Palladium-Catalyzed Arylation of Malonates and Cyanoesters Using Sterically Hindered Trialkyl- and Ferrocenyldialkylphosphine Ligands

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Palladium-catalyzed reactions of aryl bromides and chlorides with two common stabilized carbanions—enolates of dialkyl malonates and alkyl cyanoesters—are reported. An exploration of the scope of these reactions was conducted, and the processes were shown to occur in a general fashion. Using P(*t*-Bu)$_3$ (**1**), the pentaphenylferrocenyl ligand (Ph$_5$C$_5$)Fe(C$_5$H$_4$)P(*t*-Bu)$_2$ (**2**), or the adamantyl ligand (1-Ad)P(*t*-Bu)$_2$ (**3**), reactions of electron-poor and electron-rich, sterically hindered and unhindered aryl bromides and chlorides were shown to react with diethyl malonate, di-*tert*-butyl malonate, diethyl fluoromalonate, ethyl cyanoacetate, and ethyl phenylcyanoacetate. Although alkyl malonates and ethyl alkylcyanoacetates did not react with aryl halides using these catalysts, the same products were formed conveniently in one pot from diethylmalonate by cross-coupling of an aryl halide in the presence of excess base and subsequent alkylation.

Introduction

The formation of carbon−carbon bonds by the addition of stabilized carbanions to alkyl halides is one of the most fundamental processes in synthetic organic chemistry. In contrast, the reaction of stabilized carbanions with aryl halides requires a catalyst or stoichiometric additive in most cases and has been much less developed.[1−3] Until recently, reactions between aryl halides and enolates derived from dialkyl malonates or cyanoacetates were typically conducted with aryl iodides as the aryl electrophile and with stoichiometric amounts of copper additive.[4,5] In 1993, the arylation of malonates and cyanoesters was achieved using catalytic loadings of copper, but the reaction again required aryl iodides, high temperatures were used, and moderate yields were obtained.[6] The only aryl bromides that have participated in this copper chemistry have been ortho-substituted bromobenzoic acids.[7,8] Aryl chlorides have been completely unreactive. Another approach to the arylation of malonates and cyanoesters involves the complexation of aryl bromides or chlorides to a (cyclopentadienyl)iron moiety and subsequent reaction of the anions of malonates and cyanoesters to these activated aryl halides. However, this method again requires stoichiometric amounts of metal, and the metal was removed from the reaction product by photolysis.[9−11] Other arylations of malonates and cyanoesters use either toxic or specialized reagents such as bismuth,[12] lead,[13] chromium,[14] or high valent iodonium salts.[15]

Only recently has this transformation shown more synthetic potential. We reported two examples of the palladium-catalyzed α-arylation of malonates and demonstrated the first use of an aryl chloride substrate.[16] Buchwald reported a further example of the reaction of an aryl bromide with a malonate.[17] Recently, we communicated the use of an assay based on FRET (fluorescence resonance energy transfer) for reaction discovery and used the arylation of cyanoesters as a case study.[18] Using this technique, we uncovered a catalyst and procedure for the formation of α-aryl cyanoacetates and α,α′-diarylated cyanoacetates in excellent yields under mild conditions. This procedure employed catalytic loadings of palladium and sterically hindered, electron-rich phosphine ligands. This approach followed the hypothesis that such ligands should facilitate both the oxidative additions of unreactive aryl chlorides and the reductive eliminations from complexes with weakly donating ligands, such as the anions of malonates and cyanoesters.[16,19−21]

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A broad range of synthetically valuable materials is derived from the products of the malonate and cyanoester arylation. Decarboxylation provides arylacetic acids,[22] which are common synthetic building blocks, and alkylation followed by decarboxylation generates higher α-arylcarboxylic acid derivatives such as the family of Profen drugs.[23−26] Enantioselective enzymatic desymmetrization of substituted malonates forms chiral, nonracemic synthetic intermediates with one carboxylic acid and one ester unit.[27−31] Aryl malonates, themselves, have been utilized as key components of enzyme inhibitors.[32−34] In addition, these products serve as intermediates for the preparation of enantiopure, differentially protected 1,3-diols,[35−37] as well as arylbarbituric acids.[38,39] Aryl cyanoacetates can be used to generate a variety of nitrogen-containing products such as amino alcohols[40] and *β*-amino acids,[41] while also being valuable as chiral shift reagents.[42−44]

We report here a full account of the scope and limitations of the new arylations of malonates and cyanoesters. The scope of this reaction is broad and includes ortho-substituted aryl halides, aryl chlorides that are activated or deactivated, and a variety of malonate partners. In some cases catalysts bearing ligands such as $Ph_5FcP(t\text{-}Bu)_3$ or (1-Ad)P(*t*-Bu)$_3$ gave higher yields than catalysts bearing P(*t*-Bu)$_3$, but most coupling processes could be conducted with one of these three ligands. In addition, it was necessary to suitably match the anionic base and countercation with the pronucleophile to achieve high yields.

Results and Discussion

1. Arylation of Malonates. A. Initial Evaluation of Reaction Conditions. Our initial exploration of reaction conditions for the arylation of malonates focused on the coupling of diethyl malonate with bromobenzene. We evaluated a variety of bases in combination with an array of solvents. Several palladium sources were employed in 2 mol % quantities, and P(*t*-Bu)$_3$ (**1**) was used initially as ligand (Figure 1). This ligand has generated efficient catalysts for the arylation of ketones.[16] Moreover, it had broadened the scope of aromatic C−N and C−O bond formation to include weakly nucleophilic substrates such as phenols and carbamates.[45−47] The electronic properties of malonate and cyanoester anions are likely to control the scope of C−C coupling reactions in a similar way that the electronic properties of phenoxides and acidic nitrogen substrates control the scope of aromatic carbon−heteroatom coupling. Therefore, we began our studies toward the development of catalysts for arylation of malonates and cyanoesters using this ligand.

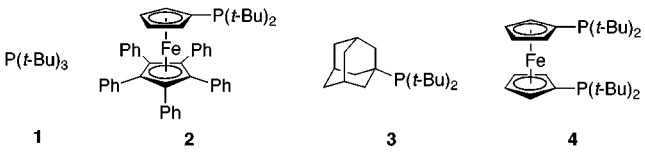

Figure 1. Ligands used in the malonate and cyanoacetate arylation.

We analyzed reactions at 70 °C using the readily available bases Na_3PO_4, K_3PO_4, Na_2CO_3, Cs_2CO_3, NaH, NaHMDS, LDA, and NaO-*t*-Bu. Reactions conducted with alkoxide bases generated materials resulting from transesterification of the starting malonate and product arylmalonate. Reactions containing NaH as base in THF solvent gave the fastest reaction rates, providing complete conversion of bromobenzene to the arylmalonate product after 1 h. THF solvent was used to ensure solubility of the malonate anion. K_3PO_4 was also a suitable base and is more convenient to use under some laboratory conditions. In this case, toluene was superior to THF as solvent. Reactions containing this base were somewhat slower, but still required only about 5 h for full conversion. Considering the results with cyanoacetates below and the suitability of NaH as base, we were surprised to observe that reactions involving Na_3PO_4 were considerably slower than those involving K_3PO_4, as were reactions involving Na_2CO_3 and Cs_2CO_3. All reactions with Na_3PO_4, Na_2CO_3, and Cs_2CO_3 failed to provide complete conversion after 10 h. Throughout this work both the cation and anion of the base influenced rates and yield. With some classes of substrate and basic anions, sodium cations produced the fastest rates and highest yields, while in other cases, potassium as cation gave better results. Thus, no trend of optimal cation was observed, and in many cases the choice of base remains empirical. No reaction was observed when using either of the two stronger bases NaHMDS or LDA.

We also evaluated the optimum catalyst precursor and metal:ligand ratio. In all cases Pd(dba)$_2$ was a superior precatalyst to Pd(OAc)$_2$. Generally, [Pd(allyl)Cl]$_2$ was an equally effective precursor. In some cases, higher turnover numbers were observed using the allyl complex. Of

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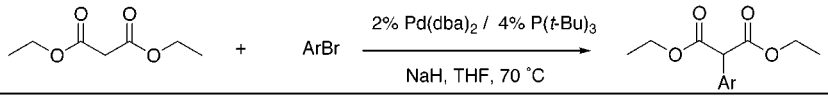
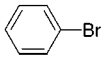
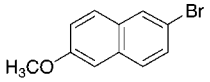
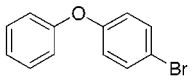
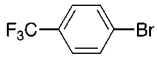
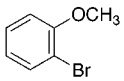
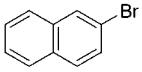
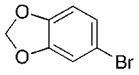
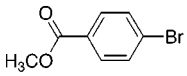
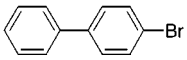
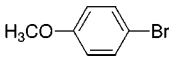
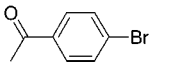
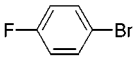
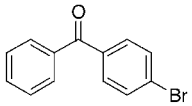
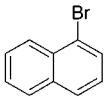
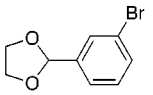
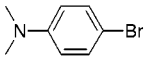
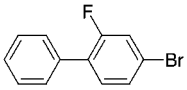
Table 1. Preparative Scale Arylation of Diethyl Malonate[a]



Entry	ArBr	Yield (%)	Time	Entry	ArBr	Yield (%)	Time
1		89	1 h	11		92	12 h[b]
2		88	5 h[b]	12		85	8 h
3		91	12 h[c]	13		91	3 h
4		89	8 h	14		89	6 h
5		84	8 h	15		83	6 h
6		91	3 h	16		91	4 h
7		89	3 h	17		89	14 h[b]
8		82	3 h	18		90	14 h[b]
9		83	6 h	19		87	6 h[b]
10		87	6 h	20		89	12 h[b]

[a] Reactions conducted in duplicate on a 1 mmol scale in THF using 1.1 equiv of diethyl malonate, 1.1 equiv of NaH, and 1.0 equiv of aryl bromide. [b] K_3PO_4 (3.0 equiv) used as base in toulene. [c] 0.050 mol % $[(allyl)PdCl]_2$, 0.10 mol % ligand 4, 3.0 equiv of K_3PO_4, in toulene at 100 °C for 12 h. Yields are an average of two runs.

course, no reaction was observed in the absence of palladium. Unlike other palladium-catalyzed bond-forming reactions using bulky alkylphosphines,[16,46,48] the palladium-to-ligand ratio was not a crucial factor in determining reactivity. Both 1:1 and 1:2 ratios were suitable, although use of a 1:2 ratio led to slightly faster reaction rates. No reaction occurred with $Pd(dba)_2$, $[Pd(allyl)Cl]_2$ or $Pd(OAc)_2$ in the absence of added phosphine ligand.

B. Coupling of Aryl Bromides with Diethyl Malonate. After optimization of the reaction conditions, we investigated the scope of the coupling of aryl bromides with diethyl malonate. These results are presented in Table 1. A broad scope of aryl bromides participated in this reaction, as demonstrated by the results in entries 4, 7, 10, 12, and 15. Even reaction of the *p*-dialkylamino-substituted aryl bromide in entry 10 gave over 85% yield. Substrates with an ortho or pseudo-ortho substituent also reacted under the standard conditions (entries 4, 5, and 9). *o*-Methoxybromobenzene, which is both electron-rich and sterically hindered, gave over 85% yield of coupled product (entry 4). Reaction of electron-poor substrates such as those in entries 6, 13, 17, and 18 all occurred in high yield.

Some of these substrates can be sensitive to the strongly basic conditions created by NaH. However, many

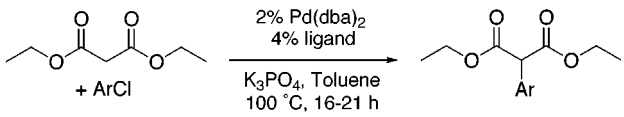
(48) Littke, A. F.; Dai, C.; Fu, G. C. *J. Am. Chem. Soc.* **2000**, *122*, 4020.

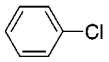
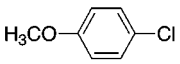
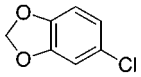
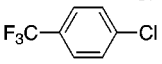
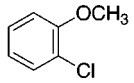
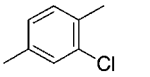
of these substrates gave high yields under appropriately modified conditions. For example, high yields for reaction of the acetophenone derivative in entry 17 were observed when employing K_3PO_4 as base and toluene as solvent instead of NaH as base in THF solvent. The origin of this requirement is not straightforward because the malonate is much more acidic than the methyl ketone. The ester in entry 6, the benzophenone in entry 18, and dioxolane-containing substrate in entry 19 gave high yields for reactions containing the phosphate, but not for those containing the hydride base. In addition 2-bromo-6-methoxynaphthalene and 1-bromo-3-fluorobiphenyl smoothly underwent coupling with diethyl malonate using K_3PO_4 as base to give precursors to the commercially important drugs Naproxen and Flurbiprofen, respectively (entries 11 and 20). In these cases, increased amounts of hydrodehalogenation products were observed when using NaH as base.

Although not investigated in detail, the malonate arylation also occurred when using substantially lower catalyst loadings than the standard conditions of 2 mol % catalyst. As shown in entry 3, the reaction of diethyl malonate with bromobenzene occurred in high yield with 0.05 mol % of the precursor $[(allyl)PdCl]_2$ at 100 °C. Higher turnover numbers were observed under these conditions than when using NaH as base.

C. Coupling of Aryl Chlorides with Diethyl Malonate. Significant success has been observed recently in the coupling of aryl chlorides in a number of processes.[16,19,49−57] These substrates are, of course, less reactive for palladium-catalyzed processes than are aryl bromides, but are less expensive and available in more derivatives from commercial sources. With the catalysts containing sterically hindered electron-rich phosphine ligands, the reactions of aryl chlorides with diethyl malonate occurred smoothly in many cases. These results are summarized in Table 2. In these cases, K_3PO_4 was a more effective base than was NaH. Although high conversions were observed when using P(*t*-Bu)$_3$ as ligand, arene that was formed from hydrodehalogenation was a significant side product. The source of the hydrogen is unclear, and we do not understand at this time the difference in selectivity as a function of halide. However, use of either the pentaphenylferrocenyl phosphine, (Ph_5C_5)-$Fe(C_5H_4)P(t\text{-}Bu)_2$ (**2**),[58] or the adamantyl phosphine, (1-Ad)P(t-Bu)$_2$(**3**)[18] (see Figure 1), instead of P(*t*-Bu)$_3$, allowed for coupling of aryl chlorides in high yields. Electron-rich (entries 3−5), electron-poor (entry 6) and sterically hindered substrates (entries 8 and 9) were suitable coupling partners when using ligand **2**. Although catalysts comprised of adamantyl ligand **3** were effective for reactions of many aryl chlorides, this catalyst system produced roughly 50% of the product from hydrodehalogenation during coupling of the dioxolane in entry 5 or the ortho-substituted aryl chlorides.

