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Tetrahedron
Tetrahedron 62 (2006) 11740–11746

# 1,4-Carbonylative addition of arylboronic acids to methyl vinyl ketone: a new synthetic tool for rapid furan and pyrrole synthesis

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Received 21 July 2006; revised 7 September 2006; accepted 12 September 2006
Available online 17 October 2006

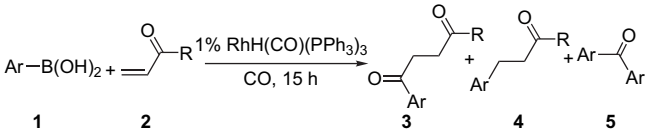
**Abstract**—The rhodium catalysed 1,4-carbonylative addition of arylboronic acids to methyl vinyl ketone under carbon monoxide pressure was studied. High yields of 1,4-diketones were obtained using a catalytic system formed from $Rh(COD)_2BF_4$ (COD=1,5-cyclooctadiene) and triphenylphosphine even at very low catalyst loading (0.02 mol %). A short synthetic procedure combining this carbonylation reaction with a subsequent cyclisation step affords pyrroles or furans.


## 1. Introduction

Five membered heterocyclic compounds such as pyrroles, furans or thiophenes and their derivatives are important products in organic chemistry since their structures can be found in many natural or therapeutic compounds.[1] Classical methods to access this class of compounds involve cyclisation reactions of 1,4-dicarbonyl reagents.[2] In this context a straightforward synthesis of 1,4-diketones is a significant objective in synthetic chemistry.

The Stetter reaction of substituted benzaldehydes with enones catalysed by thiazolium salts leads to 1,4-diketones and has already been applied for synthetic purposes but has the disadvantage of requiring high catalytic loadings.[3] Alternatively, several stoichiometric acyl–metal reagents such as acyl cobaltate,[4] ferrate,[5] cuprate,[6] nickelate,[7] molybdate[8] or chromate[9] were also used efficiently. The acyl moiety stabilised by the metal formally acts as a nucleophile with the enones playing the role of Michael acceptors. Unfortunately, the toxicity of the metal salt as well as the cost of their stoichiometric use is a strong limitation to their further development. Further improvements in the use of acyl–transition metal intermediates were dedicated to their production in the course of a catalytic cycle. Oxidative addition of aldehydes at a rhodium centre usually at high reaction temperatures,[10] or transmetallation of the acyl moiety from a acylzirconocene[11] or acylstannyl[12] derivative to a palladium metal centre allowed the use of catalytic amounts of noble metal but needed again the stoichiometric amounts of acyl reagent. In view of the wide availability and low cost of carbon monoxide, another interesting approach would be the development of a catalysed acylating reaction through in situ generation of the metal–acyl reagent via an environmentally clean carbonylation step and using simple reagents. Despite important developments of carbonylation reactions, acylation reactions of enones involving carbon monoxide source are rare.[13]

In this context, the reaction of 1,4-addition of arylboronic acids to α,β-enones attracted our attention.[14] Actually this reaction is catalysed by rhodium salts and involves a rhodium–carbon bond containing intermediate.[15] Since rhodium complexes are suitable for carbonylation reactions, it was anticipated that a molecule of CO would readily insert into the metal–carbon bond to afford a metal–acyl derivative suitable for a subsequent acylation reaction (see Scheme 1). This hypothesis was confirmed experimentally and we recently reported the rhodium catalysed carbonylative 1,4-addition of arylboronic acids to methyl vinyl ketone.[16]




**Scheme 1**. Rhodium catalysed aroylation of enones with arylboronic acids and carbon monoxide.

Under CO pressure, the reaction allows the conversion of an arylboronic acid **1** and an unsubstituted enone **2** to a 1,4-diketone **3** (Scheme 1). The product **4**, which is selectively obtained when the reaction was carried out in the absence

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doi:10.1016/j.tet.2006.09.035

of CO and diarylketone **5** are usually obtained as side products in low quantities depending on the reaction conditions. We now wish to report complementary catalytic data to our preliminary communication as well as the direct application of this new reaction in a carbonylation–cyclisation short synthetic procedure for furan or pyrrole heterocycle synthesis.

## 2. Results and discussion

### 2.1. Catalytic carbonylation reactions

Reactions performed with phenylboronic acid **1a** and 2 equiv of methyl vinyl ketone **2a** at 80 °C under 20 bar CO showed strongly differing results depending on the nature of the solvent (Table 1). The reaction is completely ineffective in dioxane (entry 3) and only partially occurring in dry THF or in THF/water solvents (entries 1 and 2). Best results were indeed obtained with MeOH as a polar and protic solvent. Dried methanol led to very similar results to those obtained if methanol is combined with 10% $H_2O$ (entries 4 and 8). This observation is rather unexpected since in the parent reaction of rhodium catalysed 1,4-addition of arylboronic acids to enones without CO, it is commonly observed that organic solvent/water solutions are preferred to water free solvents. Water is thought to be involved in a protonolysis step of a rhodium–carbon bond containing intermediate leading to ketone liberation (see Scheme 2). In the case of the carbonylation reaction, water is not necessary for high conversion and it is likely that the proton comes from the boronic acid itself. Actually, the reaction worked in dry THF in which the only source of proton was the boronic acid. The possible role of MeOH as a proton donor cannot be completely discarded. However, the high efficiency observed with this solvent could also arise from its high polarity. Less polar alcoholic solvents gave lower yield of **3** without noticeable changes in the selectivity of the reaction. Moreover, the reaction was completely ineffective in isopropanol.

