation of ketones has been met with limited success because this process requires the activation of two inert carbon–carbon bonds. All of the decarbonylation reactions of simple unstrained ketones reported to date require the addition of a stoichiometric rhodium complex. We report herein the nickel/N-heterocyclic carbene-mediated decarbonylation of simple diaryl ketones. This reaction shows unique acceleration effects based on the presence of both electron-donating and electron-withdrawing groups.

The rhodium-mediated conversion of an aldehyde to its parent alkane with the concomitant release of a single molecule of carbon monoxide is known as the Tsuji–Wilkinson decarbonylation. This reaction allows for a formyl group to be used as a removable functionality, and has consequently been widely used in organic synthesis (Scheme 1a).^{1,2}

The extension of this decarbonylation reaction to ketone substrates is highly desirable, because it would be a new method for the formation of carbon–carbon bonds (Scheme 1b). However, the realization of ketone decarbonylation reactions represent a much greater challenge than that of the corresponding aldehyde decarbonylation process, because the former process requires the cleavage of two carbon–carbon bonds,³ which are both kinetically and thermodynamically more stable than the carbon–hydrogen bond of a formyl group. In 1994, Ito and Murakami reported their pioneering work toward the decarbonylation reaction of strained and unstrained cyclic aliphatic ketones using RhCl(PPh₃)₃.⁴ Although this reaction can be performed in a catalytic fashion with strained ketones, unstrained substrates require the addition of a stoichiometric rhodium complex to reach satisfactory levels of conversion. Brookhart reported on the decarbonylation of diaryl ketones using a stoichiometric rhodium complex bearing a bulky cyclopentadienyl ligand.⁵ Existing methods for the catalytic decarbonylation of unstrained ketones are limited to 1,2- and 1,3-diketones,⁶ alkynyl ketones⁷ and ketones bearing a directing group.⁸ Furthermore, all of the decarbonylation reactions of unstrained ketones reported to date are mediated by rhodium complexes. Herein, we report the first nickel system capable of mediating the decarbonylation of simple diaryl ketones.⁹

We initially investigated the Ni(cod)₂-mediated decarbonylation of 2-naphthyl phenyl ketone (**1**) in the presence of

Scheme 1. Metal Complex-Mediated Decarbonylation of Unstrained Aldehydes and Ketones



various ligands. Our initial screening efforts revealed that electron-rich phosphines, such as tricyclohexylphosphine (PCy₃) and 1,2-bis(dicyclohexylphosphino)ethane (dcype), failed to afford any of the desired decarbonylative product **2**, with most of the starting material being recovered unchanged (Table 1, entries 1 and 2). We subsequently evaluated a series of N-heterocyclic carbene (NHC) ligands with the expectation that their strong σ-donor properties would facilitate the required C–C bond activation process. Among the NHCs examined, IMes^{Me} was found to be most effective, although the desired product was isolated in a low yield of 21% under the catalytic conditions. The yield increased to 63% when the reaction was conducted with stoichiometric Ni(cod)₂ (entries 9 in Table 1). It is noteworthy that no byproducts were formed in this reaction, and that the starting ketone **1** was recovered in 38% yield.

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Table 1. Development of the Nickel-Mediated Decarbonylation of Ketone 1^a

| entry | ligand | GC yields (%) | |
|----------------|---|----------------------|----|
| | | 2 | 1 |
| 1 | PCy ₃ (no NaO ^t Bu, 120 °C) | 0 | 93 |
| 2 | dcype (no NaO ^t Bu) | 0 | 79 |
| 3 | ICy·HCl | 0 | 97 |
| 4 | ICy ^{Me} ·HCl | 4 | 89 |
| 5 | IMes·HCl | 8 | 96 |
| 6 | IMes ^{Me} ·HCl | 21 | 72 |
| 7 | IPr·HCl | 10 | 90 |
| 8 | IPr ^{Me} ·HCl | 0 | 94 |
| 9 ^b | IMes ^{Me} ·HCl | 63 (59) ^c | 38 |

dcype

ICy (R = cyclohexyl)

ICy^{Me} (R = cyclohexyl)

