Sterically Demanding Unsymmetrical Diaryl-λ³-iodanes for Electrophilic Pentafluorophenylation and an Approach to α-Pentafluorophenyl Carbonyl Compounds with an All-Carbon Stereocenter

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A sterically demanding unsymmetrical pentafluorophenyl-tri-isopropylphenyl-λ³-iodane was developed as an effective reagent for the electrophilic pentafluorophenylation of various β-keto esters and a β-keto amide. 17 examples of α-pentafluorophenylated 1,3-dicarbonyl compounds 3 having a quaternary carbon center are provided. The resulting compounds were nicely transformed into chiral α-pentafluorophenyl ketones with an all-carbon stereogenic center in high yields and high enantioselectivities using asymmetric organocatalysis (up to 98% ee) or asymmetric metal catalysis (up to 82% ee).

Trifluoromethylation and fluorination are now key technologies in innovations in pharmaceutical, agrochemical and advanced material industries.[1] On the other hand, direct pentafluorophenylation is still undeveloped, despite the potential use of the pentafluorophenyl (C_6F_5) group in liquid crystal materials, organic semiconductors and bioactive compounds.[2] Looking at the success of chiral drug industries[3] as well as fluorinated pharmaceuticals,[1] we are interested in molecules containing the C_6F_5 group attached to a C_{sp^3} center as drug candidates in future markets.

Due to the strong electron-accepting property of the C_6F_5 group with a planar π system, characteristic stacking effects by polar π interactions have been observed between the C_6F_5 group and non-fluorinated counterparts.[4] Therefore, bioactive compounds with a C_6F_5 moiety are expected to interact with ubiquitous aromatic moieties of biomolecules such as amino acids and nucleic acids.[5] Indeed, Gellman and co-workers disclosed that the pentafluorophenyl variants of phenylalanine in a small protein enhance the stability of its tertiary structure.[5a,b] Nucleoside analogues containing a C_6F_5 instead of natural nucleobases have been used as tools for studying base pairing and DNA replication factors.[5c,d] The C_6F_5 group is also a universal base in peptide nucleic acids (PNAs).[5e] Although introduction of the C_6F_5 group into a C_{sp^2} center has been actively investigated by using radical and transition metal-catalyzed cross-coupling reactions,[6] these are not applicable for the construction of a stereogenic C_{sp^3} center. Instead, silylated or metal-C_6F_5 reagents are a suitable choice for this purpose, and their utility is limited to the nucleophilic pentafluorophenylation of carbonyls, imines and related compounds.[7] Pentafluorophenylboronate serves as an aryl donor for a rhodium-catalyzed cross-coupling reaction with α-aryldiazoacetate, producing an α-pentafluorophenyl carboxylic acid ester.[8] On the other hand, methods for the electrophilic pentafluorophenylation of a stereocenter are rare, except for a nucleophilic attack on hexafluorobenzene.[9] In this method, however, the scope of the substrate is limited due to the need for drastic conditions (high temperature and a strong base).[9]

As part of an on-going synthetic program focused on organofluorine reagents,[10] we herein disclose our studies describing the synthesis and use of aryl-pentafluorophenyl-λ³-iodanes 1 (aryl pentafluorophenyl iodonium salts) as effective electrophilic pentafluorophenylating reagents. A variety of β-keto esters 2 is nicely α-pentafluorophenylated by 1 providing α-pentafluorophenyl-1,3-dicarbonyl compounds 3 with a quaternary carbon center in good yields under mild conditions. In particular, a structurally new and sterically demanding unsymmetrical diaryl-λ³-iodane 1d was found to be most effective. The resulting α-pentafluorophenyl β-keto esters 3 were transformed into chiral α-pentafluorophenyl ketones with an all-carbon stereogenic center by organocatalysis or metal catalysis, that is, by decarboxylation followed by enantioselective alkylation under cinchona alkaloids catalysis, or asymmetric decarboxylative allylation under the Tsuji–Trost condition using palladium(II) catalysis (Scheme 1).

