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Hydroalkylation of terminal aryl alkynes with alkyl diacyl peroxides

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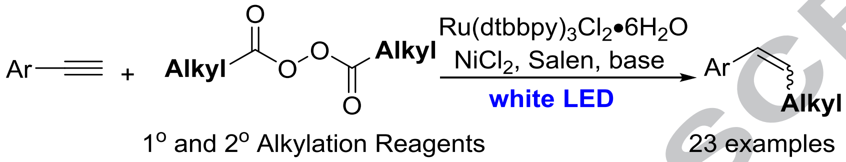
Yougui Li , Liang Ge, Bo Qian, Kaki Raveendra Babu, and Hongli Bao*



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Hydroalkylation of terminal aryl alkynes with alkyl diacyl peroxides

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ABSTRACT

A photo and nickel co-catalyzed hydroalkylation of terminal aryl alkynes enabled *Z*-preferred olefins synthesis has been developed under mild conditions. Alkyl diacyl peroxides were utilized as a new type of alkylation reagents and afforded *Z*-olefins as the major products in moderate to good yields.

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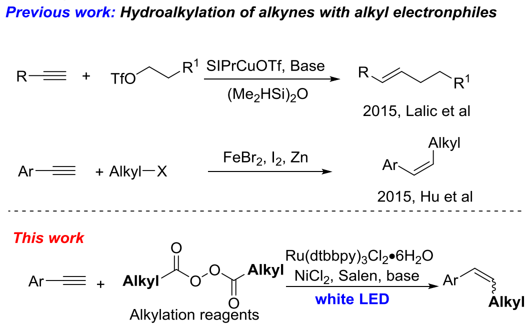
Alkenes are among the most important organic compounds and many synthetic methodologies have been developed for effective olefination such as Wittig reactions,[1] Peterson olefination,[2] Julia olefination,[3] Heck reactions,[4] olefin metathesis,[5] Negishi type addition of organometallic reagents to alkynes[6] and other type of reactions.[7] Recently, two classic examples by Lalic[8] and Hu[9] revealed that hydroalkylation of terminal alkynes with alkyl electrophiles is an effective strategy to generate alkenes from alkynes. Lalic et al. reported the first hydroalkylation of alkynes with alkyl triflate catalyzed by copper catalyst (Scheme 1) which generated *E*-olefins. Hu et al disclosed the first *Z*-selective hydroalkylation of alkynes. This iron catalyzed hydroalkylation of terminal alkynes used alkyl iodides and alkyl tosylates as the electrophiles.

Alkyl diacyl peroxides are the inexpensive chemicals commonly used in industry as radical initiators or oxidants and they are readily accessible from carboxylic acids. Nevertheless, the utilization of peroxides as alkylation reagents was under explored and there were very few documented examples so far to our knowledge.[10,11]



Scheme 1. Hydroalkylation of alkynes.

As part of our ongoing interest in developing new type of alkylating reagents for important reactions,[11d] herein we report the hydroalkylation of terminal aryl alkynes with alkyl diacyl peroxides as electrophiles. This is an alternative method for *Z*-preferred synthesis of 1,2-disubstituted olefins *via* photo and nickel catalysis.

We commenced our study by optimizing the reaction of phenyl acetylene with lauroyl peroxide (LPO). After a screening of all reaction parameters, we found that the optimized conditions involved the merger of photo and metal catalysis.[12] The reaction underwent smoothly in isopropanol in presence of photo catalyst **4a** (1 mol%), $NiCl_2$ (10 mol%), salen ligand ((*R*,*R*)-*N*,*N*'-bis(3,5-di-tert-butylsalicylidene)-1,2-cyclohexanediamine, 10 mol%), NHPI (*N*-hydroxyphthalimide, 100 mol%), and DIPEA (7 eqiuv) (Table 1, entry 1). The yield was up to 71% with the optimal conditions. The yield dropped to 51% when the reaction was heated to 70 °C and without photo catalysis. Seven photo sensors were applied and the yields range from 0-65% (entries 3-9). 1,4-Cyclohexanediene and *N*-hydroxysuccinimide were used to replace NHPI. 1,4-Cyclohexanediene showed similar reactivity but worse *Z*/*E* ratio (entry 10). Whereas *N*-hydroxysuccinimide also deliver product in good yield and good *Z*/*E* ratio (entry 11). Other controlled reactions were examined. The reaction afforded product in only 9% of product without photo catalyst (entry 12). Salen ligand is also key factor to this reaction (entries 13 and 14). NHPI can increase the yield but is not essential (entry 13) to this reaction. The reaction delivered product in a lower yield at 0 °C (entry 16) and much less product in dark (entry 15). Other metal and solvent screening did not improve the result further (entries 17-21).

