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One-pot synthesis of *N*-methylindoles from *N*-methylanilines and of benzofurans from phenols using transition-metal carbene X–H insertion reactions

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ABSTRACT

Transition-metal carbene X–H insertion reactions (X=N or O) have been employed in the simple conversion of anilines and phenols into indoles and benzofurans, respectively. Thus copper(II) catalyzed N–H insertion reactions of α-diazo-β-ketoesters with *N*-methylanilines followed by treatment with acidic ion-exchange resin gives indoles. In a similar manner, dirhodium(II) catalyzed O–H insertion reactions of α-diazo-β-ketoesters with phenols followed by treatment with PPA gives benzofurans.

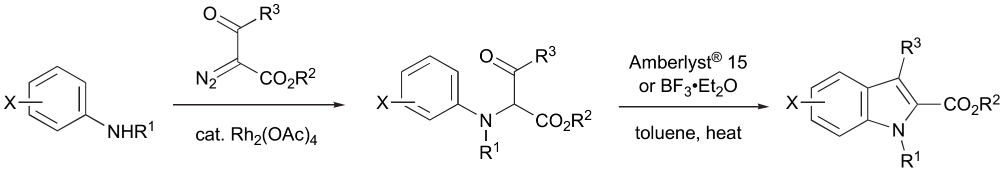
1. Introduction

The reaction of anilines with diazocarbonyl compounds is a known reaction of carbene and metal carbene intermediates, with the products being derived from an N–H insertion reaction.[1,2] The thermal reaction of ethyl diazoacetate with aniline itself was first described by Curtius over 100 years ago,[3] although nowadays the reaction is usually carried out in the presence of a metal catalyst, following Yates' first report of the copper bronze catalyzed decomposition of diazoacetophenone in the presence of aniline to give α-anilinoacetophenone in 33% yield.[4] Subsequently, reports of other reactions of anilines with diazocarbonyl compounds catalyzed by a range of transition-metal complexes, including copper,[5–8] rhodium,[9–11] rhenium[12] and ruthenium,[13] followed. We previously reported the rhodium carbene insertion reaction into the N–H bond of *N*-alkylanilines as a key step in a modified Bischler synthesis of indoles,[14,15] whilst subsequently Janda and co-workers have developed a solid-phase variant of this reaction, and applied it to the synthesis of an array of indoles.[16] In continuation of our own work on carbene N–H insertion reactions in synthesis,[17–22] we sought to develop a solution-phase, one-pot route to arrays of indoles, and we report our results herein.

2. Results and discussion

Owing to the wide-ranging biological activity of many natural and synthetic indoles, this important ring system continues to attract the attention of synthetic organic chemists.[23–26] Among the many routes to indoles, those which start from a simple aniline derivative are probably the most useful, since they do not require the presence of an additional *ortho*-substituent, such as a halide, as used in the various transition-metal mediated reactions such as the Larock method. The Bischler reaction, discovered 100 years ago,[27,28] involves the reaction of simple anilines with α-haloketones followed by acid catalyzed cyclization of the resulting α-(*N*-arylamino)ketones.

In our previously described modification of the Bischler reaction,[14,15] the key α-(*N*-arylamino)ketone intermediate was obtained by the aforementioned rhodium carbene N–H insertion reaction, and, after isolation, was subsequently cyclized using protic or Lewis acids (Scheme 1).



Scheme 1.

Initially we had hoped to exploit the Lewis acidic nature of dirhodium(II) carboxylates to effect both of the above transformations in a single operation in one pot, but this proved

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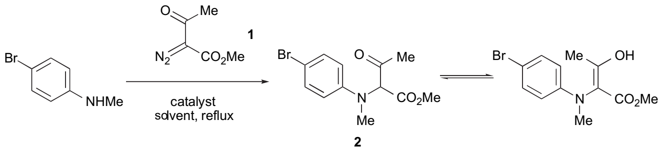
unsuccessful. Likewise, use of scandium triflate, a reagent reported to mediate carbene N–H insertion reactions,[29,30] was also unsuccessful, and therefore we resorted to a two-operation, one-pot method. In the first instance we optimized both steps (cf. Scheme 1) separately. Thus, methyl 2-diazo-3-oxobutanoate **1** was reacted with 4-bromo-*N*-methylaniline in the presence of a range of catalysts in toluene or 1,2-dichloroethane (DCE) to give the N–H insertion product **2** in a range of yields (Table 1). Although dirhodium catalysts performed satisfactorily, copper(II) trifluoroacetate generally gave better yields, and therefore was adopted for use in our one-pot synthesis. The ketone **2** appeared to exist in the enol form in solution, and in the case of the related compound derived from methyl 4-(methylamino)benzoate as the aniline component, X-ray crystallography showed that the compound existed as the enol form in the solid state also (Fig. 1).

Table 1

Catalyzed reaction of methyl 2-diazo-3-oxobutanoate **1** with 4-bromo-*N*-methylaniline



Catalyst	Solvent	Yield **2**/%
$Rh_2(OAc)_4$	Toluene	66
$Rh_2(OAc)_4$	DCE	44
$Rh_2(NHCOC_3F_7)_4$	Toluene	65
$Cu(OTf)_2$	Toluene	72
$Cu(OTf)_2$	DCE	67
$Cu(OCOCF_3)_2$	Toluene	84
$CuCl_2$	Toluene	0
$CuCl_2$	DCE	0
$InCl_3$	Toluene	19
$Sc(OTf)_3$	Toluene	20
$Sc(OTf)_3$	DCE	13
$BF_3 \cdot Et_2O$	Toluene	0

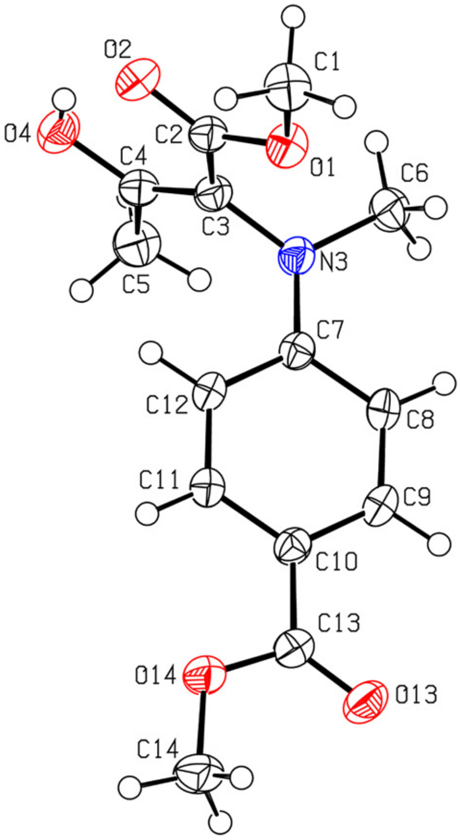


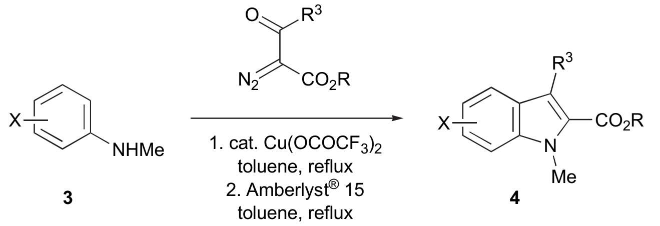
Figure 1. X-ray crystal structure of methyl 2-[*N*-(4-methoxycarbonylphenyl)-*N*-methylamino]-3-oxobutanoate (enol form) prepared by N–H insertion reaction of methyl 2-diazo-3-oxobutanoate **1** with methyl 4-(methylamino)benzoate.[31]

A number of protic acids and Lewis acids have been used to effect the cyclization of α-(*N*-arylamino)-ketones or -acetals in the classical Bischler reaction or in its Nordlander modification,[32] and therefore we screened a range of these in order to optimize the cyclization of the ketone **2** into the indole, methyl 5-bromo-1,3-dimethylindole-2-carboxylate. Of the conditions tried, the use of acidic ion-exchange resin (Amberlyst® 15) proved best—other conditions ($FeCl_3$, $AlCl_3$, $Yb(OTf)_3$, $ZnCl_2$, TFA, *p*-TsOH) were less satisfactory.