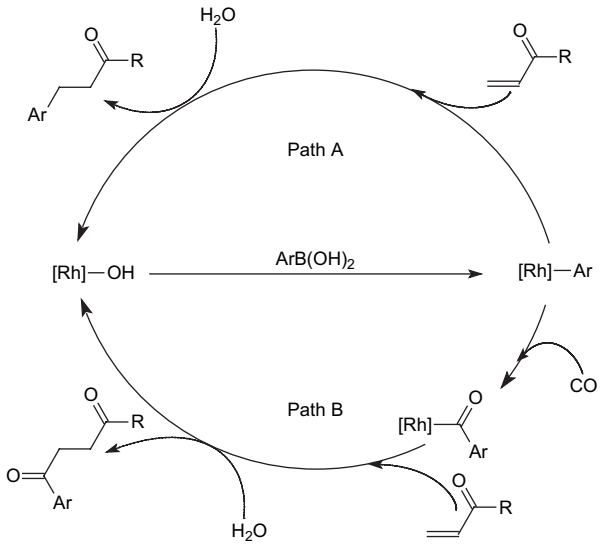
As expected with carbonylation reactions, the CO pressure has a strong effect on the selectivity of the process.[17] For example, when the CO pressure dropped from 20 bar to 1 bar, the yield of by-product **4** increased from 9 to 21% and in the mean time, the yield of carbonylated derivative **3** decreased from 78 to 52%. On the other hand, above 20 bar, the effect of the pressure on the selectivity of the reaction was rather limited (compare entries 4 and 10).

**Table 1**. Rhodium catalysed aroylation reaction of methyl vinyl ketone **2** with phenylboronic acid **1** under CO pressure[a]

| Entry | Solvent | *P* (CO) (atm) | *T* (°C) | **3** (%)[b] | **4** (%)[b] | **5** (%)[b] |
|---|---|---|---|---|---|---|
| 1 | THF | 20 | 80 | 42 | <2 | 7 |
| 2 | THF/$H_2O$ (9/1) | 20 | 80 | 46 | 3 | 9 |
| 3 | 1,4-Dioxane | 20 | 80 | 0 | 0 | 0 |
| 4 | MeOH | 20 | 80 | 78 | 9 | 7 |
| 5 | *n*-PrOH | 20 | 80 | 60 | 8 | 6 |
| 6 | *n*-BuOH | 20 | 80 | 59 | 8 | 6 |
| 7 | *i*-PrOH | 20 | 80 | 0 | 0 | 0 |
| 8 | MeOH/$H_2O$ (9/1) | 20 | 80 | 75 | 8 | 6 |
| 9 | MeOH | 1 | 80 | 52 | 21 | 7 |
| 10 | MeOH | 40 | 80 | 76 | 5 | 4 |
| 11 | MeOH | 20 | 100 | 44 | 7 | 18 |

[a] The reaction was carried out using phenylboronic acid (1.5 mmol), methyl vinyl ketone (3.2 mmol), 1% $RhH(CO)(PPh_3)_3$ and 10 mL solvent for 18 h.

[b] Yields determined by GC based on the arylboronic acid.




**Scheme 2**. Mechanism proposed for the 1,4-addition of arylboronic acids to α,β-unsaturated ketones.

The selectivity in benzophenone **5** was strongly dependent on the temperature of the reaction. If reaction temperatures higher than 80 °C were used, the quantities of **5** increased at the cost of the yields of ketones **3** and **4**. At 100 °C, the yield of **5** reached 18% and the yield of diketone **3** dropped from 78% at 80 °C to 44% at 100 °C.

In order to get better insight into the reaction, the evolution over time of the quantities of products **3–5** was checked. The reaction was carried out with a methyl vinyl ketone to phenylboronic acid ratio of 2, using $RhH(CO)(PPh_3)_3$ (0.5% vs phenylboronic acid) as a well defined catalyst precursor, at 80 °C and under 20 bar CO. Aliquot samples were taken at regular time intervals and analysed by GC with the help of an internal standard. In order to allow the analysis of enough samples the reaction medium was five times diluted compared to a typical run.

First of all, it should be noticed that the reaction performed under diluted conditions (50 mL MeOH) did not reach such high yields as in a normal catalytic run (10 mL MeOH). The yield of **3** is only 63% compared to the 78% obtained with the more concentrated catalytic run. The yields of **4** and **5** remained, on the other hand, practically unchanged. Nevertheless, Figure 1 shows that after a short activation period of approximately 30 min, the three products **3, 4** and **5** are simultaneously formed with a diketone to ketone ratio or a diketone to diphenylketone ratio that remains unchanged during the course of the reaction. This strongly supports the hypothesis of closely related catalytic cycles explaining the formation of these three products. Based on the catalytic cycle proposed by Hayashi[15] for the direct 1,4-addition of arylboronic acids to α,β-enones, we suggested a related catalytic cycle combining the non-carbonylative and the carbonylative processes and using common catalytic intermediates (Scheme 2).

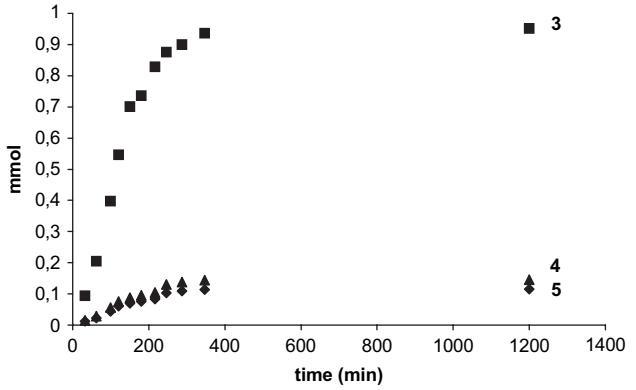



**Figure 1**. Formation profiles of the products **3**–**5** in the catalytic reaction (Scheme 1) versus time. The reaction was run at 70 °C with methyl vinyl ketone (3 mmol), $PhB(OH)_2$ (1.5 mmol), $RhH(CO)(PPh_3)_3$ (0.015 mmol) and CO (20 bar) in MeOH (50 mL).