IMes (R = 2,4,6-Me₃C₆H₂) IMes^{Me} (R = 2,4,6-Me₃C₆H₂)

IPr (R = 2,6-ⁱPr₂C₆H₃) IPr^{Me} (R = 2,6-ⁱPr₂C₆H₃)

^aReaction conditions: **1** (0.25 mmol), Ni(cod)₂ (0.025 mmol), IMes^{Me}·HCl (0.025 mmol), NaO^tBu (0.06 mmol) in toluene (0.5 mL) for 18 h at 160 °C. ^bReaction conditions: **1** (0.25 mmol), Ni(cod)₂ (0.25 mmol), IMes^{Me}·HCl (0.25 mmol), NaO^tBu (0.25 mmol) in toluene (1.0 mL) for 18 h at 160 °C. ^cIsolated yield.

Having optimized the reaction conditions, we proceeded to explore the scope of this nickel-mediated decarbonylation using a series of simple diaryl ketones (Table 2). We initially evaluated the effects of different substituents on the performance of the decarbonylation reaction. The results revealed that an electron-donating substituent such as methyl (**3a**), butyl (**3b**) or dimethylamino (**3c**) group was well tolerated at the para-position of the phenyl ring. A substrate bearing an electron-deficient trifluoromethyl group (**3d**) at the same position also successfully underwent decarbonylation. This reaction also exhibited a high level of tolerance toward substrates bearing an ortho substituent on the phenyl ring, such as ketones **4** and **5**. Polyaromatic ketone **9** bearing a phenanthrene group reacted smoothly under current conditions to give the decarbonylation product. Decarbonylation of cyclic diaryl ketone **10** successfully occurred under these conditions to form 9,10-dihydrophenanthrene. Several benzophenone derivatives (**11–13**) were also subjected to our newly developed nickel-mediated decarbonylation conditions and reacted as expected to form the corresponding substituted biphenyls. We also applied these conditions to a substrate bearing two benzoyl groups (**14**), which preferentially afforded the monodecarbonylated product **15** in 64% yield, along with the corresponding didecarbonylated product (**16**, 12%). Enolizable ketones generally failed to form the decarbonylation products, but rather led to the formation of a complicated mixture. For example, the nickel-mediated reaction of 2-acetylnaphthalene afforded the decarbonylation product in only 12%, although the conversion of the ketone substrate was 81%.

We subsequently conducted a series of competition experiments to gain a deeper insight into the effect of the electronic properties of the diaryl rings on the outcome of the

Table 2. Substrate Scope^a

| | | |
|-----------------------------------|--------------------------|--------------------|
| 1 (R = H) | 59% (29%) | 4 70% (25%) |
| 3a (R = Me) | 65% (29%) | |
| 3b (R = ⁿ Bu) | 54% (41%) | |
| 3c (R = NMe ₂) | 52% (37%) ^{b,c} | |
| 3d (R = CF ₃) | 53% (27%) | |

5 62% (16%)^d

6 55% (41%)

7 51% (32%)

8 55% (32%)

9 80% (15%)

10 52% (32%)

11 58% (35%)

12 61% (27%)

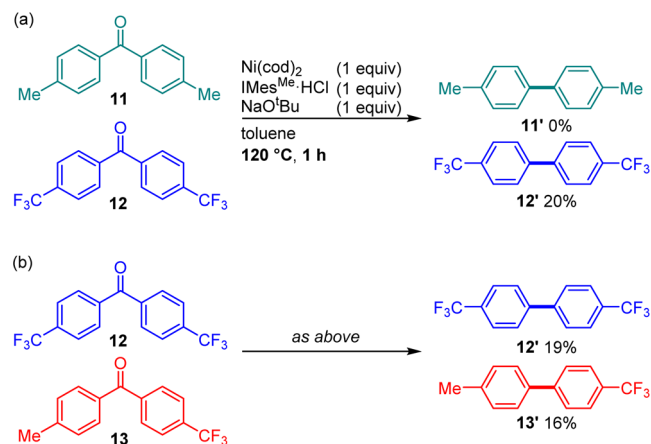
13 71% (26%)

14

→ **15** 64% + **16** 12% + recovered **14** (18%)

