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# Abnormal and regioselective Wacker oxidation of 1,5-dienes

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**Abstract**—The presence of an additional double bond can change the regioselectivity of the Wacker oxidation of a 1-alkene moiety to give the aldehyde product.

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The Wacker oxidation<sup>1</sup> of 1-alkenes (except ethene) leads selectively to methyl ketones.<sup>2</sup> We were interested in reversing this regioselectivity which seems to originate from palladiohydroxylation of the alkenes in the Markovnikov sense to afford organometallic species that subsequently undergo dehydropalladation.<sup>3</sup> Reversal of the regioselectivity has been observed in alkene systems by means of heteroatoms<sup>4–7</sup> which probably coordinate with palladium intermediates. In our study we considered  $\pi$ -complexation instead of the previously known participation of n-donors. Here we report the successful intervention in cases of certain dienes.

Diene **1a** was prepared from *p*-methylisobutyrophenone by allylation, Grignard reaction with MeMgI and dehydration (KHSO<sub>4</sub>), whereas **1b** was obtained from methyl 2,2-dimethyl-4-pentenoate, also by Grignard reaction and dehydration. To procure **1c** starting from 2,2-dimethyl-4-pentalenal the Grignard reaction, PCC oxidation and Wittig reaction sequence was employed. When submitted to conventional Wacker oxidation conditions (PdCl<sub>2</sub>, CuCl, O<sub>2</sub>, DMF–H<sub>2</sub>O) only the aldehydes **2a**, **2b**, and **2c** were generated in 73, 99, and 75% yields, respectively. We have not been able to detect any methyl ketones by NMR spectroscopy. Analogously, diene **3** also followed the same reaction pattern, furnishing **4** in 60% yield. Contrarily, alkenol **5** gave a normal product **6** which was shown to be a tautomeric mixture of the methyl ketone and the cyclic lactol.

In our opinion, the formation of **2a**, **2b**, **2c**, and **4** may be due to participation of the disubstituted double bond, such that unsymmetrical intermediates **A** appeared and then captured by water. The next inter-

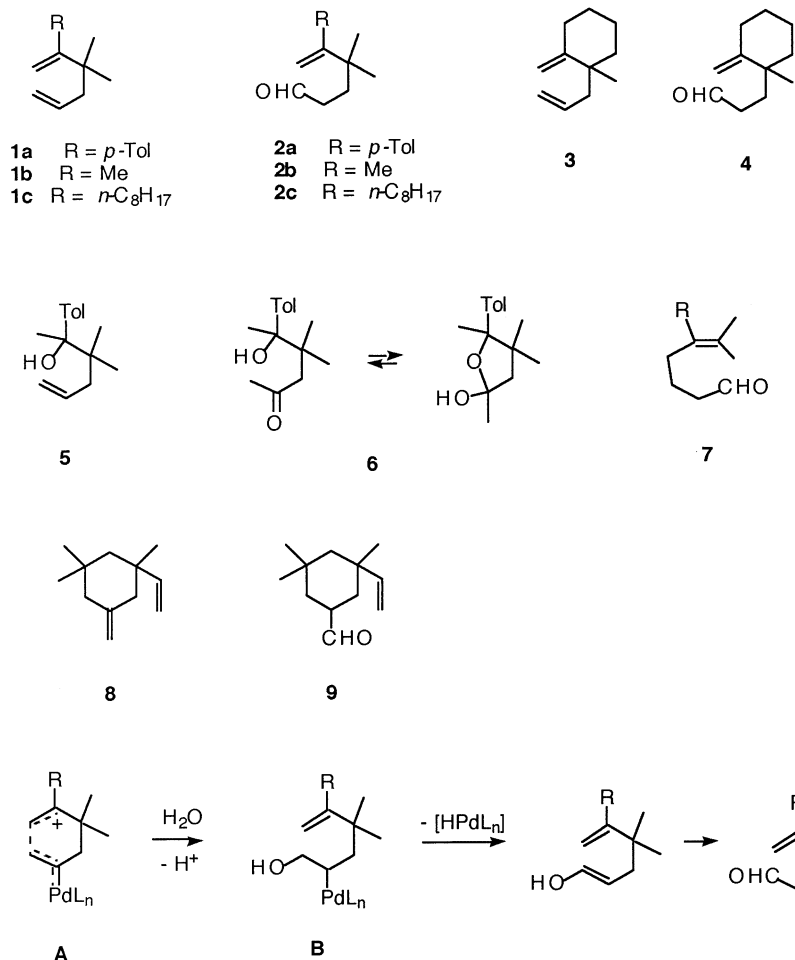
mediates **B** then underwent elimination of the [H–PdL<sub>n</sub>] species. In normal circumstances the  $\pi$ -complexes of Pd are attacked in the alternative manner, resulting in palladiohydroxylation according to the Markovnikov Rule. It should be noted that **A** has a similar structure as that proposed for the Pd-catalyzed Cope rearrangement.<sup>8</sup> The major difference in its fate is perhaps the crucial presence of water that tends to intercept it. On the other hand, in the reaction of **5** a 5-*exo-trig* process was involved.

