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LETTERS

Arylation of α-substituted acrylates in ionic liquids catalyzed by a Pd–benzothiazole carbene complex

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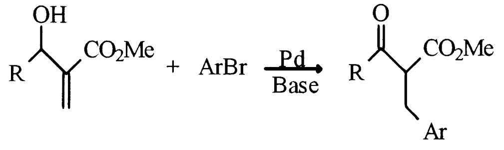
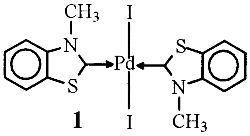
Abstract—A Pd-catalyst with benzothiazole carbene as ligands allows, in tetrabutylammonium bromide melt as solvent, very fast and efficient reactions of bromoaromatics with 3-hydroxy-2-methylenealkanoates to give β-arylketones. © 2001 Published by Elsevier Science Ltd.

The Heck reaction and related chemistry occupy a special place among basic types of palladium-catalyzed reactions.[1–3] In most of the papers dedicated to the Heck reaction, only a few examples have been reported which deal with α-substituted acrylates as olefin acceptors.[4,5] Among these, it was reported[6] that the arylation of 3-hydroxy-2-methylenealkanoates afforded β-oxoalkanoates (Scheme 1). Beside the harsh reaction conditions necessary for the reaction of α-substituted acrylates, the 3-hydroxy-2-methylenealkanoate arylation also suffers from a competitive retro-Baylis–Hillman reaction, as well as further arylation of the β-oxoalkanoate end product.[7–9]



Scheme 1.

To overcome these drawbacks, we report the application of the Pd catalyst **1** with benzothiazole carbene as ligands[10,11] for an efficient Heck arylation of 3-hydroxy-2-methylenealkanoates in the ionic liquid tetrabutylammonium bromide (TBAB) as solvent.



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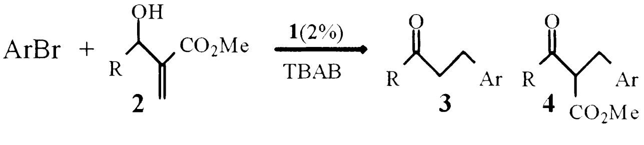
Catalyst **1** was stable in TBAB melt and efficiently allowed the reaction of various *p*-substituted bromoaromatics with hydroxymethylenealkanoates **2** to give β-arylketones **3** but not the expected Heck product, β-oxoalkanoates[6] **4** (Scheme 2).

As shown in Table 1, reaction of electron-rich and electron-poor aryl bromides gave β-aryl ketones in the presence of **1** (2%), sodium formate as reducing agent for palladium and sodium bicarbonate as base.[12] No palladium black deposition nor retro-Baylis–Hillman of **2** or further arylation of **3** was observed. The stability of **1** in TBAB, in a phosphane-free environment, cannot be regarded as simply due to the solvent polarity or phase transfer ability.[2e] Indeed, it was observed (entry 2) that in a different ionic liquid such as butylpyridinium tosylate bearing a poorly nucleophilic anion, **1** did not catalyze the reaction. We propose that both the anion and the cation of TBAB exert a double role. The bromide ion, by reaction with the rather unstable 14-electron complex $L_2Pd(0)$, the proposed catalyst in the Heck reaction, would lead to an anionic, more stable and catalytically active 16-electron complex $[L_2Pd(0)Br]^{(-)}\ {}^{(+)}NR_4$. The formation of this large com-



Scheme 2. Ar = H, *p*-MePh, *p*-MeOPh, *p*-AcPh, naphthyl; R = Ph, Me, *i*-propyl, *n*-octyl.

Keywords: β-aryl ketones; ionic liquids; carbenes; Heck reaction.