Table 2. Reaction of Diethyl Malonate with Aryl Chlorides[a]



Entry	Aryl Chloride	Llgand	Yield (%)
1		**2**	81
2		**3**	85
3		**2**	86
4		**3**	90
5		**2**	85
6		**2**	89
7		**3**	86
8		**2**	87
9		**2**	86

[a] Reactions conducted in duplicate on a 1 mmol scale in toulene using 1.1 equiv of diethyl malonate, 1.0 equiv of aryl chloride and 3.0 equiv of K_3PO_4. Yields are an average of two runs.

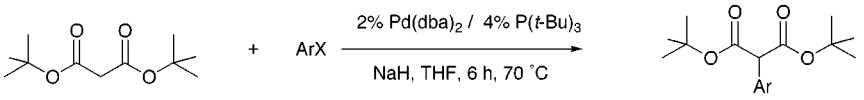
D. Coupling of Aryl Halides with Di-*tert*-butyl Malonate. It is well-known that *tert*-butyl esters are more readily deprotected than related methyl or ethyl versions. Earlier, the authors' group used palladium complexes of the sterically hindered 1,1′-bis(di-*tert*-butylphosphino)ferrocene (**4**) as catalysts for the coupling of di-*tert*-butyl malonate with chlorobenzene. Because we successfully conducted the reaction of diethyl malonate with a wide variety of aryl halides using ligands **1**−**3**, we investigated whether di-*tert*-butyl malonate would display as broad or broader a scope in its coupling with bromo- and chloroarenes than did diethyl malonate.

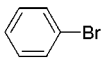
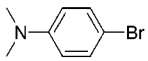
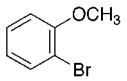
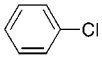
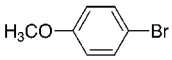
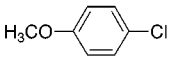
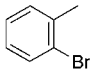
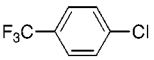
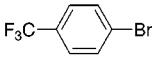
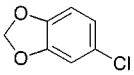
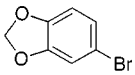
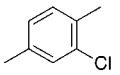
A large number of aryl bromides and chloride reagents were suitable for coupling with di-*tert*-butyl malonate (Table 3). As observed for reactions of diethyl malonate, $Pd(dba)_2$ and $[(allyl)PdCl]_2$ were useful precatalysts, but $Pd(OAc)_2$ generated catalysts of much lower activity. With di-*tert*-butyl malonate as substrate, NaO-*t*-Bu proved to be an effective base. Reactions containing NaH as base also occurred in high yields. In contrast to reactions of diethyl malonate, the reaction of di-*tert*-butyl malonate with bromobenzene using K_3PO_4 as base failed to give complete conversion, even after extended periods of heating.

Using NaH as base and P(*t*-Bu)$_3$ as ligand, the cross-coupling reactions of a diverse range of aryl bromides occurred in high yields (entries 1−7). The use of this commercially available ligand instead of the bisphosphine **4** allowed for the arylation of di-*tert*-butyl malonate with

(49) Stauffer, S.; Hauck, S. I.; Lee, S.; Stambuli, J.; Hartwig, J. F. *Org. Lett.* **2000**, *2*, 1423.
(50) Bei, X.; Turner, H. W.; Weinberg, H. W.; Guram, A. S.; Petersen, J. L. *J. Org. Chem.* **1999**, *64*, 6797.
(51) Bei, X.; Guram, A. S.; Turner, H. W.; Weinberg, W. H. *Tetrahedron Lett.* **1999**, *40*, 1237.
(52) Huang, J.; Nolan, S. *J. Am. Chem. Soc.* **1999**, *121*, 9889.
(53) Littke, A. F.; Fu, G. C. *Angew. Chem., Int. Ed.* **1998**, *37*, 3387.
(54) Littke, A. F.; Fu, G. C. *J. Org. Chem.* **1999**, *64*, 10.
(55) Wolfe, J. P.; Buchwald, S. L. *Angew. Chem., Int. Ed.* **1999**, *38*, 2413.
(56) Wolfe, J. P.; Tomori, H.; Sadighi, J. P.; Yin, J. J.; Buchwald, S. L. *J. Org. Chem.* **2000**, *65*, 1158.
(57) Zhang, C.; Huang, J.; Trudell, M. L.; Nolan, S. P. *J. Org. Chem.* **1999**, *64*, 3804.
(58) Shelby, Q.; Kataoka, N.; Mann, G.; Hartwig, J. F. *J. Am. Chem. Soc.* **2000**, *122*, 10718.

Table 3. Arylation of Di-*tert*-Butylmalonate[a]



Entry	Aryl halide	Yield (%)	Entry	Aryl halide	Yield (%)
1		89, 91[b]	7		90
2		86[c]	8		88[d]
3		90	9		84[e]
4		85[c]	10		86[d]
5		88, 90[b]	11		87[d]
6		87	12		90[e]

[a] Reactions conducted in duplicate on a 1 mmol scale in THF using 1.1 equiv of di-*tert*-butyl malonate, 1.1 equiv of NaH, and 1.0 equiv of aryl halide. [b] 1.0 mol % $[(allyl)PdCl]_2$, 1.1 equiv of NaO*t*-Bu in dioxane, 45 °C, 8 h. [c] Stirred for 12 h. [d] 1.0 mol % $[(allyl)PdCl]_2$, 1.1 equiv of NaO*t*-Bu used as base in dioxane at 100 °C for 12 h. [e] 2.0 mol % $Pd(dba)_2$, 1.1 equiv of NaO*t*-Bu used as base in dioxane at 100 °C for 12 h. Yields are an average of two runs.

chlorobenzene (entry 8) in a somewhat higher yield (88% versus 80%).[16] As did aryl bromides, a large variety of aryl chlorides successfully coupled with the anion of di-*tert*-butyl malonate (entries 8−12). For reactions of these aryl halides, NaO-*t*-Bu was superior to NaH as base. Reactions containing NaH as base formed nearly equal amounts of hydrodehalogenated arene and coupled product. In contrast, reactions containing NaO-*t*-Bu formed little hydrodehalogenation product and generated high yields of di-*tert*-butyl arylmalonates.

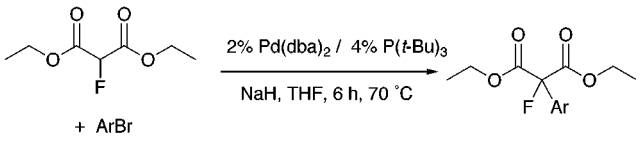
E. Coupling of Aryl Halides with Fluoromalonates. Fluorinated materials are increasingly studied because of their importance as pharmaceutical candidates.[59,60] 2-Aryl-2-fluoromalonates serve as key intermediates for the preparation of optically active, differentially protected 2-aryl-1,3-propanediols after desymmetrization with lipases.[35,36] These synthetic intermediates are generally prepared from either 2-aryl-2-fluoroacetates,[61] electrophilic fluorination of aryl malonates,[62] or nucleophilic substitution using fluoroarenes activated by chromium and the enolate of 2-fluoromalonate.[14] The direct formation of the sp^2-sp^3 bond by arylation of 2-fluoromalonate is rare and limited to reactions of metal arene complexes.[14] Because diethyl 2-fluoromalonate is isosteric with diethyl malonate, we suspected that these substrates would undergo the palladium-catalyzed arylation process.

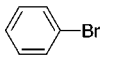
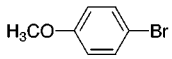
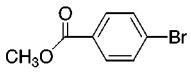
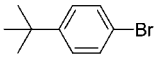
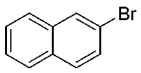
The results of reactions between diethyl 2-fluoromalonate and aryl bromides are presented in Table 4. As observed from our studies with diethyl and di-*tert*-butyl malonates, catalysts derived from $Pd(OAc)_2$ were less reactive than were those from $Pd(dba)_2$. Both K_3PO_4 and NaH were suitable bases, although reactions containing K_3PO_4 as base required substantially longer times for complete generation of the coupled product (entry 1).

F. Limitations of the Coupling of Aryl Halides with Malonates. The limitations of the catalytic arylation of malonates were principally the reactions of pyridyl halides and halobenzonitriles as electrophiles and diethyl alkylmalonates as nucleophiles. No conversion was observed when attempting the reaction of 2-, 3-, or 4-bromopyridine with diethyl or di-*tert*-butylmalonate. The origin of this absence of reactivity is unclear. Catalysts comprised of $P(t\text{-}Bu)_3$ can catalyze the amination of pyridines,[63] and we have observed clean reaction of bromopyridines with imine-protected glycinates.[64] Moreover, complexes with electron-poor, palladium-bound aryl groups generally undergo faster reductive elimination than do those with electron-rich aryl groups.[65] The 2- and

(59) Ojima, I.; McCarthy, J. R.; Welch, J. T. *Biomedical Frontiers of Fluorine Chemistry*; American Chemical Society: Washington, D. C., 1996; Vol. 639, p 356.
(60) Hintermann, L.; Togni, A. *Angew. Chem., Int. Ed.* **2000**, *39*, 4359.
(61) Fukuyama, Y.; Matoishi, K.; Iwasaki, M.; Takizawa, E.; Miyazaki, M.; Ohta, H.; Hanzawa, S.; Kakidani, H.; Sugai, T. *Biosci., Biotechnol., Biochem.* **1999**, *63*, 1664.
(62) Banks, E. R.; Lawrence, N. J.; Popplewell, A. J. *J. Chem. Soc., Chem. Commun.* **1994**, 343.
(63) Nishiyama, M.; Yamamoto, T.; Koie, Y. *Tetrahedron Lett.* **1998**, *39*, 617.
(64) Lee, S.; Beare, N. A.; Hartwig, J. F. *J. Am. Chem. Soc.* **2001**, *123*, 8410.
(65) Driver, M. S.; Hartwig, J. F. *J. Am. Chem. Soc.* **1997**, *119*, 8232.

Table 4. Palladium-Catalyzed Arylation of Diethyl Fluoromalonate[a]



Entry	Aryl Bromide	Yield (%)
1		84 88[b]
2		88
3		89
4		86
5		79

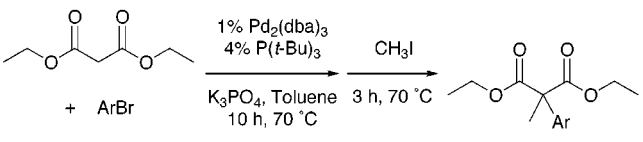
[a] Reactions conducted in duplicate on 1 mmol scale in THF using 1.1 equiv Diethyl fluoromalonate, 1.1 equiv of NaH and 1.0 equiv of aryl bromide. [b] 3.0 equiv of K_3PO_4 used as base, 14 h required for completion. Yields are an average of two runs.

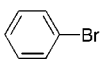
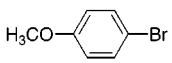
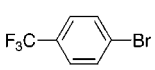
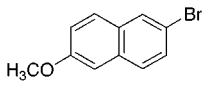
4-pyridyl groups are certainly less electron-donating substituents than a simple phenyl. The lack of reactivity of halobenzonitriles is equally perplexing. Amination of 4-bromo- and chlorobenzonitrile occurred cleanly when using catalysts generated from $Pd(dba)_2$ and P(*t*-Bu)$_3$,[63] but the malonate arylation using these substrates gave low conversions. Again, the cyano group should accelerate the reductive elimination step. The lack of reactivity of alkyl-substituted diethylmalonates is more easily rationalized. Steric hindrance could inhibit formation of the C-bound malonate anion complexes. Moreover, β-hydrogen elimination can occur from these species. When reaction did occur at elevated temperatures, products from apparent β-hydrogen elimination and Michael addition to a transient methylene diethylmalonate intermediate[66] were observed.

Although alkyl-substituted diethylmalonates have not participated in the palladium-catalyzed arylation process, sequential arylation and alkylation formed these products. Using an excess of K_3PO_4 base, we developed a one-pot process involving palladium-catalyzed arylation followed by simple alkylation (Table 5). In a typical experiment, the arylation reaction was run at 70 °C using excess base, and methyl iodide was added after the malonate was consumed. These products formed from sequential arylation and alkylation were isolated in excellent yields. For some purposes the products can be used to form acetic acid derivatives, such as the Profen drugs, by decarboxylation. As mentioned in the Introduction, the products can also be used to generate optically active building blocks by known enzymatic desymmetrizations.[27−31]

(66) Pivsa-Art, S.; Fukui, Y.; Miura, M.; Nomura, M. *Bull. Chem. Soc. Jpn.* **1996**, *69*, 2039.

Table 5. One-Pot Preparation of Diethyl 2-Aryl-2-methylmalonates[a]



Entry	Aryl Bromide	Yield (%)
1		91
2		90
3		91
4		89[b]

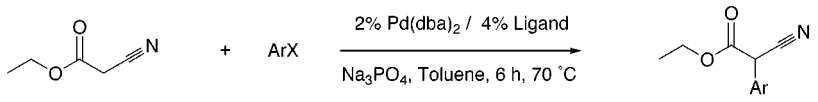
[a] Reactions conducted in duplicate on a 1 mmol scale in toulene using 1.0 equiv of diethyl malonate, 4.5 equiv of K_3PO_4, and 1.1 equiv of aryl bromide, and 3.0 equiv CH_3I added after consumption of malonate. [b] 0.5 mol % $Pd_2(dba)_3$ used. Yields are an average of two runs.

