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Control over C–O and C–C bond formation: ruthenium catalyzed regiospecific addition of carboxylic acid to alkyne and stereoselective dimerization of alkyne

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ABSTRACT

A cationic ruthenium(II) complex, $[Ru(PPh_3)_2(CH_3CN)_3Cl][BPh_4]$ (**1**), has been found to be an effective catalyst for stereoselective dimerization of alkynes in the presence of a base, and for regiospecific addition of carboxylic acids to alkynes in presence of the Lewis acid, $BF_3{\cdot}Et_2O$.

Enol esters are important intermediates in synthetic organic chemistry.[1] They are used in acylation of carbonyl compounds,[2] in the synthesis of α-halo ketones,[3] kinetic resolution of chiral alcohols[4] and in cyclopropanation[5] and cycloaddition reactions.[6] In addition, these are important monomers in polymerization reactions.[7] Similarly, enynes are important substrates for the synthesis of organic materials,[8] and metal-catalyzed carbon–carbon bond formation by coupling of alkynes offers a large number of such products.[9] Ruthenium compounds have been used as catalysts for the synthesis of enol esters[1,10] as well as for enynes.[11]

The first report on ruthenium-catalyzed addition of carboxylic acid to alkyne involves $Ru_3(CO)_{12}$ as a catalyst.[12] However, the reaction conditions were harsh and the products obtained were Markovnikov products.[12] This was followed by a large number of reports on ruthenium-catalyzed addition of carboxylic acid to alkynes.[1,10] Addition of carboxylic acid to alkynes affords three possible isomers (Scheme 1) and most of the reported reactions afford more than one isomer. Recently regio-controlled ruthenium-catalyzed addition of carboxylic acid to alkynes was reported by Goossen et al.[1c]

Ruthenium-catalyzed dimerization of terminal alkynes to *E* and *Z* 1,4-substituted enynes (A′ or B′, Scheme 2) and 2,4-disubstituted enynes (C′ Scheme 2) and butatrienes (D′, Scheme 2) was reported.[13]

Although, for both the reactions ruthenium complexes have been used as catalysts, there are only a few reports on controlled C–O and C–C bond formation using the same catalyst.[14] In a recent report it has been shown that, $RuCl_x$(*p*-cymene)(triazol-5-ylidene) compounds can catalyze both the addition of carboxylic acid to alkynes and dimerization of alkynes.[14a] However, the regio- and stereoselectivity in both the reactions were found to be very poor.[14a] Another couple of reports deal with $[Cl_2(PCy_3)_2Ru{=}CHPh]$[14b] and cationic vinylidene ruthenium complex[14c] catalyzed enol formation and dimerization of alkyne, and the nature of the product was found to be dependent on the type of acid. Here again, a mixture of products was obtained.

Only recently, Le Paih et al. have reported ruthenium-catalyzed condensation of two molecules of alkynes and one molecule of carboxylic acid.[13]

Recently, we have reported the synthesis, structure and catalytic properties of a cationic ruthenium complex, $[Ru(PPh_3)_2(CH_3CN)_3Cl][BPh_4]$ (**1**).[15] This complex catalyzes transfer hydrogenation of aldehydes and ketones[15a] and selective reduction of carbonyl group of α,β-unsaturated carbonyl compounds.[15b] The complex was also found to be an effective catalyst for monoalkylation of anilines by alcohols.[15c] In continuation of our investigations on the catalytic properties of **1**, herein we report a controlled regiospecific addition of carboxylic acid to alkynes and stereoselective dimerization of alkynes catalyzed by **1**. We have chosen the reaction of phenylacetylene with benzoic acid as the model reaction. Thus, a reaction of phenylacetylene and benzoic acid in the presence of 1 mol % of **1** in toluene at 80 °C afforded both enol ester and dimerization products (Scheme 3). Thus, it is clear that, complex **1** can catalyze addition of carboxylic acid to alkyne as well as dimerization of alkynes.

