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ARTICLE

Zr-Catalyzed Microwave Assisted Functionalization of Alkyne and Nitroalkene

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ABSTRACT

Water and zirconium(IV) as catalyst were found to be effective in the transformation of terminal aromatic alkyne to aromatic methyl ketone in the microwave. This terminal alkyne hydration reaction proceeded in excellent yield with $Zr(cp)_2Cl_2$. The reaction was moved efficiently in presence of electron donating or electron withdrawing substituent on aromatic ring. An eco-friendly synthesis of aldehyde by oxidative cleavage of nitroalkene was developed with $Zr(cp)_2Cl_2$ catalyst and water in microwave.

KEYWORDS

Microwave, Hydration, Nitroalkene cleavage, Water.

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INTRODUCTION

The success of organic reaction is depends on atom economy, catalyst recovery and use of green solvents. In green chemistry concept, water, microwave irradiation, non-toxic and less expensive catalyst has emerged as a powerful tool in synthesis and found to be environmentally benign process [1]. The microwave technique occupies broad area in organic synthesis from last three decades [2]. The oxidation of alkyne to carbonyl is interesting because of the broad scope and applications in synthetic organic chemistry. Oxidation or hydration of terminal alkyne gives methyl ketone on the basis of Markovnikov's rule [3-5].

Zirconium(IV) catalyst made complex with alkyne and then reaction was moved by addition of water, as per Markovnikov's rule to deliver ketone. In previous literature, it is observed that a many transition metal catalysts were examined for hydration, such as Pt [6], Ir [7], Pd [8], Fe [9], Ag [10,11], Sn-W [12] and Au [13-16]. Among all these metals, Au catalyst were found to be efficient for hydration of alkyne. As compared to Au catalyst, other metal catalyst have poor reactivity and selectivity [3]. Au catalyst like $(Ph_3P)AuCH_3/H_2SO_4$ [5], (IPr)AuCl/$AgSbF_6$ [17], (IPr)AuOH/$HSbF_6$ [17], $AuSPhosNTf_2$ [18] were useful for hydration of simple alkyne and bearing various functional groups. Among these catalysts, Au catalyst are costly, while most of them require co-catalyst (Ag), additives

(Hg) [19] and acid reagent [20]. Herein, a microwave assisted new method is proposed for the hydration of alkyne with cheap and easily available $Zr(cp)_2Cl_2$ in water.

Carbon-carbon double bond breaking has more importance in synthetic chemistry [21]. There are various methods widely used for oxidative C=C bond cleavage like $NaIO_4$ and ozonolysis. Bortolini *et al*. [22] achieved this transformation of nitroalkene to aldehyde with hydrogen peroxide in ionic liquid bmim(OTf). During this, in some cases of conversion of nitroalkene to aldehyde, an over oxidation product (acid) is obtained. In this work, a new method for oxidative cleavage of C=C bond in microwave with $Zr(cp)_2Cl_2$ in water is developed.

EXPERIMENTAL

All the chemicals were purchased from Sigma-Aldrich and used without further purification as received. All ^1H and ^{13}C NMR spectra were recorded in $CDCl_3$ on Avance 300 or Avance 500 spectrometers. Chemical shifts (δ) were reported in parts per million (ppm) relative to residual $CHCl_3$ (^1H: δ 7.26 ppm, ^{13}C: δ 77.00 ppm) as an internal reference. Coupling constants (*J*) were reported in Hertz (Hz). Mass spectral data were obtained using MS (EI) ESI, HRMS mass spectrometers. High resolution mass spectra (HRMS) [ESI+] were obtained using either a TOF or a double focusing spectrometer.

General procedure for ketone: The microwave tube was charged with alkyne (1 mmol), $Zr(cp)_2Cl_2$ (5 mol%) and 2 mL distilled water. This assembly was kept in microwave for 15 min at 95 ºC. After 15 min, the microwave was stopped and then allowed to cool at room temperature. Then microwave tube was removed; water was added and extracted with EtOAc (3 × 10 mL). Combined organic layers were dried over Na_2SO_4. The solvent was removed through rotary evaporator and the product was isolated using column chromatography. The isolated compounds were well characterized by IR, ^1H NMR, ^{13}C NMR and HRMS. The isolated products were identified by comparison of their mass, ^1H and ^{13}C NMR spectra with those of commercially available samples.

