ChemComm

Cite this: *Chem. Commun.*, 2012, **48**, 1320–1322

www.rsc.org/chemcomm

COMMUNICATION

Carboxylic acid anhydrides *via* Pd-catalyzed carbonylation of aryl halides at atmospheric CO pressure†

Yang Li,[a] Dong Xue,*[a] Chao Wang,[a] Zhao-Tie Liu[a] and Jianliang Xiao*[ab]

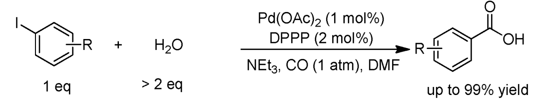
Received 25th October 2011, Accepted 25th November 2011
DOI: 10.1039/c2cc16611a

A convenient method has been developed, which allows for the direct transformation of aryl iodides into the corresponding carboxylic acid anhydrides *via* Pd-catalyzed carbonylation under atmospheric CO pressure.

Carboxylic acid anhydrides are valuable reagents for preparing carboxylic acid derivatives.[1] They are usually prepared by the reaction of an acyl halide with a metal carboxylate salt,[2] or with a carboxylic acid in the presence of a base.[3] Alternatively, carboxylic acid anhydrides can be accessed by reacting a carboxylic acid with a coupling agent, such as thionyl chloride,[4] phosgene,[5] carbodiimides,[6] phosphoranes,[7] isocyanate,[8] ethoxyacetylene,[9] 1,3,5-triazines,[10] trichloroacetonitrile/PPh_3[11] and tosyl chloride.[12] Clearly, most of these coupling reagents are either highly reactive or toxic and hence are difficult to handle. Herein we present an efficient and simple method that allows aryl iodides to be directly converted into carboxylic acid anhydrides *via* palladium-catalyzed carbonylation.

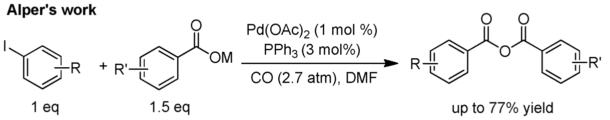
Since its initial discovery by Heck in 1974,[13] the three-component coupling of an aryl halide, carbon monoxide, and a nucleophile has undergone a great deal of development. The carbonylation reaction[14] now allows the selective synthesis of a wide range of aromatic acyl derivatives, such as acids, esters, α-ketoesters, amides, α-ketoamides, ketones, aldehydes, and anhydrides[15] (eqn (1)). Despite the considerable attention given to carbonylation over the past several decades, there is, to our knowledge, only one example of carboxylic acid anhydrides being synthesized *via* palladium-catalyzed carbonylation of aryl halides. In the reaction reported by Pri-Bart and Alper (eqn (2)),[15a] a metal carboxylate was used as nucleophile to form a carboxylic acid anhydride in the presence of CO and palladium acetate. We now report that aryl iodides can be readily converted into carboxylic acid anhydrides under 1 atm of CO with no need for an additional nucleophile (eqn (3)).

Conventional carbonylation



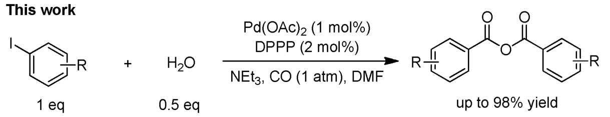
(1)

Alper's work



(2)

This work



(3)

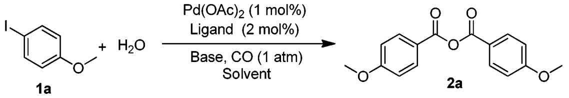
In our study of carbonylation reactions, we found that treatment of 4-iodoanisole with 1 atm of CO for 6 h afforded 4-methoxy-benzoic anhydride in 47% isolated yield alongside unreacted 4-iodoanisole in the presence of NEt_3 and a catalytic quantity of $Pd(OAc)_2/PPh_3$ at 115 °C in DMF.[16] This was somewhat surprising, as *N*,*N*-dimethylbenzamide[17] or benzoic acid would be expected as the major product. A closer look at eqn (1) suggests that if it is possible to generate the anhydride, 50 mol% water would be ideal. We then determined the water content of the DMF and found that the solution contained 27 mol% water. Subsequently, we found that controlling the amount of water in the solvent is indeed vital to product distribution (Table 1). When the amount of water in the solution was more than one equivalent,[18] *i.e.* > 100 mol%, no 4-methoxy-benzoic anhydride could be isolated, although 4-iodoanisole was completely consumed. Instead, a significant amount of 4-methoxy-benzoic acid and *N*,*N*-dimethylbenzamide was observed. Delightfully, 4-methoxy-benzoic anhydride was obtained in 90% yield when 0.5 equivalent, *i.e.* 50 mol%, water was present in the DMF solution (Table 1, entry 2). Variation of the concentrations of water around this value led to inferior results. Thus, when water was less than 0.5 equivalents, the yield of 4-methoxy-benzoic anhydride became lower and no 4-methoxy-benzoic acid could be observed (Table 1, entries 3 and 4). Similarly, when more than 0.5 equivalent of water was added, the anhydride was also lower in yield, being accompanied, however, with 4-methoxy-benzoic acid and *N*,*N*-dimethylbenzamide under such conditions (Table 1, entries 5 and 6). Together, these results point to

