Novel Synthesis of (Z)-3-Hexen-1-ol and cis-Jasmone

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Both (Z)-3-hexen-1-ol and cis-jasmone were synthesised via 1,4-selective hydrogenation of conjugated dienes in the presence of arene Cr(CO)₃ or Cr(CO)₆ catalysts as the key step.

(Z)-3-Hexen-1-ol (1) is a key component in its characteristic odor of tea leaves and cis-jasmone (2) is known as a key substance in its pleasant odor of jasmine oil. Both compounds, which occur in nature and are very useful in perfumery, have a (Z)-double bond in common. In order to afford these (Z)-double bonds, many synthetic procedures, such as selective hydrogenation of triple bonds,¹ Birch reduction,² Diels-Alder reaction,³ Wittig reaction⁴ and condensation of compounds having a (Z)-double bond,⁵ have been reported.

We report here the novel synthesis of 1 and 2 by 1,4-selective hydrogenation of conjugated dienes.⁶a,⁶b The synthetic routes for 1 and 2 are shown in Figs. 1 and 2.

At first, the synthesis of 1 is described. The preparation of the starting material, 2,4-hexadienal (3), was done by simple aldol condensation of acetaldehyde with crotonaldehyde (molar ratio, 5:1) in the presence of morpholine-aqueous H₃PO₄ catalyst in a 26% yield.⁷ We improved this condensation process to give 3 in a 38% yield by changing the molar ratio to 3:2. The reduction of 3 to the corresponding alcohol (4) was reported using Meerwein-Pondorf reduction with a 64% yield,⁸ but by utilizing the sodium borohydride reduction, we obtained 4 in a 86% yield, which was the key intermediate for 1 and was found to be a mixture of two isomers in a ca. 9 to 1 ratio by GLC (PEG 20M, 2 m x 3 mm). The major alcohol was purified by preparative GLC (PEG 20M, 2 m x 20 mm) and confirmed to be (2E,4E)-2,4-hexadien-1-ol on the basis of PMR spectral data [(CDCl₃) δ: 5.3 ~ 6.4 (4H, m, J₂₋₃ = 16 Hz, J₃₋₄ = 14 Hz, J₄₋₅ = 15 Hz)]. The other minor alcohol, however, could not be separated from the major alcohol, and was supposed to be a (Z)-(E) double bond isomer from the MS data. The resulting dien alcohol (4) was employed for the following selective hydrogenation without further purification.

The selectivity of the 1,4-selective hydrogenation of 4 was examined with various arene ligands of Cr(CO)₃ [4: 0.1 mol, catalyst⁹]: 0.005 mol, MeOH: 25 ml, initial H₂: 50 kg/cm², 190 ~ 200°C/4 hr]. The results are summarized in Table I. No remarkable differences among various arene ligands can be seen in Table I, the specific arene ligands did not seem to have any influence on this hydrogenation.

Thus, commercially available Cr(CO)₆ catalyst instead of arene Cr(CO)₃ catalysts⁶a,⁶b gave the same results for obtaining the desired 1 with high selectivity. Then, we examined the selectivity with various solvents, as summarized in Table II [4: 0.1 mol, Cr(CO)₆: 0.005 mol, MeOH: 25 ml, initial H₂: 50 kg/cm², 190 ~ 200°C/4 hr]. There were no large differences between the solvents, but methanol showed relatively good selectivity. As a result, the key step of selective hydrogenation of 4 was effected with Cr(CO)₆ catalyst in MeOH to give 1 in a 90% yield, the purity of which was more than 98% as judged by GLC analysis (PEG 20M, 2 m x 3 mm). Physical data of syn-
thetic I were entirely identical with those of an authentic sample from 3-hexyn-1-ol.

Next, the synthesis of 2 was examined. By the usual method, a mixture of two isomers (4) was treated with PBr₃ in the presence of pyridine at \(-10\sim0\)°C to give diene bromide (5) as a sole product in a 60% yield, which was confirmed to be a (2E,4E)-isomer by the PMR spectral data [(CCl₄) δ: 4.9\sim6.7 (4H, m, J₂⁻₃=16 Hz, J₃⁻₄=14 Hz, J₄⁻₅=15 Hz)]. Compound 5 was employed to introduce the side chain to the C₅-position of 2-methylfuran. Thus the condensation of 5 with 2-lithio-5-methylfuran, derived from 2-methylfuran and BuLi at \(-20\)°C, gave (2E,4E)-hexadienylfuran (6) in a 64% yield, which was the key intermediate for our synthesis of 2.

