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Synthesis of *N*-(iodophenyl)-amides via an unprecedented Ullmann–Finkelstein tandem reaction

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Abstract—Using a new Ullmann–Finkelstein tandem reaction, *N*-(iodophenyl)-amides were synthesized from the corresponding amides and iodo-bromobenzenes. The catalyst/ligand couple CuI/*N*,*N*′-dimethyl-cyclohexane-1,2-diamine was used for this reaction in dioxane with K_3PO_4 as base.

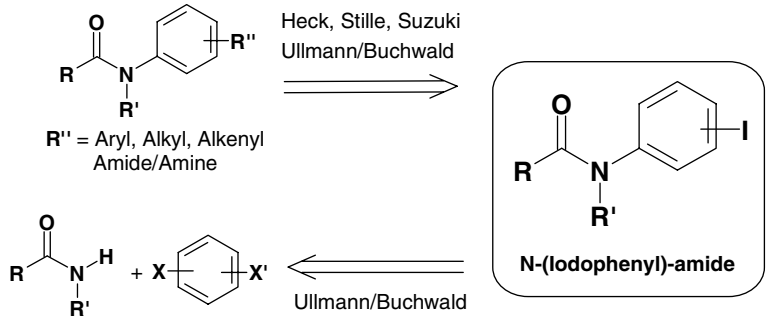
1. Introduction

Our aim was to discover an original methodology suitable for the preparation of a wide diversity of *N*-(iodophenyl)-amides. Iodine was selected among halogens due to its higher reactivity in Pd[1a,b] and Cu[2] catalyzed couplings. These iodophenylamides offer thus the possibility of being further diversified through palladium-catalyzed cross-coupling reactions like Stille,[3] Heck[4] or Suzuki–Miyaura[5] reactions, or with the copper-catalyzed N-arylation of amide[6] and amine[7] developed by Buchwald (Scheme 1). Such diverse *N*-(iodophenyl)-amides intermediates allow the preparation of original chemical libraries used in pharmaceutical investigation to the discovery of new leads.[8a,b] Although a straightforward method to access these compounds seemed to be the acylation of the corresponding anilines, their low reactivity often precludes the use of a broad diversity of acylation agents. We have thus attempted to prepare these compounds through N-arylation of amides according to the Ullmann[9a,b] reaction, which is not subjected to the same limitations, and allows tapping into the pool of complex primary amides for the diversified introduction.

In this study, we present the synthesis of *N*-(iodophenyl)-amides through the development of a tandem Ullmann–Finkelstein reaction between iodobromobenzenes **1p**, **1m** and **1o** and diverse amides.

2. Results and discussion

We first checked the possibility of using 1,4-diiodobenzene as electrophile for the copper assisted monoarylation



Scheme 1. Interest and synthesis of *N*-(iodophenyl)-amides.

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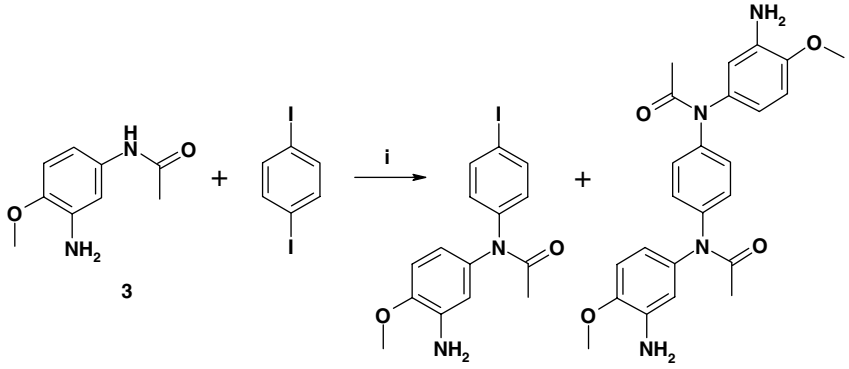
of amides. We engaged acetamide **3** with 1,4-diiodobenzene according to Buchwald's conditions. Though the expected monosubstituted compound was obtained, but the rapid and significant formation of the symmetric diamide **7** (30% after 22 h) represents the main limitation of this methodology (Table 1).

