Hypervalent Activation as Key Step for Dehydrogenative ortho C-C Coupling of Iodoarenes

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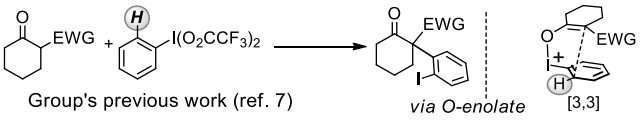
Dedication ((optional))

Abstract: Building on earlier results, we report here a direct metal-free a-arylation of substituted cyclic 1,3-diones using ArI(O_2CCF_3)$_2$ reagents; unlike other arylative approaches, the arylated products which retain the iodine substituent ortho to the newly formed C-C bond. The mechanism was explored using DFT calculation showing a vanishingly small activation barrier for the C-C bond-forming step. In fact, taking advantage of an efficient in situ hypervalent activation, the iodoarenes are shown to undergo a cross-dehydrogenative C-C coupling at the C-H *ortho* to the iodine. When using Oxone® as terminal oxidant, the process was found to benefit from a rapid initial formation of the hypervalent ArI(OR)$_2$ species and the sulphate-accelerated final coupling with a ketone. The method complements the ipso-selectivity obtained in the metal-catalysed α-arylation of carbonyl compounds..

Introduction

Carbonyl compounds bearing an α-aryl group are important targets in a wide range of chemical applications. Although their preparation is possible via the conventional S_NAr reaction of enolates,[1] the α-arylation approach became particularly practical in the late 90's with the introduction of efficient metal-catalyzed C-C coupling protocols. [2-3] Alternatively, the uncatalysed arylation using diaryliodonium or aryllead species has also been applied in the synthesis of α-arylketones,[4-6] Despite all these advances, challenges remain, particularly with respect to the selectivity and to the transfer of the ortho-substituted aryl fragments.

Our group recently reported an alternative metal-free α-arylation strategy employing phenyliodine bis(trifluoroacetate) (PIFA) as the aryl source.[7] The reaction produced arylketones bearing the iodine atom at the *ortho* position of the aromatic ring (Scheme 1). The reaction exemplifies an unusual case of aromatic CH functionalization where the outcome was rationalized by a [3,3] rearrangement of an intermediate iodonium *O*-enolate. This new dehydrogenative cross-coupling was compatible with a range of the ArI(O_2CCF_3)$_2$ reagents,[8] and the retention of the iodine atom in the coupling products provided access to hindered ortho-substituted α-arylketones and heterocycles. Notably, the method was particularly suitable for the formation of the α-(2-iodoaryl) cyanoketones, a compound class relevant in several applications, including drug design[9] (e.g. Levocabastine, an antihistamine) and crop protection, with several powerful miticides (e.g. Cyflumetofen, Cyenopyrafen, IKA-2002) based on an α-aryl-2-cyanoketone core.[10]



Scheme 1. The α-arylation employing λ^3-iodanes as aryl transfer agents.

Regarding this methodology, however, an array of questions remained concerning the mechanism, then applicability to other challenging or industrially relevant substrate families, and as to the potential for a more convenient protocol. Thus, we began by investigating the metal-free formation of 2-aryl-1,3-diones. The synthesis of such species has drawn an extraordinary amount of synthetic effort, especially given that several major commercial pesticides (spirotetramat, pinoxaden, spirodicyclophen) all feature an *ortho*-substituted aryl group at the intercarbonylic position.[11] Interestingly, the metal-catalysed α-arylation of cyclic 1,3-diketones has met with difficulty when using *ortho*-substituted aryl groups (or when forming quaternary C centres), which explains a frequent usage of stoichiometric Ar-Pb species.[12] In this context, we set out to explore the possibility of using mono-aryl hypervalent iodine reagents under metal-free conditions.