It is a well-known fact that diaryl-λ³-iodanes react with enolates providing α-arylated carbonyl compounds.[11] While one of the two aryl groups of diaryl-λ³-iodanes is transferred into the substrates, a more electron-deficient aryl group plays a fundamental role in the arylation of enolates with unsymmetrical diaryl-λ³-iodanes.[12] Despite of a large number of papers on the arylation of enolates using this concept, pentafluorophenylation using diaryl-λ³-iodanes has surprisingly never been re-

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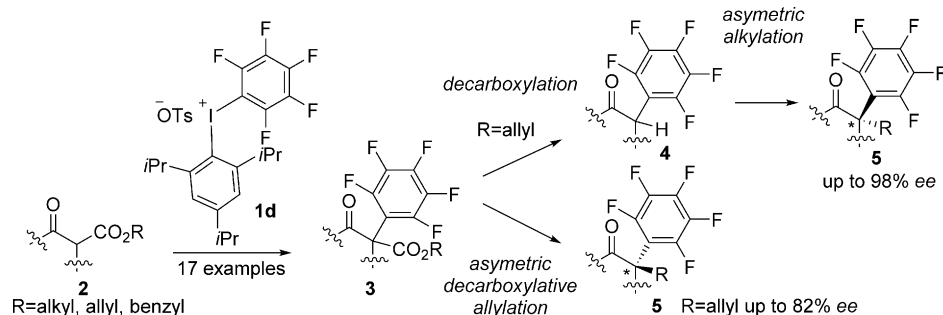
Scheme 1. Electrophilic pentafluorophenylation by **1** and transformations to chiral α-pentafluorophenyl ketones having an all-carbon stereocenter.

amined.[17] The yield improved slightly to 17% in the presence of K_2CO_3 and tetrabutylammonium iodide in *N,N*-dimethylformamide (DMF; Entry 7). In an attempt to further improve the yield, the effect of the base and solvent on the reaction was examined. The combination of organic or inorganic bases with solvents had an impact on yield (Entries 8–17), which was finally improved to 72% when the re-

ported.[11,12] This fact encouraged us to design a series of unsymmetrical C_6F_5-containing diaryl-λ^3-iodanes as electrophilic pentafluorophenylation reagents for enolates. The reasons why unsymmetrical diaryl-λ^3-iodanes are targeted are indicated next. Due to the electron-deficient nature of the C_6F_5 group, another set of aryl ligands were easily designed to stay attached to the parent iodanes. Furthermore, electron-poor symmetrical salts of bispentafluorophenyl-λ^3-iodanes are difficult to prepare.[13] The five unsymmetrical diaryl-λ^3-iodanes designed in this study were prepared in three steps from iodopentafluorobenzene via a Koser-type reagent, hydroxy-(tosyloxy)iodopentafluorobenzene **6**[14] according to a modified version of the published procedure, including oxidation and the Friedel–Crafts reaction (Scheme 2).[15]

We first examined the pentafluorophenylation of methyl indanone carboxylate **2a** using **1** (Table 1). The use of diaryl-λ^3-iodane **1a** with a mesityl (2,4,6-Me$_3$C$_6$H$_2$) group as a dummy
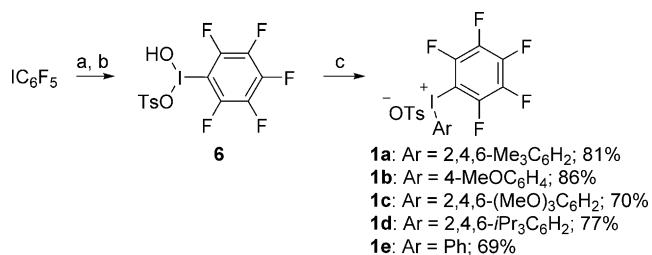
Scheme 2. Reagents and conditions: a) Oxone, TFA/CHCl$_3$, RT, 2 h; b) TsOH·H$_2$O, CH$_3$CN, RT, 3 h (87% over 2 steps); c) ArH, CF$_3$CH$_2$OH or TFA, RT, overnight.