To decrease the formation of the disubstituted product, we replaced diiodobenzene with the less reactive dibrominated derivative with the expectation that a significant drop in reactivity after the first amidation would prevent the formation of **7** (the brominated compound would then have been converted in a second step into its iodinated analogue by the Finkelstein copper-catalyzed reaction described by Klapars and Buchwald[10]). The Ullmann reaction was thus carried out with 1,4-dibromobenzene and two different amides (Table 2).

According to our expectations, thanks to the lesser reactivity of the C–Br bond, no diamide was formed. However, amide **4**[11] could not be completely arylated in these conditions. Backing on the previous results, we decided to carry out the reaction with the corresponding

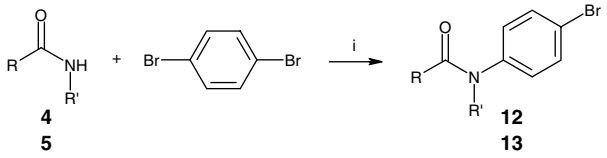
Table 1. Reaction of **3** with 1,4-diiodobenzene

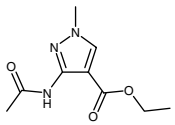


Time (h)	**8p** (%)[a]	**7** (%)[a]	Rate of conversion (%)[a,b]
2	80	20	50
22	70	30	90

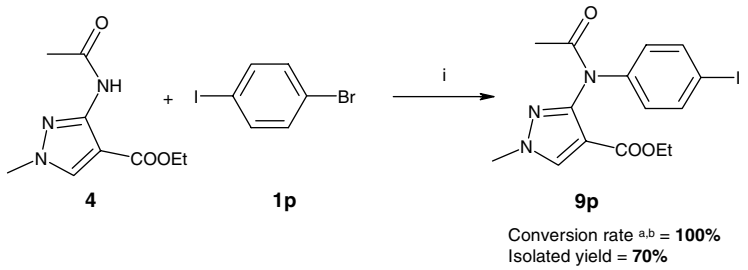
Reagents and conditions: (i) amide (1 equiv), 1,4-diiodobenzene (1.2 equiv), CuI (0.1 equiv), K_3PO_4 (2 equiv), *N*,*N*′-dimethyl-cyclohexane-1,2-diamine (0.2 equiv), Dioxane (0.5 M), 110 °C, 22 h.
[a] UV detection at 215 nm.
[b] Conversion of **3** in **8p** and **7**.

Table 2. Copper catalyzed Ullmann reaction between amides **4** or **5** and 1,4-dibromobenzene **2**



No.		Product	Rate of conversion[a,b] (%)	Yield[c] (%)
4		**12**	75	58
5		**13**	100	62

Reagents and conditions: (i) amide (1 equiv), 1,4-dibromobenzene (1.2 equiv), CuI (0.1 equiv), K_3PO_4 (2 equiv), *N*,*N*′-dimethyl-cyclohexane-1,2-diamine (0.2 equiv), Dioxane (0.5 M), 110 °C, 22 h.
[a] UV detection at 215 nm.
[b] Conversion of the amide to corresponding arylbrominated compounds.
[c] Isolated yield.



Scheme 2. Copper catalyzed tandem Ullmann–Finkelstein reaction between amides **4** and 1-bromo-4-iodobenzene **1p**. Reagents and conditions: (i) amide **4** (1 equiv), 1-bromo-4-iodobenzene (1.2 equiv), CuI (0.1 equiv), K_3PO_4 (2 equiv), *N*,*N*′-dimethyl-cyclohexane-1,2-diamine (0.2 equiv), Dioxane (0.5 M), 110 °C, 22 h. (a) UV detection at 215 nm, (b) conversion of **4** to corresponding N-arylated compounds.

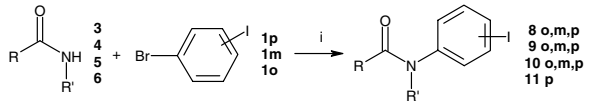
1-bromo-4-iodobenzene. Our expectation was that iodine would yield a fast substitution while the lower reactivity of the C–Br bond would prevent disubstitution. The reaction was carried out under the same conditions with 1-bromo-4-iodobenzene **1p** and amides **4** and **5**. Unexpectedly,[2] this reaction led directly to the one step formation of *N*-(iodophenyl)-amide **9p** with good yield (Scheme 2). Only trace amounts (<5%) of the *N*-(bromophenyl)-amide would be detected.

