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An Approach to the Synthesis of Unsymmetrical/Symmetrical Maleimides via Desulfitative Arylation at Different Temperatures

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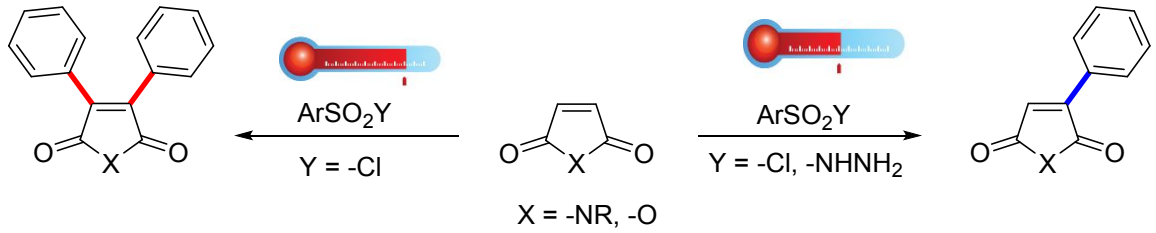
KEYWORDS: Desulfitative arylation; maleimide; C-C bond formation; Palladium; Catalysis



Abstract

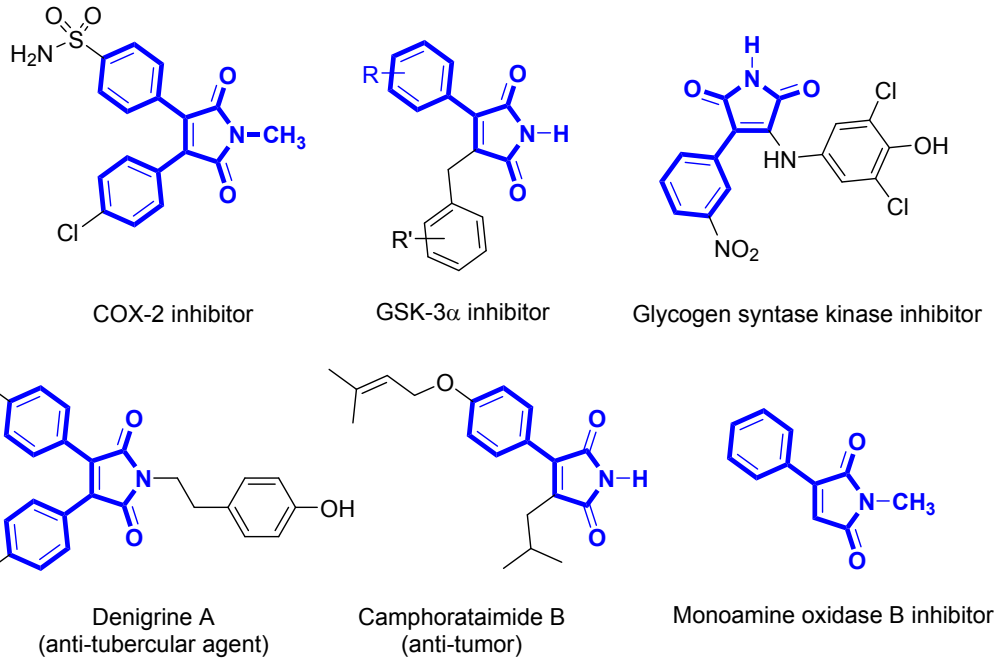
New routes toward selective synthesis of both mono- and diaryl maleimides have been innovated. The mere requirement to this end is through the increase of temperature. The method works effectively for maleic anhydride and maleic acid as well. Also, first expedient synthesis of 2-arylnaphthoquinones via the reaction of naphthoquinone with arenesulfonyl chlorides is revealed.

Introduction

In Pd-catalysed cross couplings several contributors have been used as arylating groups. In this realm, the reagents which liberate gaseous wastes such as CO[1], CO_2[2], N_2[3] and SO_2[4] have attracted great interest since the purification process are more facile. Commercially available arenesulfonyl chlorides which are precursors of arenesulfonyl hydrazides have lately found

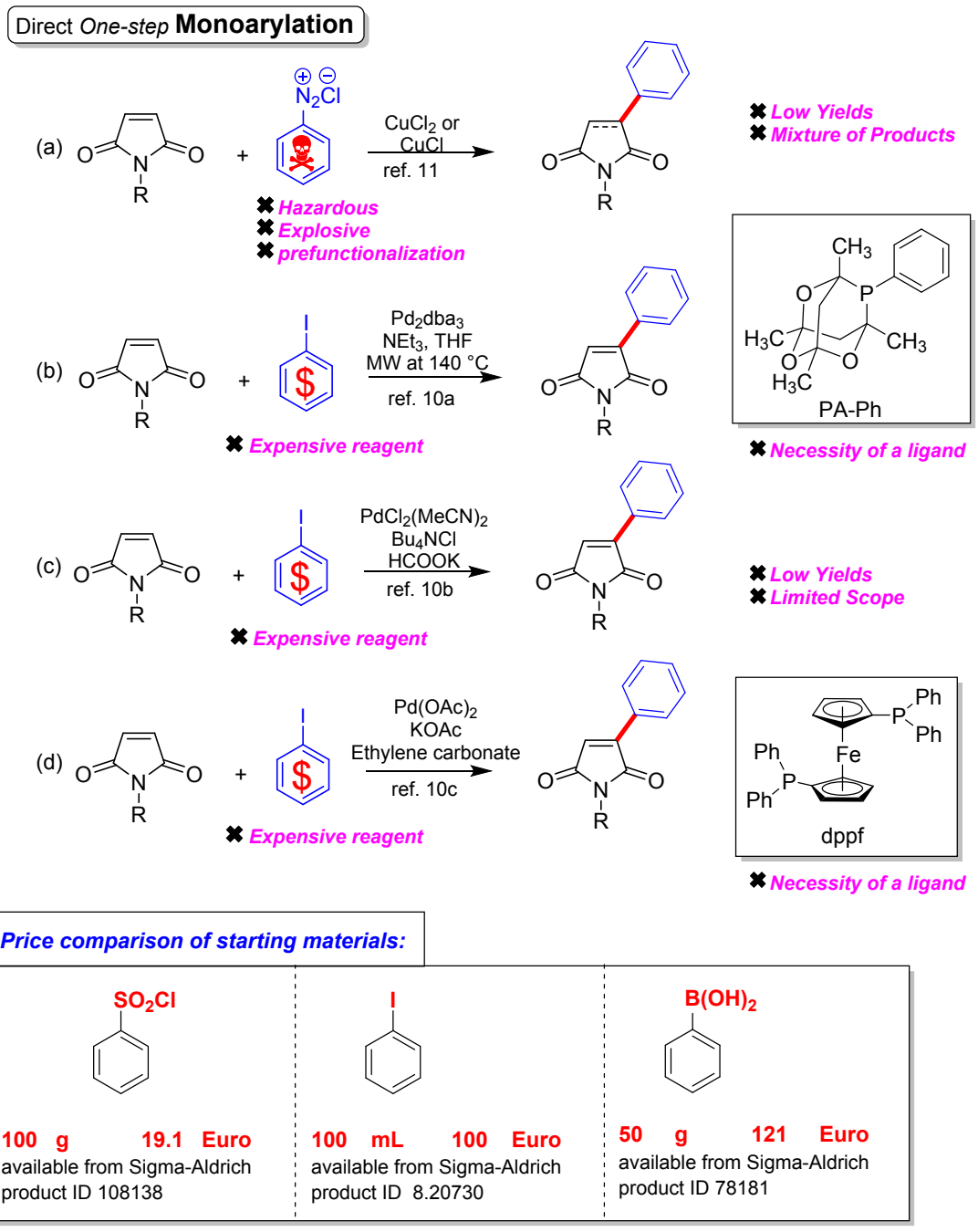
widespread application in arylation reactions due to their lower price. Arylsulfonyl hydrazides themselves are another source of arylating groups which enable one to place an aryl group on a molecule through the extrusion of SO_2 and N_2 as the only waste of the reaction. In this line, ample procedures have been disclosed showcasing the importance of these moieties in lengthening carbon chains.[4] Installation of one aryl group on another motif is a distinguished way to construct the highly sought-after π-extended systems. Regardingly and in pursuit of our ongoing program in C-H activations,[5] we focused our attention on direct arylation of maleimides. In this context, 3-aryl maleimides have found to act against Lewis lung carcinoma (LLC) cell lines.[6] They also show striking attributes in treatment of hypertention and liver cancer.[6a] Specifically, 3-aryl-*N*-methyl maleimides can act as inhibitors of monoamine oxidase.[7] Furthermore, they are precursors in the synthesis of Rubrolide E which is a bioactive compound possessing antibiotic and significant cytotoxic activities.[8] Scheme 1 represents some biological active mono- and diarylated maleimides.