Table 1

Optimization of reaction conditions[a]

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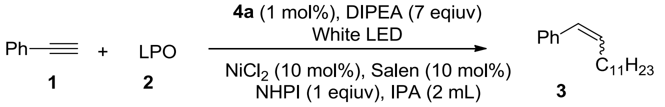
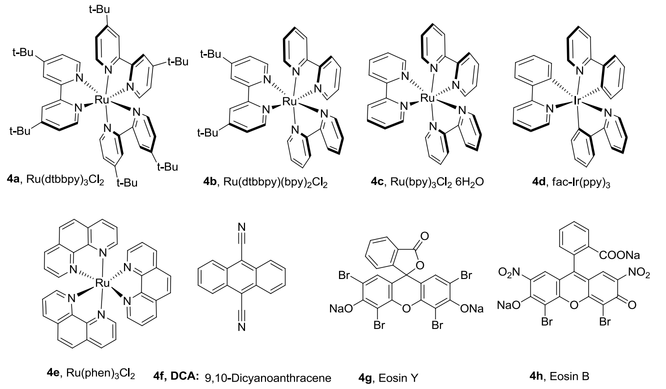




4a, Ru(dtbbpy)$_3$Cl$_2$ **4b**, Ru(dtbbpy)(bpy)$_2$Cl$_2$ **4c**, Ru(bpy)$_3$Cl$_2$ 6H$_2$O **4d**, fac-Ir(ppy)$_3$

4e, Ru(phen)$_3$Cl$_2$ **4f, DCA:** 9,10-Dicyanoanthracene **4g**, Eosin Y **4h**, Eosin B

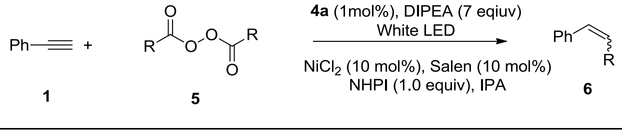
Entry	Change from the optimized condition	Yield[b] % (*Z/E*)
1	No change	71% (3.2:1)
2	Without **4a**, DIPEA, white LED, but reacted at 70 °C	51% (1:1)
3	**4b** instead of **4a**	56% (2.8:1)
4	**4c** instead of **4a**	65% (3.2:1)
5	**4d** instead of **4a**	trace
6	**4e** instead of **4a**	trace
7	**4f**, DCA instead of **4a**	39% (3.0:1)
8	**4g**, EoSin Y instead of **4a**	42% (2.9:1)
9	**4h**, Eosin B instead of **4a**	60% (3.0:1)
10	1,4-cyclohexanediene instead of NHPI	70% (2.3:1)
11	N-Hydroxysuccinimide instead of NHPI	66% (3.3:1)
12	Without **4a**	9% (3.4:1)
13	Without NHPI	58% (2.5:1)
14	Without salen and NHPI	23% (2.8:1)
15[c]	No light	18% (2.0:1)
16[c]	At 0 °C	51% (2.4:1)
17[c]	FeCl$_2$ instead of NiCl$_2$	25% (1.7:1)
18[c]	CoCl$_2$ instead of NiCl$_2$	25% (1.9:1)
19[c]	THF instead of IPA	41% (1.5:1)
20[c]	CH3CN instead of IPA	39% (1.6:1)
21[c]	DME instead of IPA	35% (2.0:1)