Application of the optimized conditions to a range of anilines **3** resulted in the formation of indoles **4** (Table 2). Thus, copper(II) trifluoroacetate catalyzed N–H insertion in boiling toluene was followed by addition of Amberlyst® 15 and further heating to give the indoles **4** in modest to good yields after chromatographic purification. The process is tolerant of a range of functional groups on the aniline, and in the case of the *m*-substituted aniline derivative **3b**, a mixture of indoles was formed on cyclization with the 6-methoxyindole predominating (ca. 3:1). In the case of indole **4j**, the use of dirhodium(II) tetraacetate as catalyst in the first step proved superior.

Table 2

One-pot conversion of *N*-methylanilines **3** into indoles **4**

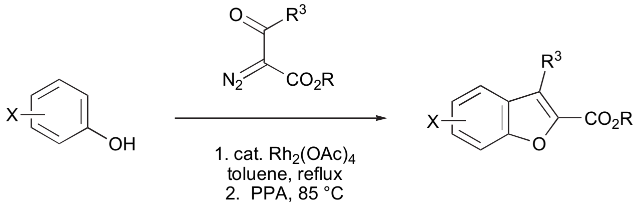


Compound **3**	X	R	R^3	Indole **4** X	**4**	Indole **4** yield/%
a	2-MeO	Me	Me	7-MeO	**a**	33
b	3-MeO	Me	Me	6-MeO	$\mathbf{b^1}$	55
				4-MeO	$\mathbf{b^2}$	19
c	4-Br	Me	Me	5-Br	**c**	75
d	4-Cl	Me	Me	5-Cl	**d**	80
e	4-F	Me	Me	5-F	**e**	81
f	$4\text{-}NO_2$	Me	Me	$5\text{-}NO_2$	**f**	52
g	4-MeO	Me	Me	5-MeO	**g**	30
h	$4\text{-}CO_2Me$	Me	Me	$5\text{-}CO_2Me$	**h**	60
i	4-Me	Me	Me	5-Me	**i**	47
f	$4\text{-}NO_2$	Et	Ph	$4\text{-}NO_2$	**j**	50[a]
d	4-Cl	Et	$4\text{-}NO_2C_6H_4$	5-Cl	**k**	36

[a] In this case dirhodium(II) tetraacetate was used as catalyst in the first step.

We next addressed the synthesis of benzofurans from phenols using a similar metal carbene based strategy but involving an O–H, rather than N–H, insertion reaction. Insertion of carbenes or metal carbenes into O–H bonds is a well known process,[33] and a number of examples involving phenolic components have been reported both from our own laboratory,[34] and by others.[35,36] In the case of O–H insertion, dirhodium(II) carboxylates are usually the catalyst of choice, and this proved to be true in the current case. No attempt was made to isolate the intermediate aryloxyketones, which were cyclized into benzofurans **6** by addition of polyphosphoric acid (PPA) at 85 °C, following removal of the toluene solvent. The results are shown in Table 3, and although the yields are for the most part fairly modest, the method tolerates a range of functional groups in the starting phenol.

Table 3
Conversion of phenols **5** into benzofurans **6**



Compound **5**	X	R	R^3	Benzofuran **6** X	**6**	Benzofuran **6** yield/%
a	2-Br	Me	Me	7-Br	**a**	67
b	3-MeO	Me	Me	6-MeO	**b**	19
c	4-Br	Me	Me	5-Br	**c**	32
d	4-Cl	Me	Me	5-Cl	**d**	47
e	4-NO_2	Me	Me	5-NO_2	**e**	26
f	4-MeO	Me	Me	5-MeO	**f**	34
g	4-CO_2Me	Me	Me	5-CO_2Me	**g**	33
d	4-Cl	Et	Ph	5-Cl	**h**	53

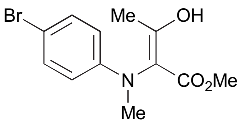
In conclusion we have demonstrated the application of transition-metal carbene X–H insertion reactions (X=N or O) in the simple conversion of anilines and phenols into indoles and benzofurans, respectively.

3. Experimental

3.1. General procedures

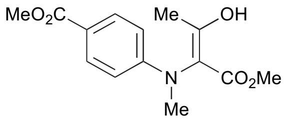
Commercially available reagents were used throughout without purification unless otherwise stated. Light petroleum refers to the fraction with bp 40–60 °C. Ether refers to diethyl ether. Analytical thin layer chromatography was carried out on aluminium backed plates coated with silica gel, and visualized under UV light at 254 and/or 360 nm. Column chromatography was carried out on silica gel unless otherwise stated. Fully characterized compounds are chromatographically homogeneous. Infrared spectra were recorded in the range 4000–600 cm^{-1}. NMR spectra were recorded at 300, 400 and 500 MHz (^{1}H frequencies, corresponding ^{13}C frequencies 75, 100 and 125 MHz). Chemical shifts are quoted in parts per million and are referenced to residual H in the deuterated solvent as the internal standard. In the ^{13}C NMR spectra, signals corresponding to CH, CH_2, or CH_3 groups are assigned from DEPT. High and low resolution mass spectra were recorded on a time-of-flight mass spectrometer.

3.2. Methyl (2*E*)-2-[(4-bromophenyl)methylamino]-3-hydroxy-2-butenoate 2



To methyl 2-diazo-3-oxobutanoate **1** (92 mg, 0.648 mmol) and 4-bromo-*N*-methylaniline (100 mg, 0.537 mmol) in dry toluene (10 mL) was added copper trifluoroacetate (2 mol %). The solution was heated at reflux for 2 h. The solvent was removed under reduced pressure and the residue was subjected to chromatography using ethyl acetate/light petroleum (1:5) to yield the *title compound* as an off-white crystalline solid (135 mg, 84%); mp 133–135 °C. Found: M+Na^+, 322.0051. $C_{12}H_{14}{}^{79}BrNO_3+Na^+$ requires 322.0049. ν_{max} ($CHCl_3$)/cm^{-1} 2954, 2881, 2817, 1651, 1616, 1592, 1491, 1386, 1361, 1345; δ_H (400 MHz; $CDCl_3$) 12.24 (1H, s, OH), 7.29 (2H, m, ArH), 6.51 (2H, m, ArH), 3.74 (3H, s, OMe), 3.03 (3H, s, NMe), 1.97 (3H, s, Me); δ_C (100 MHz; $CDCl_3$) 176.0 (C), 172.2 (C), 148.0 (C), 131.8 (CH), 113.6 (CH), 110.4 (C), 109.1 (C), 51.9 (Me), 39.0 (Me), 17.5 (Me); *m*/*z* (ESI) 322 (MNa^+, 100%), 300 (MH^+, 33), 242 (51).

