Palladium-catalyzed Enolate Arylation as a Key C-C Bond-forming Reaction for the Synthesis of Isoquinolines

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2. $^1$H and $^{13}$C Spectra of all compounds in the experimental

2-(2-(1,3-Dioxolan-2-yl)phenyl)-1-(4-methoxyphenyl)ethanone (3d)
2-(2-(1,3-Dioxolan-2-yl)phenyl)-1-(4-methoxyphenyl)ethanone (3d)
2-(2-(1,3-Dioxolan-2-yl)phenyl)-1-(3,5-bis(trifluoromethyl)phenyl)ethan-1-one (3e)
2-(2-(1,3-Dioxolan-2-yl)phenyl)-1-(3,5-bis(trifluoromethyl)phenyl)ethan-1-one (3e)
2-(2-(2-Methyl-1,3-dioxolan-2-yl)phenyl)-1-phenylethan-1-one (3g)
2-(2-(2-Methyl-1,3-dioxolan-2-yl)phenyl)-1-phenylethan-1-one (3g)
2-(2-(1,3-Dioxolan-2-yl)phenyl)-4-(tert-butyl)cyclohexan-1-one (3m)
2-(2-(1,3-Dioxolan-2-yl)phenyl)-4-(tert-butyl)cyclohexan-1-one (3m)
1-(2-(1,3-Dioxolan-2-yl)phenyl)-1-(4-methoxyphenyl)propan-2-one (3p)
1-(2-(1,3-Dioxolan-2-yl)phenyl)-1-(4-methoxyphenyl)propan-2-one (3p)
5-Methyl-1-phenylhexan-3-ol (S1)
5-Methyl-1-phenylhexan-3-ol (S1)
5-Methyl-1-phenylhexan-3-one (2n)
5-Methyl-1-phenylhexan-3-one (2n)
2-(2-(1,3-Dioxolan-2-yl)phenyl)-5-methyl-1-phenylhexan-3-one (3q)
2-(2-(1,3-Dioxolan-2-yl)phenyl)-5-methyl-1-phenylhexan-3-one (3q)
2-(2-(1,3-Dioxolan-2-yl)-4,5-dimethoxyphenyl)-1-phenylethanone (3s)
2-(2-(1,3-Dioxolan-2-yl)-4,5-dimethoxyphenyl)-1-phenylethan-1-one (3s)
2-(2-(1,3-Dioxolan-2-yl)-4-fluorophenyl)-1-phenylethanone (3y)
2-(2-(1,3-Dioxolan-2-yl)-4-fluorophenyl)-1-phenylethanone (3y)