The structure of 6 was supported by physical data. The selective hydrogenation of 6 with Cr(CO)₆ in MeOH (initial H₂: 50 kg/cm², 190 \sim 200°C/2 hr) gave (Z)-hexenylfuran (7) in a 76% yield, which was contaminated with 2% Table I. Hydrogenation of 2,4-Hexadien-1-ol with Arene Cr(CO)₃ or Cr(CO)₆ Catalysts

<table>
<thead>
<tr>
<th>Arene ligand in catalyst</th>
<th>2,4-Hexadien-1-ol</th>
<th>(Z)-3-Hexen-1-ol</th>
<th>(E)-3-Hexen-1-ol</th>
<th>4-Hexen-1-ol</th>
<th>Hexanol</th>
</tr>
</thead>
<tbody>
<tr>
<td>Methyl benzoate</td>
<td>0.0</td>
<td>92.5</td>
<td>4.6</td>
<td>2.3</td>
<td>0.6</td>
</tr>
<tr>
<td>Anisole</td>
<td>0.0</td>
<td>95.0</td>
<td>3.3</td>
<td>1.4</td>
<td>0.3</td>
</tr>
<tr>
<td>Cycloheptatriene</td>
<td>0.0</td>
<td>95.7</td>
<td>2.4</td>
<td>1.9</td>
<td>0.0</td>
</tr>
<tr>
<td>Durene</td>
<td>0.0</td>
<td>96.0</td>
<td>2.4</td>
<td>1.6</td>
<td>0.0</td>
</tr>
<tr>
<td>Cr(CO)₆</td>
<td>3.6</td>
<td>95.1</td>
<td>1.1</td>
<td>0.0</td>
<td>0.1</td>
</tr>
</tbody>
</table>

Table II. Hydrogenation of 2,4-Hexadien-1-ol with Cr(CO)₆ Catalyst in Different Solvents

<table>
<thead>
<tr>
<th>Solvent</th>
<th>2,4-Hexadien-1-ol</th>
<th>(Z)-3-Hexen-1-ol</th>
<th>(E)-3-Hexen-1-ol</th>
<th>4-Hexen-1-ol</th>
<th>Hexanol</th>
</tr>
</thead>
<tbody>
<tr>
<td>Cyclohexane</td>
<td>4.8</td>
<td>87.2</td>
<td>3.6</td>
<td>2.5</td>
<td>1.9</td>
</tr>
<tr>
<td>Benzene</td>
<td>4.3</td>
<td>90.4</td>
<td>3.6</td>
<td>1.4</td>
<td>0.3</td>
</tr>
<tr>
<td>Tetrahydrofuran</td>
<td>4.0</td>
<td>90.3</td>
<td>1.8</td>
<td>1.8</td>
<td>3.1</td>
</tr>
<tr>
<td>Acetone</td>
<td>2.9</td>
<td>88.9</td>
<td>2.0</td>
<td>4.7</td>
<td>1.5</td>
</tr>
<tr>
<td>Methanol</td>
<td>3.6</td>
<td>95.1</td>
<td>1.1</td>
<td>0.0</td>
<td>0.1</td>
</tr>
<tr>
<td>Butylamine</td>
<td>12.4</td>
<td>82.6</td>
<td>2.8</td>
<td>2.2</td>
<td>0.0</td>
</tr>
<tr>
<td>Acetonitrile</td>
<td>2.3</td>
<td>93.8</td>
<td>1.5</td>
<td>1.4</td>
<td>1.0</td>
</tr>
</tbody>
</table>
of 2-hexyl-5-methylfuran. Physical data of the resulting 7 were completely identical with those reported. 5) Finally, cis-jasmone (2) was synthesized from 7 via a dione (8) in a 70% overall yield in the same manner as reported. 5)

**EXPERIMENTAL**

All bps were uncorrected. IR spectra were determined on a JASCO IRA-2 spectrometer. PMR spectra were recorded at 60 MHz with TMS as an internal standard on a Hitachi R-24A spectrometer. MS spectra were obtained on a Hitachi RMU 6E spectrometer. GLC analyses were performed on a Hitachi 063 gas chromatograph.

2,4-**Hexadienial** (3). A mixture of 80% eq. acetaldehyde (495 g) and 90% eq. crotonaldehyde (467 g) in the presence of 50% morpholine-aq H3PO4 (molar ratio 3:1, 24 g) was heated at 90~95°C for 1 hr in an autoclave (2 liters). The reaction mixture was cooled and saturated with NaCl. The organic layer was separated and dried over MgSO4. After removal of the crotonaldehyde (408 g), the residue was distilled to give 3 (114 g, 38% based on the recovery of crotonaldehyde): bp 75~76°C/30 mmHg; IR νmax cm⁻¹: 1680, 1640, 1600; PMR (CDCl3) δ : 1.89 (3H, d, J = 4.2 Hz), 5.8~7.3 (4H, m); MS m/z: 96 (M⁺, 31%), 81 (100), 67 (41), 53 (46), 41 (63), 39 (76).