Scheme 1. Some bioactive mono- and di-arylated maleimides



Thus far all efforts for their indirect synthesis led to difunctionalized maleimidies[9] and only a few direct syntheses comprising well-established Meerwein reaction[11] (Scheme 2, a), Heck arylation[10] (Scheme 2, b-d) and pre-halogenation of maleimides[12] (Scheme 2, b) are available in this realm. However, control of these reactions towards selective synthesis of 3-monoarylated maleimides without any side reaction is still an ambitious goal and, to the best of our knowledge, in most cases either 3-halo-4-arylhydromaleimides or 3,4-diarylmaleimides were formed as by-products thus the yield of the main target molecule was usually unsatisfactory. Furthermore, according to the previous literature,[13] *N*H- and *N*-alkyl maleimides undergo rapid ring opening upon exposure to bases, hence their reactions are very sensitive and must be handled diligently. It is also worth mentioning that most transition-metals used to catalyze arylation of maleimides yielded hydroarylated maleimides[11c,14] and there are only a few reports in which the double bond of maleimides has been conserved.[12]

Scheme 2. Previous methods for monoarylmaleimides



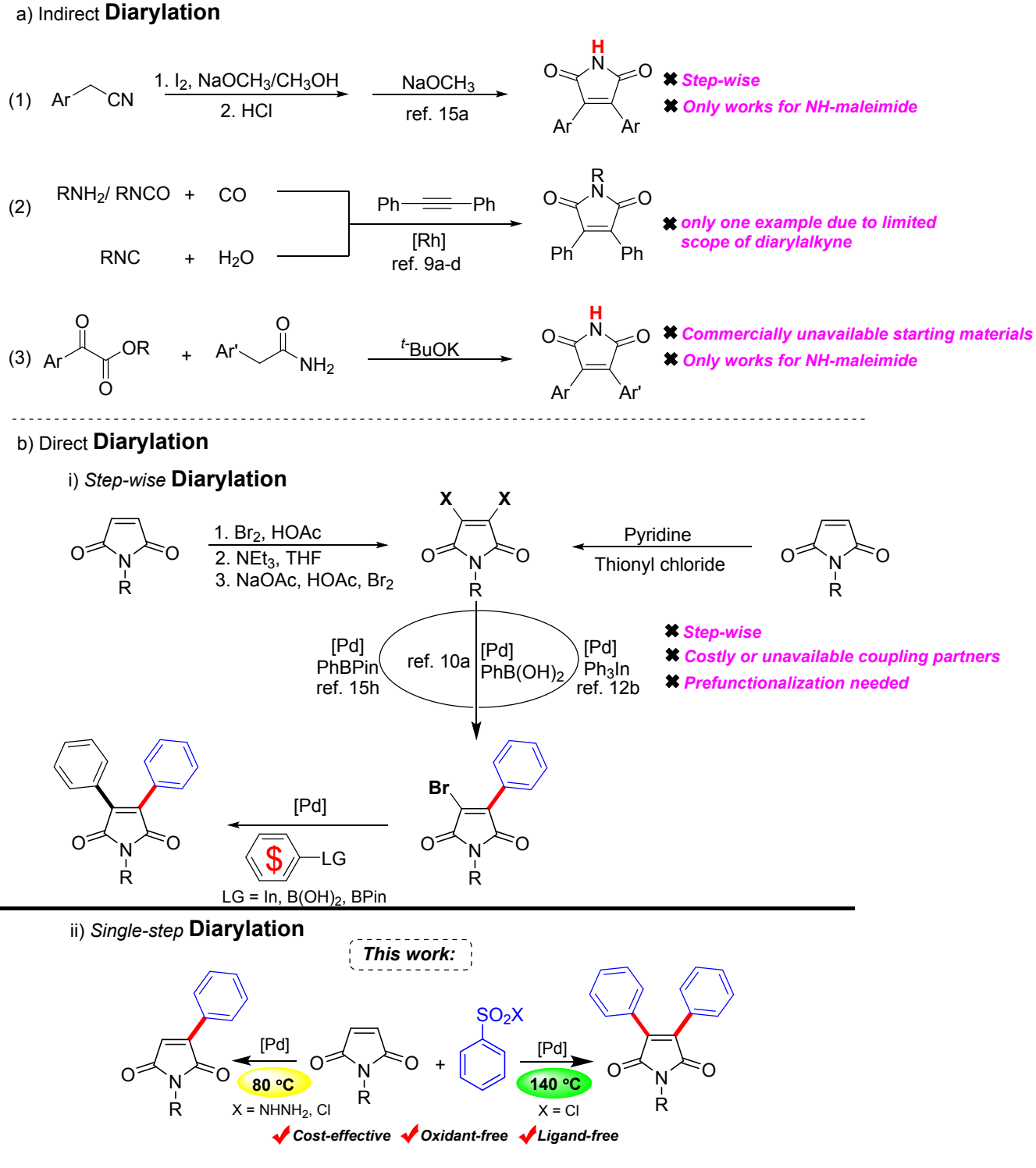
Price comparison of starting materials:

SO_2Cl	I	$B(OH)_2$
100 g 19.1 Euro	**100 mL 100 Euro**	**50 g 121 Euro**
available from Sigma-Aldrich	available from Sigma-Aldrich	available from Sigma-Aldrich
product ID 108138	product ID 8.20730	product ID 78181