3.3. Methyl (2*E*)-2-[(4-methoxycarbonylphenyl)-methylamino]-3-hydroxy-2-butenoate

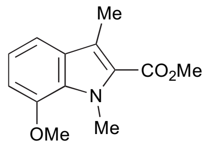


To methyl 2-diazo-3-oxobutanoate (103 mg, 0.725) and methyl 4-(methylamino)benzoate (100 mg, 0.610 mmol) in dry toluene (10 mL) was added copper trifluoroacetate hydrate (2 mol %). The solution was heated at reflux for 2 h. The solvent was removed under reduced pressure and the residue was subjected to chromatography using ethyl acetate/light petroleum (1:4) to yield the *title compound* as a colourless crystalline solid (135 mg, 80%); mp 140–141 °C. Found: M+H^+, 280.1179. $C_{14}H_{17}NO_5+H^+$ requires 280.1185. ν_{max} ($CHCl_3$)/cm^{-1} 1702, 1652, 1603, 1517, 1440, 1362, 1333, 1267, 1181, 1123, 1107; δ_H (400 MHz; $CDCl_3$) 12.27 (1H, s, OH), 7.90 (2H, d, *J* 9.0 Hz, ArH), 6.61 (2H, d, *J* 9.0 Hz, ArH), 3.85 (3H, s, OMe), 3.69 (3H, s, OMe), 3.10 (3H, s, NMe), 1.94 (3H, s, Me); δ_C (100 MHz; $CDCl_3$) 175.8 (C), 171.8 (C), 167.3 (C), 152.5 (C), 131.35 (CH), 118.5 (C), 111.1 (CH), 110.2 (C), 52.0 (Me), 51.5 (Me), 39.1 (Me), 17.5 (Me); *m*/*z* (ES^+) 302 (MNa^+, 6%), 280 (MH^+, 23).

3.4. Synthesis of indoles 4

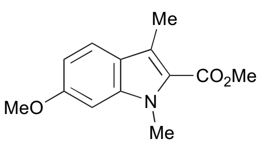
3.4.1. General method. To methyl 2-diazo-3-oxobutanoate **1** (92 mg, 0.645 mmol) and the *N*-methylaniline **3** (0.537 mmol) in toluene (10 mL) was added copper(II) trifluoroacetate hydrate (2 mol %). The reaction mixture was heated at reflux for 2 h. Amberlyst® 15 (300 mg) was added, and the mixture was heated at reflux overnight. The solvent was removed under reduced pressure and the residue was subjected to chromatography to give the indole **4**.

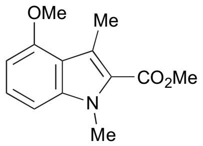
3.4.1.1. Methyl 7-methoxy-1,3-dimethylindole-2-carboxylate ***4a***.



To methyl 2-diazo-3-oxobutanoate (0.124 g, 0.873 mmol) and 2-methoxy-*N*-methylaniline (0.100 g, 0.729 mol) in toluene (10 mL) was added copper trifluoroacetate hydrate (2 mol %). The reaction mixture was heated at reflux for 2 h. Amberlyst® 15 (0.300 g) was added and the resultant mixture was heated at reflux overnight. Work up as above gave the title compound as a colourless solid (56 mg, 33%); mp 62–64 °C (lit.,[15] mp 61–63 °C); ν_{max} ($CHCl_3$)/cm^{-1} 2951, 2837, 1694, 1574, 1496, 1458, 1399, 1372, 1352, 1324, 1274, 1152, 1105, 1047; δ_H (400 MHz; $CDCl_3$) 7.26 (1H, dd, *J* 7.6, 0.8 Hz, ArH), 7.03(1H, t, *J* 7.6 Hz, ArH), 6.73 (1H, d, *J* 7.6 Hz, ArH), 4.31 (3H, s, NMe), 3.95 (3H, s, OMe), 3.94 (3H, s, OMe), 2.53 (3H, s, Me); δ_C (100 MHz; $CDCl_3$) 163.4 (C), 148.0 (C), 129.16 (C), 129.17 (C), 125.7 (C), 120.8 (C), 119.8 (CH), 113.2 (CH), 105.4 (CH), 55.5 (Me), 51.3 (Me), 35.0 (Me), 11.0 (Me).

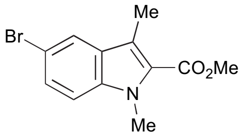
3.4.1.2. Methyl 6-methoxy-1,3-dimethylindole-2-carboxylate ***4b***^{1} *and methyl 4-methoxy-1,3-dimethylindole-2-carboxylate* ***4b***^{2}.





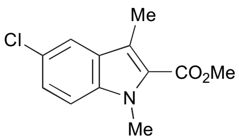
To methyl 2-diazo-3-oxobutanoate (120 mg, 0.875 mmol) and 4-chloro-*N*-methylaniline (100 mg, 0.729 mmol) in toluene (10 mL) was added copper trifluoroacetate hydrate (2.5 mol %). The reaction mixture was heated at reflux for 2 h. Amberlyst® 15 (300 mg) was added and the mixture was heated at reflux overnight. Work up as above gave (i) methyl 6-methoxy-1,3-dimethylindole-2-carboxylate **4b**^{1} as a colourless crystalline solid (94 mg, 55%); mp 94–95 °C (lit.,[15] 93–94 °C); δ_H (400 MHz; CDCl$_3$) 7.54 (1H, d, *J* 8.8 Hz, ArH), 6.83 (1H, dd, *J* 8.8, 2.0 Hz, ArH), 6.73 (1H, d, *J* 2.0 Hz, ArH), 3.97 (3H, s, OMe), 3.94 (3H, s, OMe), 3.91 (3H, s, NMe), 2.56 (3H, s, Me); and (ii) methyl 4-methoxy-1,3-dimethylindole-2-carboxylate **4b**^{2} (32 mg, 19%); mp 89–90 °C (lit.,[15] mp 90–92 °C); δ_H (400 MHz; CDCl$_3$) 7.24 (1H, t, *J* 8.0 Hz, ArH), 6.92 (1H, d, *J* 8.4 Hz, ArH), 6.45 (1H, d, *J* 7.6 Hz, ArH), 3.96 (3H, s, OMe), 3.94 (3H, s, OMe), 3.93 (3H, s, NMe), 2.79 (3H, s, Me).

3.4.1.3. Methyl 5-bromo-1,3-dimethylindole-2-carboxylate ***4c***.



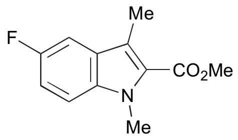
To methyl 2-diazo-3-oxobutanoate (92 mg, 0.645 mmol) and 4-bromo-*N*-methylaniline (100 mg, 0.537 mmol) in toluene (10 mL) was added copper trifluoroacetate hydrate (2 mol %). The reaction mixture was heated at reflux for 2 h. Amberlyst® 15 (300 mg) was added, and the mixture was heated at reflux overnight. Work up as above gave the *title compound* as a colourless solid (121 mg, 75%); mp 91–93 °C. Found: M+H$^+$, 303.9940. C$_{12}$H$_{12}$^{79}BrNO$_2$+Na$^+$ requires 303.9944. ν_{max} (CHCl$_3$)/cm^{-1} 2952, 1704, 1464, 1445, 1401, 1365, 1134, 1109; δ_H (400 MHz; CDCl$_3$) 7.80 (1H, s, H-4), 7.42(1H, dd, *J* 8.8, 2.0 Hz, H-6), 7.22 (1H, d, *J* 8.8 Hz, H-7), 3.99 (3H, s, NMe), 3.96 (3H, s, OMe), 2.54 (3H, s, Me); δ_C (100 MHz; CDCl$_3$) 163.2 (C), 137.3 (C), 128.6 (C), 128.1 (CH), 123.2 (C), 119.8 (CH), 112.8 (C), 111.6 (CH), 110.0 (C), 51.5 (Me), 32.2 (Me), 10.7 (Me); *m*/*z* (ESI) 282 (MH$^+$, 8%).

