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Iridium catalysed alkylation of *tert*-butyl cyanoacetate with alcohols under solvent free conditions

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ABSTRACT

Ir-catalysed alkylation of *tert*-butyl cyanoacetate with a range of substituted benzyl and heteroaryl alcohols under solvent free conditions afforded the corresponding monoalkylated products in moderate to high yields.

1. Introduction

To increase the molecular complexity of a simple organic substrate using efficient (high atom economy), selective, high yielding and environmentally benign methods is one of the contemporary challenges for synthetic organic chemists.[1] C–C bond formation is a pivotal method for achieving this goal. Indirect functionalisation of alcohols using catalytic amounts of a metal complex and base, which generates only water as a by-product is an attractive green alternative to standard C–C bond forming reactions. These cascades are termed as redox—neutral, hydrogen autotransfer or 'borrowing hydrogen' processes. We have previously reported the alkylation of active methylene and methine compounds with alcohols catalysed by iridium, rhodium and ruthenium complexes. Thus alkylation of arylacetonitriles was achieved by using rhodium[2] and more recently iridium catalysts.[3] We have also reported microwave assisted redox neutral processes for selective monoalkylation of 1,3-dimethylbarbituric acid and alcohols.[4] C-3 (methine) alkylation of indoles was also successfully carried out utilising alcohols and iridium catalysts.[5] Cho et al. have reported the direct α-alkylation of ketones with alcohols, using a Ru catalyst, to afford saturated alcohols via α-alkylated ketones.[6] The same reaction can be performed in the presence of a sacrificial hydrogen acceptor, such as 1-dodecene, when α-alkylated ketones are obtained.[7] Alternative catalysts for the α-alkylation of ketones with alcohols have been reported including the use of phosphine free catalyst $Ru(DMSO)_4Cl_4$[8] and palladium nanoparticles.[9] Ishi et al. reported the selective direct α-alkylation of ketones with alcohols using an Ir catalyst,[10] and Williams et al. reported indirect Wittig reactions with alcohols using $[Ir(cod)Cl]_2$[11] or a ruthenium carbene complex[12] and variants of aldol condensation.[13] Krische et al. reported a series of Ir-catalysed C–C coupling via hydrogen autotransfer processes involving alcohols and π-unsaturated reactants (1,3-dienes, 1,2-dienes or 1,3-enynes).[14–16] We and others reported the *N*-alkylation of amines with alcohols using iridium and rhodium catalysts[17]whilst Beller et al. have reported N-alkylation of anilines with aliphatic amines instead of alcohols using Shvo's catalyst.[18]

2. Results and discussion

Early extensive pioneering work by the Maitlis et al.[19] established simple routes to a series of halide bridged dimers **1** and pointed the way to their catalytic potential. Recently Fujita's group[17c–f] and others have reported applications of **1** in redox neutral processes. The alkylation of cyanoesters with alcohols (Scheme 1) is of interest as it provides a potential 'green' route to β-amino acids and 1,3-aminoalcohols.[20] An initial survey of a range of catalysts identified the iridium chloro bridged compound **1** [X=Cl, M=Ir(III)] as an effective catalyst for Scheme 1.

The proposed mechanism for this transformation involves dehydrogenation of the primary alcohol to generate an aldehyde and metal hydride species. Knoevenagel type condensation can then occur and hydrogenation of the double bond by in situ formed metal hydride gives the product (Scheme 2).

Prior related work by Williams et al.[21] using $[Ir(cod)Cl]_2$ on dibenzylmalonate was compromised by competing transesterification and decarboxylation resulting in mixtures with poor yields (3–34%) of the desired alkylated products. In our approach to the cyanoesters we selected the *tert*-butyl esters to both suppress the transesterification whilst providing access to the functionalised

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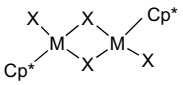
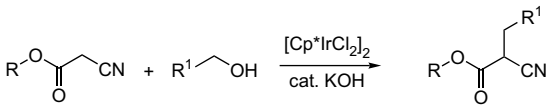
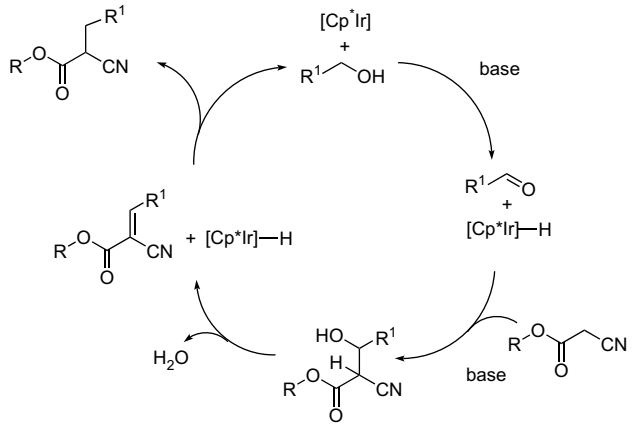


1

X = Cl, I or Br
M = Ir, Rh, Ru



Scheme 1.