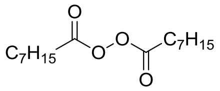
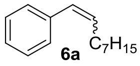
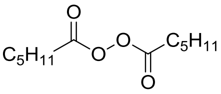
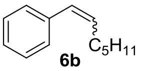
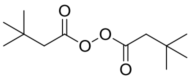
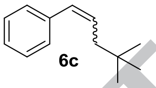
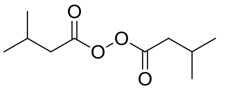
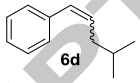
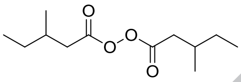
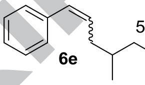
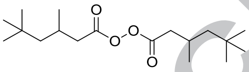
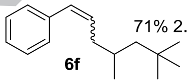
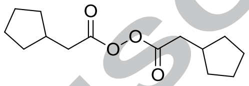
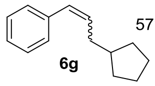
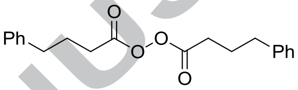
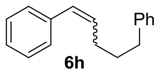
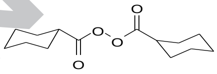
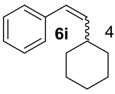
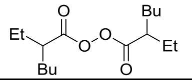
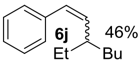
[a] Reaction conditions: phenylacetylene **1** (0.5 mmol), LPO **2** (1.125 mmol), solvent (2.0 mL), 8 h at room temperature, under argon atmosphere. [b] Yield of isolated product. [c] Yields determined by ^{1}H NMR.

With the optimal reaction conditions in hand, we studied the scope of diacyl peroxides (Table 2), which were synthesized from the corresponding carboxylic acids or acyl chlorides. Hydroalkylation of alkynes with primary and secondary alkyl diacyl peroxides afforded *Z*-olefins as the major products. The *Z/E* ratios were about 2:1 in all the cases. The alkyl dicayl peroxides which contain long chain alkyl groups and methyl substituted alkyl groups afforded the corresponding olefins with moderate yields (**6a-f**). Methyl cyclopentyl diacyl peroxide gave compound **6g**. Further, alkyl diacyl peroxides which contain phenyl group furnished **6h**. Finally, secondary diacyl peroxides delivered compound **6i** and **6j**.

Table 2

Substrate scope of alkyl diacyl peroxides[a]



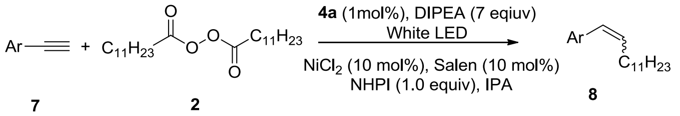
Entry	Peroxide **5**	Product and yield[b]
1		 **6a** 64% 2.6:1
2		 **6b** 51% 2.0:1
3		 **6c** 45% 2.0:1
4		 **6d** 64% 2.3:1
5		 **6e** 51% 2.3:1
6		 **6f** 71% 2.3:1
7		 **6g** 57% 2.5:1
8		 **6h** 37% 2.0:1
9		 **6i** 45%, 2.8:1
10		 **6j** 46%, 4:1

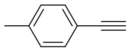
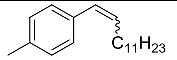
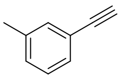
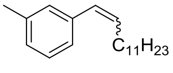
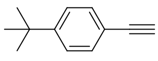
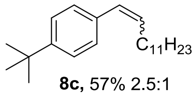
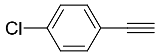
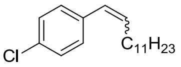
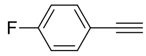
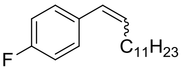
[a] Reaction conditions: phenylacetylene **1** (0.5 mmol), alkyl diacyl peroxides (1.125 mmol), solvent (2.0 mL), 8 h at room temperature, under argon atmosphere. [b] Yield of isolated products.

Next, the scope of aryl alkynes was investigated (Table 3). Alkyl substituted aryl alkynes afforded the products **8a-c**. Further, halogen substituted aryl alkynes provided the olefins **8d-i**. Furthermore, methoxy substituted aryl alkynes gave products **8j-l** in moderate yields. *Ortho*-substituents affected the reaction more than *para*-substituted groups and delivered products in lower yields (Table 3, entries 6 and 12).