3.4.1.4. Methyl 5-chloro-1,3-dimethylindole-2-carboxylate ***4d***.



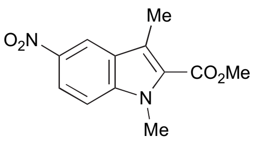
To methyl 2-diazo-3-oxobutanoate (0.120 g, 0.847 mmol) and 4-chloro-*N*-methylaniline (0.100 g, 0.706 mmol) in toluene (10 mL) was added copper trifluoroacetate hydrate (2 mol %). The reaction mixture was heated at reflux for 2 h. Amberlyst® 15 (0.300 g) was added, and the mixture was heated at reflux overnight. Work up as above gave the title compound as a colourless solid (0.134 g, 80%); mp 65–67 °C (lit.,[15] mp 64–66 °C); ν_{max} (CHCl$_3$)/cm^{-1} 2952, 1704, 1467, 1445, 1366, 1134, 1110, 871; δ_H (400 MHz; CDCl$_3$) 7.62 (1H, s, H-4), 7.26 (2H, m, ArH), 3.97 (3H, s, NMe), 3.96 (3H, s, OMe), 2.53 (3H, s, Me); δ_C (100 MHz; CDCl$_3$) 163.2 (C), 137.0 (C), 127.9 (C), 125.9 (C), 125.6 (CH), 125.4 (C), 120.0 (CH), 111.2 (CH), 110.0 (C), 51.5 (Me), 32.2 (Me), 10.7 (Me).

3.4.1.5. Methyl 5-fluoro-1,3-dimethylindole-2-carboxylate ***4e***.



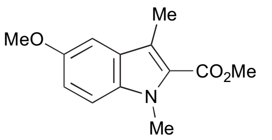
To methyl 2-diazo-3-oxobutanoate (0.140 g, 0.959 mmol) and 4-fluoro-*N*-methylaniline (0.100 g, 0.800 mmol) in toluene (10 mL) was added copper trifluoroacetate hydrate (2 mol %). The reaction mixture was heated at reflux for 2 h. Amberlyst® 15 (0.300 g) was added, and the mixture heated at reflux overnight. Work up as above gave the *title compound* as a colourless solid (134 mg, 81%); mp 107–108 °C. Found: C, 64.9; H, 5.4; N, 6.3. C$_{12}$H$_{12}$FNO$_2$ requires C, 65.2; H, 5.5; N, 6.3%. Found: M+H$^+$, 222.0929. C$_{12}$H$_{12}$FNO$_2$+H$^+$ requires 222.0930. ν_{max} (CHCl$_3$)/cm^{-1} 2952, 1704, 1625, 1490, 1461, 1400, 1385, 1368. 1122, 1105, 908; δ_H (400 MHz; CDCl$_3$) 7.27 (2H, m, ArH), 7.11 (1H, td, *J* 9.0, 2.4 Hz, ArH), 3.99 (3H, s, OMe), 3.96 (3H, s, NMe), 2.53 (3H, s, Me); δ_C (100 MHz; CDCl$_3$) 163.3 (C), 157.7 (d, *J* 236.5 Hz, CF), 135.4 (C), 127.1 (d, *J* 10.0 Hz, C), 126.7 (C), 120.2 (d, *J* 6.0 Hz, C), 114.3 (d, *J* 27.2 Hz, CH), 111.1 (d, *J* 9.1 Hz, CH), 104.9 (d, *J* 22.1 Hz, CH), 51.5 (Me), 32.3 (Me), 10.8 (Me); *m*/*z* (ESI) 222 (MH$^+$, 22%).

3.4.1.6. Methyl 1,3-dimethyl-5-nitroindole-2-carboxylate ***4f***.



To methyl 2-diazo-3-oxobutanoate (0.37 g, 2.60 mmol) and *N*-methyl-4-nitroaniline (0.300 g, 2.00 mmol) in toluene (25 mL) was added copper trifluoroacetate hydrate (11.6 mg, 0.04 mmol). The reaction mixture was heated at reflux for 150 min. Amberlyst® 15 (0.300 g) was added. The resultant mixture was heated at reflux overnight. Work up as above gave the *title compound* as a yellow solid (0.26 g, 52%); mp 179–181 °C (lit.,[15] mp 178–180 °C). Found: C, 58.1; H, 4.9; N, 11.0. C$_{12}$H$_{12}$N$_2$O$_4$ requires C, 58.1; H, 4.9, N, 11.3%. ν_{max} (CHCl$_3$)/cm^{-1} 3683, 2927, 2400, 1698, 1624, 1492, 1459, 1402, 1385, 1298, 1268, 1128, 1107, 1039; δ_H (400 MHz; CDCl$_3$) 8.65 (1H, d, *J* 2.1 Hz, H-4), 8.22 (1H, dd, *J* 9.3, 2.1 Hz, H-6), 7.38 (1H, d, *J* 9.0 Hz, H-7), 4.05 (3H, s, OMe), 3.99 (3H, s, NMe), 2.62 (3H, s, Me); δ_C (100 MHz; CDCl$_3$) 162.7 (C), 141.6 (C), 140.9 (C), 127.8(C), 126.3 (C), 123.0 (C), 120.2 (CH), 118.4 (CH), 110.2 (CH), 51.9 (Me), 32.7 (Me), 10.8 (Me).

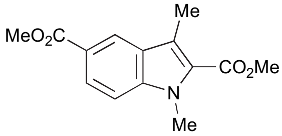
3.4.1.7. Methyl 5-methoxy-1,3-dimethylindole-2-carboxylate ***4g***.



To methyl 2-diazo-3-oxobutanoate (0.100 g, 0.873 mmol) and 4-methoxy-*N*-methylaniline (0.100 g, 0.729 mmol) in toluene (10 mL) was added copper trifluoroacetate hydrate (2.5 mol %). The reaction mixture was heated at reflux for 2.5 h. Amberlyst® 15 (0.300 g) was added and the mixture heated at reflux overnight. Work up as above gave the title compound as an off-white crystalline solid (0.10 g, 30%); mp 81–83 °C (lit.,[15] mp 81–82 °C); ν_{max} (CHCl$_3$)/cm^{-1} 3683, 2927, 2400, 1698, 1624, 1492, 1459, 1402, 1385, 1298, 1268, 1128, 1107, 1039; δ_H (400 MHz; CDCl$_3$) 7.27 (1H, m, ArH), 7.06 (2H, m, ArH), 4.00 (3H, s, OMe), 3.96 (3H, s, OMe), 3.90 (3H, s, NMe), 2.58 (3H, s Me); δ_C (100 MHz; CDCl$_3$) 163.5 (C), 154.1 (C), 134.4 (C), 127.1

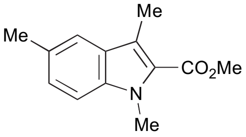
(C), 119.9 (C), 116.8 (CH), 111.0 (CH), 100.8 (CH), 55.8 (Me), 51.3 (Me), 32.2 (Me), 10.9 (Me).

3.4.1.8. Dimethyl 1,3-dimethyl-1H-indole-2,5-dicarboxylate ***4h****.*



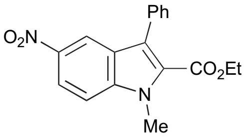
To methyl 2-diazo-3-oxobutanoate (103 mg, 0.726 mmol) and methyl 4-(methylamino)benzoate (100 mg, 0.605 mmol) in toluene (10 mL) was added copper trifluoroacetate hydrate (2 mol %). The reaction mixture was heated at reflux for 2 h. Amberlyst® 15 (300 mg) was added, and the resultant mixture heated at reflux overnight. Work up as above gave the *title compound* as an off-white solid (94 mg, 60%); mp 128–129 °C. Found: M+Na$^+$, 284.0899. $C_{14}H_{15}NO_4$+Na$^+$ requires 284.0893. ν_{max} ($CHCl_3$)/cm^{-1} 2952, 2844, 1705, 1614, 1574, 1547, 1445, 1370, 1317, 1300, 1151, 1114; δ_H (400 MHz; $CDCl_3$) 8.45 (1H, s, H-4), 8.01 (1H, d, *J* 8.8 Hz, H-6), 7.32 (1H, d, *J* 8.8 Hz, H-7), 4.00 (3H, s, NMe), 3.97 (3H, s, OMe), 3.95 (3H, s, OMe), 2.60 (3H, s, Me); δ_C (100 MHz; $CDCl_3$) 167.8 (C), 163.1 (C), 140.9 (C), 126.7 (C), 126.2 (C), 126.1 (CH), 124.1 (CH), 122.3 (C), 121.8 (C), 109.7 (CH), 52.0 (Me), 51.6 (Me), 32.4 (Me), 10.8 (Me); *m*/*z* (ESI) 284 (MNa$^+$, 100%), 262 (MH$^+$, 33), 203 (2).