Table 1. Initial studies on pentafluorophenylation of β-keto ester **2a**.[a]

Entry	1	Base	Additive	Solvent	Time [h]	Yield [%][b]
1	1a	DBU	–	CH$_2$Cl$_2$	2	6
2	1a	DABCO	–	CH$_2$Cl$_2$	18	6
3	1a	*t*BuOK	–	CH$_2$Cl$_2$	23	7
4[c]	1a	K$_2$CO$_3$	Bu$_4$NI	DMF	8	9
5[c]	1b	K$_2$CO$_3$	Bu$_4$NI	DMF	4	6
6[c]	1c	K$_2$CO$_3$	Bu$_4$NI	DMF	42	trace
7[c]	1d	K$_2$CO$_3$	Bu$_4$NI	DMF	2	17
8	1d	NaH	–	DMF	2	48
9	1d	NaH	–	toluene	4	28
10	1d	NaH	–	THF	20	8
11	1d	NaH	–	CH$_2$Cl$_2$	4	58
12	1d	*i*Pr$_2$NEt	–	CH$_2$Cl$_2$	11	21
13	1d	K$_2$CO$_3$	–	CH$_2$Cl$_2$	6	58
14	1d	Cs$_2$CO$_3$	–	CH$_2$Cl$_2$	2	53
15	1d	NaOH	–	CH$_2$Cl$_2$	6	44
16	1d	*t*BuOK	–	CH$_2$Cl$_2$	4	50
17	1d	KF	–	CH$_2$Cl$_2$	8	49
18	1d	K$_3$PO$_4$	–	CH$_2$Cl$_2$	2	72
19	1a	K$_3$PO$_4$	–	CH$_2$Cl$_2$	2	20
20	1b	K$_3$PO$_4$	–	CH$_2$Cl$_2$	2	10
21	1c	K$_3$PO$_4$	–	CH$_2$Cl$_2$	2	5
22	1e	K$_3$PO$_4$	–	CH$_2$Cl$_2$	2	11

[a] *Reagents and conditions*: a) 1a–e (1.1 equiv), base (1.2 equiv), additive (10 mol%), solvent, RT, time. All reactions were carried out on a 19.0 mg (0.100 mmol) scale. [b] Isolated yield. [c] K$_2$CO$_3$ (3.0 equiv) was used.

ligand[16] was expected to be highly suitable in chemoselective pentafluorophenylation, but the outcome was disappointing with 1,8-diazabicyclo[5.4.0]undec-7-ene (DBU)/CH$_2$Cl$_2$, yielding 6% of **3a** and a detectable amount of an α-mesitylation side-product (Entry 1, Table 1). Attempts to improve the disappointing yield by changing the base, solvent, and additive were all unsuccessful (Entries 2–4). We next fine-tuned both the electronic and steric effects of the dummy ligand on **1**. However, diaryl-λ^3-iodanes **1b–c** with electron-donating methoxy group(s) on the benzene ring were also poor reagents for this transformation (Entries 5 and 6). Hence, sterically highly demanding triisopropyl-substituted diaryl-λ^3-iodane **1d** was ex-

action of **2a** with **1d** was carried out in the presence of K$_3$PO$_4$ in CH$_2$Cl$_2$ (Entry 18). Re-optimization of reagents **1** under the best reaction conditions of K$_3$PO$_4$ in CH$_2$Cl$_2$ could not improve the yield (Entries 19–22, Table 1).

With optimized reaction conditions in hand, the substrate scope was explored (Table 2). Reagent **1d** was identified as the most practical reagent for the electrophilic pentafluorophenylation of various substrates **2** in the presence of K$_3$PO$_4$ in CH$_2$Cl$_2$ at room temperature. When the reaction was carried out with β-keto esters **2a–m** derived from 1-indanones, it proceeded efficiently affording desired products **3a–m** in good

Table 2. Substrate scope on pentafluorophenylation of β-keto esters **2**.[a]

[a] The reaction of **2** with **1d** (1.1 equiv) was carried out in the presence of K₃PO₄ (1.2 equiv) in CH₂Cl₂ at RT, unless noted otherwise. [b] **1d** (1.6 equiv) and K₃PO₄ (1.7 equiv) were used. [c] Reaction time was 22 h.