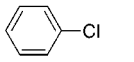
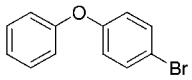
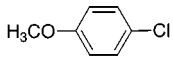
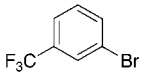
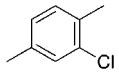
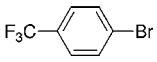
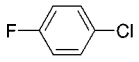
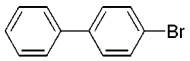
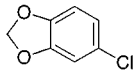
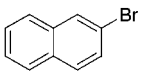
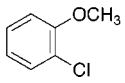
2. Arylation of Cyanoacetates. A. Reactions of Ethyl Cyanoacetate. A number of aryl bromides and chlorides reacted with ethyl cyanoacetate using bulky trialkyl phosphines and loadings of palladium as low as 0.1 mol %. In contrast to the findings on the arylation of diethyl malonate, Na_3PO_4 was the most effective base for the arylation of cyanoacetates. When we used NaH as base, no product was formed, and when we used K_3PO_4 the product was generated slowly. The poor solubility of the sodium or potassium salts of ethyl cyanoacetate in the tetrahydrofuran, dioxane, toluene, and acetonitrile solvents we investigated may be responsible for the low reactivity when using strong bases. Deprotonation of the cyanoacetate with NaH quickly generated a thick suspension. Perhaps the low levels of enolate present in the reaction media when using Na_3PO_4 as base allows the cyanoester anion to react with the catalyst before it aggregates and precipitates. Alternatively, coordinated cyanoacetate, and not free substrate, is deprotonated by this base.

Examples of the arylation of ethyl cyanoacetate are presented in Table 6. The selective monoarylation of ethyl cyanoacetate with an aryl bromide was achieved in a general fashion using 4 mol % P(*t*-Bu)$_3$ or pentaphenylferrocenyl **2** as ligand and either 2 mol % $Pd(dba)_2$ or 1 mol % $[Pd(allyl)Cl]_2$ as the palladium source.

Reactions of aryl bromides bearing electron-withdrawing substituents using catalysts ligated by P(*t*-Bu)$_3$ were significantly different from those of electron−neutral or electron-rich aryl bromides. Reactions of these substrates generated, in varying amounts, the diarylated product in competition with the major monoarylation product. This difference in reactivity as a function of electronics was particularly evident during reactions of 3- and 4-bromobenzotrifluoride. Reaction of the *meta*-substituted trifluoride produced the desired monoarylated product

Table 6. Arylation of Ethyl Cyanoacetate[a]



Entry	Aryl halide	L	Yield (%)	Entry	Aryl halide	L	Yield (%)
1		**1**	85	7		**1**	86[c]
2		**1**	90	8		**1**	90[c]
3		**1**	87	9		**1**	87[c]
4		**2**	87[b]	10		**1**	82[c]
5		**2**	91[b]	11		**2**	86[c]
6		**2**	91[b]	12		**2**	81[c]

[a] Reactions conducted in duplicate on a 1 mmol scale in toluene using 1.0 equiv of ethyl cyanoacetate, 1.0 equiv of aryl halide, and 3.0 equiv of Na_3PO_4. [b] 1.0 mol % $[Pd(allyl)Cl]_2$ used at 100 °C for 12 h. Yields are an average of two runs.

in good yield (entry 3), but reactions of the *para*-substituted trifluoride produced a mixture of the mono- and diarylated product. Although lowering of the reaction temperature and varying the ligand:metal ratio had no noticeable effect on this selectivity, a change in ligand solved this problem of selectivity. Reactions of electron-poor aryl halides, such as those in Table 6, entries 4−6, with ethyl cyanoacetate catalyzed by complexes of pentaphenylferrocenyl ligand **2** provided good yields of the monoarylcyanoacetate product.

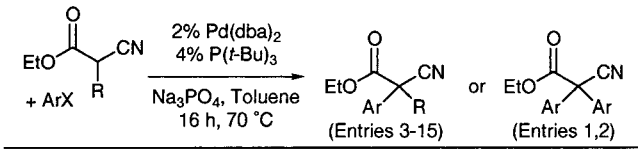
Catalysts generated from P(*t*-Bu)$_3$ were more effective for the arylation of ethyl cyanoacetate using aryl chlorides than they were for the arylation of malonates using aryl chlorides. All of the aryl halides in entries 7−12 of Table 6 had generated large amounts of hydrodehalogenation product during reactions with diethyl malonate, but they gave high yields for reaction with ethyl cyanoacetate. Although P(*t*-Bu)$_3$ was a generally effective ligand for reactions of ethyl cyanoacetate with aryl chlorides, pentaphenylferrocenyl ligand **2** again improved yields in certain cases. For example, hydrodehalogenation products were formed in 10−20% yield when coupling 3,4-methylenedioxyphenyl chloride or 2-chloroanisole with ethyl cyanoacetate catalyzed by complexes of P(*t*-Bu)$_3$. In contrast, the same reactions catalyzed by Pd(dba)$_2$ and pentaphenylferrocenyl **2** formed less arene, and the desired products were isolated in 86% and 81% yield (entries 11 and 12).

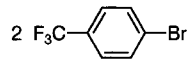
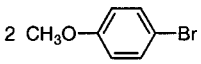
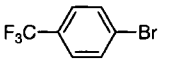
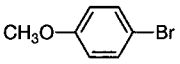
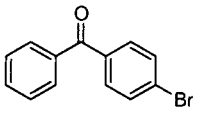
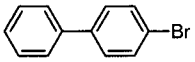
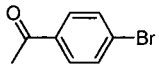
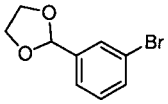
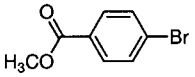
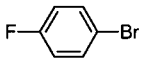
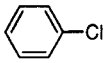
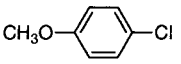
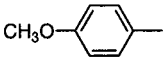
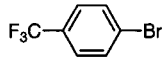
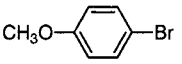
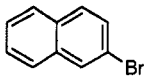
The limitations of the catalytic arylation of ethyl cyanoacetate were somewhat greater than were those for the arylation of malonates. As observed for malonate substrates, cyanoacetates did not couple with pyridyl halides or halobenzonitriles. In addition, 4-haloacetophenone, 4-halobenzophenone, and methyl 4-halobenzoate did not react with ethyl cyanoacetate. Reactions of very hindered aryl halides such as bromomesitylene also did not occur. Ethyl alkylcyanoacetates, like diethyl alkylmalonates, were unreactive toward aryl halides.

B. Arylation of Ethyl Arylcyanoacetates. As described above, we observed the diarylation of cyanoacetates as a side reaction in some couplings of electron-poor aryl halides with ethyl cyanoacetate. Thus, we investigated whether these diaryl products could be formed purposefully in high yield. Examples of the formation of quaternary diaryl-substituted products are presented in Table 7. Both symmetrical (entries 1 and 2) and unsymmetrical diaryl cyanoacetates were readily synthesized. A broad spectrum of aryl bromides coupled with ethyl phenylcyanoacetate or ethyl *p*-anisylcyanoacetate as nucleophile to give the diaryl cyanoester products in excellent yield.

Except for reactions of ortho-substituted aryl halides, the scope of the arylation of ethyl phenylcyanoacetate was even more extensive than that for arylation of the parent ethyl cyanoacetate. As expected, aryl bromides (entries 6, 8, and 10) and aryl chlorides (entries 11 and 12) that coupled with ethyl cyanoacetate also coupled with the ethyl arylcyanoacetates. In addition, several aryl bromides that were not suitable substrates for reaction with ethyl cyanoacetate were suitable substrates for reaction with ethyl phenylcyanoacetate. For example, 4-bromobenzophenone (entry 5), 4-bromoacetophenone

Table 7. Generation of Diarylated Cyanoacetates[a]



Entry	R	ArX	Yield (%)
1	H		95[b]
2			93[b]
3			91
4			93
5			93
6			90
7			92
8			94
9			92
10			89
11			89[c]
12			91[c]
13			90
14			94[d]
15			91[d]

[a] Reactions conducted in duplicate on 1.0 mmol scale in toulene using 1.0 equiv of aryl cyanoacetate, 1.1 equiv of aryl halide, and 3.0 equiv of Na_3PO_4. [b] 0.5 equiv of ethyl cyanoacetate, 1.1 equiv of aryl bromide, 4 mol % $Pd(dba)_2$, 8 mol % **1**. [c] Stirred at 100 °C for 16 h. [d] Reaction required 20 h. Yields are an average of two runs.

(entry 7), and methyl 4-bromobenzoate (entry 9) reacted to form the products with a quaternary carbon in excellent yields. Yet, substrates with ortho substituents were less reactive toward the ethyl arylcyanoacetate than they were toward the parent ethyl cyanoacetate. No reaction was observed between the phenyl cyanoacetate and 2-bromotoluene, and no reaction was observed between ethyl *o*-tolylcyanoacetate and 4-bromobenzotrifluoride.

A similar arylation of dialkyl arylmalonates was not observed. Reaction of diethyl malonate with 2 equiv of bromobenzene formed only the monophenylmalonate and left the second equivalent of phenyl bromide unreacted. Furthermore, all attempts to couple diethyl phenylmalonate with aryl bromides were unsuccessful. Although the pK_a values of diethyl malonate and ethyl cyanoacetate are similar, the values for the monoaryl versions of these materials are substantially different. Ethyl phenylcyanoacetate has a pK_a that is roughly five units lower than that of the ethyl cyanoacetate,[67] while diethyl phenylmalonate has a pK_a value that is roughly six units higher than that of the diethyl malonate.[68] Thus, the phenyl-substituted, stabilized nucleophile that is further from the ketone enolate basicity undergoes the coupling reaction more readily. Ketones, including α-aryl ketones, undergo palladium-catalyzed α-arylation in a general fashion. Thus, this difference in reactivity between arylcyanoacetates and arylmalonates is more likely to result from steric effects than electronic effects.

Conclusions: Overall Reaction Scope and Relationship to Palladium-Catalyzed C−X Bond Formation. Because the malonates and cyanoesters used in these reactions display the same oxidation level at the three central carbons, we discuss here the overall scope of the reaction using malonates and cyanoesters interchangeably. For coupling with electron-poor aryl bromides, the use of malonates is more straightforward than the use of cyanoacetates. No diarylation is observed, and ligand **2** is not necessary. In the coupling of malonates with aryl chlorides, di-*tert*-butyl malonate reacts in the most general fashion using ligand **1**. Reactions of di-*tert*-butylmalonate occurred in high yield using **1** as ligand and NaH, or in some cases NaO-*t*-Bu, as base. In contrast, it was necessary to use ligands **2** or **3** to prevent hydrodehalogenation of the chloroarene when using diethyl malonate. Fluoromalonates also reacted with aryl halides in high yield, in this case to form products with fluorine-substituted, quaternary centers. The scope for reactions of cyanoacetates was not as broad as that for reactions of malonates, but many reactions did occur smoothly. Besides introducing functionality containing nitrogen directly into the product of coupling with aryl halides, the coupling of cyanoacetates reported here provides products with diaryl-substituted quaternary carbons. Formation of analogous diarylmalonates did not occur. Finally, a straightforward, one-pot procedure for formation of dialkyl alkylarylmalonates was developed using a sequence of palladium-catalyzed arylation with excess base and subsequent addition of an alkyl halide. We presume that this process would be equally effective for reactions of cyanoacetates, considering that the alkylation step is commonplace.

Strong parallels can be found between the palladium-catalyzed, base-mediated arylations reported here and amine or alkoxide arylations. The coupling of amines with

(67) Bordwell, F. G.; Branca, J. C.; Bares, J. E.; Filler, R. *J. Org. Chem.* **1988**, *53*, 780.
(68) Zaugg, H. E.; Schaefer, A. D. *J. Am. Chem. Soc.* **1965**, *87*, 7.

aryl halides occurs with either aromatic or sterically hindered alkylphosphines, but the coupling of less basic substrates, such as such as alcohols and phenols, with unactivated aryl halides occurs more readily with the most sterically hindered of the alkylphosphine ligands.[45,58,69] The reason for this catalyst requirement in the coupling of alcohols and phenols is the slow reductive elimination to form ethers as a result of the lower basicity of the alkoxide relative to the amido ligand.[65,70,71]

The rates for reductive elimination of α-aryl carbonyl compounds are also connected, at least roughly, with the electronic properties of the carbonyl substrate. The coupling of ketones with aryl halides can be conducted with either arylphosphines[72,73] or sterically hindered alkylphosphines,[16,17] but they occur more rapidly when conducted with the alkylphosphines. However, malonate and cyanoester arylations require at this time the sterically hindered alkylphosphines. We have shown recently that arylpalladium *mono*carbonyl enolate complexes ligated by 1,2-bis(diphenylphosphino)benzene (DPPBz) undergo reductive elimination at similar rates. However, reductive elimination of these enolate complexes was slower than reductive elimination of the analogous arylpalladium methyl complex,[74] and, most important for the work here, reductive elimination of the analogous arylpalladium complex of a malonate anion did not occur at all. Thus, sterically hindered ligands, such as those used in the work described here, accelerate reductive elimination and overcome the unfavorable electronic properties of these substrates. In addition, these hindered ligands promote oxidative addition. Thus, the catalysts described here lead to reaction of weakly basic malonates and cyanoesters with aryl bromides and even unactivated aryl chlorides.

Experimental Section

General Methods. Reactions were conducted using standard drybox techniques. ^{1}H and ^{13}C NMR spectra were recorded on a Bruker DPX 400 MHz spectrometer with tetramethylsilane or residual protiated solvent used as a reference and coupling constants reported in hertz (Hz). Elemental analyses were performed by Robertson Microlabs, Inc., Madison, NJ, and by Atlantic Microlabs, Inc., Norcross, GA. Chromatographic purifications were performed by flash chromatography using silica gel (200−400 mesh) from Natland International Corporation. Yields for final products in all tables refer to isolated yields and are the average of at least two runs. Spectroscopic data and combustion analyses are reported for all new compounds. Previously reported products were isolated in greater than 95% purity as determined by ^{1}H NMR and capillary gas chromatography (GC). All ^{13}C NMR spectra were proton decoupled. GC analyses were performed on a HP-6890 instrument using a DB-1301 narrow bore column for high-temperature ramp applications (max. 120 °C/min). GCMS spectra were recorded on a HP5890 instrument equipped with a HP5971A Mass Spectral Analyzer using a HP-1 methyl silicone column. All reagents and bases were purchased from Aldrich and used without further purification. Dioxane was purchased as anhydrous grade and stored in a drybox. Toluene and tetrahydrofuran were distilled from sodium and benzophenone and were stored in a drybox. Pd(dba)$_2$ was prepared according to the literature procedure and [(allyl)PdCl]$_2$, P(*t*-Bu)$_3$, and Pd$_2$(dba)$_3$·CHCl$_3$ were purchased from Strem Chemicals. The following ligands were prepared using literature procedures or slightly modified variations thereof: **2**,[18] **3**,[18] **4**,[18] **5**,[75] and **6**.[76]

General Procedure for the Arylation of Diethyl Malonate with Aryl Bromides (Table 1). Method A: To a screw-capped vial containing diethyl malonate (1.1 mmol) was added tetrahydrofuran (1.0 mL) followed by NaH (1.1 mmol). Upon evolution of hydrogen (ca.2 min), aryl bromide (1.0 mmol), P(*t*-Bu)$_3$ (0.040 mmol), Pd(dba)$_2$ (0.020 mmol), and tetrahydrofuran (2.0 mL) were added. The vial was sealed with a cap containing a PTFE septum and removed from the drybox. The homogeneous reaction mixture was stirred at 70 °C and monitored by GC. After complete conversion of the aryl halide, the crude reaction was filtered through a plug of Celite and concentrated in vacuo. The residue was purified by chromatography on silica gel (1:2 dichloromethane/hexanes).