^aReaction conditions: **1** (0.25 mmol), Ni(cod)₂ (0.25 mmol), IMes^{Me}·HCl (0.25 mmol), NaO^tBu (0.25 mmol) in toluene (1.0 mL) for 18 h at 160 °C. Isolated yields are shown unless otherwise noted. Numbers in the parentheses refer to the yield of the recovered starting ketone. ^bNMR yield. ^cKetone **1** was formed as a byproduct (4% GC yield). ^dKetone **1** was formed as a byproduct (9% GC yield).

decarbonylation reaction. Intermolecular competitive experiments were performed using 4,4'-disubstituted benzophenones bearing different substituents at the para-positions of their phenyl rings (**11–13**). These reactions were conducted under milder conditions than those described above with shorter reaction times (Scheme 2). Although the electron-deficient ketone **12** is reacted faster than the electron-rich analogue **11** under these conditions (Scheme 2a), ketones **12** (bis-CF₃-substituted) and **13** (methyl and CF₃ substituted) reacted at similar rates (Scheme 2b). It is noteworthy that no crossover

Scheme 2. Intermolecular Competition Experiments

products were observed, indicating that this process occurs through an intramolecular mechanism.

To investigate further the substituent effect, we conducted a series of parallel reactions using substrates **11–13** to compare their initial rates of decarbonylation (Figure 1). Interestingly,

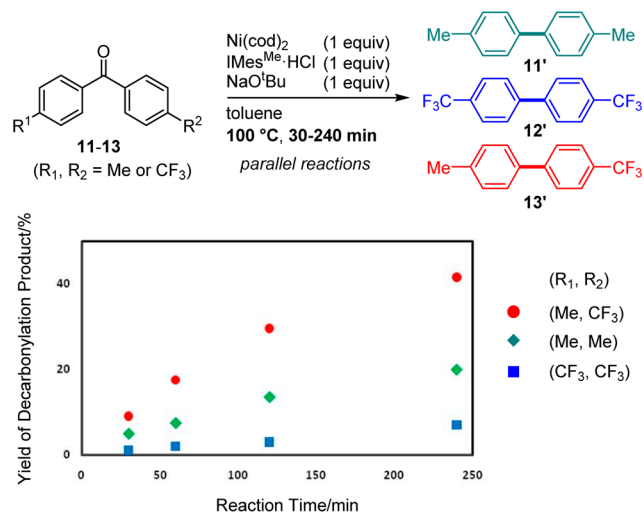
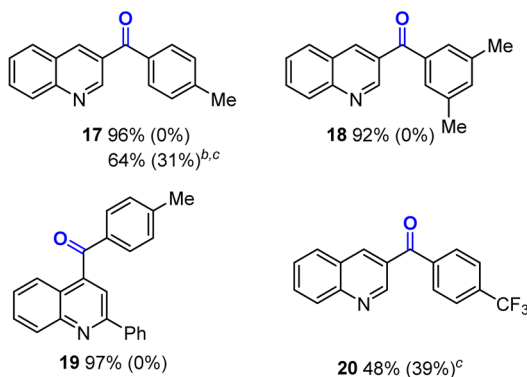


Figure 1. Measurements of the initial rates of the decarbonylation reactions of **11–13**. Data are the average of two independent experiments.

ketone **13**, which contains both electron-donating and electron-withdrawing groups, underwent the decarbonylation reaction at a much greater rate than ketones bearing two electron-donating groups (i.e., **11**) or two electron-withdrawing groups (i.e., **12**).

This unique acceleration effect resulting from the push/pull substituents on the phenyl rings was also observed with heterocyclic ketones (Table 3). 3-Quinolynyl ketones bearing a