The arylrhodium catalytic species is obtained in both cases by a transmetallation step of the phenyl from the boron to the rhodium centre. This intermediate can readily insert the olefin leading to the ketone formation. Alternatively, arylrhodium complexes are known to easily insert a CO molecule to give an aroylrhodium intermediate.[18] Insertion of the olefin into the aroylrhodium bond followed by a hydrolysis step gives the 1,4-diketone. It is noteworthy that under CO pressure, very low amounts of benzene are obtained by hydrololytic B–C bond cleavage of phenylboronic acid. Catalytic experiments with *p*-tolylboronic acid and *m*-chlorophenylboronic acid showed similar results. This is in marked contrast to the usually large excesses of organoboronic acids required for the direct 1,4-addition of arylboronic acids to α,β-enones. Such starting material degradation can be explained by a competitive Rh–C bond protonolysis. Low protonolysis of the arylboronic acid under our conditions can be explained by a fast insertion of the olefin into the arylrhodium or aroylrhodium bond compared to the hydrolysis step. Another explanation can arise from the higher stability of the aroylrhodium complex compared to the arylrhodium complex towards protonolysis. This is supported by the fact that proton NMR and GC analysis of the crude reaction mixture did not show the presence of significant amounts of benzoic acid or methylbenzoic ester as the respective products of hydrolysis and methanolysis of an aroylrhodium intermediate.

As a high loading of expensive rhodium is usually used in the corresponding non-carbonylative reaction, it was important to determine the extent to which it was possible to decrease the amount of catalyst without a dramatic loss of the yields of **3**.

Table 2 shows that as little as 0.01% of the rhodium precursor is enough to complete the reaction within one night at 80 °C using Rh(COD)Cl as the catalyst precursor combined with triphenylphosphine. Phosphine free catalytic systems showed much lower reactivity although they remained efficient if used with a higher amount of rhodium (0.5%). Using the same reaction conditions, experiments carried out with 0.005% of rhodium afforded much lower yields of 1,4-diketone **3**. The combination of different phosphorous based ligands with $Rh(COD)_2BF_4$ did not further improve the yields of **3** and the selectivity of the reaction for **3** versus the non-carbonylated derivative **4** remained rather unchanged. On the other hand, it is noteworthy that the use of low catalyst amounts afforded a better selectivity into the 1,4-diketone product **3**. Experiments carried out with less than 0.02% of rhodium showed the formation of much lower quantities of diphenylketone compared to the standard experiments made with 0.5% catalyst. Actually the use of higher reaction temperatures with high catalyst concentration induced the formation of much higher quantities of the undesired diphenylketone. This drawback can be partially avoided with a lower amount of Rh.

**Table 2**. Influence of the catalyst precursor on the aroylation reaction of methyl vinyl ketone **2** with phenylboronic acid **1**[a]

| Entry | Rhodium catalyst | Catalyst (%) | **3** (%) | **4** (%) | **5** (%) |
|---|---|---|---|---|---|
| 1 | $Rh(COD)_2BF_4+3PPh_3$ | 0.5 | 74 | 9 | 5 |
| 2 | $Rh(COD)_2BF_4+3PPh_3$ | 0.02 | 80 | 7 | 1 |
| 3 | $Rh(COD)_2BF_4$ | 0.01 | 35 | 3 | <1 |
| 4 | Rh(COD)Cl | 0.01 | 60 | 5 | <1 |
| 5 | $Rh(COD)_2BF_4+3PPh_3$ | 0.01 | 74 | 7 | 1 |
| 6 | $Rh(COD)Cl+3PPh_3$ | 0.01 | 70 | 8 | <1 |
| 7 | $Rh(COD)_2BF_4+3PPh_3$ | 0.005 | 42 | 5 | <1 |
| 8 | $Rh(COD)_2BF_4+6PPh_3$ | 0.005 | 39 | 5 | <1 |
| 9 | $Rh(COD)_2BF_4$+1dppb | 0.005 | 33 | 4 | <1 |
| 10 | $Rh(COD)_2BF_4$+2dppb | 0.005 | 45 | 5 | <1 |

[a] Reactions were carried out using phenylboronic acid (1.5 mmol) and methyl vinyl ketone (3.2 mmol) in 10 mL MeOH under 20 bar CO at 80 °C for 18 h.

Using optimised reactions conditions, high yields of diketones that can be easily isolated by column chromatography and fully characterised before further use, are obtained from variously substituted arylboronic acids (Table 3, entries 1 and 5–9).

Additional experiments made with some other well-known transmetalling reagents using the same reaction conditions showed low efficiencies. No reaction was observed with $ArSi(OEt)_3$[19] or another boron derivative such as $NaB(Ar)_4$[20] and only moderate yields was obtained with $ArSn(Bu)_3$ (Table 3, entries 2–4). Boronic acids are thus the best reactant for this carbonylation reaction. Unfortunately, attempts to change the Michael acceptor, using the same reaction conditions and catalyst, have been up until

**Table 3**. Rhodium catalysed aroylation reaction of methyl vinyl ketone under CO pressure with various boronic acids and transmetallation reagents[a]

| Entry | Transmetallation reagent | Ar | **3** (%)[b] |
|---|---|---|---|
| 1 | $ArB(OH)_2$ | $C_6H_5$ | 76 |
| 2 | $ArSn(Bu)_3$ | $C_6H_5$ | 53 |
| 3 | $NaB(Ar)_4$ | $C_6H_5$ | 0[c] |
| 4 | $ArSi(OEt)_3$ | $C_6H_5$ | 0 |
| 5 | $ArB(OH)_2$ | 4-$MeC_6H_4$ | 78 |
| 6 | $ArB(OH)_2$ | 4-$MeOC_6H_4$ | 72 |
| 7 | $ArB(OH)_2$ | 3-$ClC_6H_4$ | 65 |
| 8 | $ArB(OH)_2$ | 4-$ClC_6H_4$ | 68 |
| 9 | $ArB(OH)_2$ | 4-$FC_6H_4$ | 65 |