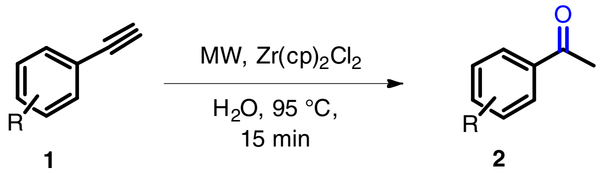
Compound 2j: ^1H NMR (500 MHz): δ 8.01 (d, $J = 7.1$ Hz, 2H), 7.55 (t, $J = 7.3$ Hz, 1H), 7.48 (t, $J = 7.4$ Hz, 2H), 7.32 (t, $J = 7.3$ Hz, 2H), 7.29 (d, $J = 9.4$ Hz, 3H), 4.27 (s, 2H); ^{13}C NMR (75 MHz, $CDCl_3$): δ 197.5, 136.5, 134.5, 133.2, 129.5, 128.5, 126.9, 45.5, 29.7; *m/z* EI-HRMS calcd. for $C_{14}H_{12}O$: 196.088; found 196.088.

General procedure for aldehyde: The microwave tube was charged with aromatic nitroalkene (1 mmol), $Zr(cp)_2Cl_2$ (5 mol%) and 1.5 mL distilled water. This assembly was kept in microwave for 10 min at 80 ºC. After 15 min, the microwave was stopped and microwave tube was allowed to cool at room temperature. Then microwave tube was removed; water was added and extracted with EtOAc (3 × 10 mL). Combined organic layers were dried over Na_2SO_4. The solvent was removed through rotary evaporator and product was isolated using column chromatography. The isolated compounds were well characterized by IR, ^1H NMR, ^{13}C NMR and HRMS. The isolated products were identified by comparison of their mass, ^1H & ^{13}C NMR spectra with those of authentic samples.

Compound 4g: ^1H NMR (400 MHz, $CDCl_3$): δ 10.65 (s, 1H), 7.94 (d, $J = 7.8$ Hz, 1H), 7.63 (d, $J = 7.7$ Hz, 1H), 7.59 - 7.53 (m, 3H), 7.46-7.35 (m, 4H); ^{13}C NMR (101 MHz, $CDCl_3$): δ 191.62, 135.87, 133.80, 133.25, 131.72, 129.11, 128.56, 127.29, 126.87, 122.37, 96.41, 84.99, 60.42.

RESULTS AND DISCUSSION

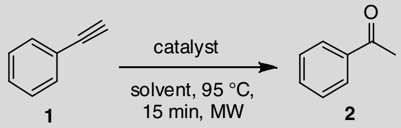
Initially, it is observed that $Zr(cp)_2Cl_2$ and water in microwave produce the hydration of alkyne (**Scheme-I**). When phenylacetylene (1mmol), $Zr(cp)_2Cl_2$ (5mol%) in water (2 mL) was heated at 95 ºC for 20 min in microwave. The phenylacetylene was consumed completely, giving acetophenone in 85% yield. First, 2 mol% catalyst was used in the reaction but alkyne was not completely consumed, which was made possible with 5 mol% catalyst. Thus, 5 mol% catalyst was found to be sufficient for complete conversion of alkyne to ketone.



Scheme-I: Hydration of alkyne

Instead of using only water, various organic solvent (DMF, THF, DCM, EtOH, MeOH, CH_3CN, C_6H_6) in combination with water (1:1) were also applied, but no satisfactory yield was obtained. When reaction proceeded in $CH_3CN:H_2O$ (1:1) gave methyl ketone in 55% yield, which was more as compared to other solvent systems. Aromatic alkyne in presence of corresponding catalyst in $DMF:H_2O$ (1:1) furnished methyl ketone in 20% yield, which found to be poor solvent system for this reaction. The remaining solvent system (Table-1) showed moderate yield of methyl ketone. In catalyst screening, other Zr catalysts were also applied and found to be effective too. Thus several zirconium(IV) compounds such as $ZrCl_4$, $Zr(cp)_2H_2$, $ZrOCl_2·8H_2O$ and $Zr(cp)_2ClH$ catalysts (5mol%) with phenyl