Scheme 2.

free carboxylic acid if required. Further optimisation showed that the reaction could be achieved under essentially solvent free conditions and identified potassium hydroxide as the base of choice. Initially we carried out the alkylation reaction of *tert*-butyl cyanoacetate (1 mmol) with benzyl alcohol (1.5 mmol), KOH (20 mol %) and $[Cp^*IrCl_2]_2$ (2.5 mol %) at 100 °C for 4 h, which afforded the monoalkylated product **2** in 77% yield (Table 1, entry 1).

Benzyl alcohols substituted with electron-withdrawing or electron-donating groups were readily alkylated to afford the corresponding α-benzylated cyanoesters **3**–**10** in high yield (Table 1, entries 2–9). The reaction was not significantly affected by either the location or the electronic nature of the substituent on the aryl ring. Under the optimised conditions all the additional functional groups (F, Cl, Br, I, NO_2) were stable. In this respect the use of nitroalcohol (Table 1, entry 5) is of interest in showing that the Knoevenagel sequence in Scheme 2 is significantly faster than nitro group reduction. In previous work[5] we have shown that nitro group reduction in a redox neutral cascade provides access to functionalised indoles. The reaction of phenethyl alcohol showed approximately 70% conversion to the alkylated product **11** (Table 1, entry 10), which was isolated in 53% yield. The heteroaromatic furfuryl alcohol was slower compared to benzylic alcohols. This retardation may be due to a non-productive π-interaction with the iridium catalyst resulting in a slower reaction leading to increased amounts of degradative by-product. However, the alkylated cyanoester **13** was obtained in 52% yield (Table 1, entry 12). In some other cases various amounts of degradative by-product (~5–20%) were observed in the ^{1}H NMR spectrum, which exhibited two triplets of the same intensity at ca. δ 2.95 and 2.55 ppm. These by-products were shown (HRMS) to be the corresponding decarboxylated products arising from hydrolysis of the ester followed by thermal decarboxylation (Scheme 3).

Table 1
Alkylation of *tert*-butyl cyanoester with alcohols[a]

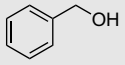
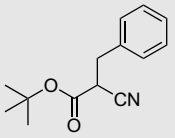
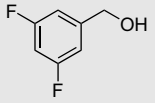
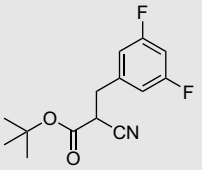
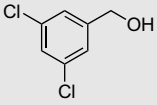
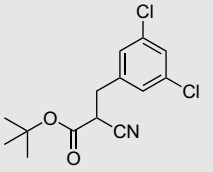
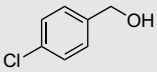
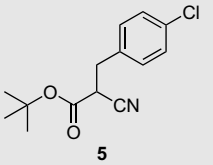
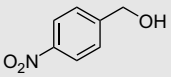
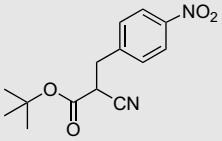
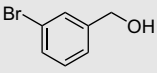
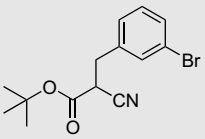
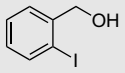
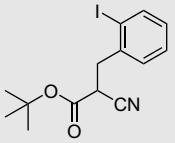
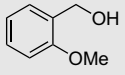
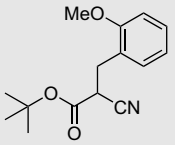
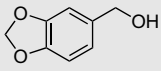
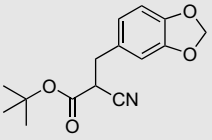
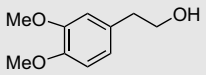
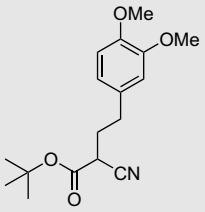
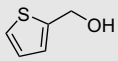
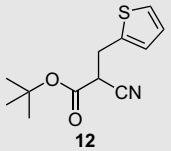
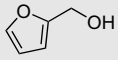
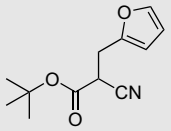
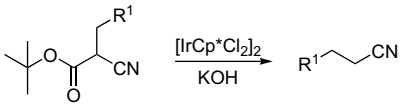
Entry	Alcohol	Product	Time (h)	Yield[b] (%)
1		 **2**	4	77
2		 **3**	4	55
3		 **4**	4	76
4		 **5**	4	77
5		 **6**	8	57
6		 **7**	8	73
7		 **8**	4	65
8		 **9**	8	86
9		 **10**	4	82