Table 3

Substrate scope of aryl alkynes[a]



entry	Aryl Alkyne	product and yield[b]
1		 **8a**, 50% 2.7:1
2[c]		 **8b**, 44% 3:1
3		 **8c,** 57% 2.5:1
4		 **8d,** 51% 2.7:1
5		 **8e,** 49% 2.6:1

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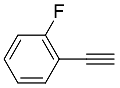
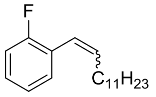
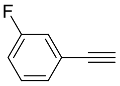
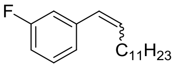
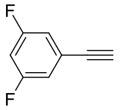
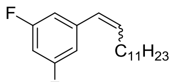
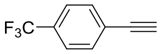
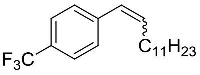
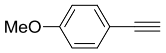
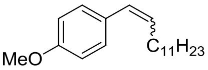
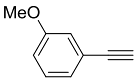
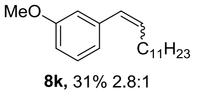
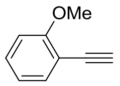
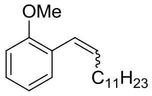
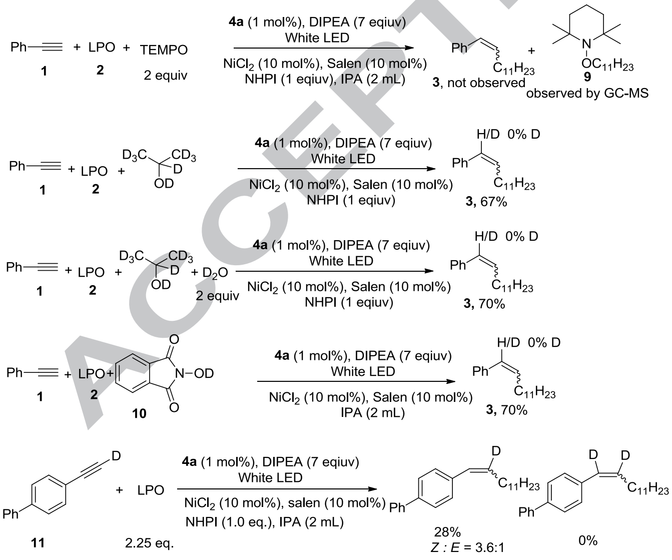
6		 **8f**, 40% 2.3:1
7		 **8g,** 44% 2.4:1
8[e]		 **8h,**58% 5.6:1
9		 **8i,** 58% 4.5:1
10		 **8j,** 55% 3.1:1
11		 **8k,** 31% 2.8:1
12		 **8l**, 30% 2.4:1

[a]Reaction conditions: phenylacetylene **1** (0.5 mmol), alkyl diacyl peroxides (1.125 mmol), solvent (2.0 mL), 8 h at room temperature, under argon atmosphere. [b]Yield of isolated products.

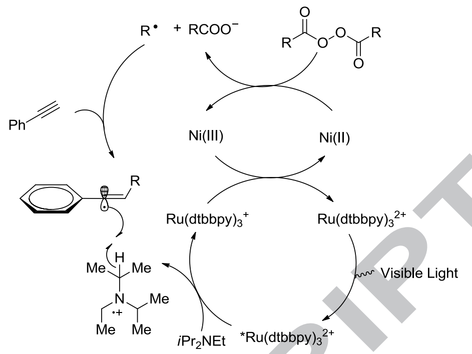
We performed mechanistic experiments to further understand the reaction. Firstly, a radical trapping experiment was conducted with TEMPO (2,2,6,6-tetramethyl-1-piperidinyloxy). The reaction was shut down and there was no desired product observed, while **9** was observed by GC-MS (Scheme 2). Next, four experiments were conducted with deuterated reagents, d_8-isopropanol, D_2O, **10** and **11**. None of these experiments afforded product bearing deuteron atom at the benzylic carbon.



Scheme 2. Initial mechanistic studies.

Based on our experimental results and previous works,[12] a mechanism involving single electron transfer catalytic and photo redox catalytic cycle is proposed here (Scheme 3). Ni(II) complex transfers an electron to the diacyl peroxide to form Ni (III) compound and an alkyl radical. Then this Ni (III) is reduced by Ru (I) species to Ni (II). The generated Ru (II) turns back to Ru (I) under the photo-catalysis condition in presence of DIPEA.

In summary, we have developed the first hydro-alkylation reaction of aryl alkynes with alkyl diacyl peroxides. This reaction enabled *Z*-preferred hydro-alkylation of aryl alkynes and delivered products in moderate yields. This reaction offers a complementary approach to the current methods.



Scheme 3. Proposed catalytic cycle.

Acknowledgments

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Highlights

(1) Diacyl peroxides as electrophiles for hydroalkylation of aryl alkynes.

(2) *Z*-selective hydroalkylation of alkynes

(3) Mild reaction condition.

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