2,4-**Hexadien-1-ol** (4). To a stirred suspension of NaBH4 (11.0 g) in water (300 ml) was added dropwise 3 (96.0 g) over 1 hr at room temperature and then the stirring was continued for 2 hr. The mixture was extracted with ether and the extract was washed with brine and dried over MgSO4. After removal of the solvent, the residue was distilled to give a mixture of (2E,4E)-4 and (2Z,4E) or (2Z,4Z)-4: IR νmax cm⁻¹: 3350, 1660, 1640, 1440, 1220, 990, 780; PMR (CDCl3) δ: 0.95 (3H, t, J = 7.6 Hz), 1.80~2.45 (4H, m), 3.59 (2H, t, J = 6.8 Hz), 5.08~5.73 (2H, m); MS m/z: 100 (M⁺, 6%), 82 (32), 69 (27), 67 (64), 55 (37), 41 (100), 31 (35). These data of synthetic 1 are completely identical with those of an authentic sample.

b) In the same manner, a solution of 4 (9.8 g) in MeOH (25 ml) was hydrogenated in the presence of (Durene) Cr(CO)3, prepared9) from durene (50 g) and Cr(CO)6 (5.0 g), under H2 (initial, 50 kg/cm²) at 190~200°C for 4 hr in an autoclave (100 ml). The cooled mixture was filtered and concentrated. The residue was shown to be a mixture of 1 (96.0%), (E)-3-hexen-1-ol (2.4%) and 4-hexen-1-ol (1.6%) by GLC (PEG 20M, 2 m x 3 mm; column temperature, 150°C; carrier gas, N2, 40 ml/min; tR: 5 min 50 sec, 5 min 20 sec and 6 min 20 sec) and MS analysis.

(2E,4E)-1-Bromo-2,4-hexadiene (5). To a stirred solution of 4 (19.6 g) and pyridine (16.6 g) in hexane (40 ml) was added dropwise PBr3 (19.0 g) over 1 hr at −10~0°C and the mixture was stirred at 0°C for 2 hr. The reaction mixture was poured into ice-water and extracted with hexane. The extract was washed with brine, dried over MgSO4 and concentrated. The residue was distilled to give 5 (19.7 g, 60%): bp 37~39°C/5 mmHg; IR νmax cm⁻¹: 3350, 1660, 1600, 1440, 1220, 990, 780; PMR (CDCl3) δ: 1.80 (3H, d, J = 6.0 Hz), 3.98 (2H, d, J = 7.2 Hz), 4.9~6.7 (4H, m), 5.74 (2H, s), 4.6~6.8 (4H, m); MS m/z: 162 (M⁺, 6%), 160 (M⁺, 61), 81 (100), 79 (35), 66 (13), 53 (35), 41 (49), 39 (31).

2-[2(E,4E)-5-Methylfuran-2-yl]-2,4-hexadienyl-5-methylfuran (6). To a solution of 2-methylfuran (10.1 g) in dry THF (50 ml) was added dropwise BuLi (10.8 g) over 1 hr at −20°C under Ar. The mixture was stirred for 1 hr. To this was added dropwise a solution of 5 (19.4 g) in dry THF (20 ml) over 30 min at −20~−10°C and then the stirring was continued for 2 hr. After stirring at room temperature for a further 15 hr, the mixture was poured into NH4Cl solution and extracted with ether. The extract was washed with brine, dried over MgSO4 and concentrated. The residue was distilled to give 6 (12.4 g, 64%): bp 71~73°C/4 mmHg; IR νmax cm⁻¹: 1650, 1570, 1220, 990, 780; PMR (CDCl3) δ: 1.72 (3H, d, J = 6.0 Hz), 2.20 (3H, s), 3.26 (2H, d, J = 6.4 Hz), 5.74 (2H, s), 4.6~6.8 (4H, m); MS m/z: 162 (M⁺, 37%), 147 (27), 129 (17), 119 (29), 95 (34), 91 (34), 43 (100), 41 (37).

2-[2(Z)-5-Methylfuran-2-yl]-2,4-hexadienyl-5-methylfuran (7). A solution of 6 (11.4 g) in MeOH (30 ml) was hydrogenated in the presence of Cr(CO)6 (0.8 g) under H2 (initial, 50 kg/cm²) at 190~200°C for 2 hr in an autoclave (100 ml). The cooled mixture was filtered and concentrated. The residue was distilled to give 7 (8.7 g, 76%) containing 2-hexyl-5-methylfuran (20%) by GC-MS analysis: bp 66~68°C/4 mmHg; IR νmax cm⁻¹: 3100, 3000, 2950, 2910, 2860, 1650,
cis-Jasmone (2). By the same procedure as described by Büchi et al., 7 (8.2 g) was converted to 2 (5.7 g, 70%): bp 74~75°C/2 mmHg; IR νmax cm⁻¹: 1700, 1645, 1440, 1385, 1340, 1300, 1180, 1070. PMR (CDCl₃) δ: 0.98 (3H, t, J = 7.0 Hz), 2.06 (3H, s), 2.85 (2H, d, J = 5.5 Hz), 4.92~5.52 (2H, m). MS m/z: 164 (M⁺, 60%), 149 (42), 135 (39), 122 (44), 110 (58), 93 (46), 91 (46), 79 (77), 55 (84), 41 (100), 39 (79). These data of synthetic 2 are completely identical with those of an authentic sample.

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REFERENCES

    b) A. Miyake and H. Kondo, Angew. Chem., 80, 663 (1968).