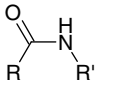
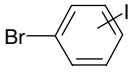
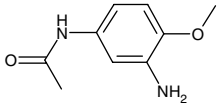
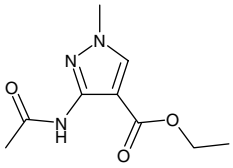
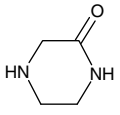
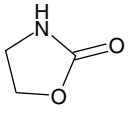
In order to study the scope and limitations of this reaction, we first examined the reactivity of the *ortho*, *meta* and *para* isomers of bromoiodobenzene, with three amides (**3**, **4** and **5**) and carbamate **6** (Table 3).

Both *para* and *meta* iodobenzene (**1p**, **1m**) gave a very good rate of conversion with the three amides and with the carbamate. On the contrary, the more hindered orthosubstituted bromoiodobenzene **1o** was less converted in the same reaction time.

The concomitance of the conditions for the Ullmann and the Finkelstein reactions led us to postulate a mechanism involving the liberation of iodide during the initial

Table 3. Copper catalyzed tandem Ullmann–Finkelstein reactions between diverse amides **3**–**6** and dihalobenzenes **1o**, **1m** and **1p**



No.			Product[a]	Rate of conversion[b,c] (%)	Yield[d] (%)
3		(**1p**) (**1m**) (**1o**)	**8p** **8m** **8o**	100 100 20	80 78 —
4		(**1p**) (**1m**) (**1o**)	**9p** **9m** **9o**	100 100 24	70 67 —
5		(**1p**) (**1m**) (**1o**)	**10p** **10m** **10o**	100 100 28	60 57 —
6		(**1p**)	**11p**	100	95

Reagents and conditions: (i) amide (1 equiv), bromoiodobenzene (1.2 equiv), CuI (0.1 equiv), K_3PO_4 (2 equiv), *N*,*N*′-dimethyl-cyclohexane-1,2-diamine (0.2 equiv), dioxane (0.5 M), 110 °C, 22 h.

[a] **p**: para, **m**: meta, **o**: ortho.

[b] UV detection at 215 nm.

[c] Conversion of amide in N-arylated compounds.

[d] Isolated yield.

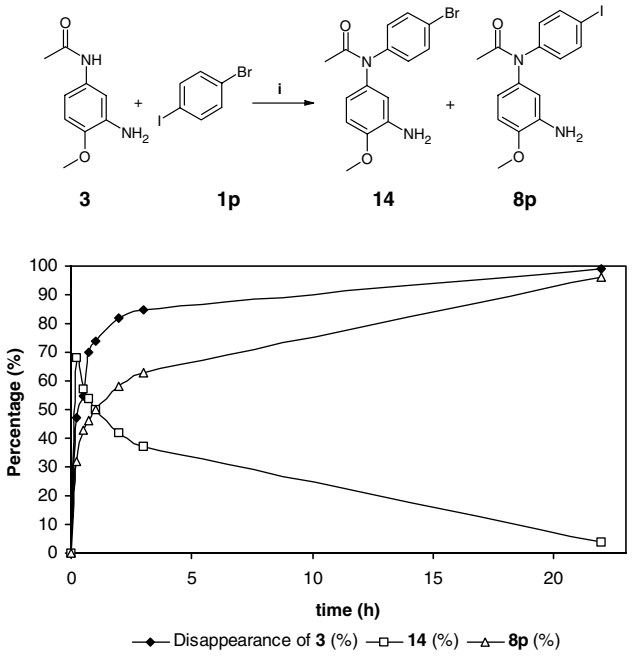
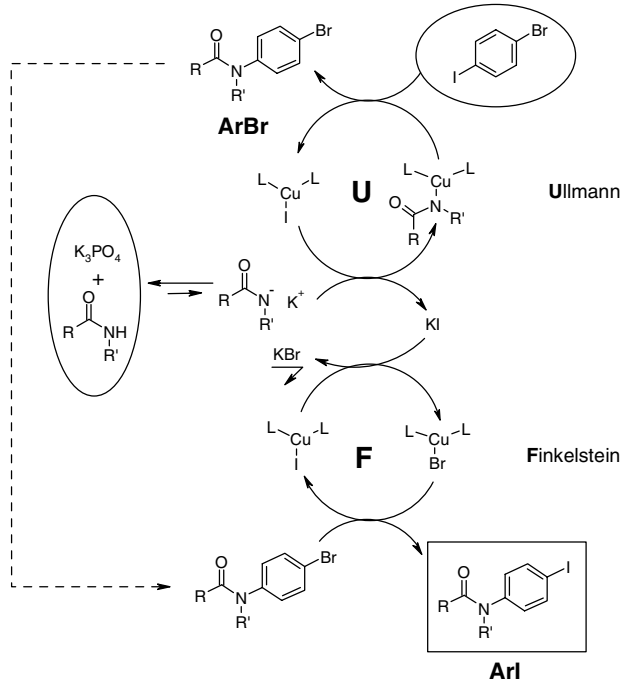