Results and Discussion

***Arylation of cyclic diones*.** Initial tests were conducted by exposing the 2-methyl-1,3-cyclohexanedione, **1a**, to PIFA (1.25 equiv). For the 1:1 CH_3CN/CF_3CO_2H solvents mixture the expected *ortho*-iodo aryl product **2a** formed in 50% yield (Table 1, entry 1). The nitromethane/trifluoroacetic acid combination was also identified as a promising medium, especially in the presence of small amounts (approx. 0.4 equiv) of the trifluoroacetic anhydride (entries 2-4). Although the role of TFAA remains unclear, it may act as a drying agent; indeed, the addition of water to the mixture proved detrimental. Under the optimised reaction conditions the target 2-(2´-iodophenyl)-2-methyl-1,3-cyclohexanedione, **2a**, was isolated in 65% yield; a similar yield was also obtained for the dimedone-based product **2a'** (Table 2). The presence of larger 2-alkyl substituents, including ethyl, n-butyl and benzyl, was also tolerated, affording the target α-(2-iodophenyl)-1,3-diketones **2b**-**d**. The introduction of substituted iodoaryl groups was achieved with additional ArI(O_2CCF_3)$_2$ reagents[13,7] to give **2e**-**i** bearing the 2-iodo-5-carboxy-phenyl,

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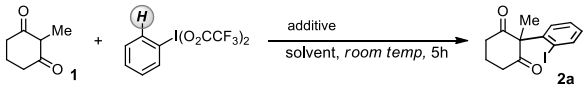
Table 1. Optimization of the arylation of **1a** with PIFA[a]

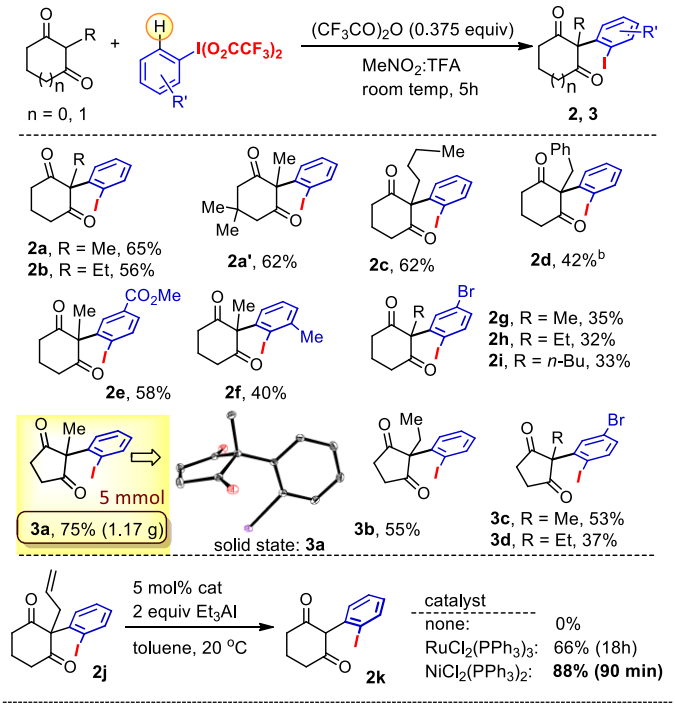


Entry	Solvent	Additive (equiv)	%Yield[b]
1	$CH_3CN + CF_3COOH$	-	50
2	$CH_3NO_2 + CF_3COOH$	-	55
3	$CH_3NO_2 + CF_3COOH$	$(CF_3CO)_2O$) (1.250)	59
4	$CH_3NO_2 + CF_3COOH$	$(CF_3CO)_2O$ (0.375)	**65**

[a] 1 mmol of **1** and 1.25 mmol of **2a** in 4 mL of solvent (1:1 mixture) for 5h at room temp.[b] % isolated product.

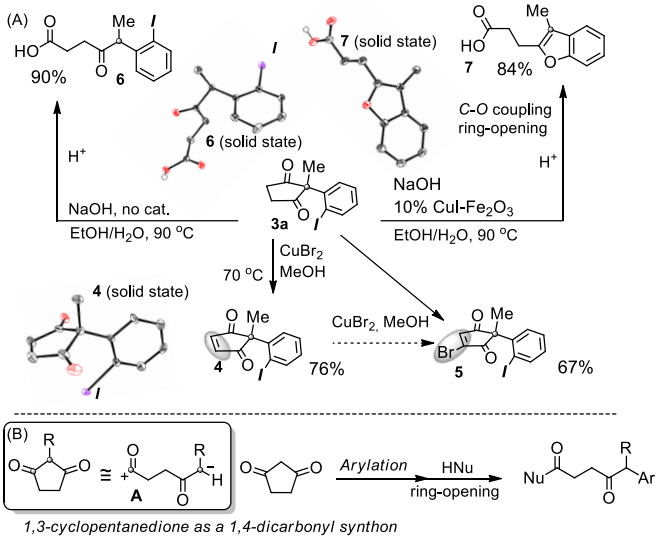
2-iodo-3-methyl-phenyl or the potentially versatile 2-iodo-5-bromophenyl moieties. The method was suitable for the 5-membered cyclic diketones (products **3a**-**d**), whereby the arylation of 1,3-cyclopentanedione on a 5 mmol scale led to 75% yield (1.17 g) of **3a** as microcrystalline solid.

