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# Synthesis of (E,E)-2,4-Dienols from (E)-β-Chloro-γ-hydroxyvinylmercurials and Olefins by Palladium(II) Salt

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Reaction of (E)-β-chloro-γ-hydroxyvinylmercurials, prepared by mercuration of propargyl alcohol and 2-methyl-3-butyne-2-ol, with olefins in the presence of a catalytic amount of $Li_2PdCl_4$ and 2 equiv of cupric chloride in methanol at 50°C gave the corresponding (E,E)-2,4-dienols in moderate yields. However, addition of 1 equiv of inorganic bases such as magnesium oxide to the reaction mixture brings a rapid and clean vinylation and gave high yields of the dienols at room temperature. In the case of hindered (E)-2-chloro-3-chloromercuri-2-buten-1,4-diol prepared from 2-butyne-1,4-diol, reaction with olefins gave the dienols only in low yields even in the presence of 2 equiv of magnesium oxide.

## Introduction

The stereo- and regiospecific synthesis of conjugated dienes are of great importance in organic chemistry, as well as in their utilization in other reactions such as Diels-Alder reaction.[1] Vinylation of organometallic compounds with olefins by exchange reaction of palladium could be a promising method for the preparation of conjugated dienes,[2,3] 1,4-dienes[4] and aryl substituted olefins.[5-7]

We have recently reported that the reaction of (E)-1-alkenylboronic acids[8] and highly hindered (E)- or (Z)-β-acetoxyvinylmercurials[9] with olefins in the presence of a catalytic amount of palladium(II) salt and cupric chloride as a reoxidant for the palladium afforded the corresponding various functionalized conjugated dienes stereo- and regiospecifically. We now report the vinylaton of (E)-β-chloro-γ-hydroxyvinylmercurials, readily obtainable by mercuration of propargylic alcohols,[10,11] with several functionalized olefins in the presence of catalytic amount of palladium(II) salt.

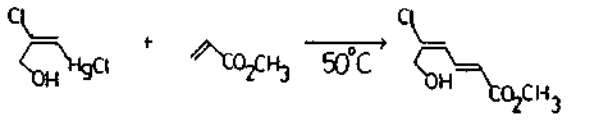
## Results and Discussion

When we attempted to carry out the reaction of (E)-2-chloro-3-chloromercuri-2-propen-1-ol(**1**) with methyl acrylate in the presence of 10 mol % $Li_2PdCl_4$ and 2 equiv of cupric chloride in methanol at room temperature, we failed to obtain the expected (E,E)-2,4-dienol, and the starting vinylmercurial **1** was recovered. However, the reaction carried out at 50°C gave (E,E)-methyl 5-chloro-6-hydroxy-2,4-hexadienoate (**4**) in 65% yield (Table 1). We examined the effect of several different solvents on the rate of vinylation and the yield. Table 1 shows that the more polar solvents give faster reactions and higher yields of the vinylated products.

We reasoned that the failure of the reaction at room temperature might be due to the strong coordination of palladium chloride to the hydroxy group of vinylmercurial so that the reaction was no longer able to give rapid transmetallation with the mercurial moiety.[11] In order to solve this problem we have run the reaction of **1** with methyl acrylate in the presence of several inorganic bases, that were expected to more strongly coordinate with the hydroxy group, freeing the palladium for transmetallation (Table 2). Addition of 1 equiv of the inorganic base to the reaction mixture brought dramatically a rapid and clean vinylation at room temperature and the magnesium oxide bringing the best result.

(E)-2-Chloro-3-chloromercuri-2-propen-1-ol(**1**), (E)-3-chloro-4-chloromercuri-2-methyl-3-buten-2-ol(**2**) and (E)-2-chloro-3-chloromercuri-2-buten-1,4-diol(**3**) were reacted with olefins in the presence of 10 mol % $Li_2PdCl_4$, 2 equiv of cupric chloride and 1 equiv of magnesium oxide in methanol at room temperature. (E,E)-2,4-Dienols were obtained stereospecifically. Results are summarized in Table 3.