Figure 1. Disappearance of **3** (%) and relative ratio of **14/8p**. Reagents and conditions (i): amide **3** (1 equiv), 1-bromo-4-iodobenzene **1p** (1.2 equiv), CuI (0.1 equiv), K_3PO_4 (2 equiv), *N*,*N*′-dimethyl-cyclohexane-1,2-diamine (0.2 equiv), Dioxane (0.5 M), 110 °C. Sampling realized under an argon overpressure. Relative ratios of **14/8p** were calculated from HPLC–MS (identification by mass and quantification by UV detection at 215 nm).

Ullmann reaction. In order to confirm this hypothesis, we have carried out the reaction between acetamide **3** and 1-bromo-4-iodobenzene **1p** and monitored the formation of the brominated and the iodinated products.



Scheme 3. Supposed mechanism of the tandem Ullmann/Finkelstein reaction.

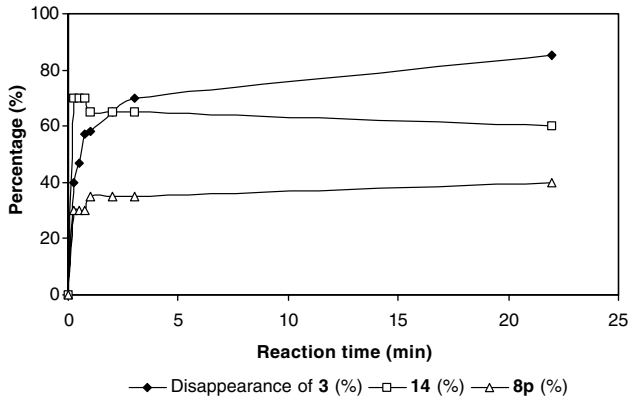


Figure 2. Disappearance of **3** (%) and relative ratio of **14/8p**. Reagents and conditions: (i) amide **3** (1 equiv), 1-bromo-4-iodobenzene **1p** (1.2 equiv), CuI (0.1 equiv), K_3PO_4 (2 equiv), *N*,*N*′-dimethyl-cyclohexane-1,2-diamine (0.2 equiv), DMF (0.5 M), 110 °C. Sampling realized under an argon overpressure. Relative ratios of **14/8p** were calculated from HPLC–MS (identification by mass and quantification by UV detection at 215 nm).

During the first 15 min the main product is **14** in agreement with the higher reactivity of the C–I bond, in copper catalyzed N-arylations[2] (Fig. 1). Then after 1 h, the copper catalyzed iodine–bromine exchange leads to the inversion of the initial proportion. The conversion curve puts forward that iodine substitution is the fastest process during the reaction (80% of disappearance after 2 h). The almost sequential course of the two steps of the tandem reaction is explained by the interdependence of the two implied catalytic cycles as represented in Scheme 3. Indeed the Ullmann catalytic cycle produces iodide required for the Finkelstein I–Br exchange in our conditions. Due to the large difference between the high solubility of the KI and the low solubility of KBr in dioxane, the reaction is eventually driven towards the formation of the iodinated compound by the precipitation of KBr.

This assumption was confirmed by carrying out the reaction in DMF. Indeed the higher solubility of KBr in this solvent precludes the displacement of the equilibrium by precipitation.[10] In these conditions both **14** and **8p** are formed and their ratio remains stable during all the reaction (Fig. 2).