Table 2. The scope of the arylation reaction.[a]



[a] Conditions: 1 mmol of diketone, 1.25 mmol of **2**, 4 mL of $MeNO_2$:TFA (1:1), rt, 5h. Yields of isolated products. [b] MeCN instead $MeNO_2$ and without TFAA.

Attempts to engage the parent 2*H* 1,3-cyclohexanedione led instead to the corresponding iodonium ylide.[15] Nevertheless, the introduction of of a 2-allyl group allowed for the formation of the "masked" arylated species **2j** which was then deprotected to the free **2k** *via* a metal-catalysed deallylation reported by Kotora *et al*.[16] Although the original protocol dealt with solely with 2-allylmalonates, exposing **2j** to Et_3Al (2 equiv) and catalytic $RuCl_2(PPh_3)_3$ yielded 66% of **2j** in 66% after 18h (Scheme 2), while switching to the $NiCl_2(PPh_3)_2$ catalyst accomplished this in an 88% yield in just 90 min.[16b] The structure of the newly generated α-aryl-1,3-diones **2** and **3** should allow for their straightforward conversion into a variety of targets, as shown in Scheme 2(A) for the **3a**. Thus, a C=C bond was readily installed by treatment with $CuBr_2$ in MeOH,[17] affording either the 2-aryl-2-methylcyclopenten-1,3-dione **4** (76%) or its 4-bromo derivative **5** (67%) depending on the amounts of the copper salt employed. Under basic conditions **3a** was opened into the 4-ketoacid **6** (90% yield) bearing an intact 2-iodophenyl fragment. Interestingly, the same reaction in the presence of catalytic CuI-Fe_2O_3 afforded 84% yield of the 3-methyl-benzofuran-based acid **7**, likely *via* an initial Cu-catalysed C-O coupling (intramolecular enolate arylation[18]), followed by a base-promoted ring opening. It is of note that the formation of **6** from **3a**, and ultimately, from 2-Me-1,3-cyclopentanedione highlights the ability of such cyclic 1,3-diones to act as convenient synthons of a formal 1,4-dicarbonyl dipole, as seen in Scheme 2(B). A related concept was recently exploited by Cramer *et al* in the synthesis of functionalised allenes.[19]



Scheme 2. Examples of the synthetic versatility of 3**a**.

***Mechanistic insights*.** As early as 1988, Oh and co-workers postulated the possibility of a [3,3] rearrangement to explain the appearance of 2-allyl-iodobenzene when attempting an *umpolung* aromatic allylation using $(PhIO)_n$ as an oxidant, and the process received full attention from the laboratories of Ochiai *et al.* in the course of the synthesis of a series of *ortho*-propargyl iodoarenes.[20] Further mechanistic studies were conducted by Norton and co-workers, and the reaction was later applied by *Zhu et al.* in a versatile approach to allyliodoarenes.[21] A series of ostensibly closely related CH functionalization *via* [3,3] rearrangement processes have also been reported for arylsufoxides by the groups of Maulide and Procter.[15b, 22]

Focusing, once again on the mechanism of the (2-iodoaryl) transfer, our failure to observe the putative iodonium enolate intermediates suggested that the rearrangement step might, in fact, be rather fast.[23] In order to shed further light on this process, the mechanis m was probed by DFT calculations applying the B3LYP/6-31+G(d,p) and augmented LAN2DZ (for I) combination. In particular, it was crucial to validate the feasibility of the key putative iodonio-[3,3] rearrangement step. Using the arylation of the 2-cyanocyclohexanone as model system, we began by locating the corresponding iodonium *O*-enolate precursor.