3.4.1.9. Methyl 1,3,5-trimethylindole-2-carboxylate ***4i****.*



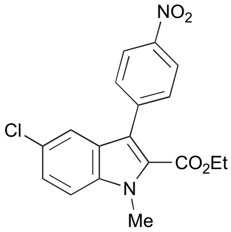
To methyl 2-diazo-3-oxobutanoate (157 mg, 1.10 mmol) and *N*-methyl-4-toluidine (121 mg, 1.00 mmol) in toluene (10 mL) was added copper trifluoroacetate hydrate (8 mg, 0.025 mmol). The reaction mixture was heated to 110 °C for 2 h. Amberlyst® 15 (300 mg) was added and the reaction mixture heated under reflux overnight. The mixture was cooled to room temperature and filtered. The filtrate was concentrated under reduced pressure and the resultant solid loaded onto a silica cartridge (20 g) and purified using a gradient of 0–50% ethyl acetate/cyclohexane over a period of 30 min. The crude produce recrystallized from methanol to yield the *title compound* as a colourless crystalline solid (101 mg, 47%); mp 34–36 °C. Found: M+H$^+$, 218.1171. $C_{13}H_{15}NO_2$+H$^+$ requires 218.1181. ν_{max} ($CHCl_3$)/cm^{-1} 2918, 1699, 1530, 1443, 1403, 1379, 1354, 1265, 1249, 1193, 1183; δ_H (400 MHz; $CDCl_3$) 7.45 (1H, s, H-4), 7.25 (1H, d, *J* 8.5 Hz, H-7), 7.21 (1H, dd, *J* 8.5, 1.3 Hz, H-6), 3.99 (3H, s, NMe), 3.95 (3H, s, OMe), 2.58 (3H, s, Me), 2.48 (3H, s, ArMe); δ_C (100 MHz; $CDCl_3$) 163.6 (C), 137.4 (C), 128.9 (C), 127.2 (CH), 124.9 (C), 122.5 (C), 120.2 (C), 120.0 (CH), 109.7 (CH), 51.3 (Me), 32.1 (Me), 21.4 (Me), 10.8 (Me); *m*/*z* (ESI) 218 (MH$^+$, 33%), 217 (M$^+$, 20), 186 (100).

3.4.1.10. Ethyl 1-methyl-5-nitro-3-phenylindole-2-carboxylate ***4j****.*



To a solution of *N*-methyl-4-nitroaniline (152 mg, 1 mmol) and ethyl 2-diazo-3-oxo-3-phenylpropanoate (263 mg, 1.200 mmol) in toluene (2 mL), stirred under an atmosphere of nitrogen at room temperature was added rhodium(II) acetate dimer (11.05 mg, 0.025 mmol). The reaction mixture was heated at reflux for 2 h. Amberlyst® 15 (300 mg) was added and the mixture heated at reflux overnight. The solution was allowed to cool to room temperature and the solvent was removed under reduced pressure. The sample was loaded in dichloromethane onto a silica cartridge (50 g) and purified using a 0–50% ethyl acetate/cyclohexane solvent system over 40 min. The resultant yellow solid was recrystallized from methanol to yield the *title compound* as light yellow crystalline needles (162 mg, 50%), mp 122–123 °C (lit.,[37] mp not given); ν_{max} ($CHCl_3$)/cm^{-1} 1693, 1609, 1519, 1335, 1251, 1092; δ_H (400 MHz; $CDCl_3$) 8.52 (1H, d, *J* 2.3 Hz, H-4), 8.27 (1H, dd, *J* 9.3, 2.3 Hz, H-6), 7.50–7.40 (6H, m, ArH), 4.24–4.19 (2H, q, *J* 7.0 Hz, OC*H*$_2$Me), 4.14 (3H, s, NMe), 1.09–1.05 (3H, t, *J* 7.1 Hz, OCH$_2$Me); δ_C (100 MHz; $CDCl_3$) 161.9 (C), 142.6 (C), 140.5 (C), 133.0 (C), 130.2 (CH), 128.1 (CH), 127.7 (CH), 126.6 (C), 126.0 (C), 125.1 (C), 120.3 (CH), 119.3 (CH), 118.5 (C), 110.4 (CH), 61.1 (CH_2), 32.6 (Me), 13.6 (Me).

3.4.1.11. Ethyl 5-chloro-1-methyl-3-(4-nitrophenyl)-indole-2-carboxylate ***4k****.*

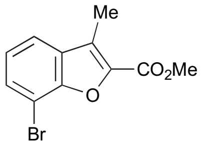


To 4-chloro-*N*-methylaniline (142 mg, 1 mmol) and ethyl 2-diazo-3-(4-nitrophenyl)-3-oxopropanoate (290 mg, 1.1 mmol) in toluene (5 mL) was added copper trifluoroacetate hydrate (7 mg, 0.025 mmol). The reaction mixture was heated to 110 °C and stirred for 2 h. Amberlyst® 15 (300 mg) was added and heated under reflux overnight. The reaction mixture was cooled and filtered. The solvent was removed under reduced pressure and the resultant oil purified over a silica cartridge (20 g) using a solvent gradient of 0–50% ethyl acetate/cyclohexane. The crude product was recrystallized from methanol to give the *title compound* as a yellow crystalline solid (129 mg, 36%); mp 108–109 °C.Found: C, 60.3; H, 4.1; N, 7.7. $C_{18}H_{15}ClN_2O_4$ requires C, 60.3; H, 4.2; N, 7.8%. Found: M+H$^+$, 359.0797. $C_{18}H_{15}{}^{35}ClN_2O_4$+H$^+$ requires 359.0799. ν_{max} ($CHCl_3$)/cm^{-1} 2976, 1701, 1594, 1512, 1485, 1463, 1384, 1345, 1278, 1257, 1242, 1181; δ_H (400 MHz; $CDCl_3$) 8.31 (2H, d, *J* 8.8 Hz, ArH), 7.59 (2H, d, *J* 8.8 Hz, ArH), 7.46 (1H, d, *J* 1.6 Hz, H-4), 7.39 (1H, d, *J* 8.8 Hz, H-7), 7.37 (1H, dd, *J* 8.8, 1.8 Hz, H-6), 4.23 (2H, q, *J* 7.0 Hz, OC*H*$_2$Me), 4.10 (3H, s, NMe), 1.10 (3H, t, *J* 7.2 Hz, OCH$_2$*Me*); δ_C (100 MHz; $CDCl_3$) 161.7 (C), 146.9 (C), 141.5 (C), 136.7 (C), 131.2 (C), 127.3 (C), 126.8 (C), 126.3 (C), 126.2 (CH), 123.1 (CH), 121.1 (CH), 120.0 (CH), 111.7 (CH), 61.1 (CH_2), 32.4 (Me), 13.8 (Me); *m*/*z* (ESI) 717 (2M+H$^+$, 100%), 359 (MH$^+$, 45).