3. Conclusion

In our attempt to synthesize *N*-iodophenylamides, as intermediates for further diversification, we have put forward an unprecedented tandem Ullmann–Finkelstein reaction based on classical Buchwald conditions. This condition works successfully with diverse functionalized aliphatic and aromatic amides and a carbamate. The limitation of this reaction depends on the steric hindrance of the bromoiodobenzene reactants. We also proposed a mechanism based on known catalytic cycles that has been verified through kinetic studies carried out in appropriate solvents.

4. Experimental

4.1. 3-Acetylamino-1-methyl-1*H*-pyrazole-4-carboxylic acid ethyl ester (4)

Compound (**4**) was synthesized from the corresponding amino-pyrazole (Schmidt et al.[11]) by acylation. Procedure: A 25 mL flask charged with the 3-aminopyrazole-4-carboxylic acid ethyl ester (170 mg, 1 mmol), Ac_2O (379 μL, 4 mmol) and acetic acid (10 mL) was heated under reflux for 1 h. The acetic acid was removed under reduced pressure, the residue was triturated in $NaHCO_3$ (10%, 20 mL). The aqueous layer was extracted with AcOEt (3 × 20 mL). The combined organic layer was then dried on $MgSO_4$, filtered and evaporated under reduced pressure to give **4**. Yield: 97%, white solid; mp 98–101 °C, ^{1}H NMR (300 MHz, $CDCl_3$): $\delta = 9.14$ (s, 1H, O=C–N*H*); 7.67 (s, 1H, C$H_{Pyrazole}$); 4.26 (q, 2H, $J_{HH} = 7$ Hz, CH_2–O); 3.85 (s, 3H, N–CH_3); 2.21 (s, 3H, O=C–CH_3); 1.31 (t, 3H, $J = 7$ Hz, CH_3–CH_2–O); ^{13}C NMR (75 MHz, $CDCl_3$): $\delta = 166.9$ (N–*C*=O); 164.1 (O–*C*=O); 148,6 (*C*q$_{Pyrazole}$); 132.6 (*C*H$_{Pyrazole}$); 110,1 (*C*q$_{Pyrazole}$); 60.5 (*C*H$_2$–O); 39.9 (N–*C*H$_3$); 24.6 (*C*H$_3$–C=O); 14.5 (*C*H$_3$–CH$_2$–O), LCMS (EI): $m/z = 212$ (base peak).

4.2. Ullmann and Ullmann/Finkelstein reaction general procedure

A dried Schlenk evacuated and backfilled with argon (2×) was charged with CuI (10 mg, 0.05 mmol), K_3PO_4 (213 mg, 1 mmol), the appropriated dihalobenzene (0.6 mmol), amide (0.5 mmol) under argon overpressure. Then the solvent DMF or dioxane (1 mL) and *N*,*N*′-dimethyl-cyclohexane-1,2-diamine (16 μL, 0.1 mmol) were injected into the tube. The sealed tube was stirred at 110 °C for 22 h. A solution of ammonia (28%, 1 mL) and water (15 mL) was sequentially added at rt to the reaction mixture. The resulting aqueous layer was extracted with AcOEt (3 × 15 mL). The combined organic layers were dried on $MgSO_4$, filtered and evaporated under reduced pressure. The residue was triturated in cyclohexane or purified on silica gel.

4.3. *N*-(3-Amino-4-methoxy-phenyl)-*N*-(4-iodo-phenyl)-acetamide (8p)

Yield: 80%, brown solid, mp: 125–127 °C, ^{1}H NMR (300 MHz, $CDCl_3$): $\delta = 7.61$ (d, 2H, $J_{HH} = 9$ Hz, CH_{PhI}); 7.03 (d, 2H, $J_{HH} = 9$ Hz, CH_{PhI}); 6.75 (m, 3H, CH_{arom}); 4.23 (s, 2H, NH_2); 3.86 (s, 3H, O–CH_3); 2.05 (s, 3H, CH_3–C=O); ^{13}C NMR (75 MHz, $CDCl_3$): $\delta = 170.8$ (N–*C*=O); 146.6 (*C*q); 142.7 (*C*q); 137.6 (*C*H$_{PhI}$); 137.3 (*C*q); 135.9 (*C*q); 127.1 (*C*H$_{PhI}$); 117.2 (*C*H$_{arom}$); 113.5 (*C*H$_{arom}$); 110.2 (*C*H$_{arom}$); 55.3 (*C*H$_3$–O); 23.5 (*C*H$_3$–C=O), LCMS (EI): $m/z = 383$ (base peak).