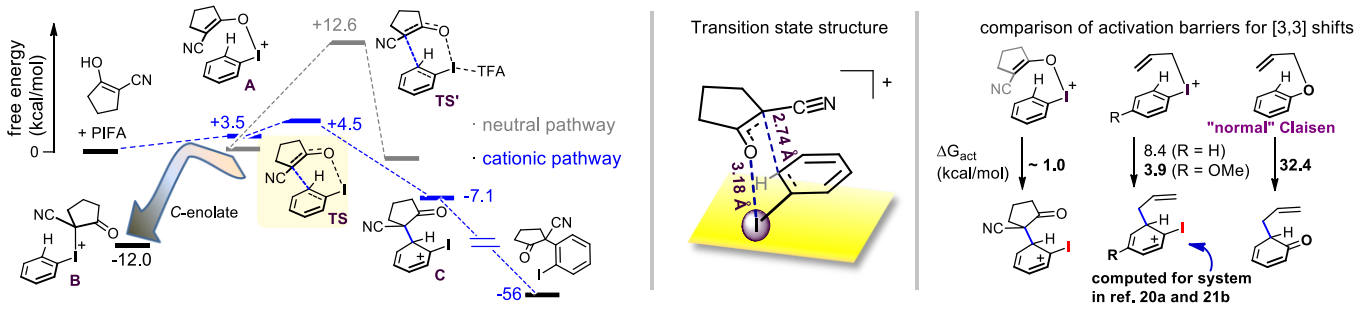
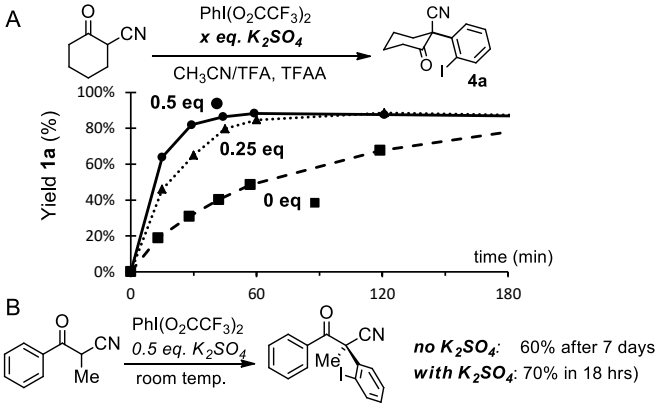


Figure 1. DFT reaction profile using Gaussian09 B3LYP/6-31+g(d,p) (C,H,N,O) and LAN2DZ augmented by p and d for Iodine. Solvent (CH_3CN) was included with SCRF PCM model. For the sake of clarity, the requisite TFAH and TFA^- have been omitted from the profile drawing (but included in the energy calculations).

Thus, the cationic [PhI-*enol*]$^+$ (**A**) resides 3.5 kcal/mol above the precursors, with one of its the chair-like conformers (~ 1 kcal/mol above the open form) pre-arranged for the [3,3] transition state (Figure 1, **TS**, 1 imag. frequency). This transition state gave rise to the protonated intermediate **C** at -7.1 kcal/mol which yields the final (2-iodophenyl) product **8a** upon deprotonation. The overall reaction was found to be exergonic by 56 kcal/mol. Although the *C*-enolate **B** lies 13 kcal/mol lower than the *O*-enolate, we believe that the key C-C bond formation occurs faster than the **A**-to-**B** tautomerization. Importantly, the activation barrier for the "neutral" pathway involving the TFA-bound **A** (see **TS'**) was found to be 12 kcal/mol higher than for the cationic **A**, in line with the idea of the charge-accelerated rearrangement.[23] For comparison, the activation barrier for a related iodonium-based *ortho*-allylation[20a] was also computed. In this case, the reaction was proposed to proceed through an Ar-I(allyl)$^+$ intermediate. A chair-like cationic transition state was now located with an activation barrier of 8 kcal/mol, which was further reduced to 4 kcal/mol for the ArI fragment substituted with a –OMe group *para* to the activated CH position, in light with documented the favourable reactivity at the position *para* to an electron-donating group.[21b] A significantly higher barrier of 32 kcal/mol was calculated at the same DFT level for the classical Claisen rearrangement of the *O*-allyl phenol. The vanishingly small activation barrier in the rearrangement step of the iodonium *O*-enolate **A** is in line with the slow step in the process actually being the ligand exchange leading to this interemediate.

The sulfate effect and the direct usage of ArI. Interestingly, the reaction was found to be susceptible to acceleration by simple sulphate salts. A control experiment using PIFA and 2-cyanocyclohexanone using 0.5 equiv of K_2SO_4 reached a 64% completion after 15 min, reaching completion in 60 min (Scheme 3A). Although the possibility of an iodonium sulphate intermediate was considered, no evidence for such species was obtained by ^{1}H NMR upon stirring a solution of PIFA with K_2SO_4 (see Support. Info). While the exact mechanism is still unclear, its effect can also be seen in the arylation of the challenging open-chain 2-acetylpropionitrile, reducing the reaction time from 7 days to just 18h at room temp. (Scheme 3B).

