## TITANIUM-MEDIATED SYNTHESIS OF CONJUGATED DIENES

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Abstract: Titanacyclobutenes, readily prepared from  $Cp_2TiCH_2$ ·Al(CH<sub>3</sub>)<sub>2</sub>Cl and alkynes, react with ketones and aldehydes to afford metallacyclic products resulting from insertion into either the titanium-alkyl or the titanium-vinyl bond of the titanacyclobutene. The latter insertion products are thermally unstable, undergoing facile retro [4+2] cycloaddition to afford substituted 1,3-dienes in good yield.

Despite their great synthetic importance, there are comparatively few good routes for the general synthesis of conjugated dienes. Reported procedures for the preparation of many dienes produce complex mixtures of difficultly separable isomers. Even simple dienes such as 2,3-diphenylbutadiene, for example, are notoriously difficult to prepare.<sup>1</sup> Herein we present a simple, titanium-mediated procedure for the stereoselective synthesis of conjugated dienes.

We recently reported unprecedented reactions of titanacyclobutenes, in which nitriles preferentially insert first into the titanium-vinyl bond of the titanacycle, then into the titanium-alkyl bond.<sup>2</sup> As we now report, ketones and aldehydes undergo analogous preferential insertions into the titanium-vinyl bond of titanacyclobutenes. This insertion is followed not by a second insertion, as observed for the nitrile reactions, but rather by facile thermal decomposition of the metallacyclic insertion product, apparently via a retro [4+2] reaction, to afford conjugated dienes in synthetically useful yields.

The dimethyltitanacyclobutene, 1, is readily preparable from  $Cp_2TiCH_2$  Al(CH<sub>3</sub>)<sub>2</sub>Cl ("Tebbe's reagent"<sup>3</sup>) and 2-butyne.<sup>4</sup> Addition of 1 equiv of acetaldehyde to a benzene solution of 1 yields complex 2, the result of insertion of the aldehyde into the titanium-vinyl bond of 1. This insertion regiochemistry, although perhaps astonishing in light of a priori expectations of the reactivity of metal-alkyl vs. metal-vinyl bonds,<sup>5</sup> appears to be intrinsically favored in the titanacyclobutenes, as we have discussed for analogous nitrile insertion chemistry.<sup>2</sup> Complex 2 decomposes over the course of several hours at room temperature or rapidly at 60°C to form a yellow precipitate of  $[Cp_2TiO]_n$ . The organic product of this decomposition, E-2,3-dimethyl-1,3-pentadiene,<sup>6</sup> is obtained as a benzene solution in 69% yield by simple vacuum transfer from the reaction mixture.<sup>7</sup>



Similar results are obtained in reactions of 1 with 2,2-dimethylpropanal and with acetone, although in these cases, formation of complexes 3a and 3b is accompanied by formation of isomeric titanacyclic products, 4a and 4b, resulting from insertion into the titanium-alkyl bond of 1. Gentle thermolysis of these reaction mixtures decomposes 3a and 3b, affording E-2,3,5,5-tetramethyl-1,3-hexadiene and 2,3,4-trimethyl-1,3-pentadiene,

respectively. The E-stereochemistry of the former product is established by its facile reaction with maleic anhydride in benzene at 100°C to form a single Diels-Alder adduct; the Z-isomer, unable to achieve the requisite scis conformation, should be completely unreactive toward dienophiles.<sup>8</sup>



Titanacyclobutenes were reported previously by Grubbs and Meinhart to react with ketones and aldehydes via insertion into the titanium-*alkyl* bond, producing intermediate titanacycles analogous to **4a** and **4b**.<sup>9</sup> Protonolysis of these titanacyclic products was suggested to provide a useful synthetic route to homoallylic alcohols. Formation of these alkyl insertion products constitutes an undesirable side reaction in our diene synthesis. As we have previously noted,<sup>2</sup> titanium-*vinyl* bond insertion appears to be exquisitely sensitive to steric effects. By the judicious choice of reacting titanacycle and substrate, we are able to minimize the formation of the undesired alkyl insertion products, thereby maximizing the yields of conjugated dienes obtained via the thermal decomposition of the vinyl insertion products.