Table 1 (*continued*)

Entry	Alcohol	Product	Time (h)	Yield[b] (%)
10		 **11**	4	53
11		 **12**	4	68
12		 **13**	24	52

[a] The reaction was carried out at 100 °C under solvent free conditions with cyanoester (1 mmol), alcohol (1.5 mmol), $[IrCp^*Cl_2]_2$ (2.5 mol %) and KOH (15–20 mol %).
[b] Isolated yield.



Scheme 3.

The same decarboxylation process has been observed by Williams et al.[21] in their alkylation reactions of various ester derivatives with alcohols. Ishii et al. have reported closely related work on $[IrCl(cod)]_2/PPh_3$ catalysed alkylation of *n*-butyl cyanoester.[22] Interestingly under their conditions the combination of $[Cp^*IrCl_2]_2$ and PPh_3 gave no conversion to the desired alkylated product.

3. Conclusion

In conclusion, *tert*-butyl cyanoacetate was successfully alkylated with a range of substituted benzyl and heteroaryl alcohols to afford the corresponding α-alkylated products in moderate to high yield. Extended reaction time leads to some product degradation via hydrolysis and decarboxylation.

4. Experimental

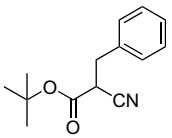
4.1. General

Unless otherwise noted all reagents were obtained from commercial suppliers and used without further purification. The $[IrCp^*Cl_2]_2$ catalyst was prepared from $Ir(III)Cl_3$ and pentamethylcyclopentadiene according to literature procedure.[23] Chromatography columns were prepared using Fisher Chemicals 60A 35–70 μm silica gel. Nuclear magnetic resonance spectra were recorded using Bruker DPX300 and DPX500 MHz spectrometers. Chemical shifts are reported in parts per million (δ) downfield relative to the internal reference tetramethylsilane. Unless otherwise specified NMR spectra were recorded in deuterochloroform at room temperature. Abbreviations used; Ar=aromatic, d=doublet, dd=doublet of doublets, dq=doublet of quartets, dt=doublet of triplets, m=multiplet, q=quartet, s=singlet, t=triplet. Mass spectra were recorded using a micromass ZMD 2000 spectrometer employing the electrospray (ES^+) ionisation technique. Accurate molecular masses were obtained from the EPSRC Swansea Mass Spectroscopy service using perfluorotributylamine or polyethylenimine as an internal standard. Infrared spectra were recorded using a Perkin–Elmer FT-IR spectrometer. IR spectra of liquids were recorded as thin films on sodium chloride plates. IR spectra of solids were recorded using the 'golden gate' apparatus. Melting points were determined on a Griffin hot-stage apparatus and are uncorrected. Microanalyses were obtained using a Carlo Erba 1108 Elemental Analyser.

4.2. General procedure for the alkylation of *tert*-butyl cyanoacetate with alcohols

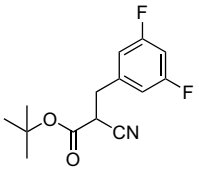
A mixture of the *tert*-butyl cyanoacetate (0.141 g, 1.0 mmol), $[Cp^*IrCl_2]_2$ (0.020 g, 2.5 mol %), KOH (0.009–0.011 g, 0.15–0.2 mmol) and the required alcohol (1.5 mmol) were combined in a thick walled glass tube. The tube was sealed with a rubber septum, purged with nitrogen and heated at 100 °C for 4–24 h. The reaction mixture was analysed by ^1H NMR spectroscopy and thereafter purified by chromatography.