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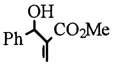
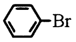
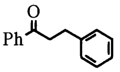
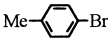
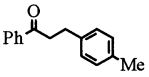
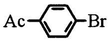
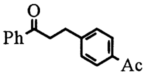
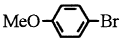
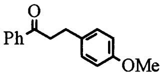
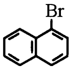
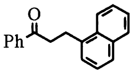
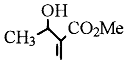
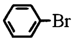
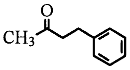
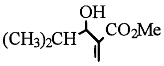
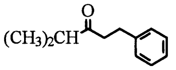
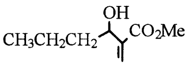
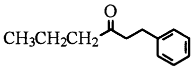
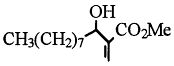
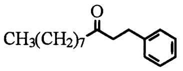
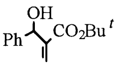
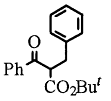
Table 1. Synthesis of β-arylketones in TBAB catalyzed by the Pd–carbene complex **1**[a]

Entry	Hydroxymethylene alkanoate[14]	Aryl bromide	Products	Time (h)	Yield (%)[b]	Ref.
1				20	77	15
2[c]	″	″	″	24	Nr	–
3	″			22	66	16
4	″			14	78	17
5	″			14	82	16
6	″			15	80	16
7				6	79	18
8		″		4	71	19
9		″		20	77	20
10		″		8	79	21
11		″		14	66[d]	22

[a] Reaction conditions: TBAB (3 g), catalyst (0.38 mmol, 2 mol%), sodium formate (0.76 mmol), bromoarene (19 mmol), sodium bicarbonate (40 mmol) and hydroxymethylene alkanoate (27 mmol) stirred at 130°C.

[b] Determined by GLC.

[c] Performed in *N*-butylpyridinium tosylate as solvent.

[d] Total yield as sum of β-oxoalkanoate and the corresponding β-arylketone.

plex, by imposing a Coulombic barrier for collision, would impede the formation of clusters growing further into metal particles. This is conceivable since it was demonstrated[3,13] that halides or acetate ions stabilize the 14-electron complex $Pd(0)[P(Ph)_3]_2$.

The stability of **1** in TBAB makes a recycling process feasible. For example, in only 3 g of TBAB, after three cycles, 8 g of bromobenzene were processed with a total TON (turn over number) roughly equal to a very decent value of 1720, thus making the whole process economically viable.

The exclusive formation of **3** is probably due to a fast decarbomethoxylation in TBAB of the β-oxoalkanoate **4**. Indeed, by using a *tert*-butylester of **2** (entry 11), we observed, beside **3**, 30% of the corresponding β-oxoalkanoate which slowly underwent decarbobutoxylation to the corresponding ketone.

Studies of the factors which govern the efficiency of metal–carbene complexes as catalysts in ionic liquids are underway.

Acknowledgements

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12. Typical procedure: A pyrex reaction flask was charged with tetrabutylammonium bromide (3 g) and heated at 130°C. To the stirred molten salt were added in strict order the catalyst (250 mg, 0.38 mmol), sodium formate (52 mg, 0.76 mmol), bromoarene (19 mmol), sodium bicarbonate (3.4 g, 40 mmol) and hydroxymethylene alkanoate (3.4 g, 27 mmol). The reaction yields were determined by GLC integrated with diethylene glycol dibutyl ether as internal standard. After completion of the reaction, the mixture was extracted in a Soxhlet apparatus with cyclohexane for 1 h. After evaporation of the solvent, the pure product was isolated in a 60–80% yield. The ionic liquid and the catalyst were then recycled.
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22. Spectral data for the *t*-butyl ester: ^{1}H NMR (500 MHz, $CDCl_3$) δ: 1.27 (9H, s, *t*-butyl), 3.28 (2H, d, J 7.5 Hz, CH_2), 4.50 (1H, t, J 7.5 Hz, CH), 7.14–7.27 (6H, m, Ph), 7.39–7.56 (4H, m, Ph); ^{13}C NMR δ: 27.65, 34.45, 57.22, 81.97, 126.42, 128.36, 128.48, 128.97, 133.21, 136.22, 136.43, 138.61, 168.30, 194.74; MS (EI) m/z 310 (M^+, 1), 254 (20), 236 (6), 209 (11), 149 (42), 131 (24), 105 (100), 91 (7), 77 (45), 57 (58), 51 (20), 41 (50); IR (liquid film) ν: 3087, 3063, 3028, 2978, 2933, 1734, 1687, 1589, 1582, 1486, 1478, 1450, 1369, 1240, 1147, 1080, 1056, 1030, 1003, 971, 944, 893, 844, 778, 745, 739, 688 cm^{-1}.