3a: R = Me, 72%
3b: R = Et, 62%
3c: R = tBu, 64%[b]
3d: R = allyl, 65%
3e: R = Bn, 76%[b]

3f: R = Me, 61%
3g: R = allyl, 65%[b]

3h: R = Me, 61%
3i: R = allyl, 66%

3j: R = Me, 61%
3k: R = allyl, 61%

3l: R = Me, 71%[b]
3m: R = allyl, 57%[b]

3n: R = Me, 37%
3o: R = allyl, 34%[c]

3p: 47%

3q: 41%

phase-transfer catalyst of choice in aqueous toluene in the presence of KOH at −40 °C. The scope of the asymmetric alkylation of **4** is shown in Table 3. In all cases, high yields with excellent enantioselectivities up to 98% *ee* were accomplished almost independent of both the electronic and steric natures of electrophiles R–Br, and substrates **4** (indanone **4a** and tetralone **4b**). The absolute configuration of **5e** was determined as *R* by X-ray crystallography (Figure 1), and the stereochemistry of **5a–d**, **5f–i** was tentatively assigned by analogy.

In another approach to chiral pentafluorophenyl compounds, direct asymmetric transformation of allyl-α-pentafluorophenyl-β-keto esters **3d** and **3o** to α-allyl-α-pentafluorophenyl-ketones **5a** and **5i** was achieved by palladium(II)-catalyzed asymmetric decarboxylative allylation[20] in the presence of the Trost ligand with high enantioselectivities (82% and 80% *ee*, respectively; Scheme 4). The absolute stereochemistry of **5** obtained by this procedure is opposite to that obtained by direct alkylation mentioned in Table 3.

In conclusion, this study discloses aryl-pentafluorophenyl-λ³-iodanes **1** as effective reagents for the electrophilic pentafluorophenylation of β-keto esters and amide **2**. Among several reagents designed, an unsymmetrical diaryl iodonium salt **1d** with a highly sterically demanding 2,4,6-triisopropyl phenyl group as a dummy ligand was most effective for the electrophilic pentafluorophenylation reaction. In the presence of K₃PO₄ in CH₂Cl₂ at room temperature, the pentafluorophenylation of nucleophiles proceeded smoothly to yield the desired products. The resulting products were

yields. Substrates with sterically demanding *tert*-butyl ester **2c** and transformable allyl ester **2d** were reacted to give desired products **3c** and **3d**. The electronic or steric nature of the benzene ring and ester moiety of the substrates might not have affected the yields of **3** that much. The yields derived from tetralone **2n** and **2o** or cyclopentanone **2p** were slightly lower due to the less enolizable nature of the substrates. Notably, β-keto amido **2q** was also reactive giving **3q** in 41% yield (see Table 2).
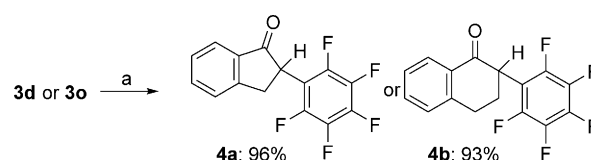
The allyl α-pentafluorophenyl-β-keto esters **3d** and **3o** that were obtained were easily transformed into α-pentafluorophenyl ketones **4d** and **4o** by palladium(II)-catalyzed decarboxylation using tris(dibenzylideneacetone)dipalladium(0) (Pd₂(dba)₃), 1,2-bis(diphenylphosphino)ethane (dppe) and Meldrum's acid as a proton source[18] in tetrahydrofuran (THF) with 96% and 93% yield, respectively (Scheme 3).

With α-pentafluorophenyl ketones **4** in hand, we were ready to investigate the enantioselective functionalization of **4** to create a quaternary chiral carbon center bearing a C₆F₅ group by asymmetric organocatalysis. Asymmetric alkylation of α-phenyl ketones has been actively researched in recent years.[19] However, there are no examples of the use of α-pentafluorophenyl ketones as substrates. Fortunately, a brief survey of reaction conditions consisting of chiral catalysts, bases and solvents for allylation (see table S1 in the Supporting Information) led to the rapid selection of cinchoninium bromide as the
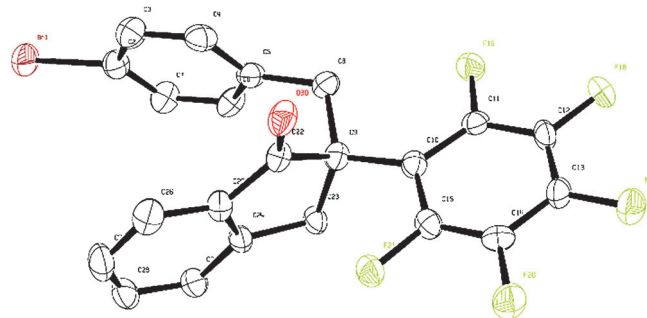