3.5. Synthesis of benzofurans 6

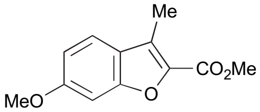
3.5.1. General method. To methyl 2-diazo-3-oxobutanoate (157 mg, 1.10 mmol) and the phenol **5** (1.00 mmol) in toluene (0.5 mL) under an atmosphere of nitrogen was added rhodium(II) acetate dimer (11 mg, 0.025 mmol). The reaction mixture was heated to 110 °C for 2 h. The mixture was allowed to cool to room temperature and the solvent removed under reduced pressure. Polyphosphoric acid (300 mg) was pre-heated to 85 °C and added to the crude reaction mixture. The viscous mixture was stirred at 85 °C overnight. The reaction mixture was cooled to 0 °C and water (20 mL) was added. The organic material was extracted with methyl *tert*-butyl ether (3×30 mL) and neutralized with sodium hydrogen carbonate. The organic layer was dried over $MgSO_4$ and the suspension was filtered and the filtrate concentrated under reduced pressure. The residue was purified over a silica cartridge (20 g) using a solvent gradient of 0–50% ethyl acetate/cyclohexane over a period of 20 min.

3.5.1.1. Methyl 7-bromo-3-methylbenzofuran-2-carboxylate ***6a****.*



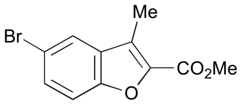
To methyl 2-diazo-3-oxobutanoate (157 mg, 1.10 mmol) and 2-bromophenol (173 mg, 1.00 mmol) in toluene (0.5 mL) under an atmosphere of nitrogen was added rhodium(II) acetate dimer (11 mg, 0.025 mmol). The reaction mixture was heated at reflux for 3 h. The resultant solution was allowed to cool and the solvent removed under reduced pressure. Polyphosphoric acid (300 mg) was pre-heated to 85 °C and added to the residue. The mixture was stirred at 85 °C overnight. The reaction mixture was cooled to 0 °C and diluted with distilled water (20 mL). Work up as above gave the *title compound* as a colourless solid (181 mg, 67%); mp 99–101 °C. Found: M+H$^+$, 268.9806. $C_{11}H_9{}^{79}BrO_3+H^+$ requires 268.9813. ν_{max} ($CHCl_3$)/cm^{-1} 2950, 1710, 1604, 1439, 1356, 1288, 1210, 1134; δ_H (400 MHz; $CDCl_3$) 7.61 (1H, d, *J* 7.8 Hz, ArH), 7.57 (1H, d, *J* 7.8 Hz, ArH), 7.19 (1H, t, *J* 7.8 Hz, ArH), 4.00 (3H, s, OMe), 2.59 (3H, s, Me); δ_C (100 MHz; $CDCl_3$) 160.5 (C), 141.5 (C), 130.7, 130.2 (C), 126.4 (C), 124.4 (CH), 120.2 (CH), 104.9 (C), 71.9, 52.1 (Me), 9.5 (C); *m*/*z* (ESI) 269 (MH$^+$, 53%).

3.5.1.2. Methyl 6-methoxy-3-methylbenzofuran-2-carboxylate ***6b****.*



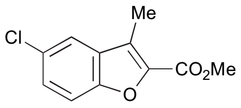
To methyl 2-diazo-3-oxobutanoate (157 mg, 1.100 mmol) and 3-methoxyphenol (124 mg, 1 mmol) in toluene (0.5 mL) under nitrogen was added rhodium(II) acetate dimer (11 mg, 0.025 mmol). The reaction mixture was heated at reflux for 2 h. The resultant solution was allowed to cool and the solvent removed under reduced pressure. Polyphosphoric acid (300 mg) was pre-heated to 85 °C and added to the residue. The mixture was stirred at 85 °C overnight. The reaction mixture was cooled to 0 °C and diluted with distilled water (20 mL). Work up as above gave the *title compound* as an off-white solid (41 mg, 19%); mp 80–81 °C (lit.,[38] mp 90 °C). Found: M+H$^+$, 221.0810. $C_{12}H_{12}O_4+H^+$ requires 221.0814. ν_{max} ($CHCl_3$)/cm^{-1} 2948, 2343, 2327, 2310, 1698, 1620, 1599, 1497, 1428, 1361, 1312, 1271, 1235, 1189, 1152, 1130; δ_H (400 MHz; $CDCl_3$) 7.49 (1H, d, *J* 8.5 Hz, H-4), 7.02 (1H, d, *J* 2.3 Hz, H-7), 6.94 (1H, dd, *J* 8.5, 2.3 Hz, H-5), 3.97 (3H, s, OMe), 3.87 (3H, s, OMe), 2.57 (3H, s, Me); δ_C (100 MHz; $CDCl_3$) 160.8 (CH), 155.7 (C), 140.1 (C), 126.4 (C), 122.4 (C), 121.4 (CH), 116.5 (C), 113.3 (CH), 95.6 (CH), 55.7 (Me), 51.8 (Me), 9.4 (Me); *m*/*z* (EI$^+$) 221 (MH$^+$, 100%), 220 (M$^+$, 18).

3.5.1.3. Methyl 5-bromo-3-methylbenzofuran-2-carboxylate ***6c****.*



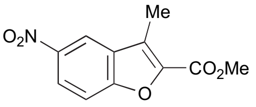
To methyl 2-diazo-3-oxobutanoate (157 mg, 1.100 mmol) and 4-bromophenol (173 mg, 1 mmol) in toluene (0.5 mL) under an atmosphere of nitrogen was added rhodium(II) acetate dimer (11 mg, 0.025 mmol). The reaction mixture was heated to 110 °C for 2 h. The mixture was allowed to cool to room temperature and the solvent removed under reduced pressure. Polyphosphoric acid (300 mg) was pre-heated to 85 °C and added to the crude reaction mixture. The viscous mixture was stirred at 85 °C overnight. The reaction mixture was cooled to 0 °C and distilled water (20 mL) added. Work up as above gave the *title compound* as a colourless crystalline solid (86 mg, 32%); mp 83–84 °C (MeOH) (lit.,[39] mp not given). Found: M+H$^+$, 268.9806. $C_{11}H_9{}^{79}BrO_3+H^+$ requires 268.9813. ν_{max} ($CHCl_3$)/cm^{-1} 3675, 2988, 2902, 1720, 1440, 1364, 1310, 1147; δ_H (400 MHz; $CDCl_3$) 7.77 (1H, d, *J* 2.0 Hz, H-4), 7.54 (1H, dd, *J* 8.8, 2.0 Hz, H-6), 7.42 (1H, d, *J* 8.8 Hz, H-7), 3.99 (3H, s, OMe), 2.56 (3H, s, Me); δ_C (100 MHz; $CDCl_3$) 160.5 (C), 153.0 (C), 130.9 (C), 130.8 (CH), 125.0 (C), 123.8 (CH), 120.0 (C), 116.3 (C), 113.7 (CH), 52.2 (Me), 9.3 (Me); *m*/*z* (ESI) 269 (MH$^+$, 100%).