4.2.1. *tert*-Butyl 2-cyano-3-phenylpropanoate (**2**)



Prepared by the general procedure from *tert*-butyl cyanoacetate (0.141 g, 1.0 mmol), KOH (0.011 g, 0.20 mmol), $[IrCp^*Cl_2]_2$ (0.020 g, 0.025 mmol) and benzyl alcohol (0.162 g, 1.5 mmol) with heating at 100 °C for 4 h. Chromatography, eluting with 7:1 v/v hexane and ethyl acetate, gave the product (0.178 g, 77%) as a colourless oil; δ_H (500 MHz, $CDCl_3$): 7.36–7.25 (m, 5H, 5×ArH), 3.63 (dd, 1H, *J* 6.0, 8.1 Hz, CH), 3.24 (dd, 1H, *J* 6.0 and 13.8 Hz, C*H*H), 3.17 (dd, 1H, *J* 8.1, 13.8 Hz, CH*H*), 1.44 (s, 9H, 3×CH_3); δ_C (75 MHz, $CDCl_3$): 164.43 (CO), 135.49 (ArC), 129.10 (2×ArCH), 128.79 (2×ArCH), 127.68 (ArCH), 116.60 (CN), 84.26 (C), 40.51 (CH), 35.77 (CH_2), 27.73 (3×CH_3); ν_{max} (cm^{-1}) (film): 2981, 2249 (CN), 1737 (CO), 1497, 1370, 1150; HRMS [ES^+] found M+Na 254.1150. $C_{14}H_{17}NNaO_2$ requires 254.1151.

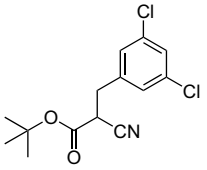
4.2.2. *tert*-Butyl 2-cyano-3-(3,5-difluorophenyl)-propanoate (**3**)



Prepared by the general procedure from *tert*-butyl cyanoacetate (0.141 g, 1.0 mmol), KOH (0.011 g, 0.20 mmol), $[IrCp^*Cl_2]_2$ (0.020 g, 0.025 mmol) and 3,5-difluorobenzyl alcohol (0.216 g, 1.5 mmol) with heating at 100 °C for 4 h. Chromatography, eluting with 7:1 v/v hexane and ethyl acetate, gave the product (0.146 g, 55%) as a pale yellow oil; δ_H (500 MHz, $CDCl_3$): 6.82 (dd, 2H, *J* 2.1, 8.1 Hz, 2×H^2), 6.76 (tt, 1H, *J* 2.1, 9.0 Hz, H^4), 3.63 (dd, 1H, *J* 6.0, 7.9 Hz, CH), 3.21 (dd, 1H, *J* 6.0, 14.1 Hz, C*H*H), 3.15 (dd, 1H, *J* 7.9, 14.1 Hz, CH*H*), 1.47 (s, 9H,

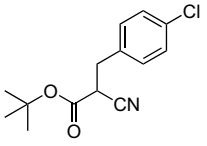
3×CH_3); δ_C (75 MHz, $CDCl_3$): 163.49 (dd, $^3J_{CF}$ 12.8 Hz, $^1J_{CF}$ 249.0 Hz, CF), 164.25 (CO), 139.48 (t, $^3J_{CF}$ 9.06 Hz, ArC), 116.14 (CN), 112.57 (d, $^2J_{CF}$ 25.1 Hz, ArCH), 103.76 (t, $^2J_{CF}$ 25.3 Hz, ArCH), 85.25 (C), 40.22 (CH), 35.52 (CH_2), 28.14 (3×CH_3); ν_{max} (cm^{-1}) (film): 2983, 1740, 1628, 1597, 1461, 1371, 1152, 1120; HRMS [ES$^+$] found M+Na 290.0962. $C_{14}H_{15}NO_2NaF_2$ requires 290.0963.

*4.2.3. tert-Butyl 2-cyano-3-(3,5-dichlorophenyl)-propanoate (**4**)*



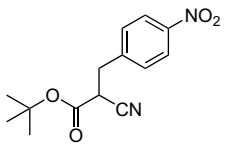
Prepared by the general procedure from *tert*-butyl cyanoacetate (0.141 g, 1.00 mmol), KOH (0.009 g, 0.152 mmol), $[IrCp^*Cl_2]_2$ (0.020 g, 0.025 mmol) and 3,5-dichlorobenzyl alcohol (0.261 g, 1.50 mmol). Work up followed by column chromatography, eluting with 1:7 v/v ether–petroleum ether, gave the product (0.227 g, 76%) as a colourless oil; δ_H (300 MHz, $CDCl_3$): 7.30 (t, 1H, *J* 1.8 Hz, H^4), 7.18 (d, 2H, *J* 1.8 Hz, H^2), 3.65 (dd, 1H, *J* 7.7 and 6.4 Hz, *CH*), 3.19 (dd, 1H, *J* 14.1 and 6.4 Hz, CH*H*) and 3.13 (dd, 1H, *J* 14.1 and 7.7 Hz, *CH*H), 1.47 (s, 9H, $C(CH_3)_3$); δ_c (75.5 MHz, $CDCl_3$): 164.2 (C=O), 139.1 (C), 135.7 (C), 128.7 (CH), 128.1 (2×CH), 116.4 (C), 85.3 (C), 40.2 (CH), 35.2 (CH_2) and 28.1 (3×CH_3); ν_{max} (cm^{-1}) (film): 3100–2850 (C–H stretching), 2247 (CN stretching), 1739 (C=O), 1592 and 1569 (aromatic), 1434, 1395, 1371, 1281 and 1151; HRMS [M+Na] $C_{14}H_{15}^{35}Cl_2NNaO_2$ calculated 322.0372, found 322.0379.