Scheme 3. Palladium-catalyzed decarboxylation of β-keto esters **3d** and **3o** to α-pentafluorophenyl ketones **4a** and **4b**. *Reagents and conditions*: a) Pd₂(dba)₃ (2.5 mol%), dppe (6.25 mol%), Meldrum's acid (2.5 equiv), THF, RT or 50 °C, 1–2 h.
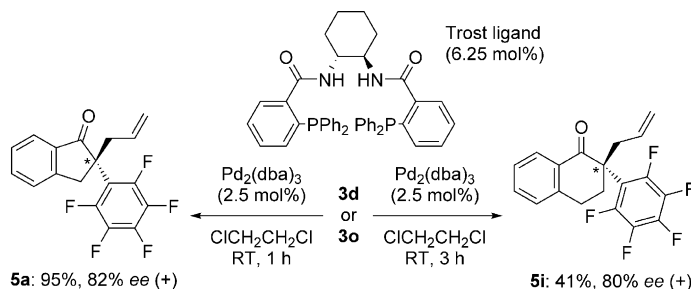
4a: 96%
4b: 93%

Figure 1. X-ray crystallographic structure of (*R*)-**5e** (CCDC 1009021).

Table 3. Creation of an all-carbon stereogenic center with C_6F_5: asymmetric alkylation of α-pentafluorophenyl ketones **4** with R–Br under organocatalysis.[a]

using:

4a: n=1
4b: n=2

7a : R^1 = Bn, R^2 = 3,5-(tBu)$_2$C$_6$H$_3$
7b : R^1 = Me, R^2 = 3,5-(tBu)$_2$C$_6$H$_3$

Entry	**4**, n	R	Time [h]	**5**	Yield[b] [%]	ee[c] [%]
1[d]	**4a**, n=1	allyl	96	**5a**	95	87 (−)
2	**4a**, n=1	benzyl	24	**5b**	95	96 (+)
3	**4a**, n=1	CH$_2$-p-Tol	48	**5c**	91	96 (−)
4[e]	**4a**, n=1	CH$_2$-p-MeOPh	72	**5d**	84	95 (−)
5	**4a**, n=1	CH$_2$-p-BrPh	48	**5e**	87	98 (−)
6	**4a**, n=1	CH$_2$-1-Naphthyl	96	**5f**	83	92 (+)
7	**4a**, n=1	CH$_2$-2-Naphthyl	24	**5g**	89	94 (−)
8	**4b**, n=2	benzyl	48	**5h**	93	96 (−)

[a] *Reagents and conditions*: a) R–Br (2.0 equiv), **7** (10 mol%), aq KOH (50 wt%), toluene, −40 °C, time. All reactions were carried out using **7a** as a catalyst unless noted otherwise. [b] Isolated yield. [c] Determined by HPLC analysis. [d] Catalyst **7b** was used instead of **7a**. [e] R–Br (1.2 equiv) was employed.

Trost ligand
(6.25 mol%)

5a: 95%, 82% *ee* (+)   **5i**: 41%, 80% *ee* (+)

Pd$_2$(dba)$_3$
(2.5 mol%)   Pd$_2$(dba)$_3$
                              (2.5 mol%)
        3d
        or
        3o
ClCH$_2$CH$_2$Cl   ClCH$_2$CH$_2$Cl
RT, 1 h   RT, 3 h

Scheme 4. Creation of an all-carbon stereogenic center with C_6F_5: Palladium-catalyzed asymmetric decarboxylative allylation of **3d** and **3o** using the Trost ligand.

transformed into chiral α-pentafluorophenyl ketones bearing an all-carbon stereogenic center by asymmetric palladium(II) catalysis and phase-transfer organocatalysis. New studies on the potential of these reagents are now in progress.[21]

Acknowledgements

[1] a) I. Ojima, *J. Org. Chem.* **2013**, *78*, 6358–6383; b) S. Purser, P. R. Moore, S. Swallow, V. Gouverneur, *Chem. Soc. Rev.* **2008**, *37*, 320–330; c) N. Shibata, S. Mizuta, H. Kawai, *Tetrahedron: Asymmetry* **2008**, *19*, 2633–2644.