On the other hand, unlike monoaryl maleimides, many indirect and direct approaches have emerged concerning the synthesis of diarylmaleimides. Among the proposed strategies, indirect methods have utilized non-maleimide starting materials. Phenylacetonitrile has been shown to

convert into NH-free maleimide in a one-pot step-wise reaction under basic condition and with the aid of I_2 as the promoter of the reaction (Scheme 3, a-1). Also, the reaction of diarylalkynes with amines or isocyanates under a CO atmosphere led to diarylmaliamide (Scheme 3, a-2). When isocyanate was replaced with isocyanide, diarylmaliamide was formed in water medium even in the absence of carbon monoxide. In a different approach, condensation of glyoxalate ester with acetamides resulted in only NH-maliamide derivatives (Scheme 3, a-3). In contrast to indirect methods, direct strategies[15] have gained more popularity since they take advantage of commercially available starting materials and offer simpler paths. Direct methods in which maleimide itself is employed as the reactant is divided into two categories: step-wise reactions and single-step reactions. The latter provide shorter routes to the favored product. Moreover, in these approaches the need for additional reagents is obviated and superfluous, tedious purifications are eliminated thus these reactions are more facile and cost-effective. Capretta reported a Pd-catalysed reaction which led to diaryl maleimides in high yields albeit in high temperatures and only by the aid of 1,3,5,7-tetramethyl-2,4,8-trioxa-6-*O*-methoxyphenyl-6-phosphaadamantane as a bulky and commercially unavailable ligand.[10a] In the same paper, authors prepared monoaryl maleimides in good yields but non-selectively and in mixture with diaryl maleimides.

Scheme 3. Various approaches to the synthesis of diarylmaleimides



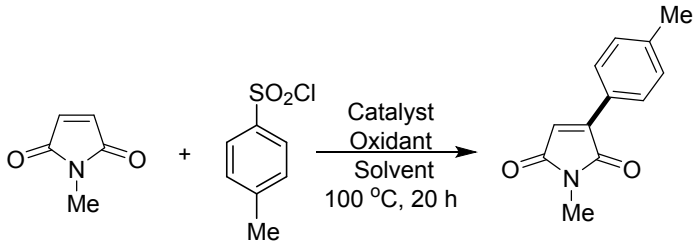
However, construction of two aryl groups on adjacent carbons in a synperiplanar mode imposes a major steric hindrance which is quite challenging and always within the aim of most chemists. It is worth mentioning that symmetrical 3,4-diaryl maleimiedes can be exemplified as stable atropisomers at room temperature [12a,16] thereby being exploited in asymmetric synthesis and drug discovery.[17] Moreover, diaryl maleimides constitute the backbone of copolymers together with showing fluorescent properties.[15f-g, 15o,18] Thus, there has been always an urge for the synthesis of these privileged moieties. Given the foregoing, we came up with an approach to prepare both monoaryl maleimides and diaryl maleimides selectively in a similar fashion with the least modulation of reaction conditions.

Results and discussion

At the outset, we reacted *N*-methyl maleimide with *p*-toluenesulfonyl chloride under $Pd(OAc)_2/NEt_3$ in acetonitrile which resulted in the 52% of the yield (Table 1, entry 1). Trying to optimize the solvent had a destructive effect on the yield (entries 2-6). Then we took advantage of other bases among which NaOAc acted superior to all others, yet the yield was not satisfactory enough (entries 7-11). Hence, we then probed the role of acids in this reaction. Although use of AcOH and *p*-TsOH lowered the yield, TFA built up the yield contently (entries 12-14). Use of $PdCl_2$ instead of $Pd(OAc)_2$ improved the yield slightly (entry 15). Then, the effect of temperature was taken into account showing that the best temperature under which the reaction can be conducted is 80 ^oC (entries 15-16). Lowering the time of the reaction to 12 h deteriorated the yield drastically (entry 18). Attainment of a better yield through adding different oxidants such as $K_2S_2O_8$ or metal oxidants (entries 19-21), Cs_2CO_3 as a base (entry 22) or PivOH as an acid (entry 23) was futile in this process. We tested a combination of $PdCl_2$/NaOAc both in

the presence (entry 24) and in the absence of TFA (entry 25). In the case of $PdCl_2$/NaOAc, the yield obtained was higher than that of achieved from the reaction under $PdCl_2$/NaOAc/TFA. Based on these observations it can be suggested that the reaction proceeds via a pseudo-Heck reaction and passes through an enolization step which can be assisted with both acids and bases. The proposed mechanism can be corroborated more firmly by using both TFA and NaOAc in the reaction. After screening various conditions, $PdCl_2$ (10%), TFA (2 equiv) in ACN under 80 ^oC provided the best result.

Table 1. Screening optimal conditions



Entry	Catalyst	Base	Acid	Oxidant	Solvent	Yield%[a]
1	$Pd(OAc)_2$	NEt_3	-	-	ACN	52
2	$Pd(OAc)_2$	NEt_3	-	-	DMF	20
3	$Pd(OAc)_2$	NEt_3	-	-	DMSO	0
4	$Pd(OAc)_2$	NEt_3	-	-	Toluene	34
5	$Pd(OAc)_2$	NEt_3	-	-	DMA	35
6	$Pd(OAc)_2$	NEt_3	-	-	Dioxane	48
7	$Pd(OAc)_2$	K_2CO_3	-	-	ACN	52
8	$Pd(OAc)_2$	Cs_2CO_3	-	-	ACN	30
9	$Pd(OAc)_2$	KO*t*-Bu	-	-	ACN	50
10	$Pd(OAc)_2$	NaOAc	-	-	ACN	62
11	$Pd(OAc)_2$	K_3PO_4	-	-	ACN	20
12	$Pd(OAc)_2$	-	HOAc	-	ACN	15
13	$Pd(OAc)_2$	-	TFA	-	ACN	62
14	$Pd(OAc)_2$	-	*p*-TsOH	-	ACN	45
15	$PdCl_2$	-	TFA	-	ACN	65
16	$PdCl_2$	-	TFA	-	ACN	67[b]
17	$PdCl_2$	-	TFA	-	ACN	60[c]
18	$PdCl_2$	-	TFA	-	ACN	38[d]
19	$PdCl_2$	-	TFA	$K_2S_2O_8$	ACN	62[b]
20	$PdCl_2$	-	TFA	$Cu(OAc)_2.H_2O$	ACN	20[b]