*4.2.4. tert-Butyl 2-cyano-3-(4-chlorophenyl)propanoate (**5**)*



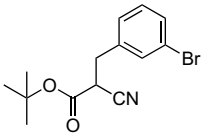
Prepared by the general procedure from *tert*-butyl 2-cyanoacetate (0.141 g, 1.00 mmol), KOH (0.009 g, 0.152 mmol), $[IrCp^*Cl_2]_2$ (0.020 g, 0.025 mmol) and 4-chlorobenzyl alcohol (0.214 g, 1.50 mmol). Work up followed by column chromatography, eluting with 1:7 v/v ether–petroleum ether, gave the product (0.205 g, 77%) as a colourless oil; δ_H (300 MHz, $CDCl_3$): 7.31 (d, 2H, *J* 8.5 Hz, 2×H^3), 7.22 (d, 2H, *J* 8.5 Hz, 2×H^2), 3.62 (dd, 1H, *J* 7.9 and 6.0 Hz, CH), 3.21 (dd, 1H, *J* 14.0 and 6.0 Hz, CH*H*) and 3.14 (dd, 1H, *J* 14.0 and 7.9 Hz, C*H*H), 1.45 (s, 9H, $C(CH_3)_3$); δ_c (75.5 MHz, $CDCl_3$): 164.6 (C=O), 134.3 (C), 134.1 (C), 131.0 (2×CH), 129.4 (2×CH), 116.8 (C), 84.9 (C), 40.7 (CH), 35.4 (CH_2) and 28.2 (3×CH_3); ν_{max} (cm^{-1}) (film): 3000–2900 (C–H stretching), 2250 (CN stretching), 1739 (CO), 1493and 1456 (aromatic), 1370, 1281, 1151 and 1093; HRMS [M+Na] $C_{14}H_{16}^{35}ClNNaO_2$ calculated 288.0762, found 288.0756.

*4.2.5. tert-Butyl 2-cyano-3-(4-nitrophenyl)propanoate (**6**)*



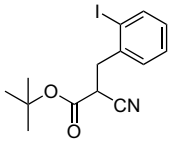
Prepared by the general procedure from *tert*-butyl cyanoacetate (0.141 g, 1.0 mmol), KOH (0.011 g, 0.20 mmol), $[IrCp^*Cl_2]_2$ (0.020 g, 0.025 mmol) and *p*-nitrobenzyl alcohol (0.230 g, 1.5 mmol) with heating at 100 °C for 8 h. Chromatography, eluting with 4:1 v/v hexane and ethyl acetate, followed by crystallisation of the residue from DCM and hexane gave the product (0.157 g, 57%) as colourless prisms; mp 74–75 °C. (Found: C, 60.70; H, 5.75; N, 10.30. $C_{14}H_{19}NO_4$ requires: C, 60.86; H, 5.84; N, 10.14%.) δ_H (500 MHz, $CDCl_3$): 8.22 (d, 2H, *J* 8.8 Hz, 2×H^3), 7.48 (d, 2H, *J* 8.8 Hz, 2×$H^{2'}$), 3.71 (dd, 1H, *J* 6.0, 8.1 Hz, CH), 3.34 (dd, 1H, *J* 6.0, 14.1 Hz, C*H*H), 3.29 (dd, 1H, *J* 8.1, 14.1 Hz, CH*H*), 1.47 (s, 9H, 3×CH_3); δ_C (75 MHz, $CDCl_3$): 164.12 (CO), 147.95 (ArC), 143.29 (ArC), 130.63 (2×ArCH), 124.40 (2×ArCH), 116.34 (CN), 85.40 (C), 40.08 (CH), 35.45 (CH_2), 28.15 (3×CH_3); ν_{max} (cm^{-1}) (film): 2982, 2250 (CN), 1739 (CO), 1522, 1348, 1151; HRMS [ES$^+$] found M+Na 299.1002. $C_{14}H_{16}N_2NaO_4$ requires 299.1002.