3.5.1.4. Methyl 5-chloro-3-methylbenzofuran-2-carboxylate ***6d****.*



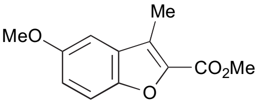
To methyl 2-diazo-3-oxobutanoate (157 mg, 1.10 mmol) and 4-chlorophenol (129 mg, 1.00 mmol) in toluene (0.5 mL) under an atmosphere of nitrogen was added rhodium(II) acetate dimer (11 mg, 0.025 mmol). The reaction mixture was heated to 110 °C for 2 h. The mixture was allowed to cool to room temperature and the solvent removed under reduced pressure. Polyphosphoric acid (300 mg) was pre-heated to 85 °C and added to the crude reaction mixture. The viscous mixture was stirred at 85 °C overnight. The reaction mixture was cooled to 0 °C and distilled water (20 mL) was added. Work up as above gave the *title compound* as a light orange solid (105 mg, 47%); mp 86–87 °C (EtOH) (lit.,[40] mp 95–95.8 °C). Found: M+H$^+$, 225.0314. $C_{11}H_9{}^{35}ClO_3+H^+$ requires 225.0318. ν_{max} ($CHCl_3$)/cm^{-1} 2951, 1730, 1713, 1602, 1581, 1446, 1358, 1308, 1278, 1224, 1145, 1132, 1100; δ_H (400 MHz; $CDCl_3$) 7.60 (1H, d, *J* 2.0 Hz, H-4), 7.46 (1H, d, *J* 8.8 Hz, H-7), 7.40 (1H, dd, *J* 8.8, 2.1 Hz, H-6), 3.99 (3H, s, OMe), 2.56 (3H, s, Me); δ_C (100 MHz; $CDCl_3$) 160.5 (C), 152.7 (C), 141.9 (C), 130.3 (C), 129.0 (C), 128.1 (CH), 125.2 (C), 120.7 (CH), 113.3 (CH), 52.1 (Me), 9.3 (Me).

3.5.1.5. Methyl 3-methyl-5-nitrobenzofuran-2-carboxylate ***6e****.*



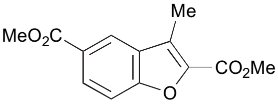
To methyl 2-diazo-3-oxobutanoate (157 mg, 1.1 mmol) and 4-nitrophenol (139 mg, 1 mmol) in toluene (0.5 mL) under an atmosphere of nitrogen was added rhodium(II) acetate dimer (11 mg, 0.025 mmol). The reaction vessel was sealed and heated to 110 °C for 2 h. The reaction mixture was allowed to cool to ambient temperature and the solvent removed under reduced pressure. Polyphosphoric acid (300 mg) was heated to 85 °C for 30 min and added to the crude reaction mixture. The viscous solution was stirred at 85 °C overnight. The reaction mixture was cooled in an ice bath and distilled water (20 mL) was added. Work up as above gave the *title compound* as a yellow solid (60 mg, 26%); mp 120–122 °C (MeOH) (lit.,[41] mp 147–148.5 °C); ν_{max} ($CHCl_3$)/cm^{-1} 2110, 2957, 2925, 1726, 1525, 1435, 1336, 1287, 1223, 1146; δ_H (400 MHz; $CDCl_3$) 8.60 (1H, d, *J* 2.3 Hz, H-4), 8.37 (1H, dd, *J* 9.1, 2.3 Hz, H-6), 7.65 (1H, d, *J* 9.1 Hz, H-7), 4.02 (3H, s, OMe), 2.66 (3H, s, Me); δ_C (100 MHz; $CDCl_3$) 160.0 (C), 156.9 (C), 144.4 (C), 143.6 (C), 129.4 (C), 126.2 (C), 123.2 (CH), 118.0 (CH), 111.8 (CH), 52.4 (Me), 9.3 (Me).

3.5.1.6. Methyl 5-methoxy-3-methylbenzofuran-2-carboxylate ***6f***.



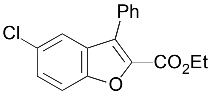
To methyl 2-diazo-3-oxobutanoate (157 mg, 1.10 mmol) and 4-methoxyphenol (124 mg, 1.00 mmol) in toluene (0.5 mL) under an atmosphere of nitrogen was added rhodium(II) acetate dimer (11 mg, 0.025 mmol). The reaction vessel was sealed and heated to 110 °C for 2 h. The reaction mixture was allowed to cool to ambient temperature and the solvent removed under reduced pressure. Polyphosphoric acid (300 mg) was heated to 85 °C and added to the crude reaction mixture. The viscous solution was stirred at 85 °C overnight. The reaction mixture was cooled in an ice bath and distilled water (20 mL) was added. Work up as above gave the *title compound* as an off-white solid (75 mg, 34%); mp 82–83 °C (MeOH) (lit.,[42] mp 88–89 °C); ν_{max} (CHCl$_3$)/cm^{-1} 2959, 1710, 1589, 1480, 1430, 1366, 1321, 1292, 1233, 1185, 1147; δ_H (400 MHz; CDCl$_3$) 7.44 (1H, d, *J* 9.0 Hz, H-7), 7.07 (1H, dd, *J* 9.0, 2.5 Hz, H-6), 7.01 (1H, d, *J* 2.5 Hz, H-4), 3.99 (3H, s, OMe), 3.88 (3H, s, OMe), 2.58 (3H, s, Me); δ_C (100 MHz; CDCl$_3$) 160.8 (C), 156.2 (C), 149.4 (C), 141.3 (C), 129.4 (C), 125.8 (C), 117.6 (CH), 112.8 (CH), 102.2 (CH), 55.8 (Me), 51.9 (Me), 9.3 (Me).

3.5.1.7. Dimethyl 3-methylbenzofuran-2,5-dicarboxylate ***6g***.



To methyl 2-diazo-3-oxobutanoate (157 mg, 1.100 mmol) and methyl 4-hydroxybenzoate (152 mg, 1 mmol) in toluene (0.5 mL) under an atmosphere of nitrogen was added rhodium(II) acetate dimer (11 mg, 0.025 mmol). The reaction vessel was sealed and heated to 110 °C for 2 h. The reaction mixture was allowed to cool to ambient temperature and the solvent removed under reduced pressure. Polyphosphoric acid (300 mg) was heated to 85 °C and added to the crude reaction mixture. The viscous solution was stirred at 85 °C for 1 h. The mixture was cooled to room temperature and ice cold water (20 mL) was added. Work up as above gave the *title compound* as a colourless solid (81 mg, 33%); mp 144–145 °C (MeOH). Found: M+H$^+$, 249.0759. C$_{13}$H$_{12}$O$_5$+H$^+$ requires 249.0763. ν_{max} (CHCl$_3$)/cm^{-1} 2969, 1713, 1596, 1434, 1290, 1223, 1145; δ_H (400 MHz; CDCl$_3$) 8.40 (1H, d, *J* 1.7 Hz, H-4), 8.17 (1H, dd, *J* 8.8, 1.7 Hz, H-6), 7.58 (1H, d, *J* 8.8 Hz, H-7), 4.01 (3H, s, OMe), 3.97 (3H, s, OMe), 2.64 (3H, s, Me); δ_C (100 MHz; CDCl$_3$) 166.8 (C), 160.5 (C), 156.8 (C), 142.0 (C), 129.2 (CH), 129.1 (C), 126.2 (C), 125.7 (C), 123.8 (CH), 112.1 (CH), 52.3 (Me), 52.2 (Me), 9.3 (Me); *m*/*z* (ESI) 249 (MH$^+$, 100%).

