Palladium-catalysed Arylation of Allylic Alcohols: Highly Selective Synthesis of β-Aromatic Carbonyl Compounds or β-Aromatic α,β-Unsaturated Alcohols.

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Abstract: The outcome of the coupling of aromatic halides with allylic alcohols can be highly controlled and the reaction directed at will towards the formation of either β -aromatic carbonyl or β -aromatic $\alpha_i\beta$ -unsaturated alcohol compounds.

The palladium-catalysed reaction of aromatic halides with allylic alcohols leads to the formation of β -aromatic carbonyl compounds ¹⁴. Reaction conditions have been investigated to favour the formation of conjugated aromatic alcohols, but they have not been of synthetic use ⁵.

We have reported that the arylation of allylic alcohols leading to the formation of aromatic carbonyl compounds - which is the usual pathway of the Heck reaction with allylic alcohols - can be performed under mild conditions upon addition of tetra-n-butylammonium chloride ⁶. We now report that a highly selective formation of conjugated aromatic alcohols can also be achieved from aromatic halides and allylic alcohols.

Indeed, the results described below show that the outcome of the coupling can be highly controlled by the catalyst systems (I) and (II).

Highly selective formation of aromatic carbonyl compounds $\underline{1}$ is realised under phase transfer conditions, in the presence of the catalyst system (I) constituted by a catalytic amount of palladium acetate and a combination of sodium bicarbonate and tetra-n-butylammonium chloride ⁶, the reaction being

performed in N,N-dimethylformamide or acetonitrile. On the other hand, highly selective formation of aromatic conjugated alcohols 2 can be achieved in N,N-dimethylformamide (or without solvent), in the presence of the catalyst system (II) constituted by silver acetate (or silver carbonate) and catalytic amounts of palladium acetate and triphenylphosphine⁷.



catalyst system (I): [cat.Pd(OAc)₂/NaHCO₂/nBu₄NCl/DMF] catalyst system (II): [cat.Pd(OAc)₂/cat.PPh₂/AgOAc/DMF]

Reactions (I) and (II) are both highly regioselective with respect to the addition of the aromatic group: only β substitution is observed. Their structural isomer selectivity is also very high: only traces of alcohol compounds are obtained when the arylation of allylic alcohols is performed in the presence of the catalyst system (I) and minor amounts of carbonyl compounds are observed when the reaction is conducted in the presence of the catalyst system (II). Reaction (II) is moreover highly stereoselective: only an (E) type double bond is formed α to the alcohol functional group (Table).

Formation of carbonyl and alcohol compounds in palladium-catalysed reactions of organic halides with allylic alcohols is determined, a priori, by a palladium hydride β -elimination and a palladium hydride reverse addition-reelimination³.

The exclusive obtention of alcohols can only result from both an absence of isomerisation and a high regiospecificity of the B-elimination step. The silver ion effect for suppressing isomerisation has been reported ^{8,9}. Our present and previous ⁷ results suggest either a formation of unsaturated alcohols (which are isomerized into carbonyl compounds in the absence of Ag⁺) as the first step of the Pd-catalysed arylation and vinylation of allylic alcohols, or a silver salt specific and determining effect for favouring the elimination of

Ar	R	Catalyst System ^{b)}	Product ^{c)}	Yield ^{d)} (%)
C ₆ H ₅	н	(1)	C ₆ H ₅ CH ₂ CH ₂ CHO	82 ^{e)}
*1	"	(II) ^{f)}	(E) C ₆ H ₅ CH=CHCH ₂ OH	73
m-CH ₃ C ₆ H ₄	н	(1)	m-CH ₃ C ₆ H ₄ CH ₂ CH ₂ CHO	90 ^{e)}
14	"	(II)	(E) m-CH ₃ C ₆ H ₄ CH=CHCH ₂ OH	60
11	"	(II) ^{f)}	M 11	63
p-ClC ₆ H ₄	C5H11	(I)	p-ClC ₆ H ₄ CH ₂ CH ₂ C(O)C ₅ H ₁₁	87
**	51	(I) ^{g)}	65 KT	76
**	*1	(II)	(E) p-ClC ₆ H ₄ CH=CHCH(OH)C ₅ H ₁₁	80
p-ClC ₆ H ₄	C ₂ H ₅	(1)	p-ClC ₆ H ₄ CH ₂ CH ₂ C(O)C ₂ H ₅	94 ^{e)}
tt	"	(II)	(E) p-ClC ₆ H ₄ CH=CHCH(OH)C ₂ H ₅	92
m-HOCH ₂ C ₆ H ₄	C ₂ H ₅	(I)	m-HOCH ₂ C ₆ H ₄ CH ₂ CH ₂ C(O)C ₂ H ₅	87
*1		(II)	(E) m-HOCH ₂ C ₆ H ₄ CH=CHCH(OH)C ₂ H ₅	85
p-CH ₃ OC(O)C ₆ H ₄	CH ₃	(1)	p-CH ₃ OC(O)C ₆ H ₄ CH ₂ CH ₂ C(O)CH ₃	90
11	"	(II) ^{h)}	(E) p-CH ₃ C(O)C ₆ H ₄ CH=CHCH(OH)CH ₃	90