*4.2.6. tert-Butyl 3-(3-bromophenyl)-2-cyanopropanoate (**7**)*



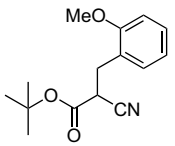
Prepared by the general procedure from *tert*-butyl cyanoacetate (0.141 g, 1.0 mmol), KOH (0.011 g, 0.20 mmol), $[IrCp^*Cl_2]_2$ (0.020 g, 0.025 mmol) and 3-bromobenzyl alcohol (0.280 g, 1.5 mmol) with heating at 100 °C for 8 h. Chromatography, eluting with 7:1 v/v hexane and ethyl acetate, gave the product (0.226 g, 73%) as a pale yellow oil; δ_H (500 MHz, $CDCl_3$): 7.45–7.42 (m, 2H, 2×ArH), 7.25–7.20 (m, 2H, 2×ArH), 3.63 (dd, 1H, *J* 6.0, 7.9 Hz, CH), 3.20 (dd, 1H, *J* 6.0, 13.7 Hz, C*H*H), 3.14 (dd, 1H, *J* 7.9, 13.7 Hz, CH*H*), 1.46 (s, 9H, 3×CH_3); δ_C (75 MHz, $CDCl_3$): 164.48 (CO), 138.08 (ArC), 132.55 (ArCH), 131.30 (ArCH), 130.80 (ArCH), 128.24 (ArCH), 123.12 (ArC), 116.64 (CN), 85.05 (C), 40.59 (CH), 35.60 (CH_2), 28.16 (3×CH_3); ν_{max} (cm^{-1}) (film): 2980, 1738, 1569, 1475, 1370, 1281, 1150, 838; HRMS [ES$^+$] found: M+Na 332.0265. $C_{14}H_{16}NO_2Na^{79}Br$ requires 332.0257.

*4.2.7. tert-Butyl 2-cyano-3-(2-iodophenyl)propanoate (**8**)*



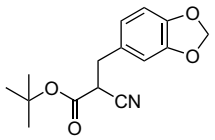
Prepared by the general procedure from *tert*-butyl cyanoacetate (0.141 g, 1.0 mmol), KOH (0.011 g, 0.20 mmol), $[IrCp^*Cl_2]_2$ (0.020 g, 0.025 mmol) and 2-iodobenzyl alcohol (0.351 g, 1.5 mmol) with heating at 100 °C for 4 h. Chromatography, eluting with 7:1 v/v hexane and ethyl acetate, gave the product (0.233 g, 65%) as a colourless oil; δ_H (500 MHz, $CDCl_3$): 7.85 (d, 1H, *J* 7.7 Hz, H^3), 7.37–7.32 (m, 2H, H^5 and H^6), 7.00 (apparent dt, 1H, *J* 2.6, 7.3 Hz, H^4), 3.82 (dd, 1H, *J* 6.2, 9.6 Hz, CH), 3.42 (dd, 1H, *J* 6.2, 13.9 Hz, C*H*H), 3.19 (dd, 1H, *J* 9.6, 13.9 Hz, CH*H*), 1.49 (s, 9H, 3×CH_3); δ_C (75 MHz, $CDCl_3$): 164.11 (CO), 139.87 (ArCH), 138.17 (ArC), 131.02 (ArCH), 129.57 (ArCH), 128.78 (ArCH), 116.18 (CN), 100.05 (ArC), 84.41 (C), 40.54 (CH_2), 38.65 (CH), 27.80 (3×CH_3); ν_{max} (cm^{-1}) (film): 2980, 1740, 1564, 1467, 1394, 1370, 1150, 1014; HRMS [ES$^+$] found M+Na 380.0112. $C_{14}H_{16}INO_2Na$ requires 380.0118.