[2] a) K. Kishikawa, K. Oda, S. Aikyo, S. Kohmoto, *Angew. Chem. Int. Ed.* **2007**, *46*, 764–768; *Angew. Chem.* **2007**, *119*, 778–782; b) M.-H. Yoon, A. Facchetti, C. E. Stern, T. J. Marks, *J. Am. Chem. Soc.* **2006**, *128*, 5792–5801; c) F. Babudri, G. M. Farinola, F. Naso, R. Ragni, *Chem. Commun.* **2007**, 1003–1022; d) T. Tsuzuki, N. Shirasawa, T. Suzuki, S. Tokito, *Adv. Mater.* **2003**, *15*, 1455–1458; e) Y. Sakamoto, T. Suzuki, A. Miura, H. Fujikawa, S. Tokito, Y. Taga, *J. Am. Chem. Soc.* **2000**, *122*, 1832–1833; f) T. Kitamura, Y. Wada, S. Yanagida, *J. Fluorine Chem.* **2000**, *105*, 305–311; g) X. de Leval, M. Ilies, A. Casini, J.-M. Dogne, A. Scozzafava, E. Masini, F. Mincione, M. Starnotti, C. T. Supuran, *J. Med. Chem.* **2004**, *47*, 2796–2804.

[3] A. M. Voutchkova, T. G. Osimitz, P. T. Anastas, *Chem. Rev.* **2010**, *110*, 5845–5882.

[4] E. A. Meyer, R. K. Castellano, F. Diederich, *Angew. Chem. Int. Ed.* **2003**, *42*, 1210–1250; *Angew. Chem.* **2003**, *115*, 1244–1287.

[5] a) M. G. Woll, E. B. Hadley, S. Mecozzi, S. H. Gellman, *J. Am. Chem. Soc.* **2006**, *128*, 15932–15933; b) G. Cornilescu, E. B. Hadley, M. G. Woll, J. L. Markley, S. H. Cellman, C. C. Cornilescu, *Protein Sci.* **2007**, *16*, 14–19; c) J. S. Lai, J. Qu, E. T. Kool, *Angew. Chem. Int. Ed.* **2003**, *42*, 5973–5977; *Angew. Chem.* **2003**, *115*, 6155–6159; d) G. Mathis, J. Hunziker, *Angew. Chem. Int. Ed.* **2002**, *41*, 3203–3205; *Angew. Chem.* **2002**, *114*, 3335–3338; e) B. K. Das, N. Shibata, Y. Takeuchi, *J. Chem. Soc. Perkin Trans. 1* **2002**, 197–206.

[6] For examples of radical coupling reaction of C_6F_5 group: a) Q.-Y. Chen, Z.-T. Li, *J. Org. Chem.* **1993**, *58*, 2599–2604; b) H. J. Frohn, A. Klose, V. V. Bardin, *J. Fluorine Chem.* **1993**, *64*, 201–215; c) R. Shang, Y. Fu, Y. Wang, Q. Xu, H.-Z. Yu, L. Liu, *Angew. Chem. Int. Ed.* **2009**, *48*, 9350–9354; *Angew. Chem.* **2009**, *121*, 9514–9518. For examples of palladium-catalyzed coupling reaction of C_6F_5 group: d) T. Korenaga, T. Kosaki, R. Fukumura, T. Ema, T. Sakai, *Org. Lett.* **2005**, *7*, 4915–4917; e) M. Lafrance, C. N. Rowley, T. K. Woo, K. Fagnou, *J. Am. Chem. Soc.* **2006**, *128*, 8754–8756; f) H.-Q. Do, O. Daugulis, *J. Am. Chem. Soc.* **2008**, *130*, 1128–1129; g) C.-Y. He, S. Fan, X. Zhang, *J. Am. Chem. Soc.* **2010**, *132*, 12850–12852; h) S. Fan, F. Chen, X. Zhang, *Angew. Chem. Int. Ed.* **2011**, *50*, 5918–5923; *Angew. Chem.* **2011**, *123*, 6040–6045; i) A. Nakatani, K. Hirano, T. Satoh, M. Miura, *Org. Lett.* **2012**, *14*, 2586–2589.