---

[a] *Key Laboratory of Applied Surface and Colloid Chemistry (Shaanxi Normal University), Ministry of Education and School of Chemistry and Chemical Engineering, Shaanxi Normal University, Xi'an, 710062, China. E-mail: Xuedong_welcome@snnu.edu.cn*
[b] *Department of Chemistry, Liverpool Centre for Materials and Catalysis, University of Liverpool, Liverpool, L69 7ZD, UK. E-mail: J.Xiao@liverpool.ac.uk*

† Electronic supplementary information (ESI) available: Experimental procedures, characterization data, ^1H, ^{13}C, IR, and HMRS spectra. See DOI: 10.1039/c2cc16611a

Table 1 Optimization of reaction conditions for the carbonylation of 4-iodoanisole[a]



Entry	Ligand	Base	Solvent	Water[b] (mol%)	Yield[c] (%)
1	No	NEt_3	DMF	50	0
2	DPPP	NEt_3	DMF	50	90
3	DPPP	NEt_3	DMF	27	55
4	DPPP	NEt_3	DMF	44	80
5	DPPP	NEt_3	DMF	72	49
6	DPPP	NEt_3	DMF	94	2
7	DPPP	NEt_3	Toluene	50	56
8	DPPP	K_2CO_3	DMF	50	65
9	BINAP	NEt_3	DMF	50	24
10	DCPP	NEt_3	DMF	50	45
11	DPPF	NEt_3	DMF	50	12
12	DPPE	NEt_3	DMF	50	40
13	D-I-PPP	NEt_3	DMF	50	52
14	D-C-PPP	NEt_3	DMF	50	53
15	A	NEt_3	DMF	50	48
16	B	NEt_3	DMF	50	70

[a] Conditions: ArI (1.0 mmol), Et_3N (2.5 mmol), $Pd(OAc)_2$ (1 mol%), ligand (2 mol%), water, solvent (2.0 mL), 115 °C, 6 h; see the ESI for more details including ligands. [b] Total water content. [c] Isolated yield.

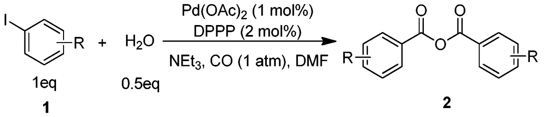
0.5 equivalent of water being the optimum water content for anhydride generation, as requested by eqn (3).

Having examined the effect of water, we turned our attention to the effect of ligands, solvents and bases on the carbonylation, aiming to optimize further the reaction conditions.[19] As can be seen from Table 1, all the ligands tested promoted the palladium-catalyzed carbonylation, regardless of monodentate or bidentate. However, the best yield was attained with DPPP in DMF with NEt_3 as base (Table 1, entry 2). Solvents also play an important role in the reaction. Among the solvents surveyed, only toluene and DMF gave the desired products. The choice of base is also critical. Amongst those tested, only NEt_3 and K_2CO_3 promoted the reaction, furnishing 90% and 65% yield, respectively (Table 1, entries 2 and 8).

With the optimized reaction conditions in hand, we next investigated the substrate scope of the reaction. As can be seen from Table 2, a wide range of aryl iodides were carbonylated, affording symmetrical anhydrides in good to excellent yields. Electron-rich and electron-deficient aryl iodides were both cleanly converted into the corresponding symmetrical anhydrides with high yields. It is notable that aryl iodides bearing fluoro and chloro substituents reacted without affecting these groups (Table 2, entries 4, 5 and 8). *ortho- meta-*, and *para*-Substituted aryl iodides worked well in the present system to give symmetrical anhydrides, demonstrating that the carbonylation tolerates substrates of diverse steric properties. Thus, the three iodoanisoles all afforded high yields of anhydrides (Table 2, entries 1, 11 and 13), and the *ortho*-substituted **1o**, **1r** and **1s** were also viable substrates (Table 2, entries 15, 18 and 19).

To gain understanding of the reaction mechanism, the following reactions were carried out. Carbonylation of iodoanisole in the presence of 1 equivalent water afforded no anhydride under otherwise the same conditions (eqn (4)). Instead, the usually expected 4-methoxy-benzoic acid was formed as the main product.