Chemical Shift (ppm)
4-Methyl-3-phenylisoquinoline (4a)
4-Methyl-3-phenylisoquinoline (4a)
1,4-Dimethyl-3-phenylisoquinoline (4b)
1,4-Dimethyl-3-phenylisoquinoline (4b)
3-(4-Methoxyphenyl)isoquinoline (4d)
3-(4-Methoxyphenyl)isoquinoline (4d)
3-(3,5-Bis(trifluoromethyl)phenyl)isoquinoline (4e)
3-(3,5-Bis(trifluoromethyl)phenyl)isoquinoline (4e)
1-Methyl-3-phenylisoquinoline (4g)
1-Methyl-3-phenylisoquinoline (4g)
4-Methoxy-3-phenylisoquinoline (4i)
4-Methoxy-3-phenylisoquinoline (4i)
2-(tert-Butyl)-1,2,3,4-tetrahydrophenanthridine (4m)
2-(tert-Butyl)-1,2,3,4-tetrahydrophenanthridine (4m)
4-(4-Methoxyphenyl)-3-methylisoquinoline (4p)
4-(4-Methoxyphenyl)-3-methylisoquinoline (4p)
4-Benzyl-3-isobutylisoquinoline (4q)
4-Benzyl-3-iso-butylisoquinoline (4q)
6,7-Dimethoxy-3-phenylisoquinoline (4s)
6,7-Dimethoxy-3-phenylisoquinoline (4s)
7-Fluoro-3-phenylisoquinoline (4y)
7-Fluoro-3-phenylisoquinoline (4y)
4-Methyl-3-phenylisoquinoline N-oxide (5a)
4-Methyl-3-phenylisoquinoline $N$-oxide (5a)
4-Methoxy-3-phenylisoquinoline N-oxide (5i)
4-Methoxy-3-phenylisoquinoline N-oxide (5i)
4-(4-Methoxyphenyl)-3-methylisoquinoline N-oxide (5p)
4-(4-Methoxyphenyl)-3-methylisoquinoline $N$-oxide (5p)
6,7-Dimethoxy-4-methyl-3-phenylisoquinoline N-oxide (5r)
6,7-Dimethoxy-4-methyl-3-phenylisoquinoline N-oxide (5r)
2,4-Dimethyl-3-phenylisoquinolin-2-ium chloride (6a)
2,4-Dimethyl-3-phenylisoquinolin-2-ium chloride (6a)
2-(2-(1,3-Dioxolan-2-yl)phenyl)-2-phenylacetonitrile (8a)
2-(2-(1,3-Dioxolan-2-yl)phenyl)-2-phenylacetonitrile (8a)
2-(2-(1,3-Dioxolan-2-yl)-4,5-dimethoxyphenyl)-2-phenylacetonitrile (8b)
2-(2-(1,3-Dioxolan-2-yl)-4,5-dimethoxyphenyl)-2-phenylacetonitrile (8b)
2-(2-(1,3-Dioxolan-2-yl)phenyl)-2-(thiophen-2-yl)acetonitrile (8c)
2-(2-(1,3-Dioxolan-2-yl)phenyl)-2-(thiophen-2-yl)acetonitrile (8c)
2-(2-(1,3-Dioxolan-2-yl)phenyl)malononitrile (8d)
2-((1,3-Dioxolan-2-yl)phenyl)malononitrile (8d)
2-(2-(1,3-Dioxolan-2-yl)phenyl)-2-(phenylsulfonyl)acetonitrile (8e)
2-(2-(1,3-Dioxolan-2-yl)phenyl)-2-(phenylsulfonyl)acetonitrile (8e)
tert-Butyl 2-(2-(1,3-dioxolan-2-yl)phenyl)-2-cyanoacetate (8f)
tert-Butyl 2-(2-(1,3-dioxolan-2-yl)phenyl)-2-cyanoacetate (8f)
4-Phenylisoquinolin-3-amine (9a)
4-Phenylisoquinolin-3-amine (9a)
6,7-Dimethoxy-4-phenylisoquinolin-3-amine (9b)
6,7-Dimethoxy-4-phenylisoquinolin-3-amine (9b)
4-(Thiophen-2-yl)isoquinolin-3-amine (9c)
4-(Thiophen-2-yl)isoquinolin-3-amine (9c)
3-Hydroxyisoquinoline-4-carbonitrile (9d)
3-Hydroxyisoquinoline-4-carbonitrile (9d)
4-(Phenylsulfonyl)isoquinolin-3-amine (9e)
4-(Phenylsulfonyl)isoquinolin-3-amine (9e)
Isoquinolin-3-amine (9f)
Isoquinolin-3-amine (9f)
**tert-Butyl 2-(2-(1,3-dioxolan-2-yl)phenyl)acetate (11)**
tert-Butyl 2-(2-(1,3-dioxolan-2-yl)phenyl)acetate (11)
Isoquinolin-3-ol (12)
Isoquinolin-3-ol (12)

[Chemical Shifts: 160.95, 144.14, 142.32, 131.67, 127.79, 124.67, 123.29, 104.88]

[Chemical Structure Image]