Method B: To a screw-capped vial containing diethyl malonate (1.1 mmol) and aryl bromide (1.0 mmol) were added P(*t*-Bu)$_3$ (0.040 mmol), Pd(dba)$_2$ (0.020 mmol), and K$_3$PO$_4$ (3.0 mmol) followed by toluene (3.0 mL). The vial was sealed with a cap containing a PTFE septum and removed from the drybox. The heterogeneous reaction mixture was stirred at 70 °C and monitored by GC. After complete conversion of the aryl halide, the crude reaction was filtered through a plug of Celite and concentrated in vacuo. The residue was purified by chromatography on silica gel (1:2 dichloromethane/hexanes).

Diethyl 2-Phenylmalonate (Table 1, Entry 1).[16] Method A of the above general procedure was followed using bromobenzene (157 mg, 1.00 mmol) and diethyl malonate (176 mg, 1.10 mmol). The reaction mixture was purified by column chromatography on silica gel (1:2 dichloromethane/hexanes) to give the desired product (204 mg, 87%) as a colorless oil: ^{1}H NMR (CDCl$_3$) δ 7.43−7.34 (m, 5H), 4.62 (s, 1H), 4.27−4.18 (m, 4H), 1.27 (t, 7.2 Hz, 6H). ^{13}C{^{1}H} NMR (CDCl$_3$) δ 168.17, 132.81, 129.27, 128.59, 128.20, 61.80, 57.96, 14.01.

Diethyl 2-(2-Methoxyphenyl)malonate (Table 1, Entry 4).[77] Method A of the above general procedure was followed using 2-bromoanisole (188 mg, 1.01 mmol) and diethyl malonate (176 mg, 1.10 mmol). The reaction mixture was purified by column chromatography on silica gel (1:2 dichloromethane/hexanes) to give the desired product (233 mg, 87%) as a colorless oil: ^{1}H NMR (CDCl$_3$) δ 7.34−7.28 (m, 2H), 6.99−6.95 (m, 1H), 6.90−6.88 (m, 1H), 5.11 (s, 1H), 4.28−4.17 (m, 4H), 3.82 (s, 3H), 1.26 (t, 7.2 Hz, 6H). ^{13}C{^{1}H} NMR (CDCl$_3$) δ 168.63, 156.89, 129.43, 129.33, 121.87, 120.67, 110.66, 61.60, 55.61, 51.28, 14.06.

Diethyl 2-(2-Methylphenyl)malonate (Table 1, Entry 5).[5] Method A of the above general procedure was followed using 2-bromotoluene (174 mg, 1.01 mmol) and diethyl malonate (176 mg, 1.10 mmol). The reaction mixture was purified by column chromatography on silica gel (1:2 dichloromethane/hexanes) to give the desired product (208 mg, 82%) as a colorless oil: ^{1}H NMR (CDCl$_3$) δ 7.41−7.37 (m, 1H), 7.24−7.17 (m, 3H), 4.87 (s, 1H), 4.29−4.17 (m, 4H), 2.34 (s, 3H), 1.26 (t, 7.2 Hz, 6H). ^{13}C{^{1}H} NMR (CDCl$_3$) δ 168.40, 136.48, 131.65, 130.50, 128.82, 128.11, 126.33, 61.76, 54.39, 19.77, 14.04.

Diethyl 2-(4-Methoxycarbonylphenyl)malonate (Table 1, Entry 6). Method A of the above general procedure was followed using methyl 2-bromobenzoate (217 mg, 1.01 mmol) and diethyl malonate (177 mg, 1.11 mmol). The reaction mixture was purified by column chromatography on silica gel (1:1 dichloromethane/hexanes) to give the desired product (276 mg, 93%) as a colorless oil: ^{1}H NMR (CDCl$_3$) δ 8.04 (d, 8.4 Hz, 2H), 7.50 (d, 8.2 Hz, 2H), 4.66 (s, 1H), 4.25−4.22 (m, 4H), 3.92 (s, 3H), 1.27 (t, 6.8 Hz, 6H). ^{13}C{^{1}H} NMR (CDCl$_3$) δ

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167.59, 166.72, 137.61, 130.00, 129.84, 129.43, 62.09, 57.88, 52.23, 14.00. Anal. Calcd for $C_{15}H_{18}O_6$: C, 61.22; H, 6.16. Found: C, 61.50: H, 5.94.

Diethyl 2-(4-Methoxyphenyl)malonate (Table 1, Entry 7).[5] Method A of the above general procedure was followed using 4-bromoanisole (189 mg, 1.01 mmol) and diethyl malonate (176 mg, 1.10 mmol). The reaction mixture was purified by column chromatography on silica gel (1:2 dichloromethane/hexanes) to give the desired product (245 mg, 91%) as a colorless oil: ^{1}H NMR ($CDCl_3$) δ 7.35−7.31 (m, 2H), 6.91−6.87 (m, 2H), 4.55 (s, 1H), 4.27−4.15 (m, 4H), 3.79 (s, 3H), 1.26 (t, 7.2 Hz, 6H). ^{13}C{^{1}H} NMR ($CDCl_3$) δ 168.46, 159.46, 130.39, 124.90, 114.00, 61.75, 57.13, 55.25, 14.03.

Diethyl 2-(4-Fluorophenyl)malonate (Table 1, Entry 8).[78] Method A of the above general procedure was followed using 4-bromofluorobenzene (175 mg, 1.00 mmol) and diethyl malonate (176 mg, 1.10 mmol). The reaction mixture was purified by column chromatography on silica gel (1:2 dichloromethane/hexanes) to give the desired product (203 mg, 80%) as a colorless oil: ^{1}H NMR ($CDCl_3$) δ 7.41−7.37 (m, 2H), 7.08−7.03 (m, 2H), 4.59 (s, 1H), 4.28−4.16 (m, 4H), 1.26 (t, 7.2 Hz, 6H). ^{13}C{^{1}H} NMR ($CDCl_3$) δ 168.06, 162.65 (d, 247.2 Hz), 131.04 (d, 8.3 Hz), 128.59 (d, 3.5 Hz), 115.54 (d, 22.5 Hz), 61.94, 57.10, 14.01.

Diethyl 2-(1-Naphthyl)malonate (Table 1, Entry 9).[5] Method A of the above general procedure was followed using 1-bromonaphthalene (207 mg, 1.00 mmol) and diethyl malonate (176 mg, 1.10 mmol). The reaction mixture was purified by column chromatography on silica gel (1:2 dichloromethane/hexanes) to give the desired product (240 mg, 84%) as a colorless oil: ^{1}H NMR ($CDCl_3$) δ 7.98 (d, 8.4 Hz, 1H), 7.90 (d, 7.6 Hz, 1H), 7.86 (d, 8.0 Hz, 1H), 7.59−7.48 (m, 4H), 5.44 (s, 1H), 4.29−4.23 (m, 4H), 1.27 (t, 7.2 Hz, 6H). ^{13}C{^{1}H} NMR ($CDCl_3$) δ 168.49, 133.88, 131.60, 129.28, 129.00, 128.89, 127.03, 126.68, 125.80, 125.40, 122.80, 61.93, 54.44, 14.03.

Diethyl 2-(4-Dimethylaminophenyl)malonate (Table 1, Entry 10).[79] Method A of the above general procedure was followed using 4-bromo-*N*,*N*-dimethylaniline (200 mg, 1.00 mmol) and diethyl malonate (176 mg, 1.10 mmol). The reaction mixture was purified by column chromatography on silica gel (1:2 dichloromethane/hexanes) to give the desired product (249 mg, 89%) as a colorless oil: ^{1}H NMR ($CDCl_3$) δ 7.27−7.25 (m, 2H), 6.71−6.69 (m, 2H), 4.50 (s, 1H), 4.26−4.14 (m, 4H), 2.94 (s, 6H), 1.26 (t, 7.6 Hz, 6H). ^{13}C{^{1}H} NMR ($CDCl_3$) δ 168.82, 150.30, 129.90, 120.32, 112.37, 61.57, 57.09, 40.46, 14.06.

Diethyl 2-(6-Methoxynaphthalen-2-yl)malonate (Table 1, Entry 11).[24] Method B of the above general procedure was followed using 2-bromo-6-methoxynaphthalene (238 mg, 1.00 mmol) and diethyl malonate (176 mg, 1.10 mmol). The reaction mixture was purified by column chromatography on silica gel (1:2 dichloromethane/hexanes) to give the desired product (283 mg, 89%) as a colorless oil: ^{1}H NMR ($CDCl_3$) δ 7.76 (m, 1H), 7.74−7.69 (m, 2H), 7.51 (dd, 8.8, 1.6 Hz, 1H), 7.13 (dd, 8.8, 2.4 Hz, 1H), 7.11 (d, 2.4 Hz, 1H), 4.75 (s, 1H), 4.28−4.16 (m, 4H), 3.88 (s, 3H), 1.25 (t, 7.2 Hz, 6H). ^{13}C{^{1}H} NMR ($CDCl_3$) δ 168.35, 158.03, 134.24, 129.50, 128.70, 128.40, 127.99, 127.25, 127.14, 119.09, 105.56, 61.80, 57.93, 55.27, 14.03.

Diethyl 2-(4-Phenoxyphenyl)malonate (Table 1, Entry 12). Method A of the above general procedure was followed using 4-bromobiphenyl ether (249 mg, 1.00 mmol) and diethyl malonate (176 mg, 1.10 mmol). The reaction mixture was purified by column chromatography on silica gel (1:2 dichloromethane/hexanes) to give the desired product (292 mg, 89%) as a colorless oil: ^{1}H NMR ($CDCl_3$) δ 7.38−7.31 (m, 4H), 7.13−7.09 (m, 1H), 7.04−7.01 (m, 2H), 7.00−6.96 (m, 2H), 4.59 (s, 1H), 4.28−4.16 (m, 4H), 1.27 (t, 7.2 Hz, 6H). ^{13}C{^{1}H} NMR ($CDCl_3$) δ 168.26, 157.42, 156.68, 130.70, 129.80, 127.34, 123.60, 119.31, 118.53, 61.87, 57.22, 14.05. Anal. Calcd for $C_{19}H_{20}O_5$: C, 69.50; H, 6.14. Found: C, 69.55: H, 6.12.

Diethyl 2-(4-Trifluoromethylphenyl)malonate (Table 1, Entry 13).[80] Method A of the above general procedure was followed using 4-bromobenzotrifluoride (226 mg, 1.00 mmol) and diethyl malonate (178 mg, 1.11 mmol). The reaction mixture was purified by column chromatography on silica gel (1:2 dichloromethane/hexanes) to give the desired product (271 mg, 89%) as a colorless oil: ^{1}H NMR ($CDCl_3$) δ 7.63 (d, 8.4 Hz, 2H), 7.55 (d, 8.4 Hz, 2H), 4.68 (s, 1H), 4.29−4.17 (m, 4H), 1.27 (t, 7.2 Hz, 6H). ^{13}C{^{1}H} NMR ($CDCl_3$) δ 167.54, 136.64, 130.49 (q, 32.5 Hz), 129.83, 125.55 (q, 3.7 Hz), 124.02 (q, 272.2 Hz), 62.18, 57.71, 14.00.

Diethyl 2-(2-Naphthyl)malonate (Table 1, Entry 14).[81] Method A of the above general procedure was followed using 2-bromonaphthalene (212 mg, 1.02 mmol) and diethyl malonate (176 mg, 1.10 mmol). The reaction mixture was purified by column chromatography on silica gel (1:2 dichloromethane/hexanes) to give the desired product (266 mg, 91%) as a colorless oil: ^{1}H NMR ($CDCl_3$) δ 7.85−7.81 (m, 4H), 7.56 (dd, 8.6, 1.6 Hz, 1H), 7.49−7.46 (m, 2H), 4.79 (s, 1H), 4.29−4.17 (m, 4H), 1.26 (t, 7.2 Hz, 6H). ^{13}C{^{1}H} NMR ($CDCl_3$) δ 168.21, 133.19, 132.98, 130.26, 128.64, 128.30, 128.00, 127.63, 126.72, 126.34, 126.23, 61.88, 58.08, 14.03.

Diethyl 2-(3,4-Methylenedioxyphenyl)malonate (Table 1, Entry 15). Method A of the above general procedure was followed using 4-bromo-1,2-(methylenedioxy)benzene (202 mg, 1.00 mmol) and diethyl malonate (177 mg, 1.11 mmol). The reaction mixture was purified by column chromatography on silica gel (1:2 dichloromethane/hexanes) to give the desired product (231 mg, 82%) as a colorless oil: ^{1}H NMR ($CDCl_3$) δ 6.96 (d, 1.6 Hz, 1H), 6.81 (dd, 8.0, 1.6 Hz, 1H), 6.77 (d, 8.0 Hz, 1H), 5.96 (s, 2H), 4.52 (s, 1H), 4.27−4.15 (m, 4H), 1.27 (t, 7.2 Hz, 6H). ^{13}C{^{1}H} NMR ($CDCl_3$) δ 168.25, 147.82, 147.62, 126.31, 122.96, 109.58, 108.21, 101.23, 61.84, 57.45, 14.03. Anal. Calcd for $C_{14}H_{16}O_6$: C, 59.99; H, 5.75. Found: C, 60.01: H, 5.80.