Table. Highly Selective Formation of β -Aromatic Carbonyl or β -Aromatic α , β -Unsaturated Alcohol Compounds from Aromatic Halides and Allylic Alcohols^{a)}.

a) Mixtures of aromatic halides (1 equiv.) and allylic alcohols (2-3 equiv.) were stirred for 16-24h in the presence of the catalyst system (I) or (II), respectively at 30-55°C and at 70-75°C; b) (I): NaHCO₃ (2.5 equiv.)/ nBu₄NCl (1 equiv.)/ Pd(OAc)₂ (0.02-0.05 equiv.) in DMF; (II): AgOAc (1 equiv.)/ Pd(OAc)₂ (0.03-0.05 equiv.)/ PPh₃ (0.06-0.1 equiv) in DMF; c) All compounds are characterized by mass spectrometry, IR, ¹H and ¹³C NMR spectroscopy; d) Non optimized yields of chromatographically isolated compounds; e) Ref. 6; f) The reaction was achieved without solvent in the presence of a large excess of allylic alcohol (8-10 equiv.); g) CH₃CN instead of DMF; h) Ag₂CO₃ (0.6 equiv.) instead of AgOAc.

the proton which is not on the carbon bearing the alcohol functional group.

In summary, the outcome of the arylation of allylic alcohols can be highly controlled by the catalyst systems (I) and (II) which are both highly selective. We can now construct at will a B-aromatic carbonyl or a B-aromatic α ,B-unsaturated alcohol functionality from an aromatic halide and an allylic alcohol, under relatively mild reaction conditions ¹⁰ and with high chemo, regio and stereocontrol.

REFERENCES AND NOTES

- 1. Melpolder, J. B.; Heck, R. F. J. Org. Chem., 1976, 41, 265.
- 2. Chalk, A. J.; Magennis, S. A. J. Org. Chem., 1976, 41, 273.
- 3. Heck, R. F. Org. React., 1982, 27, 345 and references cited.
- Heck, R. F. Palladium Reagents in Organic Syntheses; Academic Press: London, 1985; and references cited.
- 5. Chalk, A. J.; Magennis, S. A. Catal. Org. Synth., 1977; 139.
- 6. Jeffery, T. J. Chem. Soc. Chem. Commun., 1984, 1287.
- 7. We have recently reported a highly selective synthesis of conjugated dienols from vinylic halides and allylic alcohols, in the presence of silver acetate (or silver carbonate) and a catalytic amount of palladium acetate in N,N-dimethylformamide: Jeffery, T. J. Chem. Soc. Chem. Commun., in the press.
- Abelman, M. M.; Oh, T.; Overman, L. E. J. Org. Chem., 1987, 52, 4130; Abelman, M. M.; Overman, L. E. J. Am. Chem. Soc., 1988, 110, 2328.
- Larock, R. C.; Song, H.; Baker, B. E.; Gong, W. H. Tetrahedron Lett., 1988, 29, 2919; Larock, R. C.; Gong, W. H.; Baker, B. E. Tetrahedron Lett., 1989, 30, 2603; Larock, R. C.; Gong, W. H. J. Org. Chem., 1989, 54, 2047.
- The silver salt effect for enhancing the reaction rate of Heck type reactions has been first reported for the arylation of vinyl and allyl trimethylsilanes: Karabelas, K.; Hallberg, A. Tetrahedron Lett., 1985, 26, 3131; Karabelas, K.; Westerlund, C.; Hallberg, A. J. Org. Chem., 1985, 50, 3896; Karabelas, K.; Hallberg, A. J. Org. Chem., 1986, 51, 5286.

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