*4.2.8. tert-Butyl 2-cyano-3-(2-methoxyphenyl)-propanoate (**9**)*



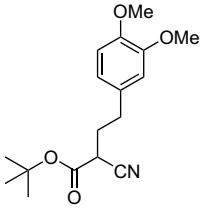
Prepared by the general procedure from *tert*-butyl cyanoacetate (0.141 g, 1.0 mmol), KOH (0.011 g, 0.20 mmol), $[IrCp^*Cl_2]_2$ (0.020 g, 0.025 mmol) and 2-methoxybenzyl alcohol (0.207 g, 1.5 mmol) with heating at 100 °C for 8 h. Chromatography, eluting with 7:1 v/v hexane and ethyl acetate, gave the product (0.225 g, 86%) as a colourless oil; δ_H (500 MHz, $CDCl_3$): 7.27 (apparent t, 1H, *J* 7.7 Hz, H^4), 7.19 (d, 1H, J 7.7 Hz, H^6), 6.91 (apparent t, 1H, *J* 8.1 Hz, H^5), 6.87 (d, 1H, *J* 8.1 Hz, H^3), 3.85 (s, 3H, OCH_3), 3.84 (dd, 1H, *J* 6.8, 9.0 Hz, CH), 3.30 (dd, 1H, 6.8, 13.3 Hz, C*H*H), 3.09 (dd, 1H, *J* 9.0, 13.3 Hz, CH*H*), 1.44 (s, 9H, 3×CH_3); δ_C (75 MHz, $CDCl_3$): 165.36 (CO), 157.87 (ArC), 131.60 (ArCH), 129.53 (ArCH), 124.27 (ArC), 121.04 (ArCH), 117.43 (CN), 110.72 (ArCH), 84.18 (C), 55.67 (OCH_3), 38.64 (CH), 32.05 (CH_2), 28.16 (3×CH_3); ν_{max} (cm^{-1}) (film): 2979, 1737, 1602, 1495, 1464, 1369, 1246, 1149; HRMS [ES^+] found M+Na 284.1254. $C_{15}H_{19}NO_3Na$ requires 284.1257.

4.2.9. *tert*-Butyl 3-(benzo[d][1,3]dioxol-5-yl)-2-cyano-propanoate (**10**)



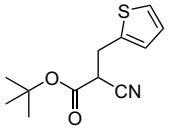
Prepared by the general procedure from *tert*-butyl cyanoacetate (0.141 g, 1.0 mmol), KOH (0.011 g, 0.20 mmol), $[IrCp^*Cl_2]_2$ (0.020 g, 0.025 mmol) and 3,4-methylenedioxy benzyl alcohol (0.228 g, 1.5 mmol) with heating at 100 °C for 4 h. Chromatography, eluting with 4:1 v/v hexane and ethyl acetate, gave the product (0.165 g, 60%) as a colourless oil; δ_H (500 MHz, $CDCl_3$): 6.78–6.72 (m, 3H, H^2,H^5 and H^6), 5.95 (s, 2H, OCH_2O), 3.57 (dd, 1H, *J* 6.0, 8.1 Hz, CH), 3.15 (dd, 1H, *J* 6.0, 13.7 Hz, C*H*H), 3.08 (dd, 1H, *J* 8.1, 13.7 Hz, CH*H*), 1.47 (s, 9H, $C(CH_3)_3$); δ_C (75 MHz, $CDCl_3$): 164.40 (CO), 147.89 (ArC), 147.12 (ArC), 129.08 (ArC), 122.43 (ArCH), 116.53 (CN), 109.39 (ArCH), 108.49 (ArCH), 101.14 (CH_2), 84.30 (C), 40.82 (CH), 35.53 (CH_2), 27.78 (3×CH_3); ν_{max} (cm^{-1}) (film): 2981, 1738, 1504, 1491, 1445, 1370, 1249, 1151; HRMS [ES^+] found M+1 276.1220. $C_{15}H_{17}NO_4$ requires 276.1230.

4.2.10. *tert*-Butyl 2-cyano-4-(3,4-dimethoxyphenyl)-butanoate (**11**)