[a] Reactions were carried out using the corresponding transmetallation reagent (1.5 mmol), methyl vinyl ketone (3.2 mmol) and 0.5% $RhH(CO)(PPh_3)_3$ in 10 mL MeOH with 40 bar CO pressure at 80 °C for 18 h.
[b] Isolated yields.
[c] PhCOPh is the only formed product.

now unsuccessful. In particular, substituted enones such as cyclohexenone failed to react even at higher reaction temperatures. The reaction does not proceed with non-activated olefins either, for example, no product was detected with 1-hexene except the diphenylketone.

### 2.2. Procedure for pyrroles and furans synthesis

For economical and environmental reasons, it is of interest to use the diketones without any previous purification for a further organic transformation. We thus evaluated the possibility to combine, in a short procedure, the diketone formation through carbonylation with a cyclisation step giving pyrrole or furan derivatives (Scheme 3). This procedure would allow simple and fast access to the pyrrole and furan heterocycles in a short catalytic multicomponent synthetic procedure.[21] The Paal–Knorr cyclisation with an amine is a common synthetic pathway to access pyrroles.[22] The procedure commonly requires high temperature reactions and an acidic media. In our case, starting from our crude catalytic mixtures the reaction remained only partially successful. Indeed, pyrroles formation proceeded more efficiently via the iodine catalysed Paal–Knorr cyclisation even though the yield for this step was not quantitative. Better results were obtained when the amount of iodine used was increased compared to the literature procedure from 3 to 40% and the reaction time at 40 °C (instead of room temperature) from 4 h to 16 h.[23]

Under these conditions, GC analysis at the end of the reaction indicated the complete disappearance of the starting diketone along with pyrrole formation. The side products, i.e., ketones **4** and **5** remained unaffected. The analytically pure pyrroles were finally isolated by alumina gel column chromatography with overall 45–60% yields from the starting boronic acid.

The 1,4-diketones can also be reacted without previous purification to form furans. After a carbonylation reaction, the solvent was evaporated. The cyclisation was promoted by *p*-toluenesulfonic acid monohydrate in refluxing toluene for one night.[24] The complete conversion of the reaction product was then confirmed by GC analysis. The furans were finally purified by alumina gel column chromatography and isolated with similar yields to the corresponding pyrroles. Following those procedures, it was possible to synthesise a series of furan and pyrrole heterocycles with good overall yields (Table 4).

To avoid any change of solvent between the catalytic and cyclisation step for furan synthesis, it is noteworthy that the carbonylation reaction could be directly performed in a toluene/water (1/1) mixture with similar yields. The water layer was then extracted and the organic layer dried with magnesium sulfate. After filtration, the toluene solution was refluxed in the presence of *p*-toluenesulfonic acid to generate the furan. This procedure performed with *p*-tolylboronic acid allowed the isolation of the corresponding furan in a similar yield. It has the main advantage of shortening the procedure by avoiding the tedious methanol evaporation step.

**Table 4**. Carbonylation–cyclisation sequences for pyrroles and furans synthesis[a]

| Entry | Ar | X=NPh[b] (%) | X=O[c] (%) |
|---|---|---|---|
| 1 | $C_6H_5$ | 56 | 49 |
| 2 | 4-$MeC_6H_4$ | 51 | 50 (54)[d] |
| 3 | 4-$MeOC_6H_4$ | 45 | 66 |
| 4 | 4-$ClC_6H_4$ | 53 | 49 |
| 5 | 3-$ClC_6H_4$ | 59 | 44 |
| 6 | 4-$FC_6H_4$ | 44 | 42 |

[a] The carbonylation reactions were carried out using the corresponding arylboronic reagent (1.5 mmol) and 0.5% $RhH(CO)(PPh_3)_3$ in 10 mL MeOH for 18 h, 20 bar CO and 80 °C.
[b] The crude mixture obtained after carbonylation was stirred overnight with aniline and iodine in dichloromethane.
[c] The crude mixture obtained after carbonylation was refluxed overnight in toluene with 1 equiv *p*-toluenesulfonic acid.
[d] The carbonylation reaction was run in a biphasic toluene (5 mL)/water (5 mL) system and the cyclisation step was run with the organic phase dried with $MgSO_4$.

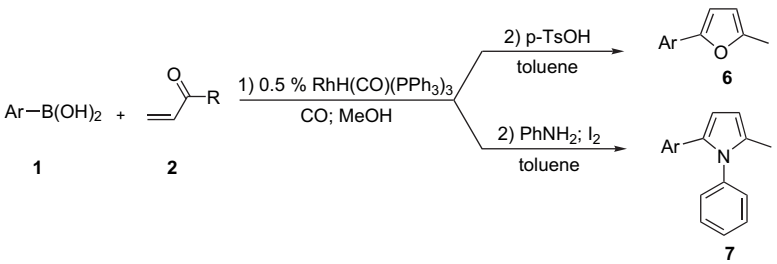
## 3. Conclusion

We have shown that the carbonylative 1,4-addition of arylboronic acids to enones affords the corresponding diketones with high selectivity even at low catalyst loadings. The reaction allows an efficient access to 1,4-diketones. Interestingly, this reaction can be coupled with a cyclisation without previous purification giving pyrrole or furan derivatives. Thus, the whole process constitutes an efficient way to access these last classes of compounds.