Such sulphate-promoted acceleration suggests the possibility of using iodoarenes directly in the presence of Oxone. Here, the process would rely on rapid in situ conversion of ArI to $ArI(O_2CCF_3)_2$ and a fast subsequent C-C coupling. Indeed, the heat flow profiles for the oxidation of several iodoarenes with Oxone in a $CHCl_3/CF_3CO_2H$ mixture revealed that the formation of $ArI(O_2CCF_3)_2$ was complete within 10-15 min (for a representative profile, see Supporting Info), leading to nearly quantitative formation of the hypervalent reagent.

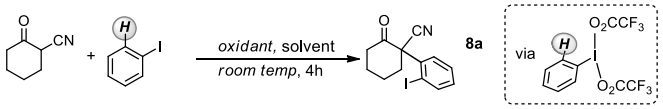


Scheme 3. Effect of K_2SO_4 on the arylation of cyanoketones.

Next, a reaction between iodobenzene and 2-cyanocyclohexanone employing Oxone® in a CH_3CN/CF_3COOH mixture afforded approximately a 50% yield of the target 2-cyano-2-(2-iodophenyl)cyclohexane, **8a** (Table 3, entries 1-2).[24] An improvement was seen by replacing acetonitrile by other polar solvents (entries 3-6), reaching an 82% yield of **8a** in a DCE–trifluoroacetic acid mixture (entry 6). Tracing the reaction progress showed the coupling in the presence of Oxone to be complete after just 1h, while 4h were required for *m*-CPBA (entries 7-9). Lending evidence for a non-radical mechanism, the addition of TEMPO had no appreciable effect on the outcome, both under present conditions or using pre-formed PIFA.[25]

Essay with several iodoarenes led to a general protocol involving an initial of 1.6 equiv of the oxidant, followed by an additional 0.5 equiv after 2h. Thus, we set out to explore whether the direct protocol would deliver the previously synthesized α-arylcyanoketones now directly from the corresponding ArI, and, especially, whether coupling could now be performed with iodoarenes for which the corresponding λ^3-iodane is either unknown or expected to be unstable. As seen in Table 4, a second halogen substituent (F, Br, Cl) was well tolerated (products **8b-e**). Iodoarenes with *p*-Me, CH_2OH, CHO and CO_2Me substituents underwent smooth coupling (entries **8g-j**), as did *o*-iodotoluene (entry **8k**) circumventing the need for the unknown alcohol- and aldehyde-bearing hypervalent species.

Table 3. Coupling between PhI and 2-cyanoketone.[a]

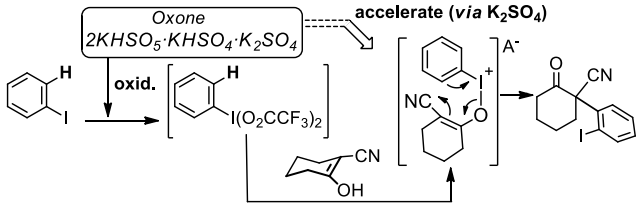


Entry	Oxidant	Solvent	%Yield[b]
1	Oxone	CH_3CN + acetic acid	25
2	Oxone	CH_3CN + CF_3COOH	52
3	Oxone	DCM + CF_3COOH	84
4	Oxone	CH_3NO_2 + CF_3COOH	81
5	Oxone	EtOAc + CF_3COOH	80
6	Oxone	DCE + CF_3COOH	86 (82)
7	Oxone	DCE + CF_3COOH	(80)[c]
8	m-CPBA	DCE + CF_3COOH	75[d]
9	m-CPBA	DCM + CF_3COOH	82 (79)[d]

[a] Using 0.5 mmol PhI, 0.6 mmol cyanoketone and 0.8 mmol [Ox] in 2 mL solvent o/n; [b] GC yield using CyCN as int. st., (% isolated); [c] 1h; [d] 4h.