**Table 1. Effect of Solvents on Vinylation[a]**




| Solvent | Catalyst | Time,h | Yield[b] |
|---|---|---|---|
| Acetonitrile | $LiPdCl_3$ | 5 | 54 |
| Methanol | $Li_2PdCl_4$ | 5 | 65 |
| THF | $Li_2PdCl_4$ | 10 | 50 |
| Benzene | $PdCl_2$ | 10 | 40 |

[a]3 mmol of (E)-2-chloro-3-chloromercuri-2-propen-1-ol, 3.5 mmol of methyl acrylate, 0.3 mmol of catalyst, 6 mmol of cupric chloride, 50°C, 30 m*l* of solvent. [b]% yield of isolated product.

Table 3 shows that this vinylation is tolerant of a wide variety of reactive functional groups such as ester, nitrile, aldehyde, amide and hydroxy on either the mercurial or olefin reagent. Reaction of **1** with methyl acrylate, styrene and N-cyclohexylacrylamide under the condition described above gave the corresponding (E,E)-2,4-dienols in high yields (**4**,**5** and **8**). Reaction of **1** with acrylonitrile and acrolein also gave the dienols in good yields (**6** and **7**). However, reaction of **1** with 1-hexene gave (E,E)-2-chloro-2,4-nonadienol(**9**) in only 45% yield.

(E)-3-Chloro-4-chloromercuri-2-methyl-3-buten-2-ol(**2**) also reacted well with methyl acrylate to give (E,E)-methyl 5-chloro-6-hydroxy-6-methyl-2,4-heptadienoate(**10**) in 75% yield. A similar result was achieved with acrylonitrile. However, in the case of hindered (E)-2-chloro-3-chloromercuri-2-buten-1,4-diol(**3**), reaction with methyl acrylate in the presence of 2 equiv of magnesium oxide gave only 24% of (E,E)-methyl 5-chloro-6-hydroxy-4-hydroxymethyl-2,4-hexadienoate(**12**) in 48 h. A similar result was obtained with acrylonitrile.

A possible mechanism of this reaction involves sequential (a) transmetallation, (b) addition of vinylpalladium species to the olefinic double bond, and (c) internal elimination, as studied in detail by Heck.[5]

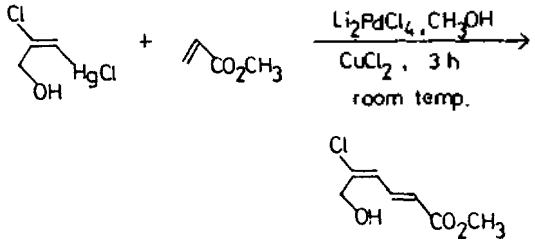
The results obtained here indicate that (E,E)-2,4-dienols can be conveniently prepared from hydroxyvinylmercurials by this procedure (the chlorine is readily removed by reduction with a Zn-Ag couple.[12])

## Experimental

The $^1$H NMR spectra were measured with a Varian Model S-60T spectrometer. Chemical shifts are given in $\delta$ units relative to tetramethylsilane as an internal standard. $^{13}$C NMR spectra were obtained on a Bruker AM-200 SY spectrometer. Infrared spectra were recorded on a Nicolet 5-DX spectrophotometer and the frequences are given in reciprocal centimeters. Mass spectra were recorded on a HP 5985-B mass spectrometer. Analytical thin layer chromatography was performed on precoated silica gel plates (0.2 mm, 60 $F_{254}$, E. Merck) and silica gel (Kieselgel 60, 70–230 mesh, E. Merck) was used for the column chromatography. Melting points were determined on a Fisher-Johns electrothermal melting point apparatus without correction.

**Materials.** Methyl acrylate, acrylonitrile, acrolein (Tokyo Kasei Co.), 1-hexene (Sigma Chemical Co.), styrene, cupric chloride, magnesium oxide, lithium chloride (Junsei Chemical Co.) and palladium chloride (Aldrich Chemical Co.) were commercial products and used without further purification.