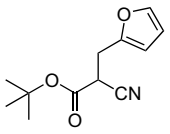
Prepared by the general procedure from *tert*-butyl cyanoacetate (0.141 g, 1.0 mmol), KOH (0.011 g, 0.20 mmol), $[IrCp^*Cl_2]_2$ (0.020 g, 0.025 mmol) and 3,4-dimethoxy phenethyl alcohol (0.270 g, 1.5 mmol) with heating at 100 °C for 4 h. Chromatography, eluting with 4:1 v/v hexane and ethyl acetate, followed by crystallisation of the residue from DCM and hexane gave the product (0.161 g, 53%) as colourless prisms; mp 62–63 °C. (Found: C, 66.85; H, 7.65; N, 4.80. $C_{17}H_{23}NO_4$ requires: C, 66.86; H, 7.59; N, 4.59%.) δ_H (500 MHz, $CDCl_3$): 6.82 (d, 1H, *J* 8.1 Hz, H^5), 6.75 (dd, 1H, *J* 1.7, 8.1 Hz, H^6), 6.72 (d, 1H, *J* 1.7 Hz, H^2), 3.88 (s, 3H, OCH_3), 3.86 (s, 3H, OCH_3), 3.34 (dd, 1H, *J* 6.8, 8.1 Hz, CH), 2.86–2.80 (m, 1H, C*H*H), 2.76–2.70 (m, 1H, CH*H*), 2.22–2.17 (m, 2H, $ArCH_2$), 1.50 (s, 9H, 3×CH_3); δ_C (75 MHz, $CDCl_3$): 165.00 (CO), 149.07 (ArC), 147.78 (ArC), 131.72 (ArC), 120.46 (ArCH), 116.82 (CN), 111.67 (ArCH), 84.09 (C), 55.93 (OCH_3), 55.88 (OCH_3), 37.69 (CH), 32.30 (CH_2), 31.59 (CH_2), 27.80 (3×CH_3); ν_{max} (cm^{-1}) (film): 2936, 2248 (CN), 1738 (CO), 1517, 1155, 1028.

4.2.11. *tert*-Butyl 2-cyano-3-(thiophen-2-yl)propanoate (**12**)



Prepared by the general procedure from *tert*-butyl cyanoacetate (0.141 g, 1.0 mmol), KOH (0.011 g, 0.20 mmol), $[IrCp^*Cl_2]_2$ (0.020 g, 0.025 mmol) and 2-thiophene methanol (0.117 g, 1.5 mmol) with heating at 100 °C for 4 h. Chromatography, eluting with 4:1 v/v hexane and ethyl acetate, gave the product (0.160 g, 68%) as a colourless oil; δ_H (500 MHz, $CDCl_3$): 7.22 (dd, 1H, *J* 1.3, 4.8 Hz, H^5), 7.01–6.95 (m, 2H, H^3 and H^4), 3.67 (dd, 1H, *J* 6.0, 7.3 Hz, CH), 3.45 (dd, 1H, *J* 6.0, 15.0 Hz, C*H*H), 3.41 (dd, 1H, *J* 7.3, 15.0 Hz, CH*H*), 1.47 (s, 9H, 3×CH_3); δ_C (75 MHz, $CDCl_3$): 163.97 (CO), 136.99 (ArC), 127.22 (ArCH), 127.18 (ArCH), 125.23 (ArCH), 116.32 (CN), 84.56 (C), 40.72 (CH), 29.96 (CH_2), 27.75 (3×CH_3); ν_{max} (cm^{-1}) (film): 2980, 2929, 1737 (CO), 1435, 1370, 1257, 1152, 836; HRMS [ES^+] found M+Na 260.0723. $C_{12}H_{15}NNaO_2S$ requires 260.0716.

4.2.12. *tert*-Butyl 2-cyano-3-(furan-2-yl)propanoate (**13**)



Prepared by the general procedure from *tert*-butyl cyanoacetate (0.141 g, 1.0 mmol), KOH (0.011 g, 0.20 mmol), $[IrCp^*Cl_2]_2$ (0.020 g, 0.025 mmol) and furfuryl alcohol (0.162 g, 1.5 mmol) with heating at 100 °C for 24 h. Chromatography, eluting with 4:1 v/v hexane and ethyl acetate, gave the product (0.115 g, 52%) as a colourless oil; δ_H (500 MHz, $CDCl_3$): 7.36 (d, 1H, *J* 1.3 Hz, H^5), 6.32 (dd, 1H, *J* 1.3, 3.4 Hz, H^4), 6.24 (d, 1H, *J* 3.4 Hz, H^3), 3.73 (dd, 1H, *J* 6.4, 7.7 Hz, CH), 3.28 (dd, 1H, *J* 6.4, 15.2 Hz, C*H*H), 3.23 (dd, 1H, *J* 7.7, 15.2 Hz, CH*H*), 1.48 (s, 9H, 3×CH_3); δ_C (75 MHz, $CDCl_3$): 164.03 (CO), 149.17 (ArC), 142.39 (ArCH), 116.24 (CN), 110.56 (ArCH), 108.28 (ArCH), 84.41 (C), 37.99 (CH), 28.57 (CH_2), 27.72 (3×CH_3); ν_{max} (cm^{-1}) (film): 2982, 1740, 1371, 1282, 1254, 1153, 1015, 839; HRMS [ES^+] found M+1 222.1123. $C_{12}H_{16}NO_3$ requires 222.1125.

Acknowledgements

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