Diethyl 2-(4-Biphenyl)malonate (Table 1, Entry 16).[82] Method A of the above general procedure was followed using 4-bromobiphenyl (232 mg, 1.00 mmol) and diethyl malonate (176 mg, 1.10 mmol). The reaction mixture was purified by column chromatography on silica gel (1:2 dichloromethane/hexanes) to give the desired product (283 mg, 91%) as a colorless oil: ^{1}H NMR ($CDCl_3$) δ 7.60−7.56 (m, 4H), 7.49−7.41 (m, 4H), 7.36−7.32 (m, 1H), 4.66 (s, 1H), 4.30−4.17 (m, 4H), 1.28 (t, 7.2 Hz, 6H). ^{13}C{^{1}H} NMR ($CDCl_3$) δ 168.16, 141.11, 140.56, 131.76, 129.68, 128.77, 127.43, 127.34, 127.12, 61.87, 57.62, 14.02.

Diethyl 2-(4-Acetylphenyl)malonate (Table 1, Entry 17).[5] Method B of the above general procedure was followed using 4-bromoacetophenone (201 mg, 1.01 mmol) and diethyl malonate (177 mg, 1.11 mmol). The reaction mixture was purified by column chromatography on silica gel (2:1 dichloromethane/hexanes) to give the desired product (250 mg, 89%) as a colorless oil: ^{1}H NMR ($CDCl_3$) δ 7.98−7.95 (m, 2H), 7.53−7.50 (m, 2H), 4.68 (s, 1H), 4.29−4.17 (m, 4H), 2.61 (s, 3H), 1.27 (t, 7.2 Hz, 6H). ^{13}C{^{1}H} NMR ($CDCl_3$) δ 197.66, 167.54, 137.79, 136.81, 129.64, 128.58, 62.11, 57.84, 26.69, 14.00.

Diethyl 2-(4-Benzoylphenyl)malonate (Table 1, Entry 18). Method B of the above general procedure was followed using 4-bromobenzophenone (261 mg, 1.00 mmol) and diethyl malonate (176 mg, 1.10 mmol). The reaction mixture was purified by column chromatography on silica gel (2:1 dichloromethane/hexanes) to give the desired product (313 mg, 92%) as a colorless oil: ^{1}H NMR ($CDCl_3$) δ 7.83−7.80 (m, 4H), 7.62−7.57 (m, 1H), 7.56−7.53 (m, 2H), 7.51−7.46 (m, 2H), 4.71 (s, 1H), 4.31−4.18 (m, 4H), 1.28 (t, 7.2 Hz, 6H). ^{13}C{^{1}H} NMR ($CDCl_3$) δ 196.20, 167.61, 137.37, 137.33, 137.10, 132.55, 130.29, 130.06, 129.36, 128.32, 62.11, 57.86, 14.01. Anal. Calcd for $C_{20}H_{20}O_5$: C, 70.57; H, 5.92. Found: C, 70.77: H, 6.05.

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Diethyl 2-[3-(1,3-Dioxolane)phenyl]malonate (Table 1, Entry 19). Method B of the above general procedure was followed using 2-(3-bromophenyl)-1,3-dioxolane (229 mg, 1.00 mmol) and diethyl malonate (176 mg, 1.10 mmol). The reaction mixture was purified by column chromatography on silica gel (2:1 dichloromethane/hexanes) to give the desired product (256 mg, 83%) as a colorless oil: ^{1}H NMR ($CDCl_3$) δ 7.50−7.36 (m, 4H), 5.81 (s, 1H), 4.63 (s, 1H), 4.26−4.16 (m, 4H), 4.15−3.98 (m, 4H), 1.25 (t, 7.2 Hz, 6H). ^{13}C{^{1}H} NMR ($CDCl_3$) δ 167.98, 138.32, 132.92, 130.04, 128.65, 127.59, 126.36, 103.40, 65.28, 61.84, 57.87, 14.00. Anal. Calcd for $C_{16}H_{20}O_6$: C, 62.33; H, 6.54. Found: C, 62.27: H, 6.53.

Diethyl 2-(2-Fluorobiphenyl-4-yl)malonate (Table 1, Entry 20).[24] Method B of the above general procedure was followed using 4-bromo-2-fluorobiphenyl (251 mg, 1.00 mmol) and diethyl malonate (176 mg, 1.10 mmol). The reaction mixture was purified by column chromatography on silica gel (1:2 dichloromethane/hexanes) to give the desired product (371 mg, 91%) as a colorless oil: ^{1}H NMR ($CDCl_3$) δ 7.55−7.52 (m, 2H), 7.45−7.41 (m, 3H), 7.38−7.36 (m, 1H), 7.28 (d, 1.6 Hz, 1H), 7.24 (dd, 6.0, 1.6 Hz, 1H), 4.64 (s, 1H), 4.30−4.19 (m, 4H), 1.29 (t, 7.2 Hz, 6H). ^{13}C{^{1}H} NMR ($CDCl_3$) δ 167.69, 159.51 (d, 248.3 Hz), 135.31, 129.99 (d, 2.9 Hz), 128.47, 128.46, 127.83, 125.35 (d, 3.3 Hz), 117.14 (d, 24.4 Hz), 62.08, 57.35, 14.03.

General Procedure for the Arylation of Diethyl Malonate with Aryl Chlorides (Table 2). To a screw-capped vial containing diethyl malonate (1.1 mmol) and aryl chloride (1.0 mmol) were added phosphine (0.040 mmol), $Pd(dba)_2$ (0.020 mmol), and K_3PO_4 (3.0 mmol) followed by toluene (3.0 mL). The vial was sealed with a cap containing a PTFE septum and removed from the drybox. The heterogeneous reaction mixture was stirred at 100 °C and monitored by GC. After complete conversion of the aryl halide, the crude reaction was filtered through a plug of Celite and concentrated in vacuo. The residue was purified by chromatography on silica gel (1:2 dichloromethane/hexanes).

Diethyl 2-(2,4-Dimethylphenyl)malonate (Table 2, Entry 9). The above general procedure was followed using 2-chloro-*p*-xylene (141 mg, 1.00 mmol) and diethyl malonate (176 mg, 1.10 mmol). The reaction mixture was purified by column chromatography on silica gel (1:2 dichloromethane/hexanes) to give the desired product (228 mg, 86%) as a colorless oil: ^{1}H NMR ($CDCl_3$) δ 7.19 (s, 1H), 7.07 (d, 8.0 Hz, 1H), 7.03−7.01 (m, 1H), 4.83 (s, 1H), 4.29−4.17 (m, 4H), 2.31 (s, 3H), 2.29 (s, 3H), 1.27 (t, 7.2 Hz, 3H). ^{13}C{^{1}H} NMR ($CDCl_3$) δ 168.50, 135.78, 133.32, 131.36, 130.38, 129.36, 128.90, 61.71, 54.35, 21.06, 19.29, 14.04.

General Procedure for the Arylation of Di-*tert*-butyl Malonate (Table 3). Method A: Into a screw-capped vial containing di-*tert*-butyl malonate (1.1 mmol) was added tetrahydrofuran (1.0 mL), followed by NaH (1.1 mmol). After the evolution of hydrogen was complete (ca. 2 min), aryl bromide (1.0 mmol), phosphine (0.040 mmol), $Pd(dba)_2$ (0.020 mmol), and additional tetrahydrofuran (2.0 mL) were added. The vial was sealed with a cap containing a PTFE septum and removed from the drybox. The homogeneous reaction mixture was stirred at 70 °C and monitored by GC. After complete conversion of the aryl bromide, the crude reaction was filtered through a plug of Celite and concentrated in vacuo. The residue was purified by chromatography on silica gel (1:2 dichloromethane/hexanes).

Method B: Into a screw-capped vial containing di-*tert*-butyl malonate (1.1 mmol) and aryl chloride (1.0 mmol) were added P(*t*-Bu)$_3$ (0.040 mmol), $Pd(dba)_2$ (0.020 mmol) or $[Pd(allyl)Cl]_2$ (0.010 mmol), and NaO-*t*-Bu (1.2 mmol) followed by dioxane (3.0 mL). The vial was sealed with a cap containing a PTFE septum and removed from the drybox. The heterogeneous reaction mixture was stirred at the required temperature and monitored by GC. After complete conversion of the aryl halide, the crude reaction was filtered through a plug of Celite and concentrated in vacuo. The residue was purified by chromatography on silica gel (1:2 dichloromethane/hexanes).

Di-*tert*-butyl 2-Phenylmalonate (Table 3, Entry 1).[16] Method A of the above general procedure was followed using bromobenzene (157 mg, 1.00 mmol) and di-*tert*-butyl malonate (177 mg, 1.10 mmol). The reaction mixture was purified by column chromatography on silica gel (1:2 dichloromethane/hexanes) to give the desired product (204 mg, 87%) as a white solid: ^{1}H NMR ($CDCl_3$) δ 7.39−7.30 (m, 5H), 4.43 (s, 1H), 1.46 (s, 18H). ^{13}C{^{1}H} NMR ($CDCl_3$) δ 167.47, 133.47, 129.31, 128.40, 127.86, 81.96, 60.08, 27.87.

Di-*tert*-butyl 2-(2-Methoxyphenyl)malonate (Table 3, Entry 2). Method A of the above general procedure was followed using 2-bromoanisole (187 mg, 1.00 mmol) and di-*tert*-butyl malonate (238 mg, 1.10 mmol). The reaction mixture was purified by column chromatography on silica gel (1:2 dichloromethane/hexanes) to give the desired product (264 mg, 82%) as a white solid: ^{1}H NMR ($CDCl_3$) δ 7.38−7.35 (m, 1H), 7.29−7.25 (m, 1H), 6.97−6.94 (m, 1H), 6.88−6.86 (m, 1H), 4.94 (s, 1H), 3.80 (s, 3H), 1.47 (s, 18H). ^{13}C{^{1}H} NMR ($CDCl_3$) δ 167.87, 156.95, 129.23, 128.93, 122.63, 120.51, 110.57, 81.59, 55.54, 53.06, 27.91. Anal. Calcd for $C_{18}H_{26}O_5$: C, 67.06; H, 8.13. Found: C, 67.30: H, 8.23.

Di-*tert*-butyl 2-(4-Methoxyphenyl)malonate (Table 3, Entry 3). Method B of the above general procedure was followed using 4-bromoanisole (145 mg, 1.01 mmol), di-*tert*-butyl malonate (238 mg, 1.10 mmol), and $[Pd(allyl)Cl]_2$ (3.4 mg, 0.0093 mmol). The reaction mixture was purified by column chromatography on silica gel (1:2 dichloromethane/hexanes) to give the desired product (278 mg, 85%) as a white solid: ^{1}H NMR ($CDCl_3$) δ 7.31 (d, 8.8 Hz, 2H), 6.88 (d, 8.8 Hz, 2H), 4.37 (s, 1H), 3.79 (s, 3H), 1.46 (s, 18H). ^{13}C{^{1}H} NMR ($CDCl_3$) δ 167.75, 159.20, 130.41, 125.62, 113.82, 81.84, 59.24, 55.21, 27.88. Anal. Calcd for $C_{18}H_{26}O_5$: C, 67.06; H, 8.13. Found: C, 67.00: H, 7.79.

Di-*tert*-butyl 2-(2-Methylphenyl)malonate (Table 3, Entry 4). Method A of the above general procedure was followed using 2-bromotoluene (171 mg, 1.00 mmol) and di-*tert*-butyl malonate (238 mg, 1.10 mmol). The reaction mixture was purified by column chromatography on silica gel (1:4 dichloromethane/hexanes) to give the desired product (266 mg, 87%) as a white solid: ^{1}H NMR ($CDCl_3$) δ 7.43−7.38 (m, 1H), 7.23−7.15 (m, 3H), 4.70 (s, 1H), 2.32 (s, 3H), 1.47 (s, 18H). ^{13}C{^{1}H} NMR ($CDCl_3$) δ 167.69, 136.45, 132.41, 130.33, 128.59, 127.73, 126.11, 81.92, 56.33, 27.89, 19.81. Anal. Calcd for $C_{18}H_{26}O_4$: C, 70.56; H, 8.55. Found: C, 70.58: H, 8.36.

Di-*tert*-butyl 2-(3,4-Methylenedioxyphenyl)malonate (Table 3, Entry 6). Method A of the above general procedure was followed using 4-bromo-1,2-(methylenedioxy)benzene (206 mg, 1.00 mmol) and di-*tert*-butyl malonate (238 mg, 1.10 mmol). The reaction mixture was purified by column chromatography on silica gel (1:2 dichloromethane/hexanes) to give the desired product (292 mg, 85%) as a colorless oil: ^{1}H NMR ($CDCl_3$) δ 6.95−6.94 (m, 1H), 6.79 (m, 1H), 6.77 (d, 8.0 Hz, 1H), 5.95 (s, 2H), 4.34 (s, 1H), 1.47 (s, 18H). ^{13}C{^{1}H} NMR ($CDCl_3$) δ 167.53, 147.63, 147.34, 127.05, 122.99, 109.63, 108.09, 101.09, 82.00, 59.57, 27.88. Anal. Calcd for $C_{18}H_{24}O_6$: C, 64.27; H, 7.19. Found: C, 60.01: H, 5.80.

Di-*tert*-butyl 2-(4-Dimethylaminophenyl)malonate (Table 3, Entry 7). Method A of the above general procedure was followed using 4-bromo-*N*,*N*-dimethylaniline (203 mg, 1.01 mmol) and di-*tert*-butyl malonate (238 mg, 1.10 mmol). The reaction mixture was purified by column chromatography on silica gel (1:1 dichloromethane/hexanes) to give the desired product (299 mg, 88%) as a white solid: ^{1}H NMR ($CDCl_3$) δ 7.26−7.22 (m, 2H), 6.72−6.69 (m, 2H), 4.32 (s, 1H), 2.93 (s, 6H), 1.46 (s, 18H). ^{13}C{^{1}H} NMR ($CDCl_3$) δ 168.08, 150.15, 129.93, 121.21, 112.42, 81.53, 59.19, 40.54, 27.91. Anal. Calcd for $C_{19}H_{29}NO_4$: C, 68.03; H, 8.71; N, 4.18. Found: C, 68.04: H, 8.82: N, 4.04.