[Chemical Shift Graph: Chemical Shift (ppm)]
3-Phenyl-4-(o-tolyl)isoquinoline (18c)
3-Phenyl-4-(o-tolyl)isoquinoline (18c)
\((E)-\text{Benzaldehyde }O\text{-methyl oxime (22a)}\)
(E)-Benzaldehyde O-methyl oxime (22a)
(E)-Acetophenone O-methyl oxime (22b)
(E)-Acetophenone O-methyl oxime (22b)
Propiophenone O-methyl oxime (22c)
Propiophenone O-methyl oxime (22c)
Benzophenone $O$-methyl oxime (22d)
Benzophenone $O$-methyl oxime (22d)
(E)-2-Bromobenzaldehyde O-methyl oxime (23a)
(E)-2-Bromobenzaldehyde O-methyl oxime (23a)
(E)-1-(2-Bromophenyl)ethanone O-methyl oxime (23b)
(E)-1-(2-Bromophenyl)ethanone \textit{O}-methyl oxime (23b)
1-(2-Bromophenyl)propan-1-one O-methyl oxime (23c)
1-(2-Bromophenyl)propan-1-one O-methyl oxime (23c)
(E)-(2-Bromophenyl)(phenyl)methanone O-methyl oxime (23d)
(E)-(2- Bromophenyl)(phenyl)methanone O-methyl oxime (23d)
(E)-2-(1-Oxo-1-phenylpropan-2-yl)benzaldehyde O-methyl oxime (24a)
(E)-2-(1-Oxo-1-phenylpropan-2-yl)benzaldehyde O-methyl oxime (24a)
(E)-2-(1-Methoxy-2-oxo-2-phenylethyl)benzaldehyde O-methyl oxime (24b)
(E)-2-(1-Methoxy-2-oxo-2-phenylethyl)benzaldehyde O-methyl oxime (24b)
(E) 2-(2-(1-(Methoxyimino)ethyl)phenyl)-1-phenylpropan-1-one (24c)
(E) 2-(2-(1-(Methoxyimino)ethyl)phenyl)-1-phenylpropan-1-one (24c)
(E)-2-(2-(1-(Methoxyimino)propyl)phenyl)-1-phenylpropan-1-one ((E)-24d)
(E)-2-(2-(1-(Methoxyimino)propyl)phenyl)-1-phenylpropan-1-one ((E)-24d)
(Z)-2-(2-(1-(Methoxyimino)propyl)phenyl)-1-phenylpropan-1-one ((Z)-24d)
(E)-2-(2-((Methoxyimino)(phenyl)methyl)phenyl)-1-phenylpropan-1-one (24e)
(E)-2-(2-((Methoxyimino)(phenyl)methyl)phenyl)-1-phenylpropan-1-one (24e)
1-Ethyl-4-methyl-3-phenylisoquinoline (25a)
1-Ethyl-4-methyl-3-phenylisoquinoline (25a)
4-Methyl-1,3-diphenylisoquinoline (25b)
4-Methyl-1,3-diphenylisoquinoline (25b)
3. Details of the X-ray crystallographic data

3-(Adamantan-1-yl)isoquinoline (4n)

Figure 1: 50% thermal ellipsoid plot of 4n

Single crystal diffraction data for 4n were collected at 150 K using a CCD Diffractometer ($\lambda = 0.71073\text{Å}$). Data were reduced using DENZO/SCALEPACK. The structure was solved with SuperFlip and refined by full-matrix least squares on $F^2$ using CRYSTALS. All non-hydrogen atoms were refined with anisotropic displacement parameters and hydrogen atoms were treated in the usual manner. Crystallographic data (excluding structure factors) will be deposited with the Cambridge Crystallographic Data Centre (CCDC 1422536) upon acceptance for publication and can be obtained via www.ccdc.cam.ac.uk/data_request/cif.

C$_{19}$H$_{21}$N, $Mr = 263.38$, monoclinic, $P21$, $a = 6.5458$ (1) Å, $b = 8.4459$ (2) Å, $c = 13.2079$ (3) Å, $\alpha = 90^\circ$, $\beta = 99.9683$ (9)$^\circ$, $\gamma = 90^\circ$, $V = 719.18$ (8) Å$^3$, Data/restraints/parameters = 1740/1/181, $R_{int} = 0.013$, $R[F^2 > 2\sigma(F^2)] = 0.031$, $wr_2 = 0.080$. 
8-Fluoro-3-(4-methoxyphenyl)isoquinoline (4z)

**Figure 2: 50% thermal ellipsoid plot of 4z**

Single crystal diffraction data for 4z were collected at 150 K\(^1\) using a CCD Diffractometer (\(\lambda = 0.71073\text{Å}\)). Data were reduced using DENZO/SCALEPACK\(^2\). The structure was solved with SIR92\(^6\) and refined by full-matrix least squares on \(F^2\) using CRYSTALS\(^4\). All non-hydrogen atoms were refined with anisotropic displacement parameters and hydrogen atoms were treated in the usual manner.\(^5\) Crystallographic data (excluding structure factors) will be deposited with the Cambridge Crystallographic Data Centre (CCDC 1422535) upon acceptance for publication and can be obtained via www.ccdc.cam.ac.uk/data_request/cif.

\[
\text{C}_{16}\text{H}_{12}\text{FNO}, \quad \text{Mr} = 253.28, \quad \text{monoclinic, P 21/n, } \quad a = 12.0003 \quad \text{(5) Å, } \quad b = 5.4759 \quad \text{(2) Å, } \quad c = 17.9308 \quad \text{(8) Å, } \quad \alpha = 90^\circ, \quad \beta = 92.310 \quad \text{(2)°, } \quad \gamma = 90^\circ, \quad V = 1177.32 \quad \text{(8) Å}^3, \quad \text{Data/restraints/parameters - 2296/0/172, } \quad R_{\text{int}} = 0.028, \quad R[F^2 > 2\sigma(F^2)] = 0.049, \quad wR_2 = 0.150.
\]
4-Methyl-3-phenylisoquinoline N-oxide (5a)