Table 2 Conversion of aryl iodides to symmetrical anhydrides *via* Pd-catalyzed carbonylation[a]



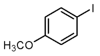
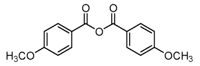
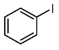
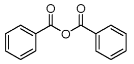
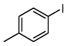
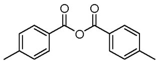
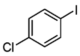
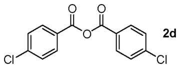
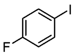
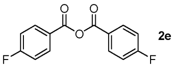
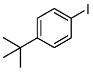
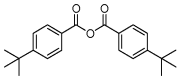
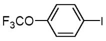
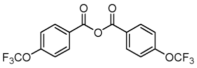
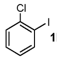
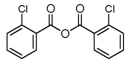
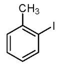
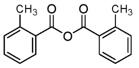
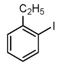
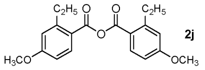
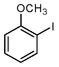
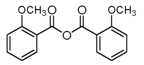
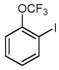
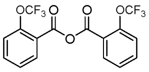
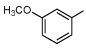
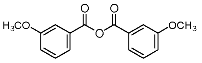
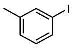
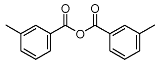
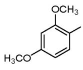
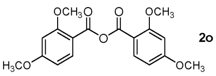
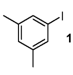
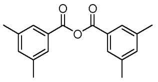
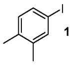
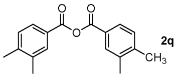
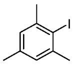
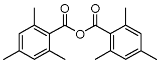
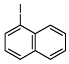
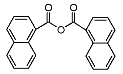
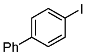
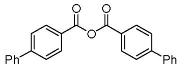
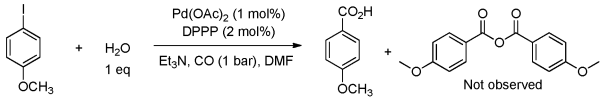
Entry	Aryl halides	Product	Yield[b] (%)
1	 1a	 2a	90
2	 1b	 2b	90
3	 1c	 2c	95
4	 1d	 2d	77
5	 1e	 2e	98
6	 1f	 2f	56
7	 1g	 2g	71
8	 1h	 2h	54
9	 1i	 2i	83
10	 1j	 2j	69
11	 1k	 2k	95
12	 1l	 2l	67
13	 1m	 2m	95
14	 1n	 2n	73
15	 1o	 2o	68
16	 1p	 2p	67
17	 1q	 2q	82
18	 1r	 2r	77[c]

Table 2 (*continued*)

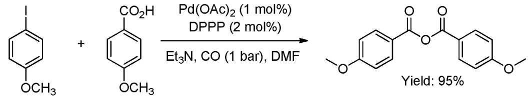
Entry	Aryl halides	Product	Yield^b (%)
19	 **1s**	 **2s**	64
20	 **1t**	 **2t**	76

^{a} Reaction conditions: ArI (1.0 mmol), Et_3N (2.5 mmol), $Pd(OAc)_2$ (1 mol%), ligand (2 mol%), water (50 mol%), DMF (2.0 mL), 115 °C, 6 h. ^{b} Isolated yield. ^{c} 48 h.

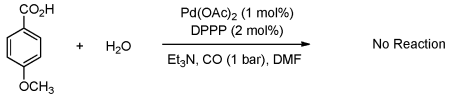
On the other hand, 4-methoxy-benzoic anhydride was obtained in a high yield of 95% when water was replaced with 4-methoxy-benzoic acid (eqn (5)), indicating that the latter participates in the formation of the anhydride. However, 4-methoxy-benzoic acid itself cannot give rise to the anhydride



(4)



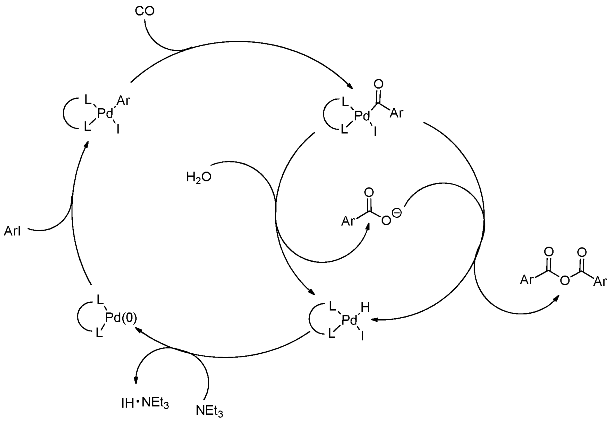
(5)