Several new α-iodoaryl derivatives were now readily readily obtained, such as those bearing the *para* $-S(Me)O_2$, $-NO_2$ and $-CF_3$ (entries **8l-n**), the latter, for examples, in a 73% yield. The use of the 3,5-disubstituted ArI allowed for the formation of the α-arylketones **8p** and **8q** possessing the highly hindered quaternary carbon centre. Such hindered quaternary centres have no precedent in the "normal" metal-catalysed α-arylation literature, highlighting the ability of the new method to fill the gaps left by other approaches. As anticipated, while the easily oxidisable *p*-iodoanisol failed, the coupling the acetyl, mesyl and tosyl esters of 4-iodophenol did afford the corresponding arylated **8r**-**8t** (σ_p= +0.31, +0.34 and +0.29 for the -OR, respectively). In addition, a 37% yield was achieved for 4-(trifluoromethoxy)iodobenzene (**8u**). The scope also included the 7- and the 5-mebered cyclic cyanoketones (products **9i**, **10a**, **10h**) and delivered the arylated 2-cyanotetralone **11a** in an 81% yield.

Oxone, therefore, appears to play a double role, serving as the oxidant in the hypervalent activation (via $KHSO_5$), and as promoter (via K_2SO_4) of the subsequent dehydrogenative C-C coupling (Scheme 4). A lack of such positive sulphate effect may also explain a more sluggish coupling when using *m*-CPBA, despite the comparable rates of the initial ArI hypervalent activation.

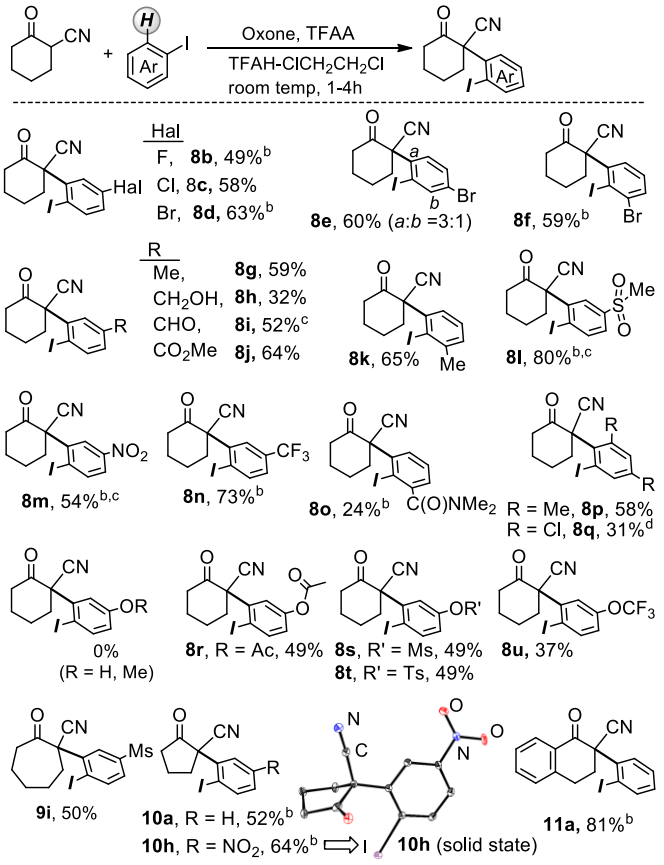


Scheme 4. The double role of Oxone in the arylation *via* hypervalent activation.

Conclusions

We have demonstrated the hypervalent activation of iodoarenes, whether prior to a reaction or *in situ* constitutes a powerful tool for the dehydrogenative α-arylation of industrially relevant substrate classes, such as cyclic 1,3-diones. A direct metal-free coupling between iodoarenes and 2-cyanoketones is possible via a key hypervalent activation step shown to occur in <15 min when using Oxone or *m*-CPBA as terminal oxidants. In the new protocol, the iodine atom is left untouched, and the new C-C bond was created at the *ortho* position, rendering the method complementary to the existing *ipso* substitutive reactions. The DFT calculation revealed that the putative Claisen-type rearrangement is indeed feasible, and indeed appears to take place with a vanishingly small activation barrier. This work also reveals that the key coupling step (involving the $ArI(O_2CCF_3)_2$) can be significantly accelerated by K_2SO_4, which we expect to help couple hitherto difficult substrate combinations.

Table 4. Coupling between ArI and 2-cyanocyclohexanone.[a]



[a] Using ArI (0.25M) and cyanoketone (1.5 eq) in TFA:DCE (1:1). [b] Using CH_3NO_2 instead of DCE. [c] Using *m*-CPBA. [d] Using $K_2S_2O_8$ and H_2SO_4

Experimental Section

All arylation reactions were conducted in air using screw-top test tube equipped with Teflon septum caps. Full experimental details are given in the Supporting Information. The X-Ray crystallographic data for compounds **3a**, **4**, **6**, **7** and **10h** has been deposited in the Cambridge Structural Database.