We were interested in controlling the catalytic properties of **1**. It has been reported that, in ruthenium-catalyzed dimerization of alkynes, addition of base promotes formation of alkenylruthenium species of the type $[L_nRu\text{-}C{\equiv}CR]$, which is the key intermediate in the dimer formation.[11c,d] Accordingly, a reaction of phenylacetylene with carboxylic acid in the presence of a base, Na_2CO_3 and **1** {1:1:1:0.01} was carried out and as expected, the tail to tail *Z*-dimerization product was found to be the major product (Table 1). The HPLC trace of the crude product confirms the formation of a small amount of unsaturated ester and *E*-dimerization product along with the *Z*-dimerization product.

Having established the reaction conditions for the dimerization reaction, we were interested in investigating the reaction condition

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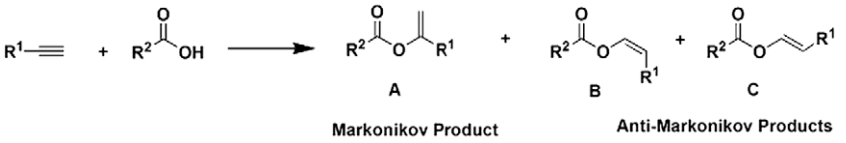
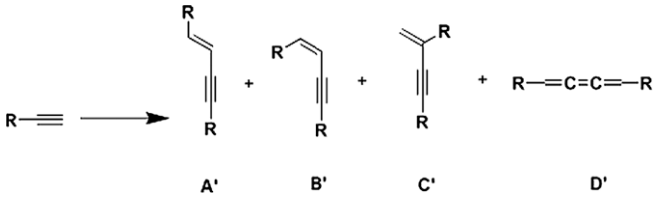


Scheme 1. Addition products of carboxylic acid to alkynes.



Scheme 2. Products of dimerization of alkynes.

for the addition of carboxylic acid to alkynes. It has been suggested that, coordination of both the reactants, that is, carboxylic acid as well as alkyne is necessary for the catalytic reaction.[12,14]

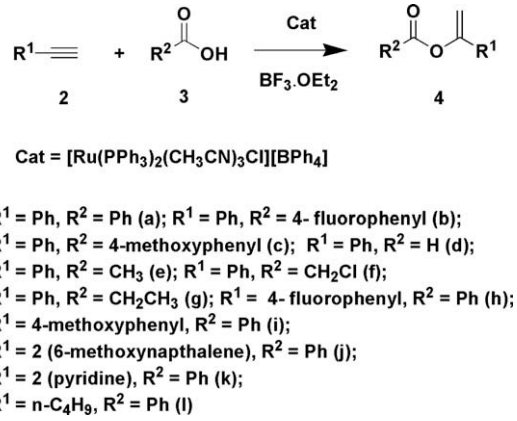
Recently, [RuCl{C(=CHPh)OC(=O)CH_2CH_3}(CO) (PPh_3)] has been isolated and structurally characterized as an intermediate in the ruthenium-catalyzed *Z*-enol ester formation.[16] However, Bruneau and Dixneuf have suggested that, formation of enol esters takes place through the attack of the external nucleophilic acid to the coordinated electrophilic alkyne. Also, it has been shown that, the presence of a coordinated monophosphine is necessary for the catalytic activity.[1a]