## 4. Experimental

### 4.1. General

All experiments were carried out with solvents, rhodium complexes, phosphines, arylboronic acids, amines, APTS and methyl vinyl ketone purchased from Aldrich or Acros and used as received.




**Scheme 3**. Pyrrole and furan synthesis via a rhodium catalysed aroylation of enones with arylboronic acids and carbon monoxide followed by a cyclisation step.

GLC analyses were performed on a Chrompack CP 9001 apparatus equipped with a flame ionisation detector and a CPSil 5CB (25 m×0.32 mm, Chrompack) column. $^{1}H$, $^{19}F$ and $^{13}C$ NMR spectra were recorded on a AC-300 Bruker spectrometer at 23 °C; chemical shifts are reported in parts per million downfield from TMS.

**4.1.1. General procedure for carbonylation reactions and enones isolation.** A 100 mL stainless steel autoclave equipped with a magnetic stirrer was charged with arylboronic acid (1.5 mmol) and the required amount of rhodium catalyst. MeOH (10 mL) was thus added followed by methyl vinyl ketone (0.25 mL, 3 mmol). The autoclave was pressurised to 20 bar and the mixture was warmed at 80 °C for 18 h. After cooling to room temperature, the reactor was vented and the orange-yellow methanol solution was evaporated to dryness. The diketones were finally purified by silica gel column chromatography using petroleum/ether (9/1) as eluent.

1-*p*-Tolylpentane-1,4-dione: white solid, 78% yield. $^{1}H$ NMR: (300 MHz, $CDCl_3$) $\delta$=7.85 (d, 2H, $^{3}J_{H-H}$=8 Hz, C*H* aromatic); 7.21 (d, 2H, $^{3}J_{H-H}$=8 Hz, C*H* aromatic); 3.21 (t, 2H, $^{3}J_{H-H}$=6.3 Hz, C$H_2$); 2.83 (t, 2H, $^{3}J_{H-H}$=6.3 Hz, C$H_2$); 2.36 (s, 3H, ArC$H_3$); 2.21 (s, 3H, COC$H_3$). $^{13}C$ NMR: ($CDCl_3$, 75 MHz) $\delta$=207.41 (s, 1C, $CH_3$*C*O); 198.10 (s, 1C, Ar*C*O); 143.90 (s, 1C, $CH_3$*C*); 134.13 (s, 1C, *C*CO); 129.22 (s, 2C, *C*H aromatic); 128.13 (s, 2C, *C*H aromatic); 37.05 (s, 1C, *C*$H_2$); 32.29 (s, 1C, *C*$H_2$); 30.09 (s, 1C, *C*$H_3$); 21.61 (s, 1C, Ar*C*$H_3$).

1-(4-Methoxyphenyl)pentane-1,4-dione: white solid, 72% yield. $^{1}H$ NMR: (300 MHz, $CDCl_3$) $\delta$=7.92 (d, 2H, $^{3}J_{H-H}$=9 Hz, C*H* aromatic); 6.89 (d, 2H, $^{3}J_{H-H}$=9 Hz, C*H* aromatic); 3.83 (s, 3H, OC$H_3$); 3.19 (t, 2H, $^{3}J_{H-H}$=6.5 Hz, C$H_2$); 2.85 (t, 2H, $^{3}J_{H-H}$=6.5 Hz, C$H_2$); 2.23 (s, 3H, COC$H_3$). $^{13}C$ NMR: ($CDCl_3$, 75 MHz) $\delta$=207.54 (s, 1C, $CH_3$*C*O); 197.01 (s, 1C, Ar*C*O); 163.51 (s, 1C, $CH_3$O*C*); 130.29 (s, 2C, *C*H aromatic); 129.12 (s, 1C, *C*CO); 113.69 (s, 2C, *C*H aromatic); 55.45 (s, 1C, O*C*$H_3$); 37.13 (s, 1C, *C*$H_2$); 32.05 (s, 1C, *C*$H_2$); 30.12 (s, 1C, *C*$H_3$).

1-(4-Chlorophenyl)pentane-1,4-dione: white solid, 68% yield. $^{1}H$ NMR: (200 MHz, $CDCl_3$) $\delta$=7.83 (d, 2H, $^{3}J_{H-H}$=8 Hz, C*H* aromatic); 7.36 (d, 2H, $^{3}J_{H-H}$=8 Hz, C*H* aromatic); 3.20 (t, 2H, $^{3}J_{H-H}$=6.3 Hz, C$H_2$); 2.80 (t, 2H, $^{3}J_{H-H}$=6.3 Hz, C$H_2$); 2.20 (s, 3H, COC$H_3$). $^{13}C$ NMR: ($CDCl_3$, 50 MHz) $\delta$=206.65 (s, 1C, $CH_3$*C*O); 196.78 (s, 1C, Ar*C*O); 138.94 (s, 1C, Cl*C* or *C*CO); 134.13 (s, 1C, Cl*C* or *C*CO); 128.94 (s, 2C, *C*H aromatic); 128.33 (s, 2C, *C*H aromatic); 36.44 (s, 1C, *C*$H_2$); 31.81 (s, 1C, *C*$H_2$); 29.46 (s, 1C, *C*$H_3$).