The synthesis of 2-(2'-iodophenyl)-2-methyl cyclopentane-1,3-dione (prod. 3a, Table 2). A 50 mL Schlenk tube was charged with with $PhI(O_2CCF_3)_2$ (2.69 g, 6.26 mmol) and a stirbar. Nitromethane (10.0 mL) and trifluoroacetic acid (10.0 mL) were added, followed by the trifluoroacetic anhydride (265 µL, 1.88 mmol). The resulting colorless solution was allowed to stir for 15 min, at which point 2-methylcyclopentane-1, 3-dione (0.56 g, 4.99 mmol) was added as a solid in a single portion to give a light-yellow solution. After stirring for 4h at room temperature, all volatiles were removed under reduced pressure. The target arylketone **3a** was obtained as white solid upon chromatographic purification: gradient 10:1 –> 4:1 cyclohexane:EtOAc, R_f = 0.11 (4:1 cyclohexane:EtOAc). White solid, yield: 1.17 g, 3.72 mmol, 75%.

^{1}H NMR (500 MHz, $CDCl_3$) δ 7.83 (dd, *J* = 7.9, 1.3 Hz, 1H), 7.52 – 7.39 (*apparent* td, 1H), 7.33 (dd, *J* = 7.9, 1.6 Hz, 1H), 7.06 (td, *J* = 7.7, 1.6 Hz, 1H), 3.15 – 3.01 (m, 4H, CH_2CH_2), 1.59 (s, 3H). ^{13}C NMR (126 MHz, $CDCl_3$) δ 212.57 (C=O), 141.65 (C), 140.33 (CH), 131.07 (CH), 130.09 (CH), 128.45 (CH), 99.86 (C-I), 67.21 (C_q), 35.93 (CH_2), 20.87 (CH_3). HRMS (ESI+) calcd m/z for $C_{12}H_{11}INaO_2$ $[M+Na]^+$ 336.9696, found: 336.9689. IR (ATR) ν (cm^{-1}) 1751, 1708 (strong, C=O asym), 1460, 1410, 1164, 1070, 764.

2-(2'-iodo-5-trifluoromethyl-phenyl)-2-cyanocyclohexanone (prod. 8n, Table 4). A 10 mL tube was charged with a stirbar, Oxone (0.8 mmol), nitromethane (1 mL) and trifluoroacetic acid (1 mL). and a stirbar. Next, 4-iodobenzotrifluoride (0.5 mmol, 96% pure, 142 mg and 2-oxocyclohexanecarbonitrile (0.75 mmol, 92 mg) were injected. The mixture was allowed to stir for 2h, at which point the second portion of Oxone (0.25 mmol) was added; the stirring was continued for an additional 2h. The mixture was first filtered via celite and concentrated to move the solvents and **8n** was isolated by column chromatography: gradient 20:1 to 10:1 Hexane : EtOAc; R_f = 0.27 (10:1, Hexane : EtOAc). White solid, yield: 73% (144 mg).

^{1}H NMR (500 MHz, $CDCl_3$) δ 8.14 (d, *J* = 8.2 Hz, 1H), 7.60 (d, *J* = 2.2 Hz, 1H), 7.33 (dd, *J* = 8.2, 2.1 Hz, 1H), 3.13 (td, *J* = 13.6, 6.1 Hz, 1H), 2.75-2.65 (m, 2H), 2.58 (td, *J* = 12.9, 3.7 Hz, 1H), 2.38 (dtt, *J* = 14.4, 12.9, 3.9 Hz, 1H), 2.33 – 2.24 (m, 1H), 2.16 (dm, *J* = 14 Hz, 1H), 1.99 (qt, *J* = 13.3, 4.2 Hz, 1H). ^{13}C NMR (126 MHz, $CDCl_3$) δ 200.32 (C=O), 142.81, 138.46, 131.23 (q, *J* = 33.2 Hz, C-CF_3), 126.83 (q, *J* = 3.6 Hz), 125.51 (q, *J* = 3.8 Hz), 123.67 (q, *J* = 272.6 Hz, CF_3), 118.12 (CN), 103.84 (C-I), 59.36, 39.92, 38.89, 27.66, 22.53. ^{19}F NMR (376 MHz, $CDCl_3$) δ 63.02 ppm. HRMS (ESI^+) m/z calcd for $C_{14}H_{11}NF_3INaO$ $[M+Na]^+$ 415.9730, found: 415.9744. IR (ATR) υ (cm^{-1}) 2964, 2934, 2873, 2227 (CN), 1725 (C=O), 1326, 1179, 1129, 1073, 1015, 834.