4.4. *N*-(3-Amino-4-methoxy-phenyl)-*N*-(3-iodo-phenyl)-acetamide (8m)

Yield: 78%, brown oil, ^{1}H NMR (300 MHz, $CDCl_3$): $\delta = 7.6$ (t, 1H, $J_{HH} = 2$ Hz, CH_{arom}); 7.5 (s, 1H, CH_{arom}); 7.24 (m, 1H, CH_{arom}); 7.02 (t, 1H, $J_{HH} = 7.5$ Hz, Harom); 6.75 (d, 1H, $J_{HH} = 9$ Hz, CH_{arom}); 6.62 (dd, 2H, $J_{HH} = 2.4$ Hz $J_{HH} = 9$ Hz, CH_{arom}); 4.0 (s, 2H, NH_2); 3.84 (s, 3H, O–CH_3); 2.03 (s, 3H, CH_3–C=O); ^{13}C NMR (75 MHz, $CDCl_3$): $\delta = 135.1$ (*C*H$_{arom}$); 135.0 (*C*H$_{arom}$); 130.4 (*C*H$_{arom}$); 125.2 (*C*H$_{arom}$); 118.8 (*C*H$_{arom}$); 115.1 (*C*H$_{arom}$); 110.9 (*C*H$_{arom}$); 55.9 (*C*H$_3$–O); 23.9 (*C*H$_3$–C=O), LCMS (EI): $m/z = 383$ (base peak).

4.5. 3-[Acetyl-(4-iodo-phenyl)-amino]-1-methyl-1*H*-pyrazole-4-carboxylic acid ethyl ester (9p)

Yield: 70%, colourless oil; ^{1}H NMR (300 MHz, $CDCl_3$): $\delta = 7.90$ (s, 1H, C$H_{Pyrazole}$); 7.60 (d, 2H, $J = 9$ Hz, CH_{PhI}); 7.21 (d, 2H, $J = 9$ Hz, CH_{PhI}); 4.25 (q, 2H, $J_{HH} = 7$ Hz, CH_2–O); 3.90 (s, 3H, N–CH_3); 2.03 (s, 3H, O=C–CH_3); 1.28 (t, 3H, $J = 7$ Hz, CH_3–CH_2–O); ^{13}C NMR (75 MHz, $CDCl_3$): $\delta = 170.5$ (N–*C*=O); 161.3 (O–*C*=O); 149.8 (*C*q$_{Pyrazole}$); 140.8 (*C*q$_{PhI}$); 137.9 (*C*H$_{PhI}$); 132.9 (*C*H$_{Pyrazole}$); 128.6 (*C*H$_{PhI}$); 110.2 (*C*q$_{Pyrazole}$); 91.3 (*C*q$_{PhI}$); 60.7 (*C*H$_2$–O); 40.1 (N–*C*H$_3$); 23.0 (*C*H$_3$–C=O); 14.5 (*C*H$_3$–CH$_2$–O), LCMS (EI): $m/z = 414$ (base peak).

4.6. 3-[Acetyl-(3-iodo-phenyl)-amino]-1-methyl-1*H*-pyrazole-4-carboxylic acid ethyl ester (9m)

Yield: 67%, white solid, mp: 117–121 °C; ^{1}H NMR (300 MHz, $CDCl_3$): $\delta = 7.91$ (s, 1H, C$H_{Pyrazole}$); 7.72 (s, 1H, CH_{PhI}); 7.53 (s, 1H, CH_{PhI}); 7.38 (s, 1H, CH_{PhI}); 7.05 (s, 1H, CH_{PhI}); 4.27 (q, 2H, $J_{HH} = 7$ Hz, CH_2–O); 3.94 (s, 3H, N–CH_3); 2.03 (s, 3H, O=C–CH_3); 1.30 (t, 3H, $J = 7$ Hz, CH_3–CH_2–O); ^{13}C NMR (75 MHz, $CDCl_3$): $\delta = 135.9$ (*C*H$_{Pyrazole}$); 135.8 (2 × *C*H$_{PhI}$); 130.3 (*C*H$_{PhI}$); 126.3 (*C*H$_{PhI}$); 60.8 (*C*H$_2$–O); 40.2 (N–*C*H$_3$); 23.0 (*C*H$_3$–C=O); 14.5 (*C*H$_3$–CH$_2$–O), LCMS (EI): $m/z = 414$ (base peak).