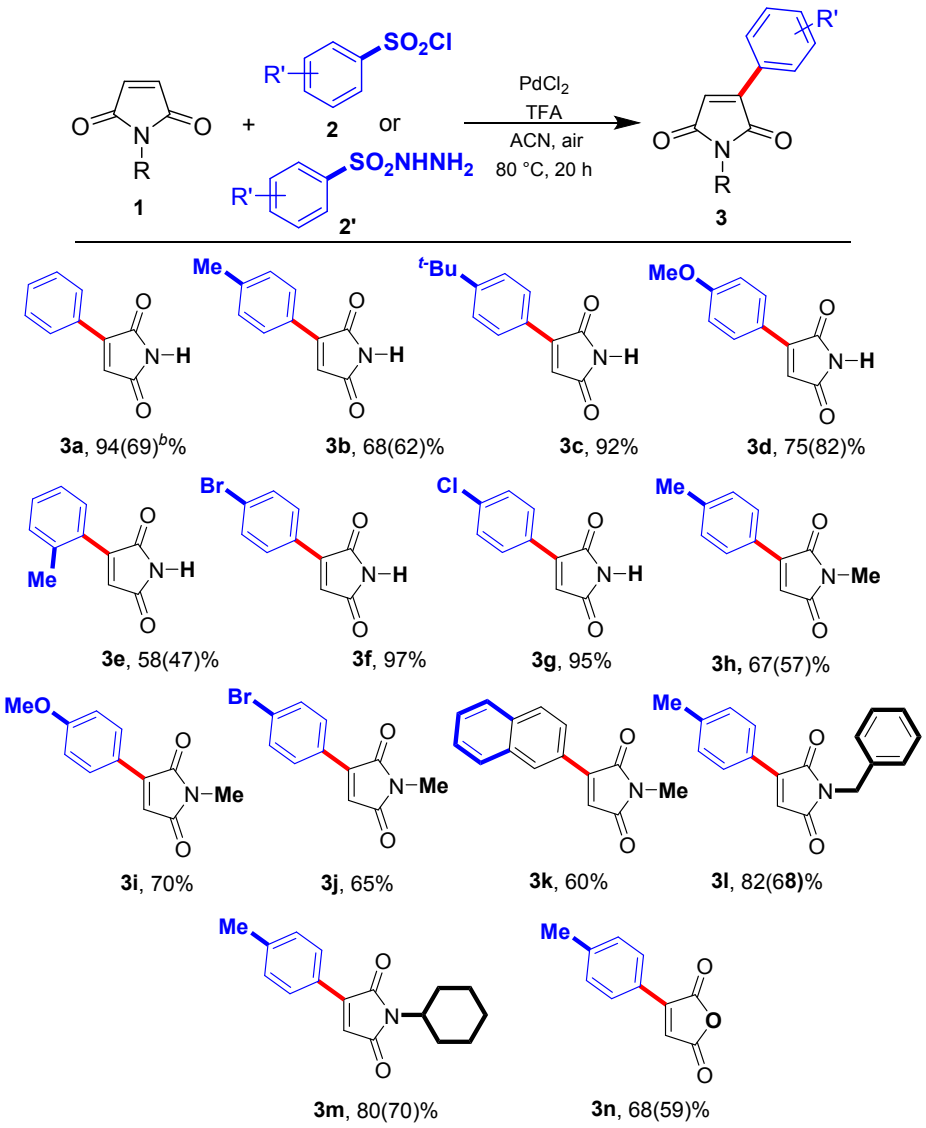
21	$PdCl_2$	-	TFA	AgOAc	ACN	20[b]
22	$PdCl_2$	Cs_2CO_3	TFA	-	ACN	15[b]
23	$PdCl_2$	-	TFA/PivOH	-	ACN	15[b]
24	$PdCl_2$	NaOAc	TFA	-	ACN	8
25	$PdCl_2$	NaOAc	-	-	ACN	38

[a] Reaction conditions unless otherwise noted: *N*-Methyl maleimide (0.1 mmol), *p*-toluenesulfonyl chloride (2 equiv), catalyst (10 mol %), base (2 equiv), acid (2 equiv), additive (2 equiv) in 0.5 mL of solvent were heated at 100 °C for 20 h. [b] The reaction was run at 80 °C. [c] The reaction was run at 60 °C. [d] The reaction time was 12 h.

Having set the optimized conditions, we then explored the scope of the reaction (Table 2). To this end, free *N*-H maleimide was reacted with different arenesulfonyl chlorides. Delightfully, the reaction proceeded well to the desired products with benzenesulfonyl chloride and arenesulfonyl chlorides bearing either neutral (**3a-c**) or electron-releasing groups (**3d**). Accommodation of a methyl group at C2 position, despite imposing significant steric hindrance, yielded the corresponding product (**3e**). Surprisingly, this reaction showed not only a great tolerance towards halo groups but it also provided higher yields than other functional groups thus paving the way for further manipulation of the prepared molecules (**3f, 3g**).[19] We then turned our attention to using *N*-methyl maleimide and employed it in the reaction with various arenesulfonyl chlorides possessing *p*-methyl, *p*-methoxy or *p*-bromo groups all of which furnished as satisfactory yields of the products as did *N*-H maleimide (**3h-j**). In addition, when 2-naphthalenesulfonyl chloride was used as the reactant, despite the steric hindrance present in the product between the C3-H of maleimide and C1-H of naphthalene attached to maleimide, the reaction led to an acceptable yield (**3k**). *N*-Benzyl maleimide and *N*-cyclohexyl maleimide afforded 80% and 82% yields respectively (**3l, 3m**). To our delight, maleic anhydride was also reactive under standard reaction conditions yielding 3-tolyl maleic anhydride (**3n**). In addition,

when arenesulfonyl hydrazides were used instead of arenesulfonyl chlorides, comparable yields were achieved which extended the scope of this reaction even more (Table 2).

Table 2. Substrate scope for construction of 3-aryl maleimides [a]

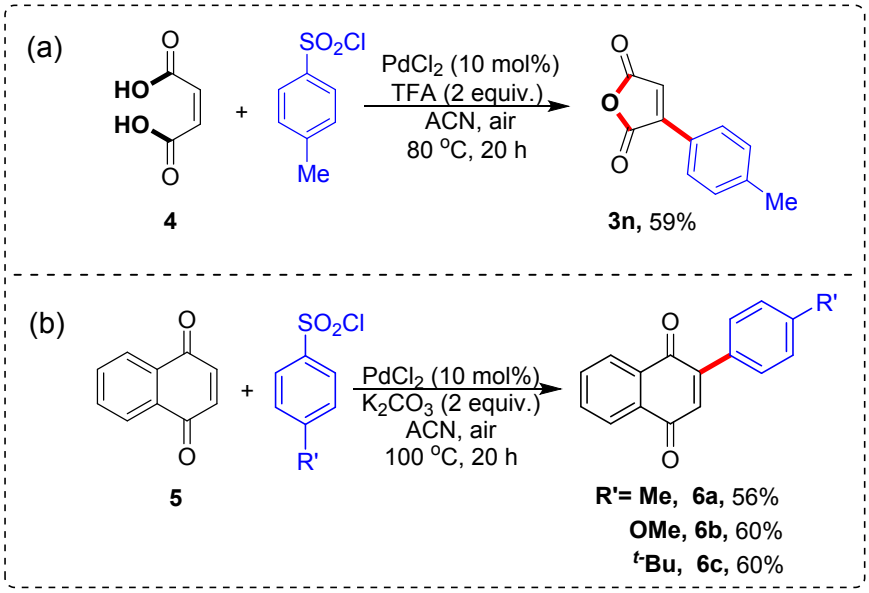


[a] Standard reaction conditions: Maleimide or maleic anhydride 1 (0.1 mmol), arenesulfonyl chloride 2 (2.0 equiv), $PdCl_2$ (10 mol %), TFA (2 equiv) in 0.5 mL ACN were heated at 80 °C for 20 h. b The yields in parenthesis were attained when arenesulfonyl hydrazides were used in the place of arenesulfonyl chlorides.