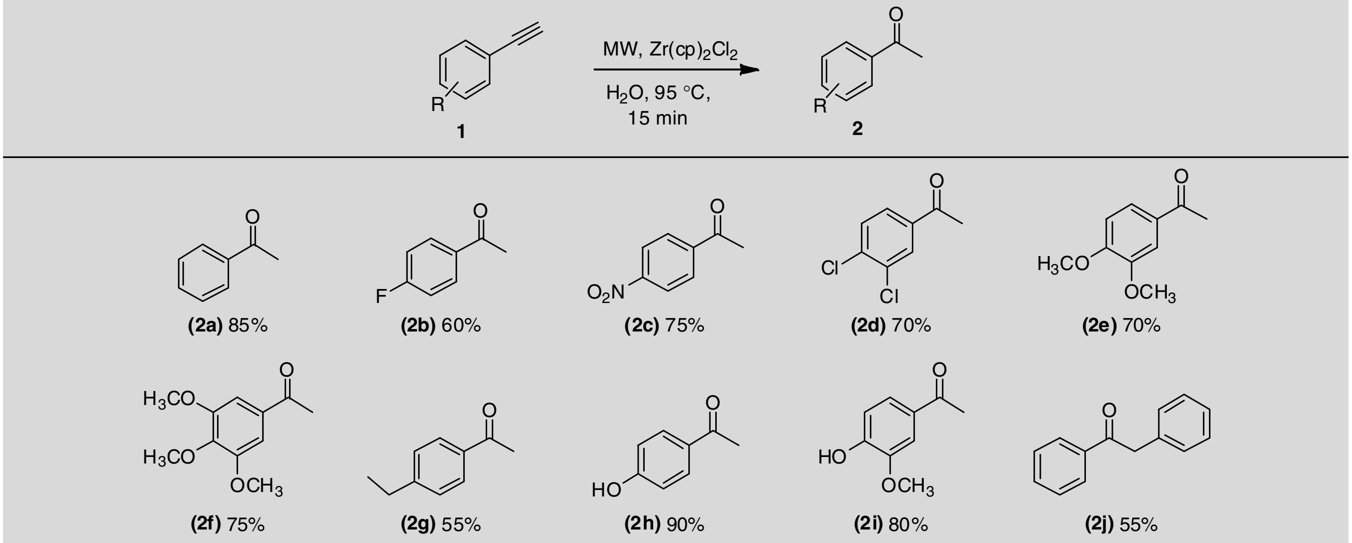
TABLE-1
SCREENING OF CATALYST AND SOLVENT FOR HYDRATION OF PHENYLACETYLENE TO ACETOPHENONE[a]



Entry	Catalyst	Mol (%)	Solvent[b]	Yield[c] (%)
1	$Zr(cp)_2Cl_2$	2	H_2O	48
2	$Zr(cp)_2Cl_2$	5	H_2O	85
3	$Zr(cp)_2Cl_2$	5	$DMF:H_2O$	20
4	$Zr(cp)_2Cl_2$	5	$THF:H_2O$	42
5	$Zr(cp)_2Cl_2$	5	$EtOH:H_2O$	38
6	$Zr(cp)_2Cl_2$	5	$C_6H_6:H_2O$	46
7	$Zr(cp)_2Cl_2$	5	$CH_3OH:H_2O$	52
8	$Zr(cp)_2Cl_2$	5	$DCM:H_2O$	48
9	$Zr(cp)_2Cl_2$	5	$CH_3CN:H_2O$	55
10	$ZrCl_4$	5	H_2O	20
11	$Zr(cp)_2H_2$	5	H_2O	28
12	$ZrOCl_2·8H_2O$	5	H_2O	35
13	$Zr(cp)_2ClH$	5	H_2O	25

[a]Reaction conditions: Phenylacetylene (1 mmol), $Zr(cp)_2Cl_2$ (5 mol%), H_2O (2 mL), 95 °C, 15 min, microwave. [b]Solvent (1:1), [c]Isolated yield.

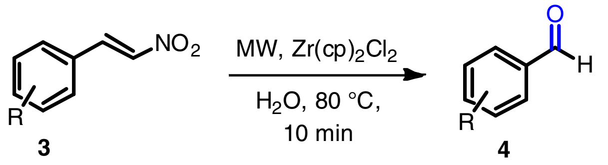
TABLE-2
HYDRATION OF TERMINAL ALKYNE (**2a-i**) AND INTERNAL ALKYNE (**2j**)



acetylene in water were applied. Among the above mentioned Zr(IV) catalysts were found to be useful for this transformation, giving acetophenone in 20-35% yields. After the optimization of reaction conditions, we further proceeded to explore scope and limitations of substrate.