In case of **1**, two triphenylphosphines are coordinated to the ruthenium centre and it was thought that, removal of one triphenylphosphine may generate catalytically active species for the addition reaction. Boron trifluoride is known to form adduct with phosphines. We thought to use BF_3 as a phosphine scavenger. The efficacy of BF_3 as phosphine scavenger was established from in situ ^{31}P (external standard: H_3PO_4) and ^{11}B NMR (external standard: $BF_3{\cdot}Et_2O$) spectra of the reaction between complex **1** and $BF_3{\cdot}Et_2O$. The $^{31}P\{^1H\}$ NMR spectrum of **1** in CD_3CN shows only one peak at 32.8 ppm. The $^{11}B\{^1H\}$ spectrum of the compound shows one broad peak at −6.3 ppm, due to $[BPh_4]^-$ anion. When $BF_3{\cdot}Et_2O$ is added to this solution and heated to about 60 °C for 15 min, the peak at 32.8 ppm disappears and three new peaks appear at 53.2, 34.9 and 8.7 ppm in the $^{31}P\{^1H\}$ NMR spectrum. The broad nature of the peak at 8.7 ppm suggests that, this signal is due to $Ph_3P{\cdot}BF_3$ adduct. Even at higher temperature (60 °C) the peak could not be resolved. The signal at 34.9 ppm has been assigned to ^{31}P signal of the ruthenium-coordinated $Ph_3P{\cdot}BF_3$. Also, with time this signal disappears. The signal at 53.2 ppm has been assigned to a monophosphine complex of ruthenium of the type $[Ru(PPh_3)(CD_3CN)_4Cl][BPh_4]$. The conclusive evidence of phosphine abstraction comes from the $^{11}B\{^1H\}$ spectrum of the solution. The $^{11}B\{^1H\}$ spectrum of the solution shows a broad signal at −0.5 ppm. This is due to the $Ph_3P{\cdot}BF_3$ species.[17] The $^{11}B\{^1H\}$ spectrum of $Ph_3P{\cdot}BF_3$ in $CDCl_3$ shows a peak at −0.4 ppm.[17] The slight shift observed is due to the solvent effect. The peak could not be resolved at higher temperature. The peak due to $[BPh_4]^-$ could not be observed, as it is merged along with the −0.5 ppm signal.

Table 1
Effect of additive on the nature of product in the **1** catalyzed reaction between phenylacetylene and benzoic acid[a]

Additive	Conv. (%)	Sel. A″[d] (%)	Sel. B″[d] (%)	Sel. C″[d] (%)
None	90	47	31	22
Na_2CO_3[b]	95	5	90	5
Et_3N[b]	85	8	56	36
$BF_3{\cdot}Et_2O$[c]	98	96	0	4

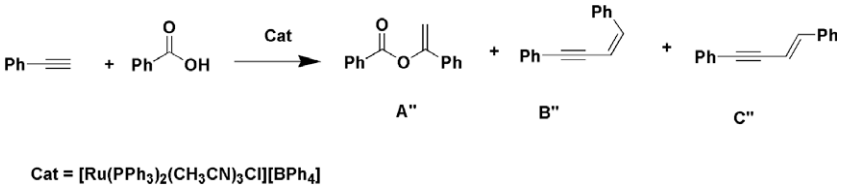
[a] Conditions: 2.5 mmol phenylacetylene, 2.5 mmol benzoic acid, 0.025 mmol **1**, toluene 80 °C.
[b] 2.5 mmol of Na_2CO_3.
[c] 0.025 mmol of $BF_3{\cdot}Et_2O$.
[d] From HPLC.



Scheme 4. Reaction of alkynes with carboxylic acid in the presence of **1** and $BF_3{\cdot}Et_2O$.

Having established the efficacy of BF_3 as phosphine scavenger, we have carried out a reaction between benzoic acid and phenylacetylene in the presence of 1 mol % of **1** and $BF_3{\cdot}Et_2O$ {1:1:0.01:0.01} in toluene at 80 °C. The major product is the Markovnikov addition product (Table 1). It may be noted that, only a few catalysts are known to afford selectively Markovnikov addition product.[1c,10]

The reaction is quite effective in the cases of aromatic and aliphatic carboxylic acids (Scheme 4) (Table 2, entries 1–7) and affords the corresponding addition product in good yields. Only in the case of acetic acid, formation of small amounts of *Z*-1,4 diphenyl-1-buten-3-yne and 2,4-diphenyl-1-buten-3-yne could be ob-



Scheme 3. Reaction of phenylacetylene with benzoic acid in the presence of **1**.