When maleic acid as the starting material was subjected to *p*-toluenesulfonyl chloride, a concomitant dehydration/arylation took place giving rise to 3-tolyl maleic anhydride. This

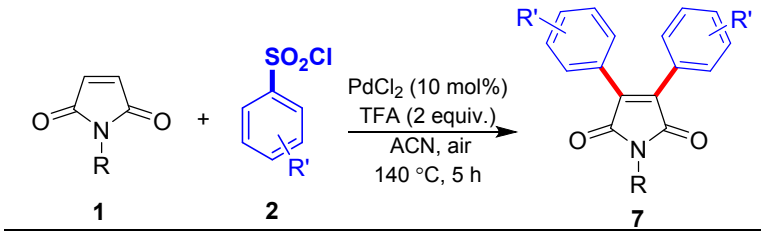
outcome gives one the opportunity to use maleic acid as a surrogate for maleic anhydride without any need for very high temperatures (Scheme 4, **3n**). In the next step, we utilized naphthoquinone in the place of maleimides. As opposed to prior work,[20] using our modified conditions, no sulfonyl naphthoquinone was formed but rather an extrusion of SO_2 occurred which culminated in 3-aryl naphthoquinone (Scheme 4, **6a-c**).

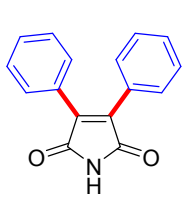
Scheme 4. The reaction of a) maleic acid and b) 1,4-naphthoquinone with arenesulfonyl chlorides

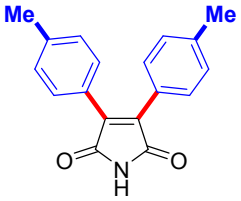


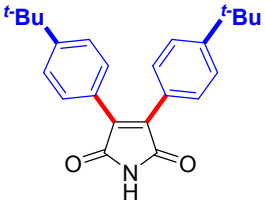
Unpredictably, when checking the different parameters of optimization table, it was found out that only with increasing the temperature to 140 °C and without any other deviation from standard conditions, a new product was formed; i.e. symmetrical 3,4-diphenyl maleimide (Table 3, **7a**). To the best of our knowledge, due to the high reactivity of both C3 and C4 of maleimides, the majority of previous reports on functionalization of this motif encountered serious difficulties attaining either monoaryl- or diaryl-maleimides selectively and in most cases a mixture of both products was gained. Having said that, we managed to get access to each series only through temperature control without any unwanted interfering side-products (Table 3).

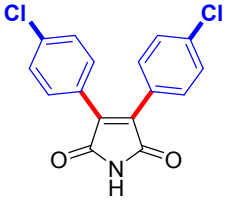
Table 3. Substrate scope for construction of 3,4-diaryl maleimides [a]

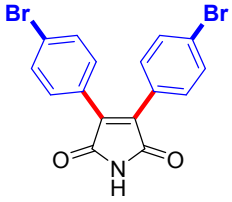


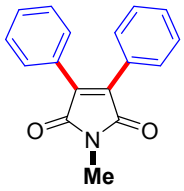

7a, 75%

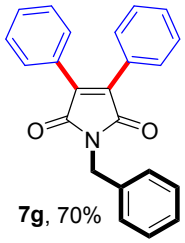

7b, 65%

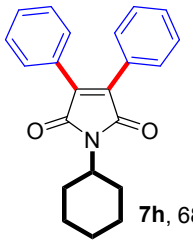

7c, 72%


7d, 78%


7e, 80%


7f, 68%


7g, 70%


7h, 68%

[a] All reactions were run under the following conditions: Maleimide 1 (0.1 mmol), arenesulfonyl chloride 2 (2.0 equiv), $PdCl_2$ (10 mol %), TFA (2 equiv) in 0.5 mL ACN were heated under air at 140 °C for 5 h.

To show the generality of this reaction, we exposed maleimide to various arenesulfonyl chlorides with different functional groups such as methyl, *tert*-butyl, halide groups (Cl and Br) which all led to the desired products in good yields (**7b-e**). Then, we replaced free *N*-H maleimide with other *N*-substituted maleimides namely *N*-methyl, *N*-benzyl and *N*-cyclohexyl

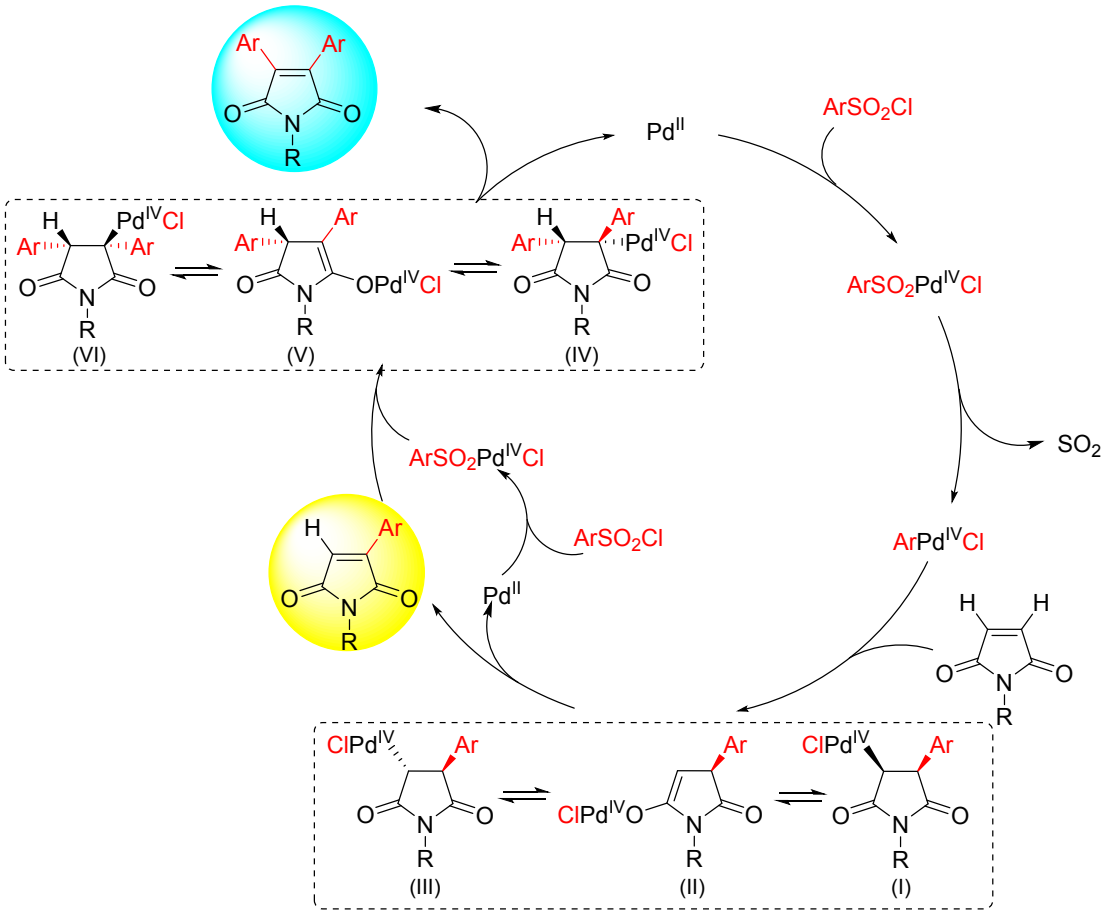
maleimides. Although we faced a slight fall in the yields comparing to *N*-H maleimide, the yields were still satisfactory thus it can be claimed that this method offers more privileges than previous methods and can be a preferred substitute for them (**7f-h**). Also, methanesulfonyl chloride and ethanesulfonyl chloride were tested under our reaction conditions to widen the scope of reaction but these reactions did not yielded any products and the starting materials remained intact at the end of the reaction.