In next step, we studied various electron donating and electron withdrawing substituent on the aromatic alkyne ring. Weakly electron withdrawing substituted aromatic ring was tested for hydration, which delivered corresponding ketone (**2b** and **2d**) in good yields. Electron-donating and electron-withdrawing groups on aromatic ring was studied and observed that electron donating group on ring such as -OCH_3, -OH produce corresponding ketone (**2e**, **2f**, **2h**, **2i**) in good to excellent yield. We also successively converted internal alkyne to respective ketone (**2j**) in moderate yield (Table-2).

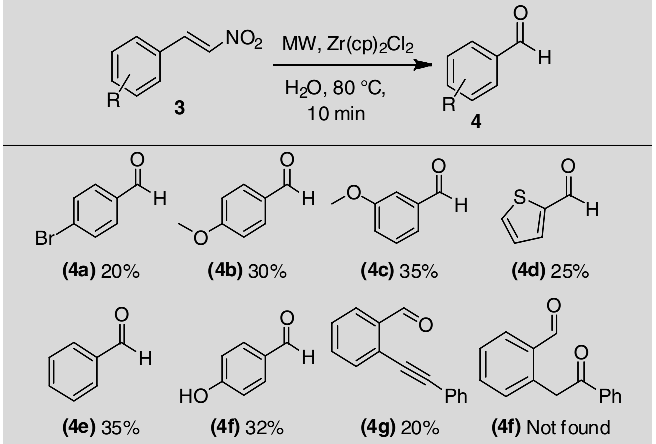
After this successful transformation of alkyne to ketone, we proceeded toward the oxidative cleavage of nitroalkene to aldehyde. When nitroalkene **3** (1 mmol), $Zr(cp)_2Cl_2$ (5 mol%) and H_2O (2 mL) was heated in microwave at 80 ºC for 10 min, it is found that nitroalkene was completely consumed to give respective aromatic aldehyde **4** (**Scheme-II**) [23]. For optimization study of this reaction ,we screened the all Zr(IV) catalyst and solvent conditions as shown in Table-1. Among all these conditions, it is observed that when (*E*)-1-bromo-4-(2-nitrovinyl)benzene treated with $Zr(cp)_2Cl_2$ (5 mol%) and H_2O (2 mL) in microwave at 80 ºC giving compound **4a** in 35% yield. To explore the scope of the present method, we studied different electron substituents on the aromatic ring. *p*-Bromo nitroalkene provided 25% yield of aldehyde while 3-OCH_3 and 4-OCH_3 nitroalkene delivered corresponding aldehyde (**4b** and **4c**) in the moderate yield.



Scheme-II: Oxidative cleavage of nitroalkene

Next, we examined heterocyclic nitroalkene, which gave aldehyde (**4d**) in 25% yield. In our protocol of hydration of alkyne and C=C bond cleavage, possess same catalyst system. So, we were interested if the similar substrate posses both reactive functional groups *i.e.* nitroalkene and alkyne then which part (alkyne or nitroalkene) will react first in reaction. To study this case, we designed a substrate from known procedure [24]. This substrate was irradiated in microwave with $Zr(cp)_2Cl_2$ (5 mol%), H_2O (2 mL) for 10 min at 90 ºC. After purification and analysis, it was found that compound **4g** formed in 20% yield and not another compounds (**4f**). From this experiment, it is concluded that nitroalkene might be ahead in competition with alkyne [23]. In this reaction of double bond cleavage, it is observed that after the completion of reaction there was formation of polar inseparable mixture. Thus, seven aldehyde compounds were synthesized from the corresponding nitroalkene in 20-35% yield (Table-3).

TABLE-3
ALDEHYDE SYNTHESIS FROM NITROALKENE



Conclusion

In conclusion, a simple and convenient microwave assisted method is developed for the hydration terminal alkyne through

Markovnikov's addition rule for the synthesis of aromatic ketone. The proposed protocol is useful in cleavage of nitroalkene for the synthesis of aldehyde.

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