4.7. 1-(4-Iodo-phenyl)-piperazin-2-one (10p)

Yield: 60%, pale yellow solid, mp: 136–138 °C; ^{1}H NMR (300 MHz, DMSOd_6): $\delta = 7.71$ (d, 2H, $J_{HH} = 9$ Hz, CH_{PhI}); 7.15 (d, 2H, $J_{HH} = 9$ Hz, CH_{PhI}); 3.57 (t, 2H, $J_{HH} = 5$ Hz, CH_2–CH_2–N); 3.36 (s, 2H, N–CH_2–C=O); 3.08 (t, 2H, $J_{HH} = 5$ Hz, CH_2–N–C=O); ^{13}C NMR (75 MHz, DMSOd_6): $\delta = 170.0$ (*C*=O); 142.9 (*C*q$_{PhI}$); 138.1 (2 × *C*H$_{PhI}$); 128.56 (2 × *C*H$_{PhI}$); 91.7 (*C*q$_{PhI}$); 51.2 (CH_2–*C*H$_2$–N + N–*C*H$_2$–C=O); 43.4 (*C*H$_2$–N–C=O), LCMS (EI): $m/z = 303$ (base peak).

4.8. 1-(3-Iodo-phenyl)-piperazin-2-one (10m)

Yield: 57%, yellow oil; ^{1}H NMR (300 MHz, DMSOd_6): $\delta = 7.71$ (t, 1H, $J_{HH} = 1.5$ Hz, CH_{PhI}); 7.61 (dt, 1H, $J_{HH} = 7.5$ Hz $J_{HH} = 1.5$ Hz, CH_{PhI}); 7.35 (m, 1H, CH_{PhI}); 7.19 (t, 1H, $J_{HH} = 7.5$ Hz, CH_{PhI}); 3.57 (t, 2H, $J_{HH} = 5$ Hz, CH_2–CH_2–N); 3.37 (s, 2H, N–CH_2–C=O); 3.00 (t, 2H, $J_{HH} = 5$ Hz, CH_2–N–C=O); ^{13}C NMR (75 MHz, DMSOd_6): $\delta = 135.4$ (*C*H$_{PhI}$); 135.1 (*C*H$_{PhI}$); 131.4 (*C*H$_{PhI}$); 125.7 (*C*H$_{PhI}$); 51.4 (CH_2–*C*H$_2$–N); 51.1 (N–*C*H$_2$–C=O); 43.3 (*C*H$_2$–N–C=O), LCMS (EI): $m/z = 303$ (base peak).

4.9. 3-(4-Iodo-phenyl)-oxazolidin-2-one (11p)

Yield: 95%, brown solid, mp: 138–140 °C; ^{1}H NMR (300 MHz, $CDCl_3$): $\delta = 7.65$ (d, 2H, $J_{HH} = 9$ Hz, CH_{PhI}); 7.31 (d, 2H, $J_{HH} = 9$ Hz, CH_{PhI}); 4.48 (t, 2H, $J_{HH} = 7.8$ Hz, CH_2–O–C=O); 4.02 (t, 2H, $J_{HH} = 7.8$ Hz, CH_2–N–C=O); ^{13}C NMR (75 MHz, $CDCl_3$): $\delta = 155.0$ (*C*=O); 138.1 (2 × *C*H$_{PhI}$); 120.1 (2 × *C*H$_{PhI}$); 87.5 (*C*q$_{PhI}$); 61.4 (*C*H$_2$–O–C=O); 45.1 (*C*H$_2$–N–C=O), LCMS (EI): $m/z = 290$ (base peak).