A tentative mechanism for this reaction is outlined in Scheme 5. As was previously put forth by Doucet [21] we assumed that in the first step Pd(II) is converted to Pd(IV) through oxidative addition into $ArSO_2$-Cl bond. Extrusion of SO_2 followed by a carbopalladation furnishes intermediate **I** which rapidly converts into its palladium-enolate tautomer **II**. Then, due to more stability of intermediate **III**, the enol form tautomerizes to its keto form.[22] Although the three intermediates are in equilibrium, it must have been intermediate **I** from which *β*-hydride elimination proceeded since only in this intermediate palladium and H are placed on adjacent carbons and in a syn mode which is an essential requirement for elimination. Pd(IV) formed in this step then undergoes a reductive elimination and restores Pd(II) to the cycle. The second arylation takes place via the same mechanism this time with 3-arylmaleimide in place of maleimide itself as the starting material.

It is worth mentioning that except for the literature reports that referred to a Pd(II)/Pd(IV) cycle for the mechanism of the palladium-catalyzed desulfitative reactions,[4a,21b] there are some reports that proposed a Pd(0)/Pd(II) cycle in the same issue.[23] In addition, in the case of entries 1-2 and 4-6 of the Table 1, in which triehtyl amine was used as the additive of the reaction, the mechanism might have passed through a Pd(0) which then undergoes an oxidative-addition into

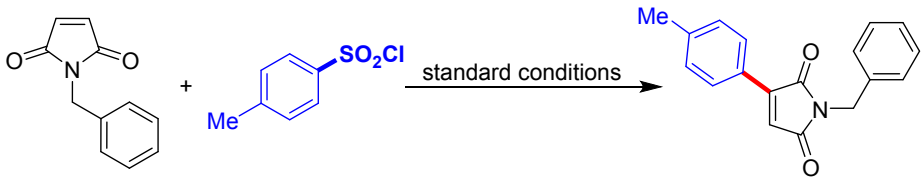
the S-Cl bond. Therefore, the reaction might involve either Pd(0)/Pd(II) or Pd(II)/(IV) intermediates and we cannot refuse any of them at this time.

Scheme 5. Plausible mechanism for regioselective C-3 arylation and 3,4-diarylation of maleimides



To demonstrate practicability of the invented new synthetic methods, the reaction of *p*-toluenesulfonyl chloride with *N*-benzyl maleimide performed in 0.3 mmol, 1 mmol and 3 mmol scales under monoarylation condition. Investigation showed that going to 0.3 mmol scale does not reduce the conversion but in larger scales it smoothly decreases. The reactions proceeded to the desired product **3l** in acceptable yields (Scheme 6).

Scheme 6. Gram-scale synthesis of monoaryl maleimides



0.3 mmol	0.07 g (80%)
1 mmol	0.20 g (71%)
3 mmol	0.49 g (59%)

Conclusion

In summary, a direct mono- and di-arylation on maleimides through concomitant Pd-catalysed two C-H functionalizations is achieved which provides an expedient access to 3-aryl- and 3,4-diaryl maleimides. This reaction is beneficial due to its simplicity and easily accessible starting materials. It is also noteworthy that temperature is the only factor that would do good and come into play for selective synthesis of either mono- or diaryl-maleimides. Good tolerance towards different functional groups and a wide scope renders this approach an alluring synthetic method as a replacement for the prior multi-step or single-step precedents.

Experimental Section

General Methods and Materials

All commercially available reagents were used without further purification. Unless noted otherwise, all reagents were purchased from Acros Organics and Merck Millipore. TLC was conducted on silica gel 250 micron, F254 plates. ^{1}HNMR spectra were recorded at room

temperature on a Bruker 400 and 500 MHz spectrometers, using DMSO-d_6 and acetone-d_6 as solvent. Chemical shifts are reported in ppm with TMS as an internal standard. ^{13}CNMR spectra are referenced from the solvent central peak. Chemical shifts are given in ppm. *N*-benzylmaleimide and *N*-cyclohexylmaleimide were prepared using the instructions given in previous papers.[24]

Typical procedure for the synthesis of 3-aryl-1H-pyrrole-2,5-diones (3a-3n)

In a vial charged by maleimide (3 mmol, 291 mg), benzenesulfonyl chloride (2 equiv, 6 mmol, 1.056 g), palladium chloride (10 mol%, 0.3 mmol, 53.1 mg) and TFA (6 equiv, 6 mmol, 684 mg), was added acetonitrile (7 mL) and capped. The resulting mixture was heated in an oil bath at 80 ^{o}C for 20 h. After washing the mixture with 10% brine solution and extraction with dichloromethane, the organic layer was dried over sodium sulfate and evaporated under reduced pressure. The organic residue was purified by a silica loaded column chromatography with 1:20 ethyl acetate in *n*-hexane as eluent. Recrystallization of the product using *n*-hexane gave pure 3-phenyl-1H-pyrrole-2,5-dione **3a** as off-white solid (280 mg), 54% yield.

Typical procedure for the synthesis of 2-arylnaphthalene-1,4-diones (6a-6c)

Naphthoquinone (1 mmol, 158 mg), *p*-toluenesulfonyl chloride (1 equiv, 1 mmol, 190 mg), palladium chloride (10 mol%, 0.1 mmol, 17.7 mg), potassium carbonate (2 equiv, 2 mmol, 276 mg) in acetonitrile (5 mL), was stirred at 100 ^{o}C for 20 h in a reaction vessel. The mixture was washed with 10% brine solution and then extracted with dichloromethane. The organic layer was dried over sodium sulfate and evaporated under reduced pressure. The organic residue was purified by a silica loaded column chromatography with 1:20 ethyl acetate in *n*-hexane as eluent. Recrystallization of the product using *n*-hexane gave pure 2-(*p*-tolyl)naphthalene-1,4-dione **6a** as white solids (139 mg), 56% yield.

Typical procedure for the synthesis of 3,4-diaryl-1H-pyrrole-2,5-diones (7a-7h)

Maleimide (1 mmol, 97 mg), benzenesulfonyl chloride (2 equiv, 2 mmol, 352 mg), palladium chloride (10 mol%, 0.1 mmol, 17.7 mg) and TFA (2 equiv, 2 mmol, 228 mg), was added acetonitrile (5 mL) and capped. The resulting mixture was heated in an oil bath at 140 ^{o}C for 5 h. The mixture was washed with 10% brine solution, extracted with dichloromethane the organic layer was dried over sodium sulfate and evaporated under reduced pressure. The organic residue was purified by a silica loaded column chromatography with 1:20 ethyl acetate in *n*-hexane as eluent. Recrystallization of the product using *n*-hexane gave pure 3,4-diphenyl-1H-pyrrole-2,5-dione **7a** as pale-yellow solid (187 mg), 75% yield.