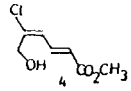
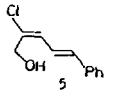
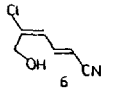
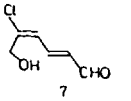
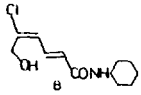
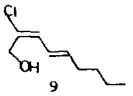
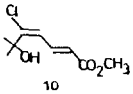
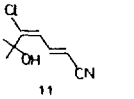
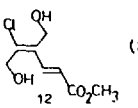
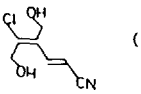
**Table 2. Effect of Added Reagents[a]**




| Reagent | Yield[b] |
|---|---|
| MgO | 95 |
| CaO | 86 |
| $K_2CO_3$ | 87 |
| $NaHCO_3$ | 84 |
| $CH_3ONa$ | 80 |
| $MgSO_4$ | 71 |

[a]3 mmol of (E)-2-chloro-3-chloromercuri-2-propen-1-ol, 3.5 mmol of methyl acrylate, 0.3 mmol of $Li_2PdCl_4$, 6 mmol of cupric chloride, 3 mmol of reagent, room temperature, 30 ml of methanol. [b]% yield of isolated product.

**Table 3. Vinylation of (E)-β-Chloro-γ-hydroxyvinylmercurials with Olefins by Palladium(II) Salt[a]**

| Mercurial | Olefin | Reaction Time, h | Product (% yield of isolated product) |
|---|---|---|---|
|  1 |  | 3 |  4 (95) |
| 1 |  | 5 |  5 (84) |
| 1 |  | 5 |  6 (70) |
| 1 |  | 6 |  7 (59) |
| 1 |  | 12 |  8 (84) |
| 1 |  | 24 |  9 (45) |
|  2 |  | 8 |  10 (75) |
| 2 |  | 24 |  11 (62) |
|  3 |  | 48 |  12 (24)[b] |
| 3 |  | 48 |  13 (13)[b] |

[a]Reactions were carried out in methanol containing 3 mmol of (E)-β-chloro-γ-hydroxyvinylmercurial, 3.5 mmol of olefin, 6 mmol of cupric chloride, 3 mmol of magnesium oxide and 0.3 mmol of $Li_2PdCl_4$ at room temperature. [b]6 mmol of magnesium oxide was used.

Methanol was purified by passage through 4A molecular sieves before use. N-Cyclohexylacrylamide,[13] (E)-2-chloro-3-chloromercuri-2-propen-1-ol(**1**)[10,11], (E)-3-chloro-4-chloromercuri-2-methyl-3-buten-2-ol(**2**)[10,11],(E)-2-chloro-3-chloromercuri-2-buten-1,4-diol(**3**)[10,11] and 0.1 M $Li_2PdCl_4$ in methanol[5] were prepared according to the literature methods.

**General procedure for the preparation of conjugated dienes.** The following procedure for the preparation of (E,E)-methyl 5-chloro-6-hydroxy-2,4-hexadienoate(**4**) is representative.

In a dry 100 m*l* flask equipped with a magnetic bar was placed 0.30 g(3.5 mmol) of methyl acrylate, 0.21 g(3 mmol) of magnesium oxide, 0.80 g(6 mmol) of cupric chloride, 3m*l* of 0.1 M $Li_2PdCl_4$ in methanol and 30 m*l* of methanol. After cooling to 0°C, 0.98 g(3 mmol) of (E)-2-chloro-3-chloromercuri-2-propen-1-ol(**1**) was added to the flask and capped. The reaction mixture was allowed to warm to room temperature and stirred for 3 h. Ether (50 m*l*) and saturated aqueous ammonium chloride (10m*l*) were added to the reaction mixture and filtered. The filtrate was washed with saturated aqueous ammonium chloride and dried over anhydrous magnesium sulfate. After removal of the solvent, the crude product was purified by column chromatography (silica gel, ethyl acetate/n-hexane = 1/2(v/v)). 0.50 g(95%) of pure (E,E)-methyl 5-chloro-6-hydroxy-2,4-hexadienoate(**4**) was obtained. $^1$H NMR($CDCl_3$) $\delta$ 3.22(*bs*,1H), 3.88(*s*,3H), 4.61(*s*,2H), 6.02(*d*,*J*=16Hz,1H), 6.54(*d*,*J*=15Hz,1H), 7.62(*dd*,*J*=12 and 15Hz,1H); $^{13}$C NMR($CDCl_3$) $\delta$ 52.79, 62.71, 123.68, 128.61, 138.13, 144.01, 168.08; IR(KBr) 3300, 1765, 1615, 975 cm$^{-1}$; MS, m/e($M^+$) calcd for $C_7H_9O_3Cl$ 176.5993, found 176.5996; mp 70-71°C.

The conjugated dienes prepared by employing the above procedure are as follows.