Di-*tert*-butyl 2-(4-Trifluoromethylphenyl)malonate (Table 3, Entry 10). Method B of the above general procedure was followed using 4-chlorobenzotrifluoride (143 mg, 1.00 mmol), di-*tert*-butyl malonate (238 mg, 1.10 mmol), and $[Pd(allyl)Cl]_2$ (3.7 mg, 0.010 mmol). The reaction mixture was purified by column chromatography on silica gel (1:2 dichloromethane/hexanes) to give the desired product (255 mg, 83%) as a white solid: ^{1}H NMR ($CDCl_3$) δ 7.62 (d, 8.2 Hz, 2H), 7.53 (d, 8.2 Hz, 2H), 4.51 (s, 1H), 1.47 (s, 18H). ^{13}C{^{1}H} NMR ($CDCl_3$) δ 166.82, 137.40, 130.14 (q, 32.5 Hz), 129.86, 125.36

(q, 3.5 Hz), 124.12 (q, 272.1 Hz), 82.37, 59.85, 27.85. Anal. Calcd for $C_{18}H_{23}F_3O_4$: C, 59.99; H, 6.43. Found: C, 59.99: H, 6.46.

Di-*tert*-butyl 2-(2,5-Dimethylphenyl)malonate (Table 3, Entry 12). Method B of the above general procedure was followed using 4-chloro-*p*-xylene (142 mg, 1.01 mmol), di-*tert*-butyl malonate (238 mg, 1.10 mmol), and $Pd(dba)_2$ (11.5 mg, 0.0200 mmol). The reaction mixture was purified by column chromatography on silica gel (1:2 dichloromethane/hexanes) to give the desired product (285 mg, 88%) as a white solid: ^{1}H NMR ($CDCl_3$) δ 7.20 (s, 1H), 7.05 (d, 8.0 Hz, 1H), 7.00 (d, 7.6 Hz, 1H), 4.66 (s, 1H), 2.31 (s, 3H), 2.26 (s, 3H), 1.48 (s, 18H). ^{13}C{^{1}H} NMR ($CDCl_3$) δ 167.80, 135.44, 133.28, 132.15, 130.19, 129.18, 128.47, 81.83, 56.31, 27.91, 21.11, 19.31. Anal. Calcd for $C_{19}H_{28}O_4$: C, 71.22; H, 8.81. Found: C, 71.21: H, 8.89.

General Procedure for the Arylation of Diethyl 2-Fluoromalonate (Table 4). Into a screw-capped vial containing diethyl 2-fluoromalonate (1.1 mmol) was added tetrahydrofuran (1.0 mL), followed by NaH (1.1 mmol). After complete evolution of hydrogen (ca. 2 min), aryl bromide (1.0 mmol), P(*t*-Bu)$_3$ (0.040 mmol), $Pd(dba)_2$ (0.020 mmol), and tetrahydrofuran (2.0 mL) were added. The vial was sealed with a cap containing a PTFE septum and removed from the drybox. The homogeneous reaction mixture was stirred at 70 °C and monitored by GC. After complete conversion of the aryl halide, the crude reaction was filtered through a plug of Celite and concentrated in vacuo. The residue was purified by chromatography on silica gel (1:2 dichloromethane/hexanes).

Diethyl 2-Fluoro-2-phenylmalonate (Table 4, Entry 1).[35] The above general procedure was followed using bromobenzene (157 mg, 1.00 mmol) and diethyl fluoromalonate (196 mg, 1.10 mmol). The reaction mixture was purified by column chromatography on silica gel (1:2 dichloromethane/hexanes) to give the desired product (219 mg, 86%) as a colorless oil: ^{1}H NMR ($CDCl_3$) δ 7.61−7.58 (m, 2H), 7.43−7.41 (m, 3H), 4.34 (q, 7.2 Hz, 4H), 1.32 (t, 7.62 Hz, 6H). ^{13}C{^{1}H} NMR ($CDCl_3$) δ 165.60 (d, 25.8 Hz), 133.13 (d, 22.0 Hz), 129.42 (d, 1.2 Hz), 128.30 (d, 1.1 Hz), 125.65 (d, 8.8 Hz), 94.05 (d, 200.1 Hz), 63.02, 13.92.

Diethyl 2-Fluoro-2-(4-methoxyphenyl)malonate (Table 4, Entry 2).[82] The above general procedure was followed using 4-bromoanisole (187 mg, 1.00 mmol) and diethyl fluoromalonate (195 mg, 1.10 mmol). The reaction mixture was purified by column chromatography on silica gel (1:2 dichloromethane/hexanes) to give the desired product (244 mg, 86%) as a colorless oil: ^{1}H NMR ($CDCl_3$) δ 7.52−7.48 (m, 2H), 6.95−7.91 (m, 2H), 4.38−4.27 (m, 4H), 3.82 (s, 3H), 1.31 (t, 7.2 Hz, 6H). ^{13}C{^{1}H} NMR ($CDCl_3$) δ 165.85 (d, 26.1 Hz), 160.36, 127.25 (d, 8.4 Hz), 125.19 (d, 22.7 Hz), 113.71, 93.99 (d, 199.5 Hz), 62.94, 55.31, 13.95.

Diethyl 2-Fluoro-2-(4-methoxycarbonylphenyl)malonate (Table 4, Entry 3). The above general procedure was followed using methyl 4-bromobenzoate (215 mg, 1.00 mmol) and diethyl fluoromalonate (195 mg, 1.10 mmol). The reaction mixture was purified by column chromatography on silica gel (1:2 dichloromethane/hexanes) to give the desired product (262 mg, 84%) as a colorless oil: ^{1}H NMR ($CDCl_3$) δ 8.10−8.07 (m, 2H), 7.71−7.69 (m, 2H), 4.34 (q, 7.2 Hz, 4H), 3.93 (s, 3H), 1.31 (t, 7.2 Hz, 6H). ^{13}C{^{1}H} NMR ($CDCl_3$) δ 166.44, 165.07 (d, 25.6 Hz), 137.57, (d, 21.9 Hz), 131.08, 129.47 (d, 1.3 Hz), 125.77 (d, 9.2 Hz), 93.81 (d, 202.0 Hz), 63.30, 52.33, 13.91. Anal. Calcd for $C_{15}H_{17}FO_6$: C, 57.69; H, 5.49. Found: C, 57.67: H, 5.59.

Diethyl 2-Fluoro-2-(4-*tert*-butylphenyl)malonate (Table 4, Entry 4). The above general procedure was followed using 1-bromo-4-*tert*-butylbenzene (217 mg, 1.02 mmol) and diethyl fluoromalonate (196 mg, 1.10 mmol). The reaction mixture was purified by column chromatography on silica gel (1:2 dichloromethane/hexanes) to give the desired product (275 mg, 87%) as a colorless oil: ^{1}H NMR ($CDCl_3$) δ 7.52−7.49 (m, 2H), 7.44−7.41 (m, 2H), 4.38−4.27 (m, 4H), 1.32 (s, 9H), 1.32 (t, 7.2 Hz, 6H). ^{13}C{^{1}H} NMR ($CDCl_3$) δ 165.76 (d, 26.0 Hz), 152.46 (d, 1.2 Hz), 130.15 (d, 22.1 Hz), 125.45 (d, 8.4 Hz), 125.36 (d, 9.8 Hz), 94.11 (d, 199.6 Hz), 62.94, 34.66, 31.20, 13.95. Anal. Calcd for $C_{17}H_{23}FO_4$: C, 65.79; H, 7.47; F, 6.12. Found: C, 65.96: H, 7.37: F, 6.26.

Diethyl 2-Fluoro-2-(2-naphthyl)malonate (Table 4, Entry 5).[35] The above general procedure was followed using 2-bromonaphthalene (209 mg, 1.01 mmol) and diethyl fluoromalonate (195 mg, 1.10 mmol). The reaction mixture was purified by column chromatography on silica gel (1:2 dichloromethane/hexanes) to give the desired product (236 mg, 77%) as a colorless oil: ^{1}H NMR ($CDCl_3$) δ 8.09 (d, 1.6 Hz, 1H), 7.89−7.82 (m, 3H), 7.69 (dd, 8.8, 2.0 Hz, 1H), 7.54−7.48 (m, 2H), 4.34 (q, 7.2 Hz, 4H), 1.31 (t, 7.2 Hz, 6H). ^{13}C{^{1}H} NMR ($CDCl_3$) δ 165.64 (d, 25.5 Hz), 133.45, 132.56, 130.50 (d, 21.6 Hz), 128.58, 128.11 (d, 1.1 Hz), 127.61, 127.07, 126.58, 125.16 (d, 10.3 Hz), 123.06 (d, 7.3 Hz), 94.28 (d, 211.6 Hz), 63.08, 13.94.

General Procedure for the Sequential Arylation/Alkylation of Diethyl Malonate (Table 5). Into a screw-capped vial containing diethyl malonate (1.0 mmol) and aryl bromide (1.1 mmol) were added P(*t*-Bu)$_3$ (0.040 mmol), $Pd(dba)_2$ (0.020 mmol), and K_3PO_4 (4.5 mmol) followed by toluene (2.0 mL). The vial was sealed with a cap containing a PTFE septum and removed from the drybox. The heterogeneous reaction mixture was stirred at 70 °C and monitored by GC. After complete conversion of the aryl bromide, iodomethane (2.0 mmol) was injected and the thick slurry was stirred at 70 °C until all of the arylmalonate was converted. The crude reaction was filtered through a plug of Celite and concentrated in vacuo. The residue was purified by chromatography on silica gel (1:2 dichloromethane/hexanes).

Diethyl 2-Methyl-2-phenylmalonate (Table 5, Entry 1).[83] The above general procedure was followed using bromobenzene (174 mg, 1.11 mmol), diethyl malonate (161 mg, 1.01 mmol), and iodomethane (0.130 μL, 2.09 mmol). The reaction mixture was purified by column chromatography on silica gel (1:2 dichloromethane/hexanes) to give the desired product (225 mg, 89%) as a colorless oil: ^{1}H NMR ($CDCl_3$) δ 7.39−7.25 (m, 5H), 4.26−4.19 (m, 4H), 1.86 (s, 3H), 1.25 (t, 7.2 Hz, 6H). ^{13}C{^{1}H} NMR ($CDCl_3$) δ 171.54, 138.36, 128.14, 127.55, 127.42, 61.68, 58.79, 22.37, 13.97.

Diethyl 2-Methyl-2-(4-methoxyphenyl)malonate (Table 5, Entry 2).[15] The above general procedure was followed using 2-bromoanisole (213 mg, 1.14 mmol), diethyl malonate (162 mg, 1.01 mmol), and iodomethane (0.130 μL, 2.09 mmol). The reaction mixture was purified by column chromatography on silica gel (1:2 dichloromethane/hexanes) to give the desired product (257 mg, 91%) as a colorless oil: ^{1}H NMR ($CDCl_3$) δ 7.33−7.29 (m, 2H), 6.89−6.85 (m, 2H), 4.28−4.16 (m, 4H), 3.79 (s, 3H), 1.85 (s, 3H), 1.25 (t, 7.2 Hz, 6H). ^{13}C{^{1}H} NMR ($CDCl_3$) δ 171.79, 158.86, 130.23, 128.66, 113.47, 61.63, 57.98, 55.21, 22.18, 13.99.

Diethyl 2-Methyl-2-(4-trifluoromethylphenyl)malonate (Table 5, Entry 3). The above general procedure was followed using 4-bromobenzotrifluoride (174 mg, 1.11 mmol), diethyl malonate (161 mg, 1.01 mmol), and iodomethane (0.130 μL, 2.09 mmol). The reaction mixture was purified by column chromatography on silica gel (1:2 dichloromethane/hexanes) to give the desired product (289 mg, 90%) as a colorless oil: ^{1}H NMR ($CDCl_3$) δ 7.61 (d, 8.4 Hz, 2H), 7.52 (d, 8.4 Hz, 2H), 4.30−4.19 (m, 4H), 1.89 (s, 3H), 1.26 (t, 7.2 Hz, 6H). ^{13}C{^{1}H} NMR ($CDCl_3$) δ 170.95, 142.30, 129.84 (q, 32.5 Hz), 128.10, 125.13 (q, 3.7 Hz), 124.10, (q, 272.06 Hz), 62.07, 58.79, 22.28, 13.97. Anal. Calcd for $C_{15}H_{17}F_3O_4$: C, 56.60; H, 5.38. Found: C, 56.77: H, 5.27.

Diethyl 2-Methyl-2-(6-methoxynaphthalen-2-yl)malonate (Table 5, Entry 4).[26] The above general procedure was followed using 2-bromo-6-methoxynaphthalene (264 mg, 1.11 mmol), diethyl malonate (162 mg, 1.01 mmol), and iodomethane (0.130 μL, 2.09 mmol). The reaction mixture was purified by column chromatography on silica gel (1:2 dichloromethane/hexanes) to give the desired product (301 mg, 90%) as a colorless oil: ^{1}H NMR ($CDCl_3$) δ 7.72−7.70 (m, 3H), 7.48 (dd, 8.8, 2.0 Hz, 1H), 7.14 (dd, 9.0, 2.4 Hz, 1H), 7.11 (d, 2.4

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Hz, 1H), 4.31−4.19 (m, 4H), 3.91 (s, 3H), 1.96 (s, 3H), 1.26 (t, 7.2 Hz, 6H). $^{13}C\{^1H\}$ NMR ($CDCl_3$) δ 171.70, 157.99, 133.76, 133.44, 129.74, 128.40, 126.67, 126.50, 125.65, 118.88, 105.38, 61.72, 58.70, 55.31, 22.25, 14.01.

General Procedure for the Arylation of Ethyl Cyanoacetate (Table 6). Method A: Into a screw-capped vial containing ethyl cyanoacetate (1.1 mmol) and aryl bromide (1.0 mmol) were added phosphine (0.040 mmol), $Pd(dba)_2$ (0.020 mmol) or $[Pd(allyl)Cl]_2$ (0.010 mmol), and Na_3PO_4 (3.0 mmol), followed by toluene (3.0 mL). The vial was sealed with a cap containing a PTFE septum and removed from the drybox. The heterogeneous reaction mixture was stirred at 70 °C and monitored by GC. After complete conversion of the aryl bromide, the crude reaction was filtered through a plug of Celite and concentrated in vacuo. The residue was purified by chromatography on silica gel (1:3 dichloromethane/hexanes).

Method B: Into a screw-capped vial containing ethyl cyanoacetate (1.1 mmol) and aryl chloride (1.0 mmol) were added P(*t*-Bu)$_3$ (0.040 mmol), $[Pd(allyl)Cl]_2$ (0.010 mmol), and Na_3PO_4 (3.0 mmol), followed by toluene (3.0 mL). The vial was sealed with a cap containing a PTFE septum and removed from the drybox. The heterogeneous reaction mixture was stirred at 100 °C and monitored by GC. After complete conversion of the aryl chloride, the crude reaction was filtered through a plug of Celite and concentrated in vacuo. The residue was purified by chromatography on silica gel (1:3 dichloromethane/hexanes).

