ORGANIC LETTERS

2004
Vol. 6, No. 3
377−380

Transition-Metal-Catalyzed Formation of *trans* Alkenes via Coupling of Aldehydes

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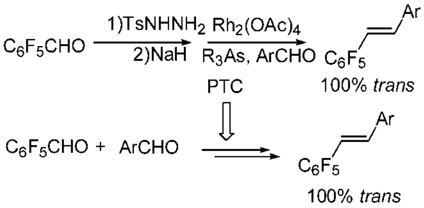
Received November 10, 2003

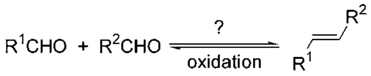
ABSTRACT



$Rh_2(OAc)_4$ catalyzed the formation of exclusively *trans* fluorinated alkenes from aldehydes and pentafluorobenzaldehyde tosylhydrazone salts, which were readily prepared from pentafluorobenzaldehyde using the Bamford–Stevens reaction. A series of pentafluorophenyl-containing alkenes were synthesized from aldehydes in moderate to good yields under mild reaction conditions in a one-pot reaction. It is the first report of coupling two different aldehydes to form exclusively *trans* alkenes.

Aldehydes can be readily prepared from the oxidation of olefins.[1] However, coupling two different aldehydes to form olefins is still a challenge for organic chemists (Scheme 1).[2]

Scheme 1



Among all of the previous methods for constructing carbon−carbon double bonds, the Wittig reaction and its modified versions are the most reliable choices.[3] To avoid the basic conditions for the generation of phosphorus precursors, there is a growing interest in developing alternative protocols that can use diazo compounds directly under neutral conditions.[4] More recently, there has been growing interest in fluoroaromatic alkenes owing to fluorine's unique physical properties.[5] The introduction of fluorine atoms onto phenyl and phenylene rings always greatly improves the properties of the corresponding alkenes.[6] Therefore fluoroaromatic alkenes can have uses in liquid crystalline materials,[7] intermolecular noncovalent π-stacking interactions,[8,2c]

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10.1021/ol036197s CCC: $27.50

Table 1. Reaction Results of **1** with **2** in Different Reaction Conditions

entry	Ar in **2**	XR_3	solvent	T (°C)	catalyst	t (h)	product	yield (%) of **3**[b]
	conditions[a]							
1	p-BrPh	Ph_3As	CH_3CN	60	$Rh_2(OAc)_4$	6	**3aa**	trace
2	p-BrPh	Ph_3As	CH_3CN	40	$Rh_2(OAc)_4$	6	**3aa**	48
3	p-BrPh	Ph_3As	CH_3CN	35	$Rh_2(OAc)_4$	8	**3aa**	60
4	p-BrPh	Ph_3As	1,4-dioxane	35	$Rh_2(OAc)_4$	6	**3aa**	60
5	p-BrPh	Ph_3As	1,4-dioxane	35	$Cu(acac)_2$	6	**3aa**	53
6	p-BrPh	Ph_3As	1,4-dioxane	35	$RhCl(PPh_3)_3$	6	**3aa**	29
7	p-NO_2Ph	Ph_3As	1,4-dioxane	35	$Rh_2(OAc)_4$	6	**3ab**	64
8	p-NO_2Ph	Ph_3As	1,4-dioxane	35	TPPFe(III)Cl	8	**3ab**	47
9	p-NO_2Ph	Ph_3As	toluene	35	TPPFe(III)Cl	12	**3ab**	11
10	p-NO_2Ph	Et_3As	1,4-dioxane	35	$Rh_2(OAc)_4$	6	**3ab**	59
11	p-NO_2Ph	Ph_3P	1,4-dioxane	35	$Rh_2(OAc)_4$	6	**3ab**	0
12	p-NO_2Ph	Ph_3P	toluene	35	TPPFe(III)Cl	6	**3ab**[c]	55
13	p-NO_2Ph	$(EtO)_3P$	toluene	35	TPPFe(III)Cl	6	**3ab**[d]	13

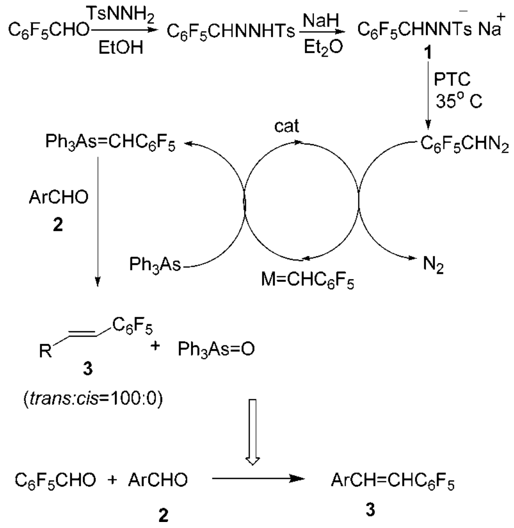
[a] 5 mol % of 18-crown-6 used as the PTC. [b] Isolated yield based on aldehyde. [c] E:Z = 3.1:1. [d] E:Z = 3.6:1

solid-state photocycloaddition reactions,[8] and fluorinated conducting polymers.[9] For example, polyphenylenevinylene (PPV) derivatives have wide applications in electroluminescence (EL) devices.[10] Recent research disclosed that the fluorinated phenylene ring showed considerable red-shifted EL[6] and antioxidation activity.[11]