3-(3-methylbenzofuran-2-yl)propanoic acid from aryldione 3a (prod. 7, Scheme 2). 2-(2-iodophenyl)-2-methylcyclopentane-1,3-dione (**3a**, 79 mg, 0.25 mmol) was dissolved in EtOH (1.5 mL). CuI (4.8 mg, 0.025 mmol), Fe_2O_3 (4 mg, 0.025 mmol), and NaOH (22 mg, 0.55 mmol in 2 mL of water) were added. The resulting red suspension was heated to 90 °C and allowed to stir overnight in a pressure-proof reaction tube. The reaction mixture was then cooled to rt., transferred to a separatory funnel and washed with EtOAc (2 x 10 mL). The aqueous phase was then acidified with 20 % HCl (aq) and extracted with CH_2Cl_2 (3 x 30 mL). Column chromatography: silca gel, cyclohexane:EtOAc 10:1->1:1 (Rf = 0.19 cyclohexane:EtOAc 3:1). Colourless crystals, 43 mg, 0.21 mmol, 84%.

^{1}H NMR (500 MHz, $CDCl_3$) δ 7.45–7.42 (m, 1H, Ar), 7.40–7.36 (m, 1H, Ar CH), 7.26–7.18 (m, 2H, Ar), 3.08 (t, *J* = 7.5 Hz, 2H, CH_2), 2.81 (t, *J* = 7.5 Hz, 2H, CH_2), 2.19 (s, 3H, CH_3). ^{13}C NMR (126 MHz, $CDCl_3$) δ 178.80 (COOH), 154.07 (C), 151.59 (C), 130.30 (C), 123.63 (CH), 122.26 (CH), 119.05 (CH), 110.80 (C), 110.78 (CH), 32.46 (CH_2), 21.60 (CH_2), 7.97 (CH_3). HRMS (ESI-) calcd m/z for $C_{12}H_{11}O_3$ $[M-H]^-$ 203.0714, found: 203.0714.

Acknowledgements

This work was financed through grants from Fundació ICIQ, MINECO (CTQ2013-46705-R and 2014-2018 Severo Ochoa Excellence Accreditation SEV-2013-0319) and the Generalitat de Catalunya (2014 SGR 1192). Financial support from CELLEX Foundation through the CELLEX-ICIQ High Throughput Experimentation platform is gratefully acknowledged.

Keywords: dehydrogenative C-C coupling • α-arylation • hypervalent iodine • *C-H* functionalization • cross-coupling

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[24] Oxidative degradation of the cyanoketone was also observed.

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[26] CCDC-1407045 (**3a**), CCDC-1407046 (**4**), CCDC-1407047 (**6**), CCDC-1407048 (**7**) and CCDC-1429539 (**10n**) contain the supplementary crystallographic data for this paper. These data can be obtained free of charge from The Cambridge Crystallographic Data Centre via www.ccdc.cam.ac.uk/data_request/cif.

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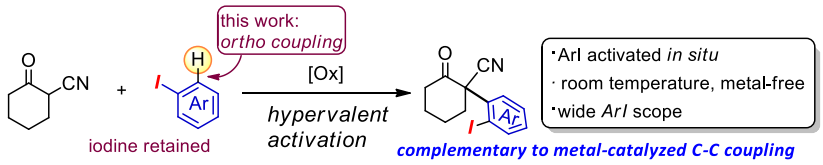

*Yichen Wu, Ismael Arenas, Lewis Broomfield, Eddy Martin and Alexandr Shafir **

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Hypervalent Activation as Key Step for Dehydrogenative ortho C-C Coupling of Iodoarenes

We report a direct metal-free a-arylation of substituted cyclic 1,3-diones using $ArI(O_2CCF_3)_2$ reagents, with the arylated products retaining the C-I moiety *ortho* to the newly formed C-C bond. DFT calculation showed a vanishingly small activation barrier for the C-C bond-forming [3,3] rearrangement. Finally, simple iodoarenes are shown to undergo a direct cross-dehydrogenative C-C coupling at the C-H ortho to the iodine. The method complements the ipso-selectivity obtained in the metal-catalysed α-arylation of carbonyl compounds.

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