3.5.1.8. Ethyl 5-chloro-3-phenylbenzofuran-2-carboxylate ***6h***.



To ethyl 2-diazo-3-oxo-3-phenylpropanoate (240 mg, 1.100 mmol) and 4-chlorophenol (129 mg, 1 mmol) in toluene (0.5 mL) under an atmosphere of nitrogen was added rhodium(II) acetate dimer (11 mg, 0.025 mmol) and heated to 110 °C for 3 h. The reaction mixture was allowed to cool to ambient temperature and the solvent removed under reduced pressure. Polyphosphoric acid (300 mg) was heated to 85 °C and added to the crude mixture. The viscous solution was stirred at 85 °C overnight. The mixture was cooled to 0 °C and ice cold water (20 mL) was added. Work up as above gave the *title compound* as a colourless solid (158 mg, 53%); mp 91–92 °C (MeOH) (lit.,[43] mp 105–106 °C). Found: M+H$^+$, 301.0625. C$_{17}$H$_{13}$^{35}ClO$_3$+H$^+$ requires 301.0631. ν_{max} (CHCl$_3$)/cm^{-1} 3661, 2987, 2902, 1720, 1371, 1272, 1261, 1226, 1145; δ_H (400 MHz; CDCl$_3$) 7.58–7.43 (8H, m, ArH), 4.36 (2H, q, *J* 7.0 Hz, OC*H*$_2$Me), 1.29 (3H, t, *J* 7.1 Hz, OCH$_2$*Me*); δ_C (100 MHz; CDCl$_3$) 159.5 (C), 152.8 (C), 141.3 (C), 130.0 (C), 129.9 (CH), 129.7 (C), 129.6 (C), 128.7 (CH), 128.6 (C), 128.3 (CH), 128.3 (CH), 121.6 (CH), 113.4 (CH), 61.5 (CH$_2$), 14.1 (Me); *m*/*z* (ESI) 323 (MNa$^+$, 42%), 301 (MH$^+$, 70), 255 (100).

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References and notes

1. Doyle, M. P.; McKervey, M. A.; Ye, T. *Modern Catalytic Methods for Organic Synthesis with Diazo Compounds*; John Wiley: New York, NY, 1998.
2. Zhang, Z.; Wang, J. *Tetrahedron* **2008**, *64*, 6577–6605.
3. Curtius, T. *J. Prakt. Chem.* **1888**, *38*, 396–440.
4. Yates, P. *J. Am. Chem. Soc.* **1952**, *74*, 5376–5381.
5. Bachmann, S.; Fielenbach, D.; Jorgensen, K. A. *Org. Biomol. Chem.* **2004**, *2*, 3044–3049.
6. Liu, B.; Zhu, S. F.; Zhang, W.; Chen, C.; Zhou, Q. L. *J. Am. Chem. Soc.* **2007**, *129*, 5834–5835.
7. Lee, E. C.; Fu, G. C. *J. Am. Chem. Soc.* **2007**, *129*, 12066–12067.
8. Moody, C. J. *Angew. Chem., Int. Ed.* **2007**, *46*, 9148–9150.
9. Aller, E.; Buck, R. T.; Drysdale, M. J.; Ferris, L.; Haigh, D.; Moody, C. J.; Pearson, N. D.; Sanghera, J. B. *J. Chem. Soc., Perkin Trans. 1* **1996**, 2879–2884.
10. Ferris, L.; Haigh, D.; Moody, C. J. *J. Chem. Soc., Perkin Trans. 1* **1996**, 2885–2888.
11. Yamazaki, K.; Kondo, Y. *J. Chem. Soc., Chem. Commun.* **2002**, 210–211.
12. Zhu, Z.; Espenson, J. H. *J. Am. Chem. Soc.* **1996**, *118*, 9901–9907.
13. Galardon, E.; LeMaux, P.; Simonneaux, G. *J. Chem. Soc., Perkin Trans. 1* **1997**, 2455–2456.
14. Moody, C. J.; Swann, E. *Synlett* **1998**, 135–136.
15. Bashford, K. E.; Cooper, A. L.; Kane, P. D.; Moody, C. J.; Muthusamy, S.; Swann, E. *J. Chem. Soc., Perkin Trans. 1* **2002**, 1672–1687.
16. Lee, S. H.; Clapham, B.; Koch, G.; Zimmermann, J.; Janda, K. D. *J. Comb. Chem.* **2003**, *5*, 188–196.
17. Moody, C. J.; Bagley, M. C. *J. Chem. Soc., Perkin Trans. 1* **1998**, 601–607.
18. Bagley, M. C.; Bashford, K. E.; Hesketh, C. L.; Moody, C. J. *J. Am. Chem. Soc.* **2000**, *122*, 3301–3313.
19. Buck, R. T.; Clarke, P. A.; Coe, D. M.; Drysdale, M. J.; Ferris, L.; Haigh, D.; Moody, C. J.; Pearson, N. D.; Swann, E. *Chem.—Eur. J.* **2000**, *6*, 2160–2167.
20. Davies, J. R.; Kane, P. D.; Moody, C. J.; Slawin, A. M. Z. *J. Org. Chem.* **2005**, *70*, 5840–5851.
21. Hughes, R. A.; Thompson, S. P.; Alcaraz, L.; Moody, C. J. *J. Am. Chem. Soc.* **2005**, *127*, 15644–15651.
22. Linder, J.; Blake, A. J.; Moody, C. J. *Org. Biomol. Chem.* **2008**, *6*, 3908–3916.
23. Sundberg, R. J. *The Chemistry of Indoles*; Academic: New York, NY, 1970.
24. Sundberg, R. J. *Indoles*; Academic: London, 1996.
25. Gribble, G. W. *J. Chem. Soc., Perkin Trans. 1* **2000**, 1045–1075.
26. Cacchi, S.; Fabrizi, G. *Chem. Rev.* **2005**, *105*, 2873–2920.
27. Bischler, A.; Brion, H. *Chem. Ber.* **1892**, *25*, 2860–2879.
28. Bischler, A.; Firemann, P. *Chem. Ber.* **1893**, *26*, 1336–1349.
29. Pansare, S. V.; Jain, R. P.; Bhattacharyya, A. *Tetrahedron Lett.* **1999**, *40*, 5255–5258.
30. Jung, J. C.; Avery, M. A. *Tetrahedron Lett.* **2006**, *47*, 7969–7972.
31. Crystallographic data can be obtained free of charge via www.ccdc.cam.ac.uk/conts/retrieving.html (or from the Cambridge Crystallographic Data Centre, 12 Union Road, Cambridge, CB21EZ, UK; fax: +44 1223 336 033; or deposit@ccdc.cam.ac.uk) CCDC 743574.
32. Nordlander, J. E.; Catalane, D. B.; Kotian, K. D.; Stevens, R. M.; Haky, J. E. *J. Org. Chem.* **1981**, *46*, 778–782.
33. Miller, D. J.; Moody, C. J. *Tetrahedron* **1995**, *51*, 10811–10843.
34. Cox, G. G.; Miller, D. J.; Moody, C. J.; Sie, E.-R. H. B.; Kulagowski, J. J. *Tetrahedron* **1994**, *50*, 3195–3212.
35. Lecercle, D.; Taran, F. *Synlett* **2007**, 1863–1868.
36. Chen, C.; Zhu, S. F.; Liu, B.; Wang, L. X.; Zhou, Q. L. *J. Am. Chem. Soc.* **2007**, *129*, 12616–12617.
37. Bhagwat, S. S.; Gude, C. *Tetrahedron Lett.* **1994**, *35*, 1847–1850.
38. Whalley, W. B. *J. Chem. Soc.* **1951**, 665–671.
39. Li, J. C.; Rush, T. S.; Li, W.; DeVincentis, D.; Du, X. M.; Hu, Y. H.; Thomason, J. R.; Xiang, J. S.; Skotnicki, J. S.; Tam, S.; Cunningham, K. M.; Chockalingam, P. S.; Morris, E. A.; Levin, J. I. *Bioorg. Med. Chem. Lett.* **2005**, *15*, 4961–4966.
40. Suzuki, T.; Horaguchi, T.; Shimizu, T.; Abe, T. *Bull. Chem. Soc. Jpn.* **1983**, *56*, 2762–2767.
41. Suzuki, T. *Bull. Chem. Soc. Jpn.* **1985**, *58*, 2821–2825.
42. Salvi, V. S.; Sethna, S. *J. Indian Chem. Soc.* **1968**, *45*, 433–438.
43. Walker, G. N.; Smith, R. T. *J. Org. Chem.* **1971**, *36*, 305–308.