(6)

with or without added water under the reaction conditions (eqn (6)), suggesting that the anhydride is derived from the iodide and 4-methoxy-benzoic acid or 4-methoxy-benzoate. In addition, when the carbonylation of iodoanisole was performed under the optimized conditions (Table 2) but quenched at 2 h reaction time, the anhydride and iodoanisole were isolated in 38% and 54% yield, respectively; the yield of 4-methoxy-benzoic was less than 2%, indicating that the acid is consumed once generated. Taking these observations into account, a plausible mechanism is presented in Scheme 1. The main features are that water attacks the Pd–acyl intermediate, resulting in the formation of a carboxylate under the basic conditions employed; the carboxylate, being more nucleophilic than water, reacts with a new Pd–acyl species, furnishing the symmetric anhydride. Clearly, over-stoichiometric water will lead to the formation of a carboxylic acid, whereas a sub-stoichiometric amount encourages attack of the acyl by DMF.[17]

In summary, a convenient method for the preparation of carboxylic acid anhydrides has been developed. The wide scope, mild reaction conditions and high yields showcase the potential of the method in chemical synthesis.



Scheme 1 A plausible mechanism for anhydride formation.

We are grateful for the financial support of the National Science Foundation (20602024), Program for Changjiang Scholars and Innovative Research Team in University (IRT 1070) and the Fundamental Research Funds for the Central Universities (GK200902009).

Notes and references

1 M. A. Ogliaruso and J. F. Wolfe, *Synthesis of Carboxylic Acids, Esters and Their Derivatives*, John Wiley & Sons, New York, 1991, pp. 198–217.
2 E. C. Tayor, G. W. McLay and A. McKillop, *J. Am. Chem. Soc.*, 1968, **90**, 2422.
3 W. Nakanishi, Y. Ikeda and H. Iwamura, *J. Org. Chem.*, 1982, **47**, 2275.
4 W. K. Fife and Z. D. Zhang, *Tetrahedron Lett.*, 1986, **27**, 4937.
5 R. Kocz, J. Roestamadji and S. Mobashery, *J. Org. Chem.*, 1994, **59**, 2913.
6 P. A. Clarke, N. E. Kayalech, M. A. Smith, J. R. Baker, S. J. Bird and C. Chan, *J. Org. Chem.*, 2002, **67**, 5226.
7 Y. Kawamura, Y. Sato, T. Horie and M. Tsukayama, *Tetrahedron Lett.*, 1997, **38**, 7893.
8 K. S. Keshavamurthy, D. Y. Vankar and D. N. Dhar, *Synthesis*, 1982, 506.
9 Y. Kita, S. Akai, N. Ajimura, M. Yoshigi, T. Tsugoshi, H. Yasuda and Y. Tamura, *J. Org. Chem.*, 1986, **51**, 4150.
10 Z. J. Kamiński, B. Kolesińska and M. Malgorzata, *Synth. Commun.*, 2004, **34**, 3349.
11 J.-G. Kim and D. O. Jang, *Synth. Commun.*, 2001, **31**, 395.
12 F. Kazemi, H. Sharghi and M. A. Nasseri, *Synthesis*, 2004, 205.
13 (*a*) A. Schoenberg, I. Bartoletti and R. F. Heck, *J. Org. Chem.*, 1974, **39**, 3318; (*b*) A. Schoenberg and R. F. Heck, *J. Org. Chem.*, 1974, **39**, 3327.
14 For reviews see: (*a*) A. Brennführer, H. Neumann and M. Beller, *Angew. Chem., Int. Ed.*, 2009, **48**, 4114; (*b*) C. F. J. Barnard, *Organometallics*, 2008, **27**, 5402.
15 (*a*) I. Pri-Bart and H. Alper, *J. Org. Chem.*, 1989, **54**, 36; (*b*) K. Nagira, K. Kikukawa, F. Wada and T. Matauda, *J. Org. Chem.*, 1980, **45**, 2365; (*c*) K. Kikukawa, K. Kono, K. Nagira, F. Wada and T. Matsuda, *J. Org. Chem.*, 1981, **46**, 4413.
16 A trace amount of *N*,*N*-dimethylbenzamide was also observed. DMF (99.5%) was used as received.
17 (*a*) Y.-Q. Wan, M. Alterman, M. Larhed and A. Hallberg, *J. Org. Chem.*, 2002, **67**, 6232; (*b*) K. Hosoi, K. Nozaki and T. Hiyama, *Org. Lett.*, 2002, **4**, 2849; (*c*) D. N. Sawant, Y. S. Wagh, K. D. Bhatte and B. M. Bhanage, *J. Org. Chem.*, 2011, **76**, 5489.
18 Referring to water added to DMF plus background water from the reaction system. As to how the water content was determined and the detailed data, please see the ESI†.
19 For more details including ligands used, please see the ESI†.