Diene **8** is a structural variant of **3**. The intermediate involving both double bonds resembles necessarily a bridged-ring system wherein the complexed double bonds are axially oriented. We observed the formation of an aldehyde from reaction at the methylene moiety, albeit **9** was isolated in only 19% yield. The result was due to partial decomposition during chromatographic purification and also probably reflects a higher strain and therefore less favorable reaction. Absence of oxidation at the vinyl substituent may also indicate the importance of steric factors. Interestingly, the active Wacker oxidation catalyst is supposed to be a polymeric Pd–Cu–DMF complex with a Pd:Cu stoichiometry of 2:1, in which the two different metal centers are linked by a chlorine atom (apical to Cu), while the Cu center is also coordinated by four DMF molecules.<sup>9</sup>

We also believed that the  $\pi$ -participation did not turn into a  $\sigma$ -bonding event. Otherwise aldehydes with a tetrasubstituted double bond (e.g. **7**) would have appeared. This latter scenario is dominant in the Pd-mediated Cope rearrangement.<sup>8</sup>

In conclusion, we have observed a change in the regioselectivity in the polar addition of 1-alkenes from the Markovnikov sense to an anti-Markovnikov fash-

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ion, when another double bond is judiciously placed in the same molecule. The through-space interaction<sup>10</sup> of two double bonds seems unique for such a phenomenon. On the other hand, *n*-donors actually accentuate the normal course of addition as shown in the case of **5**. A previous observation that an acrylamide underwent transformation into the  $\beta,\beta$ -dimethoxypropanamide derivative<sup>11</sup> is electronically biased, therefore quite different from that of ours. The unusual behavior of certain *N*-acyllallyl amines has been attributed to the coordination of palladium atom by the carbonyl group which led to the formation of *N*-acylaminopropanals.<sup>12</sup>

A representative example of the Wacker oxidation follows: Preparation of **2a**: A mixture of **1a** (0.42 g, 2.1 mmol), PdCl<sub>2</sub> (0.08 g, 1.1 mmol), and CuCl (0.21 g, 2.1 mmol) in DMF (1 mL) and water (0.1 mL) was stirred under an oxygen atmosphere for 24 h at room temperature. It was diluted with dichloromethane, washed with water, dried over anhydrous Na<sub>2</sub>SO<sub>4</sub>, and concentrated in a rotary evaporator. The residual oil was chromatographed over silica gel [eluent:hexane:AcOEt 10:1] to afford **2a** (0.33 g, 72.8%).  $\nu$  (C=O) 1725 cm<sup>-1</sup>. <sup>1</sup>H NMR (300 MHz, CDCl<sub>3</sub>)  $\delta$  0.99 (s, 6H), 1.56 (t, *J*=7.0 Hz, 2H), 2.20 (s, 3H), 2.33 (t, *J*=7.0 Hz, 2H), 4.78 (s, 1H), 5.01 (s, 1H), 6.86 (d, *J*=8.1 Hz, 2H), 6.94 (d, *J*=8.1 Hz, 2H), 9.59 (br s, 1H). <sup>13</sup>C NMR (75 MHz,

CDCl<sub>3</sub>)  $\delta$  20.8 (q), 27.4 (q), 32.1 (t), 38.5 (s), 39.8 (t), 114.0 (t), 128.0 (d), 128.3 (d), 135.7 (s), 139.6 (s), 156.4 (s), 201.5 (d). HRMS *m/z* 216.1517 (calcd for C<sub>15</sub>H<sub>20</sub>O 216.1515).

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