However, there are still no effective methods to synthesize stereochemically pure *trans* fluoroaromatic alkenes. The classic Wittig olefination[12] and Heck reactions[13] not only have low stereoselectivity but also have strict requirements for the substrates, which seriously limit their further applications. It is known that semistabilized and stable arsonium ylides react with aldehydes to give *trans* alkenes with high stereoselectivity (in contrast, non- or semistabilized arsonium ylides react with aldehydes to give epoxides).[14,16c] Aggarwal used aryl arsonium ylide intermediates from nonfluoroaromatic diazomethanes in reactions with aldehydes to give epoxides with high stereoselectivity.[16c] Thus, if semistabilized or stable arsonium ylides could be generated in situ from diazo compounds and trapped with aldehydes, it should provide alkenes in high stereoselectivity. Because of the troublesome handling properties of diazo compounds, such as their thermal instability, sensitivity to impact, and potential explosivity,[15] it is preferred to generate the diazo compound in situ using a one-pot reaction process.[16]

Herein we describe the first example of the catalytic formation of *trans* olefins **3** through coupling of the arsonium ylide, generated in situ from the reaction of triphenylarsine with pentafluorobenzaldehyde tosylhydrazone salt **1** in the presence of $Rh_2(OAc)_4$, with a second aldehyde **2** (Scheme 2).

Scheme 2



The diazo compound precursor aryl tosylhydrazone salt **1** could be readily prepared from pentafluorobenzaldehyde using the Bamford−Stevens reaction.[17] Initially, 4-bromobenzaldehyde was chosen as the reactant and triphenylarsine was used to trap the carbenoid. We found that the optimized reaction temperature is 35 °C. Higher reaction temperatures (60−80 °C) did not produce the desired product. Among all tested catalysts, $Rh_2(OAc)_4$ was the most effective catalyst. $Cu(acac)_2$ and TPPFe(III)Cl (Table 1, entries 5 and 8) could also efficiently catalyze this reaction

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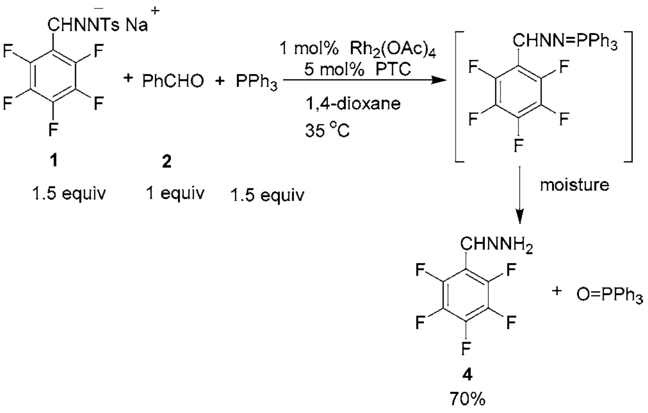
Scheme 3

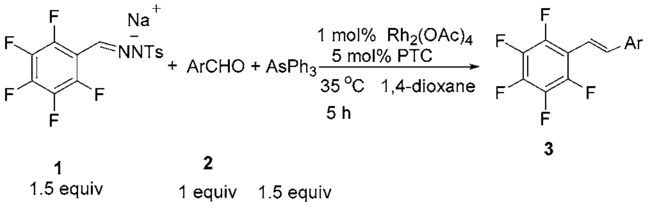


with slightly lower yields. Wilkinson's catalyst, RhCl(PPh$_3$)$_3$, was a much less efficient catalyst (Table 1, entry 6). The solvent did not affect the reaction significantly (Table 1, entries 3 and 4). When using more active triethylarsine instead of triphenylarsine, similar results were obtained (Table 1, entry 10).

Interestingly, under the same conditions, Ph$_3$P did not give the expected alkene (Table 1, entry 11); hydrazine **4** was isolated in 70% yield, which came from the intermediate phosphazine (Scheme 3).[18]

When TPPFe(III)Cl was used instead of Rh$_2$(OAc)$_4$, the expected alkene was isolated in 55% yield; however, it gave a low stereselectivity (E:Z = 3.1:1) (Table 1, entry 12). Using (EtO)$_3$P to trap the carbenoid and TPPFe(III)Cl as the catalyst, a low yield and stereoselectivity were observed (Table 1, entry 13). We cannot account for this finding at this time. The results are summarized in Table 1.