Ethyl 2-(2-Methylphenyl)cyanoacetate (Table 6, Entry 1).[84] Method A of the above general procedure was followed using 2-bromotoluene (172 mg, 1.00 mmol), ethyl cyanoacetate (125 mg, 1.11 mmol), P(*t*-Bu)$_3$ (40 μL, 1.0 M in toluene, 0.040 mmol), and $[Pd(allyl)Cl]_2$ (3.7 mg, 0.010 mmol). The reaction mixture was purified by column chromatography on silica gel (1:3 dichloromethane/hexanes) to give the desired product (180 mg, 88%) as a colorless oil: ^1H NMR ($CDCl_3$) δ 7.47−7.45 (m, 1H), 7.32−7.22 (m, 3H), 4.89 (s, 1H), 4.31−4.19 (m, 2H), 2.40 (s, 3H), 1.28 (t, 7.2 Hz, 3H). $^{13}C\{^1H\}$ NMR ($CDCl_3$) δ 165.03, 136.23, 131.24, 129.34, 128.93, 128.62, 127.05, 115.90, 63.25, 41.06, 19.42, 13.92.

Ethyl 2-(4-Phenoxyphenyl)cyanoacetate (Table 6, Entry 2). Method A of the above general procedure was followed using 4-bromobiphenyl ether (250 mg, 1.00 mmol), ethyl cyanoacetate (125 mg, 1.10 mmol), P(*t*-Bu)$_3$ (40 μL, 1.0 M in toluene, 0.040 mmol), and $Pd(dba)_2$ (11.5 mg, 0.0200 mmol). The reaction mixture was purified by column chromatography on silica gel (1:3 dichloromethane/hexanes) to give the desired product (247 mg, 88%) as a colorless oil: ^1H NMR ($CDCl_3$) δ 7.42−7.34 (m, 4H), 7.17−7.13 (m, 1H), 7.05−6.99 (m, 4H), 4.69 (s, 1H), 4.31−4.20 (m, 2H), 1.29 (t, 7.2 Hz, 3H). $^{13}C\{^1H\}$ NMR ($CDCl_3$) δ 165.06, 158.41, 156.17, 129.95, 129.42, 124.18, 124.07, 119.55, 118.91, 115.74, 63.34, 43.00, 13.91. Anal. Calcd for $C_{17}H_{15}NO_3$: C, 72.58; H, 5.37; N, 4.98. Found: C, 72.80: H, 5.37: N, 4.93.

Ethyl 2-(3-Trifluoromethylphenyl)cyanoacetate (Table 6, Entry 3).[85] Method A of the above general procedure was followed using 3-bromobenzotrifluoride (225 mg, 1.00 mmol), ethyl cyanoacetate (124 mg, 1.10 mmol), P(t-Bu)$_3$ (40 μL, 1.0 M in toluene, 0.040 mmol), and $Pd(dba)_2$ (11.5 mg, 0.0200 mmol). The reaction mixture was purified by column chromatography on silica gel (1:3 dichloromethane/hexanes) to give the desired product (211 mg, 82%) as a colorless oil: ^1H NMR ($CDCl_3$) δ 7.73−7.68 (m, 3H), 7.60−7.56 (m, 1H), 4.79 (s, 1H), 4.31−4.24 (m, 2H), 1.30 (t, 7.2 Hz, 3H). $^{13}C\{^1H\}$ NMR ($CDCl_3$) δ 164.36, 131.91 (q, 33.0 Hz), 131.46, 131.04, 130.05, 126.27 (q, 4.1 Hz), 124.99 (q, 3.9 Hz), 123.59 (q, 273.3 Hz), 115.09, 63.80, 43.46, 13.88.

Ethyl 2-(4-Trifluoromethylphenyl)cyanoacetate (Table 6, Entry 4).[86] Method A of the above general procedure was followed using 4-bromobenzotrifluoride (226 mg, 1.01 mmol), ethyl cyanoacetate (123 mg, 1.09 mmol), ligand **7** (14 mg, 0.020 mmol), and $Pd(dba)_2$ (6.0 mg, 0.010 mmol). The reaction mixture was purified by column chromatography on silica gel (1:3 dichloromethane/hexanes) to give the desired product (213 mg, 82%) as a colorless oil: ^1H NMR ($CDCl_3$) δ 7.71−7.69 (m, 2H), 7.63−7.60 (m, 2H), 4.80 (s, 1H), 4.27 (dq, 7.2, 1.2 Hz, 2H), 1.30 (t, 7.2 Hz, 3H). $^{13}C\{^1H\}$ NMR ($CDCl_3$) δ 164.28, 133.81, 131.66 (q, 33.0 Hz), 128.55, 126.38 (q, 3.7 Hz), 123.68 (q, 272.3 Hz), 115.00, 63.78, 43.52, 13.89.

Ethyl 2-(4-Biphenyl)cyanoacetate (Table 6, Entry 5).[87] Method A of the above general procedure was followed using 4-bromobiphenyl (233 mg, 1.00 mmol), ethyl cyanoacetate (124 mg, 1.10 mmol), ligand **7** (28 mg, 0.040 mmol), and $Pd(dba)_2$ (11.6 mg, 0.0200 mmol). The reaction mixture was purified by column chromatography on silica gel (1:3 dichloromethane/hexanes) to give the desired product (234 mg, 88%) as a colorless oil: ^1H NMR ($CDCl_3$) δ 7.64−7.62 (m, 2H), 7.58−7.56 (m, 2H), 7.54−7.52 (m, 2H), 7.46−7.43 (m, 2H), 7.39−7.35 (m, 1H), 4.76 (s, 1H), 4.31−4.20 (m, 2H), 1.29 (t, 7.2 Hz, 3H). $^{13}C\{^1H\}$ NMR ($CDCl_3$) δ 164.98, 142.19, 139.91, 128.91, 128.83, 128.33, 127.99, 127.84, 127.12, 115.68, 63.40, 43.40, 13.91.

Ethyl 2-(2-Naphthyl)cyanoacetate (Table 6, Entry 6).[6] Method A of the above general procedure was followed using 2-bromonaphthalene (208 mg, 1.00 mmol), ethyl cyanoacetate (123 mg, 1.09 mmol), ligand **8** (6.0 mg, 0.020 mmol), and $Pd(dba)_2$ (6.0 mg, 0.010 mmol). The reaction mixture was purified by column chromatography on silica gel (1:3 dichloromethane/hexanes) to give the desired product (214 mg, 89%) as a colorless oil: ^1H NMR ($CDCl_3$) δ 7.94 (s, 1H), 7.89−7.82 (m, 3H), 7.55−7.50 (m, 3H), 4.88 (s, 1H), 4.29−4.20 (m, 2H), 1.26 (t, 7.2 Hz, 3H). $^{13}C\{^1H\}$ NMR ($CDCl_3$) δ 165.00, 133.21, 133.16, 129.35, 128.07, 127.76, 127.51, 127.21, 127.08, 126.96, 124.81, 115.75, 63.38, 43.90, 13.89.

Ethyl 2-Phenylcyanoacetate (Table 6, Entry 7).[84] Method B of the above general procedure was followed using 4-chlorobenzene (112 mg, 1.00 mmol) and ethyl cyanoacetate (124 mg, 1.10 mmol). The reaction mixture was purified by column chromatography on silica gel (1:3 dichloromethane/hexanes) to give the desired product (162 mg, 86%) as a colorless oil: ^1H NMR ($CDCl_3$) δ 7.49−7.42 (m, 5H), 4.73 (s, 1H), 4.29−4.21 (m, 2H), 1.29 (t, 7.2 Hz, 3H). $^{13}C\{^1H\}$ NMR ($CDCl_3$) δ 165.00, 129.97, 129.34, 129.23, 127.91, 115.70, 63.32, 43.73, 13.88.

Ethyl 2-(4-Fluorophenyl)cyanoacetate (Table 6, Entry 9).[84] Method B of the above general procedure was followed using 4-chlorobenzotrifluoride (131 mg, 1.01 mmol) and ethyl cyanoacetate (125 mg, 1.11 mmol). The reaction mixture was purified by column chromatography on silica gel (1:3 dichloromethane/hexanes) to give the desired product (172 mg, 83%) as a colorless oil: ^1H NMR ($CDCl_3$) δ 7.48−7.43 (m, 2H), 7.15−7.09 (m, 2H), 4.70 (s, 1H), 4.31−4.20 (m, 2H), 1.29 (t, 6.8 Hz, 3H). $^{13}C\{^1H\}$ NMR ($CDCl_3$) δ 165.00, 163.21 (d, 249.1 Hz), 130.01 (d, 8.4 Hz), 125.94, 116.64 (d, 21.9 Hz), 115.67, 64.00, 43.20, 14.11.

Ethyl 2-(2,5-Dimethylphenyl)cyanoacetate (Table 6, Entry 10).[10] Method B of the above general procedure was followed using 4-chloro-*p*-xylene (141 mg, 1.00 mmol) and ethyl cyanoacetate (124 mg, 1.10 mmol). The reaction mixture was purified by column chromatography on silica gel (1:3 dichloromethane/hexanes) to give the desired product (190 mg, 87%) as a colorless oil: ^1H NMR ($CDCl_3$) δ 7.27 (s, 1H), 7.12−7.07 (m, 2H), 4.85 (s, 1H), 4.31−4.18 (m, 2H), 2.34 (s, 3H), 2.33 (s, 3H), 1.28 (t, 7.2 Hz, 3H). $^{13}C\{^1H\}$ NMR ($CDCl_3$) δ 165.17, 136.74, 133.0, 131.10, 130.06, 129.13, 128.63, 116.05, 63.19, 40.98, 20.88, 18.93, 13.92.

Ethyl 2-(3,4-Methylenedioxyphenyl)cyanoacetate (Table 6, Entry 11). Method B of the above general procedure was followed using 4-chloro-1,2-(methylenedioxy)benzene (157 mg, 1.00 mmol) and ethyl cyanoacetate (124 mg, 1.10 mmol). The reaction mixture was purified by column chromatography on silica gel (1:3 dichloromethane/hexanes) to give the desired

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product (191 mg, 82%) as a colorless oil: ^{1}H NMR ($CDCl_3$) δ 6.93−6.90 (m, 2H), 6.83−6.80 (m, 1H), 6.00 (s, 2H), 4.62 (s, 1H), 4.30−4.19 (m, 2H), 1.29 (t, 7.2 Hz, 3H). ^{13}C{^{1}H} NMR ($CDCl_3$) δ 165.07, 148.46, 148.44, 123.33, 121.76, 115.75, 108.79, 108.25, 101.68, 63.34, 43.31, 13.92. Anal. Calcd for $C_{12}H_{11}NO_4$: C, 61.80; H, 4.75; N, 6.01. Found: C, 62.08: H, 4.62: N, 6.13.

Ethyl 2-(2-Methoxyphenyl)cyanoacetate (Table 6, Entry 12).[84] Method B of the above general procedure was followed using 2-chloroanisole (143 mg, 1.01 mmol) and ethyl cyanoacetate (125 mg, 1.11 mmol). The reaction mixture was purified by column chromatography on silica gel (1:3 dichloromethane/hexanes) to give the desired product (191.4 mg, 87%) as a colorless oil: ^{1}H NMR ($CDCl_3$) δ 7.40−7.35 (m, 2H), 7.03−6.99 (m, 1H), 6.93 (d, 8.0 Hz, 1H), 5.03 (s, 1H), 4.30−4.22 (m, 2H), 3.86 (s, 3H), 1.29 (t, 7.2 Hz, 3H). ^{13}C{^{1}H} NMR ($CDCl_3$) δ 165.19, 156.48, 130.73, 129.44, 121.11, 119.11, 115.92, 111.12, 62.97, 55.72, 38.18, 13.97.

Ethyl 2,2-(Bis-4-trifluoromethylphenyl)cyanoacetate (Table 6, Entry 1). Into a screw-capped vial containing ethyl cyanoacetate (57 mg, 0.50 mmol) and 4-bromobenzotrifluoride (248 mg, 1.10 mmol) were added P(*t*-Bu)$_3$ (40 μL, 1.0 M in toluene, 0.040 mmol), Pd(dba)$_2$ (11.5 mg, 0.0200 mmol), and Na_3PO_4 (500 mg, 3.05 mmol), followed by toluene (3.00 mL). The vial was sealed with a cap containing a PTFE septum and removed from the drybox. The heterogeneous reaction mixture was stirred at 70 °C until GC analysis indicated the reaction was complete (12 h). After this time, the crude reaction was filtered through a plug of Celite and concentrated in vacuo. The residue was purified by chromatography on silica gel (1:2 dichloromethane/hexanes) to give the product (192 mg, 96%) as a colorless oil: ^{1}H NMR ($CDCl_3$) δ 7.71−7.69 (m, 4H), 7.56−7.53 (m, 4H), 4.40 (q, 7.2 Hz, 2H), 1.35 (t, 7.2 Hz, 3H). ^{13}C-{^{1}H} NMR ($CDCl_3$) δ 165.98, 138.90, 131.62 (q, 33.1 Hz), 128.48, 126.22 (q, 3.5 Hz), 123.53 (q, 272.4 Hz), 117.46, 64.50, 58.24, 13.87. Anal. Calcd for $C_{19}H_{13}F_6NO_2$: C, 56.87; H, 3.27; N, 3.49. Found: C, 56.95: H, 3.41: N, 3.62.

Ethyl 2,2-(Bis-4-methoxyphenyl)cyanoacetate (Table 6, Entry 2). Into a screw-capped vial containing ethyl cyanoacetate (60 mg, 0.53 mmol) and 4-bromoanisole (215 mg, 1.15 mmol) were added P(*t*-Bu)$_3$ (40 μL, 1.0 M in toluene, 0.040 mmol), Pd(dba)$_2$ (11.5 mg, 0.0200 mmol), and Na_3PO_4 (496 mg, 3.02 mmol), followed by toluene (3.00 mL). The vial was sealed with a cap containing a PTFE septum and removed from the drybox. The heterogeneous reaction mixture was stirred at 70 °C until GC analysis indicated the reaction was complete (12 h). After this time, the crude reaction was filtered through a plug of Celite and concentrated in vacuo. The residue was purified by chromatography on silica gel (1:2 dichloromethane/hexanes) to give the product (167.0 mg, 97%) as a colorless oil: ^{1}H NMR ($CDCl_3$) δ 7.32−7.29 (m, 4H), 6.92−6.88 (m, 4H), 4.33 (q, 7.2 Hz, 2H), 3.81 (s, 6H), 1.31 (t, 7.2 Hz, 3H). ^{13}C{^{1}H} NMR ($CDCl_3$) δ 167.69, 159.80, 129.18, 128.02, 119.08, 114.19, 63.53, 57.46, 55.35, 13.92. Anal. Calcd for $C_{19}H_{19}NO_4$: C, 70.14; H, 5.89; N, 4.31. Found: C, 70.36: H, 5.98: N, 4.30.