Figure 3: 50% thermal ellipsoid plot of 5a

Single crystal diffraction data for 5a were collected at 150 K using a CCD Diffractometer (\(\lambda = 0.71073\text{Å}\)). Data were reduced using DENZO/SCALEPACK. The structure was solved with SuperFlip and refined by full-matrix least squares on \(F^2\) using CRYSTALS. All non-hydrogen atoms were refined with anisotropic displacement parameters and hydrogen atoms were treated in the usual manner. Crystallographic data (excluding structure factors) will be deposited with the Cambridge Crystallographic Data Centre (CCDC 1422538) upon acceptance for publication and can be obtained via www.ccdc.cam.ac.uk/data_request/cif.

\[
\text{C}_{16}\text{H}_{13}\text{NO}, \ Mr = 235.29, \ \text{monoclinic}, \ P 21/n, \ a = 6.0190 (1) \text{Å}, \ b = 8.0659 (2) \text{Å}, \ c = 23.9029 (2) \text{Å}, \ \alpha = 90^\circ, \ \beta = 91.3683 (11)^\circ, \ \gamma = 90^\circ, \ V = 1160.12 (4) \text{Å}^3, \ \text{Data/restraints/parameters} = 2618/0/163, \ R_{\text{int}} = 0.027, \ R[F^2 > 2\sigma(F^2)] = 0.045, \ wR_2 = 0.116. \]
1,4-Dimethyl-3-phenylisoquinoline N-oxide (5b)

Figure 4: 50% thermal ellipsoid plot of 5b

Single crystal diffraction data for 5b were collected at 150 K\(^1\) using a CCD Diffractometer ($\lambda = 0.71073\text{Å}$). Data were reduced using DENZO/SCALEPACK.\(^2\) The structure was solved with SuperFlip\(^3\) and refined by full-matrix least squares on $F^2$ using CRYSTALS.\(^4\) All non-hydrogen atoms were refined with anisotropic displacement parameters and hydrogen atoms were treated in the usual manner.\(^5\) Crystallographic data (excluding structure factors) will be deposited with the Cambridge Crystallographic Data Centre (CCDC 1422537) upon acceptance for publication and can be obtained via www.ccdc.cam.ac.uk/data_request/cif.

C\(_{17}\)H\(_{15}\)NO, $Mr = 249.31$, monoclinic, $P 21/c$, $a = 9.4554$ (1) Å, $b = 10.6808$ (2) Å, $c = 12.7524$ (2) Å, $\alpha = 90^\circ$, $\beta = 92.8615$ (7)$^\circ$, $\gamma = 90^\circ$, $V = 1286.28$ (3) Å\(^3\), Data/restraints/parameters = 2314/0/172, $R_{int} = 0.014$, $R[F^2 > 2\sigma(F^2)] = 0.040$, $wR_2 = 0.094$. 
4-(2-Bromoallyl)-3-phenylisoquinoline (15f)

Figure 5: 50% thermal ellipsoid plot of 20f

Single crystal diffraction data for 20f were collected at 150 K\(^1\) using a CCD Diffractometer (\(\lambda = 0.71073\text{Å}\)). Data were reduced using DENZO/SCALEPACK.\(^2\) The structure was solved with SuperFlip\(^3\) and refined by full-matrix least squares on \(F^2\) using CRYSTALS.\(^4\) All non-hydrogen atoms were refined with anisotropic displacement parameters and hydrogen atoms were treated in the usual manner.\(^5\) Crystallographic data (excluding structure factors) will be deposited with the Cambridge Crystallographic Data Centre (CCDC 1422539) upon acceptance for publication and can be obtained via www.ccdc.cam.ac.uk/data_request/cif.

\[\text{C}_{18}\text{H}_{14}\text{BrN}, \text{Mr} = 324.22, \text{monoclinic, } P\ 21/a, a = 8.8066 (1) \text{Å}, b = 13.3703 (2) \text{Å}, c = 12.5739 (2) \text{Å}, \alpha = 90^\circ, \beta = 105.1056 (5)^\circ, \gamma = 90^\circ, V = 1429.38 (4) \text{Å}^3, \text{Data/restraints/parameters } - 3256/0/181, \text{Rint} = 0.013, R[F^2 > 2\sigma(F^2)] = 0.033, wR_2 = 0.077.\]