Table 2
Addition of carboxylic acid to alkynes catalyzed by **1**[a]

Entry	Alkyne	Acid	Product	Yield[b] (%)
1	2a	3a	4a	78
2	2b	3b	4b	82
3	2c	3c	4c	73
4	2d	3d	4d	73
5	2e	3e	4e	70
6	2f	3f	4f	72
7	2g	3g	4g	70
8	2h	3a	4h	74
9	2i	3a	4i	70
10	2j	3a	4j	62
11	2k	3a	4k	65
12	2l	3a	4l	71

[a] Conditions: 10 mmol alkynes, 10 mmol carboxylic acid, 0.1 mmol **1**, 0.1 mmol $BF_3{\cdot}Et_2O$, toluene 80 °C.
[b] Isolated yield.

served. The reaction fails in the cases of amino acids, oxalic acid and cinnamic acid. This may be due to the chelation of the metal centre by the acid, thus preventing coordination of phenylacetylene to the ruthenium centre. The reaction is also, effective in the case of substituted phenylacetylenes such as 1-ethynyl-4-fluorobenzene, or 1-ethynyl-4-methoxybenzene (Table 2, entries 8 and 9) and other substituted aromatic and heteroaromatic alkynes such as 2-ethynyl-6-methoxynaphthalene and 2-ethynylpyridine (Table 2entries 10 and 11) and aliphatic alkyne, 1-hexyne (Table 2, entry 12).

The ^1H NMR spectrum of the CD_3CN solution of **1**, $BF_3{\cdot}Et_2O$ and acetic acid at room temperature shows a peak at 2.22 ppm (singlet) along with other peaks due to **1**, diethyl ether and unreacted acetic acid. The signal at 2.22 ppm can be assigned to the $-CH_3$ protons of the ruthenium-coordinated acetate.[18] When phenylacetylene is added to this solution new signals appear at 3.45 ppm (singlet) and in the 7.35 to 7.65 ppm region. The singlet at 3.45 ppm is due to the H–C proton of the coordinated phenylacetylene as evidenced by the marked shift of the acetylinic proton of the uncoordinated phenylacetylene, which appears at 3.05 ppm. Thus it is clear that, in the present case both the substrates are coordinated to the ruthenium centre.

It may be noted that, Goossen et al. have used the ruthenium catalyst precursor, $[(p\text{-cumene})RuCl_2]_2$ and 2 equiv of phosphine ligand as the catalyst for the reaction between carboxylic acid and alkyne.[1c] Reaction of neutral ligands with $[(p\text{-cumene})RuCl_2]_2$ produces complex of the type, $[(p\text{-cumene})Ru(L)Cl_2]$.[19] Thus it is expected that, addition of 2 equiv of phosphine ligands to $[(p\text{-cumene})RuCl_2]_2$ will generate complex of the type$[(p\text{-cumene})Ru(L)Cl_2]$. Coordination of both alkyne and carboxylate to the ruthenium centre in such complexes is not easy. Thus, it has been suggested that, addition of base facilitates the formation of carboxylate anion which attacks ruthenium-coordinated alkyne and unsaturated esters are formed.[1c] However, in this case due to the labile nature of coordinated acetonitrile, both alkyne and carboxylate get coordinated to the ruthenium centre as evidenced by ^1H NMR spectrum of the reaction mixture and the reaction takes place by the insertion of triple bond into Ru–O bond.

Effect of base on the **1** catalyzed dimerization of phenylacetylene has also been studied. In the presence of Et_3N, *Z*-dimerization product is obtained as a major product (56%). Along with the *Z*-dimerization product, *E*-dimerization product (36%) and addition product (8%) are also obtained (Table 1). Thus it is clear that, Na_2CO_3 is the ideal base for dimerization reaction.

In summary, we have demonstrated that the same catalyst can be used for C–C and C–O bond formation when reaction conditions are changed. In addition, the catalyst can be synthesized very easily from a reaction of commercially available $[Ru(PPh_3)_3Cl_2]$ with $NaBPh_4$ in acetonitrile.[15a] In contrast to the catalytic system reported earlier[1c] the present catalyst does not require any expensive phosphine additives such as, $P(p\text{-}Cl\text{–}C_6H_4)_3$ or $P(Fur)_3$. We are now investigating the details of the dimerization reactions of alkynes.

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Supplementary data

Supplementary data associated with this article can be found, in the online version, at doi:10.1016/j.tetlet.2009.06.039.

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