4.10. 3-[Acetyl-(4-bromo-phenyl)-amino]-1-methyl-1*H*-pyrazole-4-carboxylic acid ethyl ester (12)

Yield: 58%, colourless oil; ^{1}H NMR (300 MHz, $CDCl_3$): $\delta = 7.91$ (s, 1H, CH_{arom}); 7.35 (m, 4H, CH_{arom}); 4.27 (q, 2H, $J_{HH} = 7$ Hz, CH_2–O); 3.91 (s, 3H, N–CH_3); 2.04 (s, 3H, O=C–CH_3); 1.29 (t, 3H, $J = 7$ Hz, CH_3–CH$_2$–O); ^{13}C NMR (75 MHz, $CDCl_3$): $\delta = 135.8$ (*C*H$_{Pyrazol}$); 131.9 (*C*H$_{PhBr}$); 128.4 (*C*H$_{PhBr}$); 60.8 (*C*H$_2$–O); 40.1 (N–*C*H$_3$); 22.9 (*C*H$_3$–C=O); 14.5 (*C*H$_3$–CH$_2$–O), LCMS (EI): $m/z = 366$, 368 (base peak).

4.11. 1-(4-Bromo-phenyl)-piperazin-2-one (13)

Yield: 62%, yellowish solid, mp: 99–102 °C; ^{1}H NMR (300 MHz, DMSOd_6): $\delta = 7.58$ (d, 2H, $J_{HH} = 9$ Hz, CH_{PhBr}); 7.31 (d, 2H, $J_{HH} = 9$ Hz, CH_{PhBr}); 3.58 (t, 2H, $J_{HH} = 5$ Hz, CH$_2$–CH_2–N); 3.37 (s, 2H, N–CH_2–C=O); 3.0 (t, 2H, $J_{HH} = 5$ Hz, CH_2–N–C=O); ^{13}C NMR (75 MHz, DMSOd_6): $\delta = 132.2$ (2 × *C*H$_{PhBr}$); 128.4 (2 × *C*H$_{PhBr}$); 51.2 (CH$_2$–*C*H$_2$–N); 51.1 (N–*C*H$_2$–C=O); 43.4 (*C*H$_2$–N–C=O), LCMS (EI): $m/z = 255$, 257 (base peak).

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References and notes

1. (a) Amatore, C. et al. *J. Am. Chem. Soc.* **1991**, *113*, 8375–8384; (b) Smith, G. B. et al. *J. Org. Chem.* **1994**, *59*, 8151–8156.
2. Klapars, A.; Huang, X.; Buchwald, S. L. *J. Am. Chem. Soc.* **2002**, *124*, 7421–7428.
3. (a) Stille, J. K. *Angew. Chem., Int. Ed. Engl.* **1986**, *25*, 508; (b) Achab, S.; Velay, L. *Tetrahedron. Lett.* **2005**, *46*, 2627–2630.
4. Withcombe, N. J.; Hii, K. K.; Gibson, S. E. *Tetrahedron* **2001**, *57*, 7449–7476.
5. Miyaura, N.; Suzuki, A. *Chem. Rev.* **1995**, *95*, 2457–2483.
6. Klapars, A. et al. *J. Am. Chem. Soc.* **2001**, *123*, 7727–7729.
7. Kwong, F. Y.; Buchwald, S. L. *Org. Lett.* **2003**, *5*, 793–796.
8. (a) Deprez-Poulain, R.; Deprez, B. *Curr. Top. Med. Chem.* **2004**, *4*, 569–580; Poulain, R. F. et al. *J. Med. Chem.* **2001**, *44*, 3378–3390; Poulain, R. F. et al. *J. Med. Chem.* **2001**, *44*, 3391–3401; (b) Jacoby, E. et al. *Curr. Top. Med. Chem.* **2005**, *5*, 397–411.
9. (a) Ullmann, F. *Ber. Dtsh. Chem. Ges.* **1903**, *36*, 2389–2391; (b) Ullmann, F. *Ber. Dtsh. Chem. Ges.* **1904**, *37*, 853–857.
10. Klapars, A.; Buchwald, S. L. *J. Am. Chem. Soc.* **2002**, *124*, 14844–14845.
11. Schmidt, P. et al. *Helv. Chim. Acta* **1959**, *42*, 349.