General Procedure for the Arylation of Ethyl Arylcyanoacetates (Table 7). Into a screw-capped vial containing ethyl arylcyanoacetate (1.0 mmol) and aryl bromide (1.1 mmol) were added P(*t*-Bu)$_3$ (0.040 mmol), Pd(dba)$_2$ (0.020 mmol), and Na_3PO_4 (3.0 mmol), followed by toluene (3.0 mL). The vial was sealed with a cap containing a PTFE septum and removed from the drybox. The heterogeneous reaction mixture was stirred at 70 °C and monitored by GC. After complete conversion of the ethyl arylcyanoacetate, the crude reaction was filtered through a plug of Celite and concentrated in vacuo. The residue was purified by chromatography on silica gel (1:2 dichloromethane/hexanes).

Ethyl 2-Phenyl-2-(4-trifluoromethylphenyl)cyanoacetate (Table 7, Entry 3). The above general procedure was followed using 4-bromobenzotrifluoride (249 mg, 1.10 mmol) and ethyl 2-phenylcyanoacetate (188 mg, 0.990 mmol). The reaction mixture was purified by column chromatography on silica gel (1:2 dichloromethane/hexanes) to give the desired product (308.1 mg, 93%) as a colorless oil: ^{1}H NMR ($CDCl_3$) δ 7.70−7.66 (m, 2H), 7.59−7.56 (m, 2H), 7.47−7.40 (m, 5H), 4.39 (q, 7.2 Hz, 2H), 1.35 (t, 7.2 Hz, 3H). ^{13}C{^{1}H} NMR ($CDCl_3$) δ 166.73, 139.91, 135.23, 131.01 (q, 32.9 Hz), 129.48, 129.41, 128.82, 127.94, 126.30 (q, 3.8 Hz), 123.84 (q, 272.4 Hz), 118.28, 64.27, 58.71, 14.02. Anal. Calcd for $C_{18}H_{14}F_3NO_2$: C, 64.86; H, 4.23; F, 17.10; N, 4.20. Found: C, 65.04: H, 4.28: F, 17.35: N, 4.27.

Ethyl 2-Phenyl-2-(4-methoxyphenyl)cyanoacetate (Table 7, Entry 4).[88] The above general procedure was followed using 4-bromoanisole (207 mg, 1.10 mmol) and ethyl 2-phenylcyanoacetate (190 mg, 1.01 mmol). The reaction mixture was purified by column chromatography on silica gel (1:2 dichloromethane/hexanes) to give the desired product (288 mg, 97%) as a colorless oil: ^{1}H NMR ($CDCl_3$) δ 7.41−7.36 (m, 5H), 7.33−7.29 (m, 2H), 6.92−6.89 (m, 2H), 4.36−4.31 (m, 2H), 3.80 (s, 3H), 1.31 (t, 7.2 Hz, 3H). ^{13}C{^{1}H} NMR ($CDCl_3$) δ 167.42, 159.84, 136.10, 129.26, 128.91, 128.86, 127.88, 127.70, 63.61, 58.11, 55.34, 13.89.

Ethyl 2-(4-Benzoylphenyl)-2-phenylcyanoacetate (Table 7, Entry 5). The above general procedure was followed using 4-bromobenzophenone (289 mg, 1.11 mmol) and ethyl 2-phenylcyanoacetate (189 mg, 1.00 mmol). The reaction mixture was purified by column chromatography on silica gel (2:1 dichloromethane/hexanes) to give the desired product (335 mg, 91%) as a colorless oil: ^{1}H NMR ($CDCl_3$) δ 7.84−7.80 (m, 4H), 7.62−7.58 (m, 1H), 7.56−7.53 (m, 2H), 7.51−7.46 (m, 2H), 7.45−7.40 (m, 5H), 4.38 (q, 7.2 Hz, 2H), 1.34 (t, 7.2 Hz, 3H). ^{13}C{^{1}H} NMR ($CDCl_3$) δ 195.69, 166.65, 139.88, 137.97, 136.97, 135.17, 132.82, 130.43, 130.05, 129.22, 129.16, 128.42, 128.12, 127.84, 118.23, 64.00, 56.69, 13.89. Anal. Calcd for $C_{24}H_{19}NO_3$: C, 78.03; H, 5.18; N, 3.79. Found: C, 77.66: H, 5.28: N, 3.65.

Ethyl 2-(4-Biphenyl)-2-phenylcyanoacetate (Table 7, Entry 6). The above general procedure was followed using 4-bromobiphenyl (256 mg, 1.10 mmol) and ethyl 2-phenylcyanoacetate (189 mg, 1.00 mmol). The reaction mixture was purified by column chromatography on silica gel (1:2 dichloromethane/hexanes) to give the desired product (307 mg, 90%) as a colorless oil: ^{1}H NMR ($CDCl_3$) δ 7.62−7.55 (m, 4H), 7.49−7.32 (m, 10H), 4.35 (q, 7.2 Hz, 2H), 1.31 (t, 7.2 Hz, 3H). ^{13}C-{^{1}H} NMR ($CDCl_3$) δ 167.15, 141.79, 139.86, 135.76, 134.70, 128.98, 128.97, 128.87, 128.41, 128.20, 127.93, 127.55, 127.10, 118.69, 63.74, 58.51, 13.88. Anal. Calcd for $C_{23}H_{19}NO_2$: C, 80.92; H, 5.61; N, 4.10. Found: C, 80.87: H, 5.82: N, 4.21.

Ethyl 2-(4-Acetylphenyl)-2-phenylcyanoacetate (Table 7, Entry 7). The above general procedure was followed using 4-bromoacetophenone (259 mg, 1.30 mmol) and ethyl 2-phenylcyanoacetate (223 mg, 1.18 mmol). The reaction mixture was purified by column chromatography on silica gel (2:1 dichloromethane/hexanes) to give the desired product (341 mg, 94%) as a colorless oil: ^{1}H NMR ($CDCl_3$) δ 8.00−7.97 (m, 2H), 7.54−7.51 (m, 2H), 7.43−7.38 (m, 5H), 4.37 (q, 7.2 Hz, 2H), 2.61 (s, 3H), 1.33 (t, 7.2 Hz, 3H). ^{13}C{^{1}H} NMR ($CDCl_3$) δ 197.18, 166.59, 140.55, 137.27, 135.16, 129.22, 129.16, 128.79, 128.41, 127.80, 118.17, 64.00, 58.65, 26.72, 13.87. Anal. Calcd for $C_{19}H_{17}NO_3$: C, 74.25; H, 5.58; N, 4.56. Found: C, 74.46: H, 5.44: N, 4.58.

Ethyl 2-[3-(1,3-Dioxolane)phenyl]-2-phenylcyanoacetate (Table 7, Entry 8). The above general procedure was followed using 2-(3-bromophenyl)-1,3-dioxolane (260 mg, 1.13 mmol) and ethyl 2-phenylcyanoacetate (189 mg, 1.00 mmol). The reaction mixture was purified by column chromatography on silica gel (2:1 dichloromethane/hexanes) to give the desired product (311 mg, 92%) as a colorless oil: ^{1}H NMR ($CDCl_3$) δ 7.57−7.56 (m, 1H), 7.53−7.50 (m, 1H), 7.43−7.36 (m, 7H), 5.79 (s, 1H), 4.34 (q, 7.2 Hz, 2H), 4.10−3.98 (m, 4H), 1.30 (t, 7.2 Hz, 3H). ^{13}C{^{1}H} NMR ($CDCl_3$) δ 166.98, 139.00, 135.83, 135.80, 129.02, 128.95, 128.87, 127.97, 127.12, 126.15, 118.57, 103.13, 65.32, 63.75, 58.75, 13.85. Anal. Calcd for $C_{20}H_{19}NO_4$: C, 71.20; H, 5.68; N, 4.15. Found: C, 70.91: H, 5.59: N, 4.00.

Ethyl 2-(4-Carbomethoxyphenyl)-2-phenylcyanoacetate (Table 7, Entry 9). The above general procedure was followed using methyl 4-bromobenzoate (239 mg, 1.11 mmol)

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and ethyl 2-phenylcyanoacetate (193 mg, 1.02 mmol). The reaction mixture was purified by column chromatography on silica gel (2:1 dichloromethane/hexanes) to give the desired product (307 mg, 93%) as a colorless oil: ^{1}H NMR ($CDCl_3$) δ 8.08−8.06 (m, 2H), 7.52−7.49 (m, 2H), 7.42−7.38 (m, 5H), 4.37 (q, 7.2 Hz, 2H), 3.92 (s, 3H), 1.32 (t, 7.2 Hz, 3H). ^{13}C{^{1}H} NMR ($CDCl_3$) δ 166.62, 166.19, 140.45, 135.23, 130.72, 130.09, 129.20, 129.14, 128.20, 127.84, 118.22, 63.97, 56.69, 52.36, 13.87. Anal. Calcd for $C_{19}H_{17}NO_4$: C, 70.58; H, 5.30; N, 4.33. Found: C, 70.46: H, 5.40: N, 4.49.

Ethyl 2-(4-Fluorophenyl)-2-phenylcyanoacetate (Table 7, Entry 10). The above general procedure was followed using 4-bromofluorobenzene (193 mg, 1.10 mmol) and ethyl 2-phenylcyanoacetate (191 mg, 1.00 mmol). The reaction mixture was purified by column chromatography on silica gel (1:2 dichloromethane/hexanes) to give the desired product (257 mg, 90%) as a colorless oil: ^{1}H NMR ($CDCl_3$) δ 7.42−7.36 (m, 7H), 7.10−7.04 (m, 2H), 4.35 (q, 7.2 Hz, 2H), 1.31 (t, 7.2 Hz, 3H). ^{13}C-{^{1}H} NMR ($CDCl_3$) δ 167.05, 162.80 (d, 249.4 Hz), 135.68, 131.79, 131.76, 130.03 (d, 8.5 Hz), 129.09, 127.81, 118.56, 115.91 (d, 21.9 Hz), 63.82, 58.14, 13.87. Anal. Calcd for $C_{17}H_{14}FNO_2$: C, 72.07; H, 4.98; N, 4.94. Found: C, 72.18: H, 5.06: N, 4.88.

Ethyl 2,2-Diphenylcyanoacetate (Table 7, Entry 11).[89] The above general procedure was followed using chlorobenzene (124 mg, 1.10 mmol) and ethyl 2-phenylcyanoacetate (191 mg, 1.01 mmol) at 100 °C. The reaction mixture was purified by column chromatography on silica gel (1:2 dichloromethane/hexanes) to give the desired product (233 mg, 87%) as a colorless oil which solidified on standing: ^{1}H NMR ($CDCl_3$) δ 7.41−7.37 (m, 10H), 4.35 (q, J = 6.8 Hz, 2H), 1.31 (t, J = 6.8 Hz, 3H). ^{13}C{^{1}H} NMR (d_4-MeOD) δ 168.54, 137.51, 130.23, 130.20, 129.18, 120.03, 64.94, 60.42, 14.29.

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Ethyl 2-(4-Methoxyphenyl)-2-(4-trifluoromethylphenyl)cyanoacetate (Table 7, Entry 13). The above general procedure was followed using 4-bromobenzotrifluoride (248 mg, 1.10 mmol) and ethyl 2-(4-methoxy)phenylcyanoacetate (221 mg, 1.00 mmol). The reaction mixture was purified by column chromatography on silica gel (1:2 dichloromethane/hexanes) to give the desired product (333 mg, 91%) as a colorless oil: ^{1}H NMR ($CDCl_3$) δ 7.66 (d, 8.4 Hz, 2H), 7.55 (d, 8.4 Hz, 2H), 7.33−7.29 (m, 2H), 6.95−6.92 (m, 2H), 4.36 (q, 7.2 Hz, 2H), 3.82 (s, 3H), 1.32 (t, 7.2 Hz, 3H). ^{13}C{^{1}H} NMR ($CDCl_3$) δ 166.85, 160.15, 140.14, 131.13 (q, 33.0 Hz), 129.13, 128.60, 126.92, 125.89 (q, 3.5 Hz), 123.72 (q, 272.3 Hz), 118.31, 114.54, 64.02, 57.92, 55.41, 13.89. Anal. Calcd for $C_{19}H_{16}F_3NO_3$: C, 62.81; H, 4.44; N, 3.86. Found: C, 62.92: H, 4.45: N, 3.79.

Ethyl 2-(4-Methoxyphenyl)-2-(2-naphthyl)cyanoacetate (Table 7, Entry 15). The above general procedure was followed using 2-bromonaphthalene (239 mg, 1.15 mmol) and ethyl 2-(4-methoxy)phenylcyanoacetate (221 mg, 1.01 mmol). The reaction mixture was purified by column chromatography on silica gel (1:2 dichloromethane/hexanes) to give the desired product (310 mg, 89%) as a colorless oil: ^{1}H NMR ($CDCl_3$) δ 7.92 (d, 1.6 Hz, 1H), 7.86−7.81 (m, 3H), 7.55−7.48 (m, 2H), 7.45 (dd, 8.8, 2.0 Hz, 1H), 7.36−7.32 (m, 2H), 6.93−6.89 (m, 2H), 4.36 (q, 7.2 Hz, 2H), 3.80 (s, 3H), 1.32 (t, 7.2 Hz, 3H). ^{13}C{^{1}H} NMR ($CDCl_3$) δ 167.41, 159.89, 133.22, 133.00, 132.83, 129.36, 128.89, 128.40, 127.70, 127.60, 127.23, 127.15, 126.82, 125.19, 118.89, 114.28, 63.67, 58.26, 55.35, 13.92. Anal. Calcd for $C_{22}H_{19}NO_3$: C, 76.50; H, 5.54; N, 4.06. Found: C, 76.26: H, 5.67: N, 4.07.

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