Table 3. Decarbonylation of Quinolynyl Ketones^a

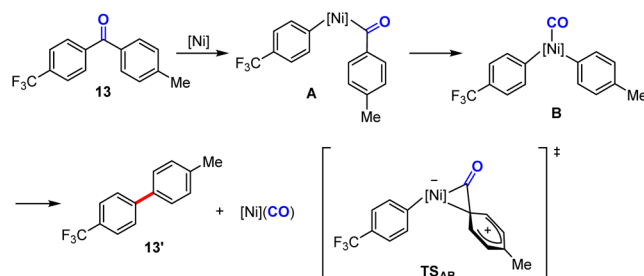


^aReaction conditions: same as Table 2. Numbers in the parentheses refer to the yield of the recovered starting ketone. ^bRun using 20 mol % of Ni(cod)₂/IMes^{Me}·HCl and 25 mol % of NaO^tBu. ^cNMR yields.

relatively electron-rich aryl group, such as **17** and **18**, exhibited high reactivity toward the nickel-mediated decarbonylation, whereas those bearing an electron-withdrawing aryl group (i.e., **20**) were less reactive. A similar trend was also observed for the 4-quinolynyl ketone **19** bearing an electron-rich phenyl ring. It is noteworthy that a promising turnover was observed with ketone **17**.

A mechanistic model to account for the unique electronic effects observed in this reaction is shown in Scheme 3. The

Scheme 3. Possible Mechanism



initial oxidative addition of one of the C(aryl)—C(=O) bonds to nickel(0) species would lead to the formation of arylnickel(II) intermediate **A**, which would undergo a decarbonylation reaction to form diarylnickel complex **B**. Finally, reductive elimination from **B** would afford the desired biaryl product, along with a nickel carbonyl species, which would be unable to undergo an oxidative addition of the C(aryl)—C(=O) bond. Indeed, a new signal was observed at 1980 cm⁻¹ in the IR spectra of the crude reaction mixture (see SI for details). As is the case for the oxidative addition of other strong σ -bonds by nickel,¹⁰ the initial oxidative addition process (**14** → **A**) would require an electron-rich nickel species bearing a strong σ -donor ligand. Conversely, the introduction of an electron-withdrawing group to the substrate undergoing activation by the electron-rich nickel species would therefore accelerate this process. Although the oxidative addition of unstrained C—C(=O) has been reported to be mediated by rhodium-based complexes,^{4–8,11,12} no examples have been reported using nickel complexes except for those involving the use of special chelating substrates.^{9,13} We propose that the subsequent decarbonylation of **A** would proceed through transition state **TS_{AB}**, where the nickel(II) center in **A** would act as an electrophile and attack the ipso carbon of the aryl ligand. A similar mechanism has been proposed for the palladium(II)-mediated decarboxylation of benzoic acid derivatives.¹⁴ According to the current decarbonylation mechanism, the presence of an electron-donating substituent on the aryl group of the aryl ligand would make this group more reactive. This mechanistic model can therefore account for the unique electronic effect observed in the current decarbonylation reaction (Figure 1). The overall rate for this ketone decarbonylation reaction should be determined based on the rates of the two C—C bond cleavage processes, because the effect of the relatively facile reductive elimination process on the rate would be negligible. Substrates bearing both electron-donating and electron-withdrawing groups would therefore undergo the decarbonylation reaction with greater ease because both of the C—C bond cleavage processes would be accelerated by these different substituents. The results of the competition experiments (Scheme 2) can be explained by assuming that initial oxidative addition of the C(aryl)—C=O bond would occur irreversibly. Under these conditions, the selectivity would be determined by the rate of the initial C—C bond cleavage, and electron-deficient ketones would therefore be expected to react at a much greater rate than their electron-rich counterparts.¹⁵

In conclusion, we have developed a nickel-mediated reaction for the decarbonylation of simple aromatic ketones that proceeds via the cleavage of two carbon—carbon bonds. This reaction represents the first reported example of a nickel-mediated decarbonylation of unstrained simple ketones. This

new reactivity of nickel complexes toward C–C bond activation, as well as the unique electronic effects of the substituents on the outcome of these processes, could provide valuable insights for the development of new organometallic reactions. Studies aimed at expanding this new reactivity of nickel complexes to catalytic transformations are ongoing in our laboratories.

■ ASSOCIATED CONTENT

Supporting Information

The Supporting Information is available free of charge on the ACS Publications website at DOI: 10.1021/jacs.6b12293.

Detailed experimental procedures and characterization of new compounds (PDF)

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Notes

The authors declare no competing financial interest.

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