

## PALLADIUM-CATALYZED COUPLING OF ALLYLIC ACETATES WITH ZINC

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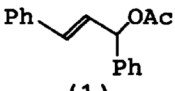
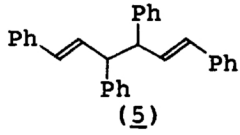
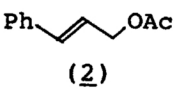
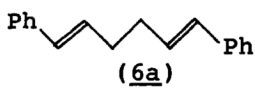
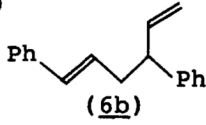
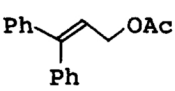
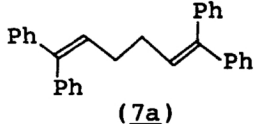
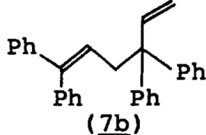
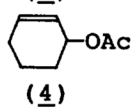
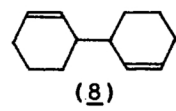
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Allylic acetates were coupled with zinc dust in the presence of a catalytic amount of  $[\text{Pd}(\text{PPh}_3)_4]$  to give the corresponding 1,5-dienes under mild conditions in high yields. Significant co-solvent effects were found with methanol or 1,2-ethanediol in tetrahydrofuran.

Various kinds of methods for the coupling of allylic halides<sup>1-11)</sup> and their derivatives<sup>12)</sup> have been reported to form 1,5-diene system, which is frequently encountered in structures of natural products. However, little has been reported about the coupling reaction of allylic acetates,<sup>13)</sup> which are easier to prepare and to store than allylic halides. Herein we report a very facile method for the reductive coupling of allylic acetates with zinc dust in the presence of a catalytic amount of  $[\text{Pd}(\text{PPh}_3)_4]$  under mild conditions.

In the course of our investigation on the palladium-catalyzed reactions of allylic acetates and sulfones,<sup>14)</sup> we have examined the coupling of allylic halides which seemed to be formed in the reaction of allylic acetates and alkali halides catalyzed by  $[\text{Pd}(\text{PPh}_3)_4]$ .<sup>14d)</sup> Namely, when (E)-3-acetoxy-1,3-diphenyl-1-propene (1) was treated with zinc (3.2 equiv.) and sodium iodide (2.6 equiv.) in the presence of 5 mol% of  $[\text{Pd}(\text{PPh}_3)_4]$  in dimethylformamide (DMF) at room temperature for 3 h under nitrogen, the corresponding coupling product, (1E,5E)-1,3,4,6-tetraphenyl-1,5-hexadiene (5), was formed in 61% yield. As a consequence of a lot of experiments under different conditions, it was found that sodium iodide was not necessary for the coupling. The results of the several coupling reactions of allylic acetates carried out in tetrahydrofuran (THF) in the absence of sodium iodide are summarized in Table 1. It is noteworthy that the stereochemistry was

Table 1.

| Entry | Allylic acetates   | Reaction conditions <sup>a)</sup> | Coupling product  | Yield/%<br>(a : b) <sup>b)</sup>  |                 |
|-------|--|-----------------------------------|---|---|-----------------|
| 1     | <br>(1) | THF, r.t.<br>overnight            | <br>(5) | 85  |                 |
| 2     | <br>(2) | THF, r.t.<br>0.5 h                | <br>(6a) | <br>(6b) | 93<br>(35 : 65) |
| 3     | <br>(3) | THF-MeOH<br>(2-1)<br>r.t., 2 h    | <br>(7a) | <br>(7b) | 83<br>(70 : 30) |
| 4     | <br>(4) | THF, r.t.<br>overnight            | <br>(8) | 70  |                 |

a) 1.8 equiv. of Zn and 5 mol% of [Pd(PPh<sub>3</sub>)<sub>4</sub>] were used.

b) The product ratios were determined by GLPC and 400 MHz <sup>1</sup>H-NMR spectra, respectively.

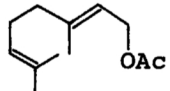
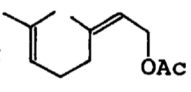
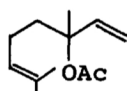
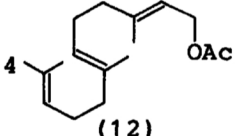
preserved in Entries 1 and 2 and that the use of methanol as co-solvent was essential for the progress of the reaction in the case of Entry 3.

To investigate the stereospecificity and the regioselectivity of the present reaction, the coupling of terpenoid allylic acetates such as geranyl (9), neryl (10), linalyl (11), and farnesyl (12) acetates were then examined as shown in Table 2. The relative proportions of isomers, head-to-tail coupling products (13a,b) and head-to-head ones (14c-e), were determined by GLPC analyses. They were isolated by preparative GLPC and separately identified by spectroscopic methods. The possible tail-to-tail isomers were not detected.<sup>12)</sup>

From the results summarized in Table 2, it was found that the ratios of 13/14 were similar in every case, around 25/75, and the preservation of stereochemistry of the substrates was improved by the use of methanol or 1,2-ethanediol (EG) as a co-solvent in THF. Such co-solvent could also accelerate the reaction except in the case of 11 in which the reaction proceeded fast enough without the co-solvent. The yields of the coupling products were higher in THF-EG than in THF-MeOH. From the fact that the formation of the low-boiling products was observed by GLPC in THF-MeOH, hydrogenolysis might have competed with the coupling.