(E,E)-2-Chloro-5-phenyl-2,4-pentadienol(**5**): $^1$H NMR($CDCl_3$) $\delta$ 3.28(*bs*,1H), 4.43(*s*,2H), 6.18-7.01(*m*,3H), 7.28(*s*,5H); IR(KBr) 3390, 3010, 1605, 968 cm$^{-1}$; mp 85-87°C.

(E,E)-5-Chloro-6-hydroxy-2,4-hexadienenitrile(**6**): $^1$H NMR($CDCl_3$) $\delta$ 3.42(*bs*,1H), 4.48(*s*,2H), 5.42(*d*,*J*=16Hz,1H), 6.45(*d*,*J*=15Hz,1H), 7.42(*dd*,*J*=12 and 15Hz,1H); IR(neat) 3430, 2220, 1625, 966 cm$^{-1}$.

(E,E)-5-Chloro-6-hydroxy-2,4-hexadienal(**7**): $^1$H NMR($CDCl_3$) $\delta$ 3.32(*bs*,1H), 4.48(*s*,2H), 6.13(*d*,*J*=16Hz,1H), 6.56(*d*,*J*=15Hz,1H), 7.46(*dd*,*J*=11 and 15Hz, 1H), 9.58(*d*,*J*=7Hz,1H); IR(neat) 3395, 1678, 1629, 975 cm$^{-1}$.

(E,E)-N-Cyclohexyl-5-chloro-6-hydroxy-2,4-hexadienamide(**8**): $^1$H NMR($CDCl_3$) $\delta$ 1.02-2.25(*m*,10H), 2.65-2.85(*m*,1H), 3.18(*s*,2H), 4.24(*bs*,1H), 5.83(*d*,*J*=16Hz,1H), 6.18(*bs*,1H), 6.28(*d*,*J*=15Hz,1H), 7.28(*dd*,*J*=11 and 15Hz,1H); IR(KBr) 3284, 1651, 1614, 1545, 974 cm$^{-1}$.

(E,E)-2-Chloro-2,4-nonadienol(**9**): $^1$H NMR($CDCl_3$) $\delta$ 0.82(*bs*,3H), 1.22(*bs*,4H), 2.08(*bs*,2H), 3.26(*bs*,1H), 4.22(*s*,2H), 5.24-5.75(*m*,3H), 6.22(*d*,*J*=16Hz,1H); IR (neat) 3338, 1633, 970 cm$^{-1}$.

(E,E)-Methyl 5-chloro-6-hydroxy-6-methyl-2,4-heptadienoate(**10**): $^1$H NMR($CDCl_3$) $\delta$ 1.52(*s*,6H) 2.78(*bs*,1H), 3.76(*s*,3H), 5.96(*d*,*J*=16Hz,1H), 6.46(*d*,*J*=15Hz,1H), 7.56 (*dd*,*J*=11 and 15Hz,1H); IR(neat) 3475, 1708, 1631, 982 cm$^{-1}$.

(E,E)-5-Chloro-6-hydroxy-6-methyl-2,4-heptadienenitrile(**11**): $^1$H NMR($CDCl_3$) $\delta$ 1.58(*s*,6H), 2.98(*bs*,1H), 5.38(*d*,*J*=16Hz,1H), 6.32(*d*,*J*=15Hz,1H), 7.35(*dd*,*J*=11 and 15Hz,1H); IR(neat) 3489, 2217, 1622, 969 cm$^{-1}$.

(E,E)-Methyl 5-chloro-6-hydroxy-4-hydroxymethyl-2,4-hexadienoate(**12**): $^1$H NMR($CDCl_3$) $\delta$ 3.42(*bs*,2H), 3.68(*s*,3H), 4.43(*s*,4H), 6.21(*d*,*J*=16Hz,1H), 7.58(*d*,*J*=16Hz,1H); IR(neat) 3360, 1787, 1623, 971 cm$^{-1}$.

(E,E)-5-Chloro-6-hydroxy-4-hydroxymethyl-2,4-hexadienenitrile(**13**): $^1$H NMR($CDCl_3$) $\delta$ 3.62(*bs*,2H), 4.38 (*s*,4H), 6.12(*d*,*J*=16Hz,1H), 7.52(*d*,*J*=16Hz,1H); IR(neat) 3410, 2219, 1627, 975 cm$^{-1}$.

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