3-Phenyl-1H-pyrrole-2,5-dione (3a); 54% yield (280 mg). White solid, mp. 160-162 ^{o}C, ^{1}HNMR (500 MHz, DMSO-d_6) δ 10.99 (s, 1H), 7.95-7.97 (m, 2H), 7.47-7.48 (m, 3H) 7.14 (s, 1H). Known compound.[11c]

3-p-Tolyl-1H-pyrrole-2,5-dione (3b); 41% yield (230 mg). White crystalline solid, mp. 174-176 ^{o}C, ^{1}HNMR (400 MHz, DMSO-d_6) δ 7.85 (d, *J* = 8.0 Hz, 2H) 7.37 (s, 1H), 7.29 (d, *J* = 8.0 Hz, 2H), 6.69 (s, 1H), 2.43 (s, 3H). ^{13}C{^{1}H} NMR (100 MHz, DMSO-d_6) δ 172.8, 172.3, 143.6, 141.4, 129.9, 129.0, 126.5, 125.0, 21.5. Anal. Calcd for $C_{11}H_9NO_2$: C, 70.58; H, 4.85; N, 7.48. Found: C, 70.67; H, 4.91; N, 7.53.

3-(4-tert-Butylphenyl)-1H-pyrrole-2,5-dione (3c); 52% yield (357 mg). Pale green sheet crystalline solid, mp. 188-192 ^{o}C, ^{1}HNMR (500 MHz, DMSO-d_6) δ 10.93 (s, 1H), 7.89 (dd, *J* = 6.5, 2.0 Hz, 2H), 7.48 (dd, *J* = 7.0, 2.0 Hz, 2H) 7.07 (s, 1H), 1.28 (s, 9H). ^{13}C{^{1}H} NMR (125 MHz, DMSO-d_6) δ 172.9, 172.5, 154.3, 143.7, 129.1, 126.8, 126.3, 125.5, 35.3, 31.4. Anal. Calcd for $C_{14}H_{15}NO_2$: C, 73.34; H, 6.59; N, 6.11. Found: C, 73.25; H, 6.55; N, 6.04.

3-(4-Methoxyphenyl)-1H-pyrrole-2,5-dione (3d); 46% yield (267 mg). Yellow solid, mp. 128-130 ^{o}C, ^{1}HNMR (500 MHz, DMSO-d_6) δ 10.86 (s, 1H), 7.97 (d, *J* = 8.5 Hz, 2H), 7.03 (d, *J* = 9.0 Hz, 2H), 6.99 (s, 1H), 3.80 (s, 3H). Known compound.[11c]

3-o-Tolyl-1H-pyrrole-2,5-dione (3e); 37% yield (207 mg). White solid, mp. 148-150 °C, ^{1}HNMR (500 MHz, DMSO-d_6) δ 11.01 (s, 1H), 7.88 (d, *J* = 8.0 Hz, 1H), 7.65-7.71 (m, 1H), 7.39 (d, *J* = 7.5 Hz, 1H), 7.34 (t, *J* = 7.0 Hz, 1H), 2.31 (s, 3H). ^{13}C{^{1}H} NMR (125 MHz, DMSO-d_6) δ 172.7, 172.5, 145.5, 137.7, 131.2, 130.7, 130.0, 129.3, 129.2, 126.2, 20.9. Anal. Calcd for $C_{11}H_9NO_2$: C, 70.58; H, 4.85; N, 7.48. Found: C, 70.50; H, 4.91; N, 7.42.

3-(4-Bromophenyl)-1H-pyrrole-2,5-dione (3f); 57% yield (429 mg). Yellow solid, mp. 184-186 °C, ^{1}HNMR (500 MHz, DMSO-d_6) δ 11.03 (s, 1H), 7.92 (dd, *J* = 7.0, 2.0 Hz, 2H), 7.69 (dd, *J* = 7.0, 2.0 Hz, 2H), 7.20 (s, 1H). ^{13}C{^{1}H} NMR (100 MHz, DMSO-d_6) δ 171.3, 170.5, 142.7, 132.0, 130.5, 128.8, 126.1, 124.8. Anal. Calcd for $C_{10}H_6BrNO_2$: C, 47.65; H, 2.40; N, 5.56. Found: C, 47.58; H, 2.31; N, 5.51.

3-(4-Chlorophenyl)-1H-pyrrole-2,5-dione (3g);) 60% yield (372 mg). Yellow solid, mp. 180-182 °C, ^{1}HNMR (500 MHz, DMSO-d_6) δ 11.02 (s, 1H), 8.00 (d, *J* = 8.5 Hz, 2H), 7.55 (d, *J* = 8.5 Hz, 2H), 7.20 (s, 1H). Known compound.[11c]

1-Methyl-3-p-tolyl-1H-pyrrole-2,5-dione (3h); 49% yield (295 mg). Greenish white crystalline solid, mp. 110-112 °C, ^{1}HNMR (500 MHz, DMSO-d_6) δ 7.93 (d, *J* = 8.0 Hz, 2H), 7.31 (d, *J* = 8.0 Hz, 2H), 7.21 (s, 1H), 2.92 (s, 3H), 2.36 (s, 3H). Known compound.[25]

3-(4-Methoxyphenyl)-1-methyl-1H-pyrrole-2,5-dione (3i); 47% yield (305 mg). Yellow crystalline solid, mp. 142-145 °C, ^{1}HNMR (400 MHz, DMSO-d_6) δ 8.04 (dd, *J* = 6.8, 2.0 Hz, 2H), 7.15 (s, 1H), 7.08 (dd, *J* = 7.2, 2.0 Hz, 2H), 3.84 (s, 3H), 2.93 (s, 3H). ^{13}C{^{1}H} NMR (100 MHz, DMSO-d_6) δ 171.5, 171.2, 161.9, 142.8, 130.8, 129.1, 121.9, 114.9, 55.9, 23.7. Anal. Calcd for $C_{12}H_{11}NO_3$: C, 66.35; H, 5.10; N, 6.45. Found: C, 66.25; H, 5.06; N, 6.49.

3-(4-Bromophenyl)-1-methyl-1H-pyrrole-2,5-dione (3j); 41% yield (326 mg). White solid, mp. 128-130 °C, ^{1}HNMR (500 MHz, DMSO-d_6) δ 7.95 (d, *J* = 8.5 Hz, 2H), 7.71 (d, *J* = 8.0 Hz, 2H), 7.33 (s, 1H), 2.28 (s, 3H). ^{13}C{^{1}H} NMR (125 MHz, DMSO-d_6) δ 170.4, 170.2, 141.5, 131.9, 131.5, 130.3, 125.9, 124.6, 23.6. Anal. Calcd for $C_{11}H_8BrNO_2$: C, 49.65; H, 3.03; N, 5.26. Found: C, 49.69; H, 2.99; N, 5.19.

1-Methyl-3-(naphthalen-3-yl)-1H-pyrrole-2,5-dione (3k); 45% yield (320 mg). Yellow solid, mp. 144-146 °C, ^{1}HNMR (300 MHz, DMSO-d_6) δ 8.66 (s, 1H), 7.81-7.91 (m, 4H), 7.46-7.50 (m,

2H), 7.05 (s, 1H), 2.91 (s, 1H). $^{13}C\{^{1}H\}$ NMR (75 MHz, DMSO-d_6) δ 167.1, 166.5, 146.1, 132.6, 131.2, 129.4, 129.2, 128.8, 128.6, 128.3, 126.9, 126.8, 124.9, 124.9, 124.7, 23.6. Anal. Calcd for $C_{15}H_{11}NO_2$: C, 75.94; H, 4.67; N, 5.90. Found: C, 75.88; H, 4.74; N, 5.82.