1-(3-Chlorophenyl)pentane-1,4-dione: yellow liquid, 65% yield. $^{1}H$ NMR: (300 MHz, $CDCl_3$) $\delta$=7.89 (s, 1H, C*H* aromatic); 7.80 (d, 1H, $^{3}J_{H-H}$=7.7 Hz, C*H* aromatic); 7.47 (d, 1H, $^{3}J_{H-H}$=7.7 Hz, C*H* aromatic); 7.36 (t, 1H, $^{3}J_{H-H}$= 7.7 Hz, C*H* aromatic); 3.19 (t, 2H, $^{3}J_{H-H}$=5.8 Hz, C$H_2$); 2.85 (t, 2H, $^{3}J_{H-H}$=5.8 Hz, C$H_2$); 2.21 (s, 3H, COC$H_3$). $^{13}C$ NMR: ($CDCl_3$, 75 MHz) $\delta$=207.01 (s, 1C, $CH_3$*C*O); 197.24 (s, 1C, Ar*C*O); 138.12 (s, 1C, Cl*C* or *C*CO); 134.85 (s, 1C, Cl*C* or *C*CO); 133.03 (s, 1C, *C*H aromatic); 129.93 (s, 1C, *C*H aromatic); 128.12 (s, 1C, *C*H aromatic); 126.71 (s, 1C, *C*H aromatic); 36.93 (s, 1C, *C*$H_2$); 32.44 (s, 1C, *C*$H_2$); 29.99 (s, 1C, *C*$H_3$).

1-(4-Fluorophenyl)pentane-1,4-dione: yellow liquid, 62% yield. $^{1}H$ NMR: (200 MHz, $CDCl_3$) $\delta$=7.94 (m, 2H, C*H* aromatic); 7.36 (m, 2H, C*H* aromatic); 3.21 (t, 2H, $^{3}J_{H-H}$=5.9 Hz, C$H_2$); 2.84 (t, 2H, $^{3}J_{H-H}$=5.9 Hz, C$H_2$); 2.20 (s, 3H, COC$H_3$). $^{13}C$ NMR: ($CDCl_3$, 75 MHz) $\delta$=206.65 (s, 1C, $CH_3$*C*O); 196.38 (s, 1C, Ar*C*O); 165.24 (d, 1C, $^{1}J_{F-C}$=254.4 Hz, F*C*); 132.62 (s, 1C, *C*CO); 131.42 (d, 2C, $^{2}J_{F-C}$=117.1 Hz, *C*H aromatic); 115.1 (s, 2C, $^{3}J_{F-C}$=21.6 Hz, *C*H aromatic); 36.48 (s, 1C, *C*$H_2$); 31.75 (s, 1C, *C*$H_2$); 29.48 (s, 1C, *C*$H_3$).

**4.1.2. General procedure for pyrroles synthesis.** In the first part of the synthesis, the carbonylation reaction was run according to the procedure used for the enones synthesis (vide supra). The mixture obtained was evaporated and the residue dissolved in a solution of iodine (0.183 g, 0.72 mmol) and aniline (0.194 mL, 2.1 mmol) in THF (10 mL). The resulting solution was then heated at 40 °C for one night. The reaction was monitored by GC and ended once the GC peak corresponding to the starting enone has disappeared. The solvent was evaporated and the pyrrole purified by alumina gel column chromatography using petroleum/ether (9/1) as eluent.

2-*p*-Tolyl-5-methyl-1-phenyl-1*H*-pyrrole: yellow-orange solid, 51% yield. $^{1}H$ NMR: (300 MHz, $CDCl_3$) $\delta$=7.2–7.3 (m, 3H, C*H* aromatic); 7.06 (m, 2H, C*H* aromatic); 6.86 (m, 4H, C*H* aromatic); 6.45 (d, 1H, $^{3}J_{H-H}$=1.9 Hz, C$H_{Pyrr}$); 6.21 (d, 1H, $^{3}J_{H-H}$=1.9 Hz, C$H_{Pyrr}$); 2.35 (s, 3H, C$H_3$); 2.25 (s, 3H, C$H_3$). $^{13}C$ NMR: ($CDCl_3$, 50 MHz) $\delta$=139.15 (s, 1C, N$C_{ipso}$); 134.83 (s, 1C, *C*q); 133.84 (s, 1C, *C*q); 130.88 (s, 1C, *C*q); 130.36 (s, 1C, *C*q); 128.54 (s, 2C, *C*H aromatic); 128.31 (s, 2C, *C*H aromatic); 128.12 (s, 2C, *C*H aromatic); 127.32 (s, 2C, *C*H aromatic); 126.92 (s, 1C, *C*H aromatic); 107.87 (s, 1C, *C*H$_{Pyrr}$); 107.09 (s, 1C, *C*H$_{Pyrr}$); 20.65 (s, 1C, *C*$H_3$); 12.95 (s, 1C, *C*$H_3$).

2-(4-Methoxyphenyl)-5-methyl-1-phenyl-1*H*-pyrrole: red-orange solid, 45% yield. $^{1}H$ NMR: (300 MHz, $CDCl_3$) $\delta$=7.42 (m, 3H, C*H* aromatic); 7.22 (d, 2H, $^{3}J_{H-H}$=6.4 Hz, C*H* aromatic); 7.06 (d, 2H, $^{3}J_{H-H}$=8.8 Hz, C*H* aromatic); 6.75 (d, 2H, $^{3}J_{H-H}$=8.8 Hz, C*H* aromatic); 6.36 (d, 1H, $^{3}J_{H-H}$=2.9 Hz, C$H_{Pyrr}$); 6.15 (d, 1H, $^{3}J_{H-H}$=2.9 Hz, C$H_{Pyrr}$); 3.77 (s, 3H, OC$H_3$); 2.21 (s, 3H, C$H_3$). $^{13}C$ NMR: ($CDCl_3$, 75 MHz) $\delta$=157.84 (s, 1C, O*C*q); 139.53 (s, 1C, N$C_{ipso}$); 134.05 (s, 1C, *C*q); 130.99 (s, 1C, *C*q); 129.18 (s, 2C, *C*H aromatic); 128.99 (s, 2C, *C*H aromatic); 128.60 (s, 2C, *C*H aromatic); 127.37 (s, 1C, *C*H aromatic); 126.42 (s, 1C, *C*q); 113.52 (s, 2C, *C*H aromatic); 107.81 (s, 1C, *C*H$_{Pyrr}$); 107.38 (s, 1C, *C*H$_{Pyrr}$); 55.15 (s, 1C, O*C*$H_3$); 13.42 (s, 1C, *C*$H_3$).