[7] a) T. Nishimine, K. Fukushi, N. Shibata, H. Taira, E. Tokunaga, A. Yamano, M. Shiro, N. Shibata, *Angew. Chem. Int. Ed.* **2014**, *53*, 517–520; *Angew. Chem.* **2014**, *126*, 527–530; b) L. Bernardi, E. Indrigo, S. Pollicino, A. Ricci, *Chem. Commun.* **2012**, *48*, 1428–1430; c) A. A. Zemtsov, V. V. Levin, A. D. Dilman, M. I. Struchkova, P. A. Belyakov, V. A. Tartakovsky, *J. Hu, Eur. J. Org. Chem.* **2010**, 6779–6785; d) M. Fujita, M. Obayashi, T. Hiyama, *Tetrahedron* **1988**, *44*, 4135–4145; e) A. D. Dilman, V. V. Gorokhov, P. A. Belyakov, M. I. Struchkova, V. A. Tartakovsky, *Russian. Chemical. Bulletin.* **2007**, *56*, 1522–1525; f) Z. Li, V. Gevorgyan, *Angew. Chem. Int. Ed.* **2012**, *51*, 1225–1227; *Angew. Chem.* **2012**, *124*, 1251–1253.

[8] Y.-T. Tsoi, Z. Zhou, W.-Y. Yu, *Org. Lett.* **2011**, *13*, 5370–5373.

[9] a) R. G. Plevey, P. Sampson, *J. Chem. Soc. Perkin Trans. 1* **1987**, 2129–2136; b) H. Amii, K. Uneyama, *Chem. Rev.* **2009**, *109*, 2119–2183.

[10] T. Liang, C. N. Neumann, T. Ritter, *Angew. Chem. Int. Ed.* **2013**, *52*, 8214–8264; *Angew. Chem.* **2013**, *125*, 8372–8423.

[11] For recent review on diaryl-λ^3-iodanes: a) E. A. Merritt, B. Olofsson, *Angew. Chem. Int. Ed.* **2009**, *48*, 9052–9070; *Angew. Chem.* **2009**, *121*, 9214–9234; b) V. V. Zhdankin, *Chem. Rev.* **2008**, *108*, 5299–5358; c) T. Dohi, Y. Kita, *Chem. Commun.* **2009**, 2073. For examples of α-arylation of enolates with diaryl-λ^3-iodanes: d) J. Guo, S. Dong, Y. Zhang, Y. Kuang, X. Liu, Li. Lin, X. Feng, *Angew. Chem. Int. Ed.* **2013**, *52*, 10245–10249; *Angew. Chem.* **2013**, *125*, 10435–10439; e) M. Ito, I. Itani, Y. Toyoda, K. Morimoto, T. Dohi, Y. Kita, *Angew. Chem. Int. Ed.* **2012**, *51*, 12555–12558; *Angew. Chem.* **2012**, *124*, 12723–12726; f) J. S. Harvey, S. P. Simonovich, C. R. Jamison, D. W. C. MacMillan, *J. Am. Chem. Soc.* **2011**, *133*, 13782–13785; g) A. Bigot, A. E. Williamson, M. J. Gaunt, *J. Am. Chem. Soc.* **2011**, *133*, 13778–13781; h) A. E. Allen, D. W. C. MacMil-

lan, *J. Am. Chem. Soc.* **2011**, *133*, 4260–4263; i) P.-O. Norrby, T. B. Petersen, M. Bielawski, B, Olofsson, *Chem. Eur. J.* **2010**, *16*, 8251–8254; j) V. K. Aggarwal, B. Olofsson, *Angew. Chem. Int. Ed.* **2005**, *44*, 5516–5519; *Angew. Chem.* **2005**, *117*, 5652–5655; k) M. Ochiai, Y. Kitagawa, N. Takayama, Y. Takaoka, M. Shiro, *J. Am. Chem. Soc.* **1999**, *121*, 9233–9234; l) C. H. Oh, J. S. Kim, H. H. Jung, *J. Org. Chem.* **1999**, *64*, 1338–1340.

