Unprecedented Palladium catalyzed Homo-Coupling Reaction of terminal E-diiodoalkanes towards the synthesis of Buta-1,3-diynes

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ABSTRACT

An efficient method for the synthesis of Buta-1,3-diynes have been developed via homocoupling reaction of terminal (E)-1,2-diiodoalkene under Suzuki reaction condition. The method has been successfully applied both on aliphatic and aromatic E-diiodoalkene resulting buta-1,3-diynes prepared in good yields.

Keywords: Cycloaddition, Cross-coupling, Cyclocondensation, Alkynes, Homocoupling

INTRODUCTION

Buta-1,3-diynes have been found to be versatile building blocks for the construction of natural product analogues\(^1\) corbocycles and heterocycles using cycloaddition and cyclocondensation reactions.\(^2\) Recently these moieties have been utilized for the construction of corbocycles benzene\(^3\) and naphthalene,\(^4\) oxygen based heterocycles furan\(^5\) and pyrrole,\(^6\) nitrogen containing 5/6-membered heterocycles pyrrole,\(^7\) pyrazole,\(^7\) triazole,\(^8\) naphthatriaazoles,\(^9\) benzo[a]phenanthridine,\(^10\) benzoquinolines,\(^11\) sulphur and selenium containing heterocycles thiophenes\(^12\) and selenothiophenes.\(^13\) In the literature various methods for the synthesis of buta-1,3-diynes have been reported,\(^14\) out of them copper (II) catalyzed homocoupling of terminal alkynes reported by Eglinton\(^15\) being a simplest method for the synthesis of these scaffolds. In the literature\(^16\), selective synthesis of unsymmetrical buta-1,3-diynes via Pd-catalyzed cross-coupling reactions of E-1,2-diiodoalkenes with terminal alkynes is reported, so we armed the synthesis of triphenylalkenes using E-1,2-diiodoalkenes and phenylboronic acid via Suzuki cross coupling reaction.\(^17\) Triphenylalkenes are the core structure of anticancer agent tamoxifen used for the treatment of breast cancer.\(^18\) For this purpose (E)-1,2-diiodoalkene 1a was subjected with phenylboronic acid using bistriphenylphosphinepalladium (II) chloride (10 mol%), tetrabutylammoniumhydrogensulphate (1.0 mol), and sodiumcarbonate (5.0 mol) in 5.0 mL of water : acetonitrile (5:1) at 100 °C for overnight. After completion of the reaction as monitored by TLC, out of two intense spots the minor product was isolated in trace amount and characterized as biphenyl\(^19\) while the major product was characterized as 1,4-bis(4-tert-butylphenyl)butha-1,3-diyne 2a. Thus, in Suzuki reaction condition, homo coupled products of both the starting materials were obtained unprecedentedly instead of cross-coupled product.

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Expected product 1,4-bis(4-tert-butylphenyl)buta-1,3-diyne alone under the above reaction condition, again homo coupled for 24h.

The optimal condition that led to the synthesis of 2a in 73% isolated yield (Table 1, entry 7) involved treatment of 1a with 10 mol % Pd(PPh₃)₂Cl₂, Na₂CO₃, (n-Bu)₄NHSO₄ in H₂O:CH₃CN(5:1) at 100 °C for 24h. Attempts to further improve the yield by either increasing the concentration of palladium salts or by extending reaction timings were not fruitful.

The generality of the method, 1,3-diynes 2 were synthesized by treating terminal diiodoalkene 1a-d with bistriphenylphosphinepalladium (II) chloride (10 mol %), tetrabutylammoniumhydrogensulphate (1.0 mol), and sodiumcorbonate (5.0 mol) in 5.0 mL of water: acetonitrile (5:1) at 100 °C for 24 h (Scheme 2).

The crude products obtained after work up were purified on a silica gel column using ethyl acetate/hexane to afford 2a-d in 46-81% isolated yields (table 2). To the best of our knowledge literature does not relive any report for the conversion of diiodoalkene to buta-1,3-diyne.

**RESULT AND DISCUSSION**

To establish this reaction method of bisalkynation of E-dioiodoalkenes, we treated terminal (E)-1,2-diodoalkene 1a alone under the above reaction condition, again homo coupled product 1,4-bis(4-tert-butylphenyl)buta-1,3-diyne 2a was formed.

Scheme 1: Reagents and optimal conditions (a) 10 mol % Pd(PPh₃)₂Cl₂, Na₂CO₃, (n-Bu)₄NHSO₄ in H₂O:CH₃CN(5:1) at 100 °C for 24h.

To optimize the reaction condition for improving the yield of buta-1,3-diyne 2a, we carried out this reaction by employing a change in Palladium salts, additives and solvents.