2-(4-Chlorophenyl)-5-methyl-1-phenyl-1*H*-pyrrole: orange solid, 53% yield. $^{1}H$ NMR: (300 MHz, $CDCl_3$) $\delta$=7.8–6.8 (m, 9H, C*H* aromatic); 6.41 (br s, 1H, C$H_{Pyrr}$); 6.15 (br s, 1H, C$H_{Pyrr}$); 2.18 (s, 3H, C$H_3$). $^{13}C$ NMR: ($CDCl_3$, 75 MHz) $\delta$=138.71 (s, 1C, N$C_{ipso}$); 132.45 (s, 1C, *C*q); 131.69 (s, 1C, *C*q); 131.57 (s, 1C, *C*q); 130.95 (s, 1C, *C*q); 128.65 (s, 2C, *C*H aromatic); 128.34 (s, 2C, *C*H aromatic); 127.96 (s, 2C, *C*H aromatic); 127.69 (s, 2C, *C*H aromatic);

127.16 (s, 1C, *C*H aromatic); 108.61 (s, 1C, *C*H$_{Pyrr}$); 107.29 (s, 1C, *C*H$_{Pyrr}$); 13.91 (s, 1C, *C*H$_3$).

2-(3-Chlorophenyl)-5-methyl-1-phenyl-1*H*-pyrrole: orange solid, 59% yield. $^1$H NMR: (300 MHz, $CDCl_3$) $\delta$=7.40–7.30 (m, 3H, C*H* aromatic); 7.00–7.23 (m, 5H, C*H* aromatic); 6.88 (m, 1H, C*H* aromatic); 6.41 (d, 1H, $^3J_{H-H}$=2.9 Hz, C*H*$_{Pyrr}$); 6.13 (d, 1H, $^3J_{H-H}$=2.9 Hz, C*H*$_{Pyrr}$); 2.16 (s, 3H, C*H*$_3$). $^{13}$C NMR: ($CDCl_3$, 75 MHz) $\delta$=139.07 (s, 1C, N*C*$_{ipso}$); 135.27 (s, 1C, *C*q); 133.81 (s, 1C, *C*q); 132.63 (s, 1C, *C*q); 132.49 (s, 1C, *C*q); 129.16 (s, 2C, *C*H aromatic); 129.12 (s, 1C, *C*H aromatic); 128.41 (s, 2C, *C*H aromatic); 127.73 (s, 1C, *C*H aromatic); 127.50 (s, 1C, *C*H aromatic); 125.57 (s, 2C, *C*H aromatic); 109.51 (s, 1C, *C*H$_{Pyrr}$); 107.81 (s, 1C, *C*H$_{Pyrr}$); 13.32 (s, 1C, *C*H$_3$).

2-(4-Fluorophenyl)-5-methyl-1-phenyl-1*H*-pyrrole: red-orange solid, 44% yield. $^1$H NMR: (300 MHz, $CDCl_3$) $\delta$=7.37 (m, 3H, C*H* aromatic); 7.16 (m, 2H, C*H* aromatic); 7.02 (m, 2H, C*H* aromatic); 6.84 (m, 2H, C*H* aromatic); 6.31 (d, 1H, $^3J_{H-H}$=3.42 Hz, C*H*$_{Pyrr}$); 6.10 (d, 1H, $^3J_{H-H}$=3.42 Hz, C*H*$_{Pyrr}$); 2.16 (s, 3H, C*H*$_3$). $^{13}$C NMR: ($CDCl_3$, 75 MHz) $\delta$=161.92 (d, 1C, $^1J_{F-C}$=245.1 Hz, F*C*); 139.20 (s, 1C, N*C*$_{ipso}$); 138.15 (s, 1C, *C*q); 132.77 (s, 1C, *C*q); 131.13 (s, 1C, *C*q); 128.90 (d, 2C, $^3J_{F-C}$=7.9 Hz, *C*H aromatic); 128.59 (s, 2C, *C*H aromatic); 128.09 (s, 2C, *C*H aromatic); 127.08 (s, 1C, *C*H aromatic); 114.31 (d, 2C, $^2J_{F-C}$=21.6 Hz, *C*H aromatic); 108.22 (s, 1C, *C*H$_{Pyrr}$); 107.17 (s, 1C, *C*H$_{Pyrr}$); 13.13 (s, 1C, *C*H$_3$).

**4.1.3. General procedure for furans synthesis.** In the first part of the synthesis, the carbonylation reaction is run according to the procedure used for the enones synthesis (vide supra). The mixture obtained is evaporated and the residue dissolved in a solution of *p*-toluenesulfonic acid monohydrate (60 mg, 1.5 mmol) in toluene (10 mL). The resulting solution is then refluxed overnight. After evaporation of the solvent, the furan is purified by alumina gel column chromatography using petroleum/ether (9/1) as eluent. Alternatively, the carbonylation reaction can be run in a toluene/$H_2O$ biphasic system. After one night of reaction with 20 bar of CO at 80 °C, the organic layer is then separated from the aqueous phase, dried over $MgSO_4$ and filtered. Addition of *p*-toluenesulfonic acid monohydrate to the toluene solution followed by overnight refluxing allows the complete transformation of the diketone in the corresponding furan heterocycle.

