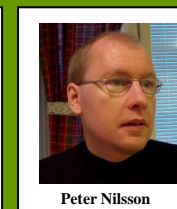
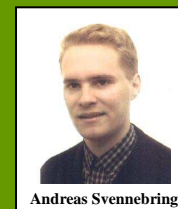


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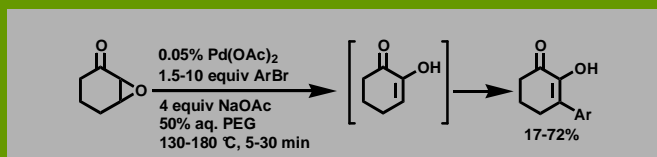
Fast microwave-assisted Heck arylation of 2,3-epoxycyclohexanone

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METHOD

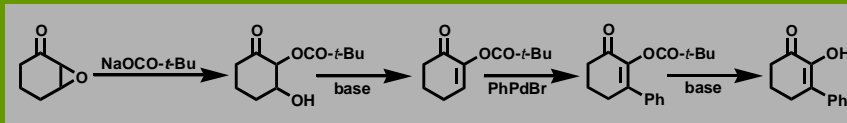
An environmentally benign protocol for fast microwave enhanced isomerization – C3-arylation of 2,3-epoxycyclohexanone yielding the corresponding 3-aryl-1,2-cyclohexandiones via 1,2-cyclohexandione has been developed:



- ✓ No more than 0.05% (500 ppm) of palladium is used
- ✓ Aqueous polyethylene glycol is used as solvent
- ✓ No stabilizing phosphines are required
- ✓ Sodium acetate is utilized as a base and isomerization catalyst
- ✓ Reaction is heated by controlled microwave irradiation

MECHANISTIC INVESTIGATION

No reaction intermediates besides 1,2-cyclohexandione were detected throughout the presented reaction. In order to elucidate the reaction pathway, acetate was successfully replaced by the sterically hindered pivalate equivalent revealing a series of stable reaction intermediates:



We suggest that the presented preparative method can be rationalized by a similar mechanism, although cleavage of the acetate ester was found to precede arylation. This was in contrast to what was observed with the corresponding pivalate mediated model reactions.

PREPARATIVE RESULTS

The reported preparative method has been evaluated using a total of 13 different aryl bromides as substrates, altogether representing electronically rich (entry 1-3), neutral (entry 4-7) and poor (entry 8-11), as well as sterically congested (entry 12, 13) arylpalladium precursors (see Table below). High yields were achieved besides for the case of electron-poor bromides.

An alternative thermally heated classical method has also been developed for comparison. Although considerably larger catalyst loading and longer reaction times were required, the classical protocol was more productive only in one case (*p*-MeCO-Ph).

Entry	Ar-	Microwave conditions ^a			Classical conditions ^b	
		T (°C)	t (min)	Yield (%)	Yield (%)	
1.	<i>m</i> -Me ₂ N-Ph-	180	30	71		
2.	<i>p</i> -MeO-Ph-	180	20	58 ^c		0 ^e
3.	<i>m</i> -MeO-Ph-	150	20	64		45 ^c
4.	<i>p</i> -Et-Ph-	150	20	66		61
5.	<i>p</i> -Me-Ph-	150	20	63		57
6.	<i>m</i> -MePh-	150	20	72		72
7.	Ph-	150	20	72		64
8.	<i>p</i> -F-Ph-	150	20	60		
9.	<i>p</i> -CF ₃ -Ph-	150	20	33		
10.	<i>p</i> -(PhCO)-Ph-	130	5	19 ^d		
11.	<i>p</i> -MeCO-Ph-	130	5	17		40
12.	<i>o</i> -Me-Ph-	180	10	63		14
13.	α-Naphthyl-	180	10	50		24

^a Microwave conditions: 1.0 mmol 2,3-epoxycyclohexanone, 0.5 μmol Pd(OAc)₂, 1.5 (entry 3-7), 4 (entry 1, 2, 8-11), or 10 (entry 12, 13) mmol aryl bromide, 4 mmol NaOAc, 3 mL 50% aq. PEG in sealed vessels. ^b Classical Conditions: 1.0 mmol 2,3-epoxycyclohexanone, 0.05 mmol Pd(OAc)₂, 0.12 mmol PPh₃, 4 mmol aryl bromide, 4 mmol DIEA, 0.75 mL water, 4.25 mL DMF in sealed vessels. Reactions were heated at 100 °C for 21 h. ^c 75% aq. PEG was used as solvent. ^d Water:PEG:*t*-BuOH 2:1:1 was used as solvent. ^e 41 h of heating was employed.

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