**Table 1. Optimization of reaction conditions for the conversion of 1a to 2a**

<table>
<thead>
<tr>
<th>Entry</th>
<th>Reaction Conditions</th>
<th>Solvent</th>
<th>Time (h)</th>
<th>% Yield (2a)</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>10 mol % Pd(PPh₃)₂Cl₂/(n-Bu)₄NHSO₄ /Na₂CO₃</td>
<td>H₂O:CH₃CN (5:1)</td>
<td>24</td>
<td>65</td>
</tr>
<tr>
<td>2</td>
<td>10 mol % Pd(PPh₃)₂Cl₂/(n-Bu)₄NHSO₄ /K₂CO₃</td>
<td>H₂O:CH₃CN (5:1)</td>
<td>24</td>
<td>63</td>
</tr>
<tr>
<td>3</td>
<td>10 mol % Pd(PPh₃)₂Cl₂/(n-Bu)₄NHSO₄ / Pyridine</td>
<td>H₂O:CH₃CN (5:1)</td>
<td>24</td>
<td>43</td>
</tr>
<tr>
<td>4</td>
<td>10 mol % Pd[(C₆H₅)₂]₃/(n-Bu)₄NHSO₄ /Na₂CO₃</td>
<td>H₂O:CH₃CN (5:1)</td>
<td>45</td>
<td>64</td>
</tr>
<tr>
<td>5</td>
<td>10 mol % Pd(PPh₃)₂Cl₂/(n-Bu)₄NHSO₄ /Na₂CO₃</td>
<td>H₂O:THF (5:1)</td>
<td>48</td>
<td>40</td>
</tr>
<tr>
<td>6</td>
<td>10 mol % Pd(PPh₃)₂Cl₂/(n-Bu)₄NHSO₄ /Na₂CO₃</td>
<td>H₂O:CH₃CN (5:1)</td>
<td>24</td>
<td>68</td>
</tr>
<tr>
<td>7</td>
<td>10 mol % Pd(PPh₃)₂Cl₂/(n-Bu)₄NHSO₄ /Na₂CO₃</td>
<td>H₂O:CH₃CN (7:1)</td>
<td>24</td>
<td>73</td>
</tr>
<tr>
<td>8</td>
<td>10 mol % Pd(PPh₃)₂Cl₂/(n-Bu)₄NHSO₄ /Na₂CO₃</td>
<td>CH₃CN</td>
<td>48</td>
<td>42</td>
</tr>
</tbody>
</table>

The optimal condition that led to the synthesis of 2a in 73% isolated yield (Table 1, entry 7) involved treatment of 1a with 10 mol % Pd(PPh₃)₂Cl₂, Na₂CO₃, (n-Bu)₄NHSO₄ in H₂O:CH₃CN(5:1) at 100 °C for 24h. Attempts to further improve the yield by either increasing the concentration of palladium salts or by extending reaction timings were not fruitful.

The generality of the method, 1,3-diynes 2 were synthesized by treating terminal diiodoalkene 1a-d with bistriphenylphosphinepalladium (II) chloride (10 mol %), tetrabutylammoniumhydrogensulphate (1.0 mol), and sodiumcorbonate (5.0 mol) in 5.0 mL of water: acetonitrile (5:1) at 100 °C for 24 h (Scheme 2).

Scheme 2: Synthesis of Buta-1,3-diynes

**Table 2. Synthesis of Buta-1,3-diynes**

<table>
<thead>
<tr>
<th>Entry</th>
<th>Substrate (1)</th>
<th>Product (2)</th>
<th>Yield (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>2a</td>
<td>3a</td>
<td>73</td>
</tr>
<tr>
<td>2</td>
<td>2b</td>
<td>3b</td>
<td>78</td>
</tr>
<tr>
<td>3</td>
<td>2c</td>
<td>3c</td>
<td>81</td>
</tr>
<tr>
<td>4</td>
<td>2d</td>
<td>3d</td>
<td>46</td>
</tr>
</tbody>
</table>
General procedure for the synthesis of Buta-1,3-diynes(2a-d):
A mixture of E-diiodoalkenes 1a-d (0.2 g, 1.0 eq) in H2O:CH3CN (9:1), Pd(PPh3)2Cl2 (0.2 eq), Na2CO3 (5.0 eq) and (n-Bu)4NHSO4 (1.0 eq) was placed round bottom flask containing a stirring bar. The reaction mixture was heated and stirred at 100 °C for 24h. The reaction mixture was cooled to ambient temperature and extracted with ethylacetate. The solvent was removed in vacuo. The crude product was purified on a silica gel column using ethyl acetate/hexane (v/v 1:9) as eluent to afford 2a-d.

1,4-bis(4-tert-butylphenyl)buta-1,3-diyne (2a):
Yield = 0.104 g (73%), white solid, mp 195-197 °C, [ Li16 mp 195-196 °C] Rf = 0.70 (Hexane) IR (KBr) νmax 3458, 2959, 1716, 1653, 1464, 1397, 1262, 1101, 832, cm−1; 1H NMR (300 MHz, CDCl3) δ = 7.45 (4H, d, J = 8.3 Hz, ArH), 1.31 (18H, s, CH3), 13C NMR (75 MHz, CDCl3) δ = 152.7, 132.4, 125.6, 119.0, 81.6, 73.7, 35.0, 31.2 ppm. mass (ES+) m/z 315.2 (M+ + 1). Anal. Calcd for C24H26: C, 91.67; H, 8.33 Found: C, 91.65; H, 8.34.

CONCLUSION
In conclusion we have developed an efficient approach for the conversion of E-diiodoalkenes into very useful scaffolds buta-1,3-diynes under suzuki reaction conditions.

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REFERENCES AND NOTES