1-Benzyl-3-p-tolyl-1H-pyrrole-2,5-dione (3l); 59% yield (490 mg). Pale yellow solid, mp. 92-94 °C, ^{1}HNMR (500 MHz, DMSO-d_6) δ 7.93 (d, *J* = 8.0 Hz, 2H), 7.30-7.34 (m, 4H), 7.26-7.27 (m, 4H), 4.64 (s, 2H), 2.34 (s, 3H). Known compound.[26]

1-Cyclohexyl-3-p-tolyl-1H-pyrrole-2,5-dione (3m); 52% yield (419 mg). Pale yellow solid, mp. 104-106 °C, ^{1}HNMR (500 MHz, DMSO-d_6) δ 7.91 (d, *J* = 8.0 Hz, 2H), 7.31 (d, *J* = 8.0 Hz, 2H), 7.17 (s, 1H), 3.80-3.87 (m, 1H), 2.36 (s, 1H), 1.93-2.01 (m, 2H), 1.78 (d, *J* = 13.0 Hz, 2H), 1.64 (t, *J* = 13.0 Hz, 3H), 1.23-1.35 (m, 3H). Known compound.[27]

3-p-Tolylfuran-2,5-dione (3n); 38% yield (214 mg). White solid, mp. 98-100 °C, ^{1}HNMR (400 MHz, Acetone-d_6) δ 8.03 (d, *J* = 8.0 Hz, 2H), 7.74 (s, 1H), 7.41 (d, *J* = 8.0 Hz, 2H), 2.44 (s, 3H). Known compound.[28]

2-p-Tolylnaphthalene-1,4-dione (6a); 56% yield (139 mg). Yellow solid, mp. 101-103 °C, ^{1}HNMR (400 MHz, DMSO-d_6) δ 8.11-8.09 (m, 1H), 8.02-8.04 (m, 1H), 7.69-7.71 (m, 2H), 7.41 (d, *J* = 8.0 Hz, 2H), 7.20 (d, *J* = 8.0 Hz, 2H), 6.98 (s, 1H), 2.3 (s, 3H). Known compound.[29]

2-(4-Methoxyphenyl)naphthalene-1,4-dione (6b); 60% yield (160 mg). Yellow solid, mp. 114-116 °C, ^{1}HNMR (500 MHz, DMSO-d_6) δ 8.07-8.08 (m, 1H), 8.00-8.01 (m, 1H), 7.87-7.90 (m, 2H), 7.61 (d, *J* = 9.0 Hz, 2H), 7.10 (s, 1H), 7.03 (d, *J* = 8.5 Hz, 2H), 3.82 (s, 3H). Known compound.[30]

2-(4-tert-Butylphenyl)naphthalene-1,4-dione (6c); 60% yield (174 mg). Yellow solid, mp. 122-125 °C, ^{1}HNMR (500 MHz DMSO-d_6) δ 8.06-8.08 (m, 1H), 7.99-8.01 (m, 1H), 7.87-7.89 (m, 2H), 7.54 (d, *J* = 8.5 Hz, 2H), 7.48 (d, *J* = 8.0 Hz, 2H), 7.12 (s, 1H), 1.30 (s, 9H). Known compound.[31, 9d]

3,4-Diphenyl-1H-pyrrole-2,5-dione (7a); 75% yield (218 mg). Yellow crystalline solid, mp. 171-173 °C, ^{1}HNMR (500 MHz, DMSO-d_6) δ 11.36 (s, 1H), 7.48-7.51 (m, 6H), 7.45-7.47 (m, 4H). Known compound.[32]

3,4-Di-p-tolyl-1H-pyrrole-2,5-dione (7b); 65% yield (181 mg). Yellow solid, mp. 170-172 °C, ^{1}HNMR (500 MHz, DMSO-d_6) δ 11.16 (s, 1H), 7.24 (d, *J* = 8.0 Hz, 4H), 7.17 (d, *J* = 8.5 Hz, 4H), 2.29 (s, 6H). Known compound.[10a,15c]

3,4-bis(4-tert-Butylphenyl)-1H-pyrrole-2,5-dione (7c); 72% yield (200 mg). Green-yellow solid, mp. 212-216 °C, ^{1}HNMR (500 MHz, DMSO-d_6) δ 11.20 (s, 1H), 7.42 (d, *J* = 8.0 Hz, 4H), 7.35 (d, *J* = 8.0 Hz, 4H), 1.28 (s, 18 H). ^{13}C{^{1}H} NMR (125 MHz, DMSO-d_6) δ 172.3, 152.6, 136.2, 129.8, 126.5, 125.7, 35.0, 31.4. Anal. Calcd for $C_{24}H_{27}NO_2$: C, 79.74; H, 7.53; N, 3.87. Found: C, 79.81; H, 7.59; N, 3.84.

3,4-bis(4-Chlorophenyl)-1H-pyrrole-2,5-dione (7d); 78% yield (248 mg). Yellow crystalline solid, mp. 208-210 °C, ^{1}HNMR (500 MHz, DMSO-d_6) δ 11.32 (s, 1H), 7.47 (dt, *J* = 8.5, 2.5 Hz, 4H), 7.36 (dt, *J* = 8.5, 2.5 Hz, 4H). Known compound.[10a,15c]

3,4-bis(4-Bromophenyl)-1H-pyrrole-2,5-dione (7e); 80% yield (295 mg). Yellow crystalline solid, mp. 172-174 °C, ^{1}HNMR (500 MHz, DMSO-d_6) δ 11.30 (s, 1H), 7.61 (d, *J* = 8.5 Hz, 4H), 7.30 (d, *J* = 8.5 Hz, 4H). ^{13}C{^{1}H} NMR (125 MHz, DMSO-d_6) δ 171.8, 136.5, 132.3, 132.2, 128.3, 124.0. Anal. Calcd for $C_{16}H_9Br_2NO_2$: C, 47.21; H, 2.23; N, 3.44. Found: C, 47.25; H, 2.31; N, 3.52.

1-Methyl-3,4-diphenyl-1H-pyrrole-2,5-dione (7f); 68% yield (251 mg). Yellow crystalline solid, mp. 138-141 °C, ^{1}HNMR (500 MHz, DMSO-d_6) δ 7.48-7.50 (m, 4H), 7.36-7.42 (m, 6H), 3.19 (s, 3H). Known compound.[15a]

1-Benzyl-3,4-diphenyl-1H-pyrrole-2,5-dione (7g); 70% yield (258 mg). Yellow solid, mp. 98-102 °C, ^{1}HNMR (500 MHz, DMSO-d_6) δ 7.36-7.41 (m, 15H), 4.75 (s, 2H). Known compound.[15b]

1-Cyclohexyl-3,4-diphenyl-1H-pyrrole-2,5-dione (7h); 68% yield (226 mg). Green-yellow crystalline solid, mp. 140-142 °C, ^{1}HNMR (500 MHz, DMSO-d_6) δ 7.65-7.71 (m, 2H), 7.34-7.40

(m, 8H), 3.88-3.95 (m,1H), 1.97-2.04 (m, 2H), 1.79 (d, J = 11.5 Hz, 2H), 1.60-1.64 (m, 2H), 1.32-1.36 (m, 4H). Known compound.[12c]

ASSOCIATED CONTENT

Supporting Information. Copies of ^{1}H and $^{13}C\{^{1}H\}$ NMR spectra. This material is available free of charge via the Internet at http://pubs.acs.org.

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Notes

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