[12] M. Ochiai, Y. Kitagawa, M. Toyonari, *ARKIVOC (Gainesville, FL, U.S.)* **2003**, *2003*, 43–48.

[13] a) M. Bielawski, B. Olofsson, *Org. Synth.* **2009**, *86*, 308–314; b) J. Helber, H.-J. Frohn, A. Klose, T. Scholten, *ARKIVOC (Gainesville, FL, U.S.)* **2003**, *2003*, 71–82; c) W. Tyrra, H. Butler, D. Naumann, *J. Fluorine Chem.* **1993**, *60*, 79–83; d) S. Schäfer, T. Wirth, *Angew. Chem. Int. Ed.* **2010**, *49*, 2786–2789; *Angew. Chem.* **2010**, *122*, 2846–2850; e) M. E. Hirschberg, P. Barthen, H.-J. Frohn, D. Bläser, B. Tobey, G. Jansen, *J. Fluorine Chem.* **2014**, *163*, 28–33.

[14] a) A. A. Zagulyaeva, M. S. Yusubov, V. V. Zhdankin, *J. Org. Chem.* **2010**, *75*, 2119–2122; b) R. M. Moriarty, R. Penmasta, I. Prakash, *Tetrahedron Lett.* **1987**, *28*, 877–880; c) M. D. Hossain, T. Kitamura, *Bull. Chem. Soc. Jpn.* **2006**, *79*, 142–144.

[15] T. Dohi, N. Yamaoka, Y. Kita, *Tetrahedron* **2010**, *66*, 5775–5785.

[16] a) J. Malmgren, S. Santoro, N. Jalalian, F. Himo, B. Olofsson, *Chem. Eur. J.* **2013**, *19*, 10334–10342; b) K. M. Lancer, G. H. Wiegand, *J. Org. Chem.* **1976**, *41*, 3360–3364.

[17] R. J. Phipps, N. P. Grimster, M. J. Gaunt, *J. Am. Chem. Soc.* **2008**, *130*, 8172–8174.

[18] a) M. P. Carroll, H. Müller-Bunz, P. J. Guiry, *Chem. Commun.* **2012**, *48*, 11142–11144; b) S. C. Marinescu, T. Nishimata, J. T. Mohr, B. M. Stoltz, *Org. Lett.* **2008**, *10*, 1039–1042.

[19] a) T. Kano, Y. Hayashi, K. Maruoka, *J. Am. Chem. Soc.* **2013**, *135*, 7134–7137; b) X.-Q. Dong, H.-L. Teng, M.-C. Tong, H. Huang, H.-Y. Taoa, C.-J. Wang, *Chem. Commun.* **2010**, *46*, 6840–6842; c) B. M. Trost, G. M. Schroeder, J. Kristensen, *Angew. Chem. Int. Ed.* **2002**, *41*, 3492–3495; *Angew. Chem.* **2002**, *114*, 3642–3645; d) U.-H. Dolling, P. Davis, E. J. J. Grabowski, *J. Am. Chem. Soc.* **1984**, *106*, 446–447.

[20] a) C. M. Reeves, C. Eidamshaus, J. Kim, B. M. Stoltz, *Angew. Chem. Int. Ed.* **2013**, *52*, 6718–6721; *Angew. Chem.* **2013**, *125*, 6850–6853; b) B. M. Trost, J. Xu, *J. Am. Chem. Soc.* **2005**, *127*, 2846–2847; c) T. Nemoto, T. Matsumoto, T. Masuda, T. Hitomi, K. Hatano, Y. Hamada, *J. Am. Chem. Soc.* **2004**, *126*, 3690–3691; d) A. Chieffi, K. Kamikawa, J. Åhman, J. M. Fox, S. L. Buchwald, *Org. Lett.* **2001**, *3*, 1897–1900.

[21] The reaction of other substrates such as acyclic β-esters and pyrroles under similar conditions gave poor yields.