Scheme 4



Under the optimized reaction conditions (Scheme 4), a series of aldehydes was used to prepare pentafluorophenyl-containing alkenes. The results are summarized in Table 2. The yields of the reactions with electron-deficient aldehydes (entries 2, 7, and 11) are higher than with electron-rich aldehydes (Table 2, entries 8−10), which is consistent with our speculation that electron-deficient aldehydes have better reactivity in this reaction.

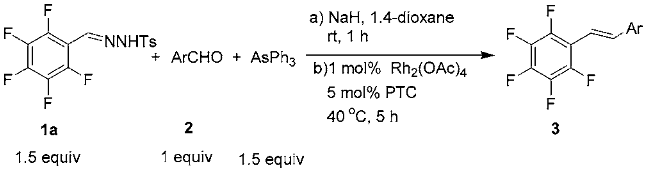
Table 2. Preparation of Alkenes **3** from the Reaction of **1**, **2**, and As$_3$Ph$_3$[a]

entry	Ar in **2**	time (h)	product (*trans*:*cis*)[b]	yield of **3** (%)[c]
1	*p*-BrPh (**2a**)	6	**3a** (100:0)	60
2	*p*-NO$_2$Ph (**2b**)	6	**3b** (100:0)	64
3[d]	Ph (**2d**)	12	**3d** (100:0)	59
4	Ph (**2d**)	6	**3d** (100:0)	70
5	*trans*-PhCH=CH(**2c**)	8	**3c** (100:0)	57
6	2-furfuryl- (**2e**)	6	**3e** (100:0)	62
7	*o*-NO$_2$Ph (**2f**)	4	**3f** (100:0)	64
8	*p*-CH$_3$OPh (**2g**)	12	**3g** (100:0)	45
9	2,4-(CH$_3$O)$_2$ Ph (**2h**)	12	**3h** (100:0)	39
10	*p*-CH$_3$Ph (**2i**)	12	**3i** (100:0)	41
11	*p*-CNPh (**2j**)	6	**3j** (100:0)	65
12	*o*-ClPh (**2k**)	6	**3k** (100:0)	67
13	*p*-CHOPh (**2l**)[e]	6	**3l**	35

[a] 1 mol % Rh$_2$(OAc)$_4$ was used as the catalyst, 1,4-dioxane as solvent, and 15% BnNEt$_3$Cl as the PTC. [b] Determined by NMR spectroscopy. [c] Isolated yield. [d] Et$_3$As was used. [e] *trans,trans*-1,4-Bis(2-phenyl-ethenyl)-2,3,5,6-tetrafluoro-benzene **3l** was formed in 35% yield, and the byproduct 4-(2-pentafluorophenyl-vinyl) benzaldehyde was formed in 16% yield.

Encouraged by the above results, we decided to employ the in situ tosylhydrazone salts in the catalytic cycle (Scheme 5). As a result, the yields of the alkenes were lower than stepwise, but the stereoselectivity was unchanged (Table 3).

Scheme 5



In summary, we described a novel and straightforward method for the synthesis of pure *trans* pentafluorophenyl-containing alkenes from aldehydes in moderate to good yields in a one-pot reaction. The present strategy capitalizes on the reaction of aldehydes with arsonium ylides. Moreover, this

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Table 3. Yields and Ratios of Alkenes Formed from Pentafluorobenzaldehyde and Tosylhydrazones Using 1.5 Equiv of $AsPh_3$[a]

entry	Ar in **2**	*T* (°C)	*t* (h)	alkene (*trans*:*cis*)[b]	yield[c] of **3** (%)
1	Ph	35	12	**3d** (100:0)	59[d]
2	*p*-NO_2Ph	35	12	**3b** (100:0)	56
3	2,4-(CH_3O) Ph	35	12	**3h** (100:0)	19

[a] Using 1 mol % $Rh_2(OAc)_4$ as the catalyst and 18-crown-6 as the PTC. [b] Determined by NMR spectroscopy. [c] Isolated yield. [d] Et_3As was used for easier isolation.

is the first report on the coupling of two aldehydes to form pure *trans* alkenes. Owing to the salt-free ylide and mild reaction conditions, this reaction will be the choice for the synthesis of *trans* aromatic alkenes, especially pentafluorophenyl-containing alkenes.

Acknowledgment. The authors thank the National Natural Science Foundation of China (NNSFC) (nos. 20372077 and 20032010).

Supporting Information Available: Experimental procedures and characterization for all new compounds. This material is available free of charge via the Internet at http://pubs.acs.org.

OL036197S