2-*p*-Tolyl-5-methylfuran: orange oil, 50% yield. $^1$H NMR: (300 MHz, $CDCl_3$) $\delta$=7.48 (m, 2H, C*H* aromatic); 7.09 (m, 2H, C*H* aromatic); 6.41 (d, 1H, $^3J_{H-H}$=3.3 Hz, C*H*$_{Fur}$); 5.97 (dq, 1H, $^4J_{H-H}$=1.1 Hz, $^3J_{H-H}$=3.3 Hz, C*H*$_{Fur}$); 2.29 (s, 3H, OC*H*$_3$); 2.28 (s, 3H, C*H*$_3$). $^{13}$C NMR: ($CDCl_3$, 75 MHz) $\delta$=152.73 (s, 1C, *C*q); 151.62 (s, 1C, *C*q); 136.58 (s, 1C, *C*q); 129.51 (s, 2C, *C*H aromatic); 128.81 (s, 1C, *C*q); 107.78 (s, 2C, *C*H aromatic); 105.28 (s, 1C, *C*H$_{Fur}$); 21.33 (s, 1C, O*C*H$_3$); 13.79 (s, 1C, *C*H$_3$).

2-(4-Methoxyphenyl)-5-methylfuran: orange oil, 66% yield. $^1$H NMR: (300 MHz, $CDCl_3$) $\delta$=7.60 (d, 2H, $^3J_{H-H}$=6.8 Hz, C*H* aromatic); 6.94 (d, 2H, $^3J_{H-H}$=6.8 Hz, C*H* aromatic); 6.45 (d, 1H, $^3J_{H-H}$=2.9 Hz, C*H*$_{Fur}$); 6.08 (br s, 1H, C*H*$_{Fur}$); 3.83 (s, 3H, OC*H*$_3$); 2.40 (s, 3H, C*H*$_3$). $^{13}$C NMR: ($CDCl_3$, 75 MHz) $\delta$=158.69 (s, 1C, *C*q); 152.40 (s, 1C, *C*q); 151.18 (s, 1C, *C*q); 124.78 (s, 2C, *C*H aromatic); 124.70 (s, 1C, *C*q); 114.11 (s, 2C, *C*H aromatic); 107.60 (s, 1C, *C*H$_{Fur}$); 104.28 (s, 1C, *C*H$_{Fur}$); 55.23 (s, 1C, O*C*H$_3$); 13.68 (s, 1C, *C*H$_3$).

2-(4-Chlorophenyl)-5-methylfuran: orange solid, 53% yield. $^1$H NMR: (300 MHz, $CDCl_3$) $\delta$=7.55 (d, 2H, $^3J_{H-H}$=8.6 Hz, C*H* aromatic); 7.32 (d, 2H, $^3J_{H-H}$=8.6 Hz, C*H* aromatic); 6.53 (br s, 1H, C*H*$_{Fur}$); 6.07 (br s, 1H, C*H*$_{Fur}$); 2.38 (s, 3H, C*H*$_3$). $^{13}$C NMR: ($CDCl_3$, 75 MHz) $\delta$=151.80 (s, 1C, *C*q); 150.76 (s, 1C, *C*q); 131.78 (s, 1C, *C*q); 129.21 (s, 1C, *C*q); 128.51 (s, 2C, *C*H aromatic); 124.01 (s, 2C, *C*H aromatic); 107.41 (s, 1C, *C*H$_{Fur}$); 105.90 (s, 1C, *C*H$_{Fur}$); 13.19 (s, 1C, *C*H$_3$).

2-(3-Chlorophenyl)-5-methylfuran: orange solid, 44% yield. $^1$H NMR: (300 MHz, $CDCl_3$) $\delta$=7.64 (s, 1H, C*H* aromatic); 7.50 (d, 1H, $^3J_{H-H}$=7.8 Hz, C*H* aromatic); 7.28 (dd, 1H, $^3J_{H-H}$=7.8 Hz, C*H* aromatic); 7.18 (d, 1H, $^3J_{H-H}$=7.8 Hz, C*H* aromatic); 6.57 (d, 1H, $^3J_{H-H}$=3.0 Hz, C*H* aromatic); 6.08 (d, 1H, $^3J_{H-H}$=2.8 Hz, C*H* aromatic); 2.38 (s, 3H, C*H*$_3$). $^{13}$C NMR: ($CDCl_3$, 75 MHz) $\delta$=152.63 (s, 1C, *C*q); 150.84 (s, 1C, *C*q); 134.66 (s, 1C, *C*q); 132.85 (s, 1C, *C*q); 129.89 (s, 1C, *C*H aromatic); 126.59 (s, 1C, *C*H aromatic); 123.26 (s, 1C, *C*H aromatic); 121.13 (s, 1C, *C*H aromatic); 107.98 (s, 1C, *C*H$_{Fur}$); 107.09 (s, 1C, *C*H$_{Fur}$); 13.70 (s, 1C, *C*H$_3$).

2-(4-Fluorophenyl)-5-methylfuran: orange solid, 42% yield. $^1$H NMR: (300 MHz, $CDCl_3$) $\delta$=7.55 (dd, 2H, $^3J_{H-H}$=8.6 Hz, C*H* aromatic); 7.32 (d, 2H, $^3J_{H-H}$=8.6 Hz, C*H* aromatic); 6.53 (br s, 1H, C*H*$_{Fur}$); 6.07 (br s, 1H, C*H*$_{Fur}$); 2.38 (s, 3H, C*H*$_3$). $^{13}$C NMR: ($CDCl_3$, 75 MHz) $\delta$=151.80 (s, 1C, *C*q); 150.76 (s, 1C, *C*q); 131.78 (s, 1C, *C*q); 129.21 (s, 1C, *C*q); 128.51 (s, 2C, *C*H aromatic); 124.01 (s, 2C, *C*H aromatic); 107.41 (s, 1C, *C*H$_{Fur}$); 105.90 (s, 1C, *C*H$_{Fur}$); 13.19 (s, 1C, *C*H$_3$).

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