In the light of these results, optimum conditions for the coupling of terpenoid allylic acetates with zinc in the presence of a catalytic amount of

Table 2. The Coupling Reaction of Terpenoid Allylic Acetates with Zinc

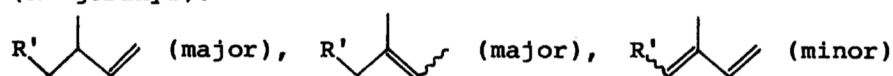
| Entry | Allylic acetate   | Reaction conditions                   | Total Yield/% <sup>a)</sup> | Ratios <sup>a)</sup> |                          |                          |
|-------|---|---------------------------------------|-----------------------------|----------------------|--------------------------|--------------------------|
|       |   |                                       |                             | <u>13</u><br>(a : b) | <u>14</u><br>(c : d : e) |                          |
|       |   | THF, 4 h                              | 78                          | 25                   | : 75                     | (11 : 89) (3 : 21 : 76)  |
| 1     |    | THF-MeOH, 2 h<br>(2-1)                | 59                          | 27                   | : 73                     | (2 : 98) (1 : 10 : 89)   |
|       | ( <u>9</u> )  | THF-EG, <sup>b)</sup> 2 h<br>(10-1)   | 84 (76) <sup>c)</sup>       | 24                   | : 76                     | (4 : 96) (2 : 10 : 88)   |
|       |   | THF, 8 h                              | 85                          | 21                   | : 79                     | (89 : 11) (68 : 27 : 5)  |
| 2     |   | THF-MeOH, 4 h<br>(2-1)                | 54                          | 23                   | : 77                     | (95 : 5) (85 : 13 : 2)   |
|       | ( <u>10</u> )   | THF-EG, <sup>b)</sup> 4 h<br>(10-1)   | 82 (81) <sup>c)</sup>       | 24                   | : 76                     | (94 : 6) (84 : 13 : 3)   |
|       |   | THF, 2 h                              | 83                          | 23                   | : 77                     | (47 : 53) (23 : 51 : 26) |
| 3     |  | THF-MeOH, 2.5 h<br>(2-1)              | 56                          | 26                   | : 74                     | (42 : 58) (19 : 49 : 32) |
|       | ( <u>11</u> )   | THF-EG, <sup>b)</sup> 2.5 h<br>(10-1) | 86 (71) <sup>c)</sup>       | 24                   | : 76                     | (43 : 57) (21 : 50 : 29) |
|       |   | THF, 5 h                              | 69                          | 24                   | : 76                     | (9 : 91) (3 : 19 : 78)   |
| 4     |  | THF-MeOH, 2.5 h<br>(2-1)              | 55 <sup>d)</sup>            | 27                   | : 73                     | (2 : 98) (1 : 10 : 89)   |
|       | ( <u>12</u> )   | THF-EG, <sup>b)</sup> 2.5 h<br>(10-1) | 81                          | 26                   | : 74                     | (3 : 97) (2 : 12 : 86)   |

a) Determined by GLPC [2% OV-17/Chromosorb W (AW-DMCS), 60-80 mesh, 3 m; N<sub>2</sub>, 30 ml/min; 150 °C (Entries 1, 2, and 3), 200 °C (Entry 4)]. 1,2,3,4-Tetrahydronaphthalene was used as an internal standard. R of 13 and 14 exhibits 4-methyl-3-pentenyl or 4,8-dimethyl-3,7-nonadienyl group corresponding to 9-11 and 12, respectively.

b) EG means ethylene glycol (1,2-ethanediol).

c) Isolated yields with preparative TLC were shown in parentheses.

d) The following compounds were isolated as low-boiling by-products by GLPC (R'=geranyl):



[Pd(PPh<sub>3</sub>)<sub>4</sub>] were established as described in the following representative procedure: To a flask containing 118 mg of zinc (1.8 atom) was introduced a solution of 10 (196 mg, 1.00 mmol) in dry THF (2.5 ml) and 1,2-ethanediol (0.4 ml) under nitrogen. After addition of a solution of [Pd(PPh<sub>3</sub>)<sub>4</sub>] (58 mg, 0.05 mmol) in THF (1.5 ml), the mixture was stirred for 4 h at room temperature and then quenched with aqueous KCN solution. Insoluble substances were filtered off and washed well with ethyl acetate and water. After evaporation of organic solvent, the products were extracted with ethyl acetate and dried over Na<sub>2</sub>SO<sub>4</sub>. The residue obtained by evaporation of solvent was separated with a preparative TLC (SiO<sub>2</sub>, hexane) to afford the coupling products (111 mg) consisting of 13a,b and 14c-e (R=4-methyl-3-pentenyl) as a colorless oil in 81% yield.

It is generally assumed that the coupling reaction occurs via radical combination, however, the exact mechanism of the present reaction is still ambiguous.

Further work is in progress to elucidate the scope and limitation and to increase the stereospecificity and the regioselectivity of the above reactions.

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