The stereoselectivity of the decompositions of the aldehyde insertion products, 2 and 3a, with only the Ediene produced, suggests that these may be concerted retro [4+2] cycloadditions, with diene stereochemistry determined by either orbital symmetry or simple steric considerations, although we have not carried out the mechanistic studies required to confirm this. Complexes 4a and 4b do not have a similar electrocyclic reaction path available to them, and are stable to the reaction conditions.



This reaction chemistry may be extended to other titanacyclobutenes as well. Thus, the diethyl analog, prepared from Tebbe's reagent and 3-hexyne,<sup>4</sup> reacts with acetaldehyde to give only the titanium-vinyl insertion product, which decomposes to give 2,3-diethyl-1,3-pentadiene in 80% yield (Table 1). 2,2-Dimethylpropanal and acetone give mixtures of the isomeric insertion products with this titanacyclobutene (Table 1). Consistent with our studies in the nitrile series,<sup>2</sup> titanium-alkyl insertion is more significant for this complex than in the case of the sterically less encumbered dimethyl titanacycle.

Table 1. Alkyl insertion product and diene yields for reactions of titanacyclobutenes with ketones and aldehydes.

\_ <sup>¶</sup> [ <sup>P</sup>]

с	P₂TI → R	+ R: R"			$\left[\begin{array}{c} & & \\ & &$	
entry	R	R'	R''	Ti-alkyl	diene yield	High res MS
				insertion (%) <sup>a</sup>	(%) <sup>a</sup>	Found (Calcd)
1	CH <sub>3</sub>	CH <sub>3</sub>	Н	< 2	> 98 <sup>b</sup>	-
2		(CH <sub>3</sub> ) <sub>3</sub> C	Н	10	90 <sup>b</sup>	138.1396 (138.1408) <sup>d</sup>
3		CH <sub>3</sub>	CH <sub>3</sub>	34	66	
4	CH <sub>3</sub> CH <sub>2</sub>	CH <sub>3</sub>	Н	< 2	> 98 <sup>b</sup>	124.1247 (124.1252) <sup>d</sup>
5		(CH <sub>3</sub> ) <sub>3</sub> C	Н	30	70	166.1719 (166.1721) <sup>d</sup>
6		CH <sub>3</sub>	CH <sub>3</sub>	45	55 <sup>b</sup>	-
7	C <sub>6</sub> H <sub>5</sub>	Н	Н	25	75 <sup>c</sup>	206.1093 (206.1095) <sup>d</sup>
8		CH <sub>3</sub>	Н	50	50 <sup>c</sup>	220.1254 (220.1252) <sup>d</sup>
9		C <sub>6</sub> H <sub>5</sub>	Н	60	40	-
10		(CH <sub>3</sub> ) <sub>3</sub> C	H	> 98	< 2	456.1917 (456.1932) <sup>e</sup>
11		CH <sub>3</sub>	CH <sub>3</sub>	> 98	< 2	428.1615 (428.1619) <sup>e</sup>
12		CH <sub>3</sub> CH <sub>2</sub>	CH <sub>3</sub> CH <sub>2</sub>	> 98	< 2	456.1921 (456.1932) <sup>e</sup>
13		C <sub>6</sub> H <sub>5</sub>	CH <sub>3</sub>	> 98	< 2	490.1792 (490.1776) <sup>e</sup>
14		C <sub>6</sub> H <sub>5</sub>	C <sub>6</sub> H <sub>5</sub>	> 98	< 2	552.1955 (552.1932) <sup>e</sup>

a. Yields by <sup>1</sup>H NMR integration relative to residual  $C_6D_5H$  solvent peak; b. Unoptimized yields of dienes as solutions in  $C_6D_6$ : entry 1: 69%; entry 2: 53%; entry 4: 80%; entry 6: 35%; c. Unoptimized isolated yield: entry 7: 50%; entry 8: 36%; d. MS of diene product; e. MS of Ti-alkyl insertion product.

The diphenyl analog of titanacyclobutene 1 reacts with formaldehyde to provide a 3:1 mixture of 2,3diphenylbutadiene and the titanium-alkyl insertion product, from which the 2,3-diphenylbutadiene may be isolated by filtration through a short column of silica gel.<sup>10</sup> Acetaldehyde provides a 50:50 mixture of E-2,3diphenylpentadiene and the alkyl insertion product,<sup>11</sup> while benzaldehyde gives a 40:60 mixture. Bulkier aldehydes, such as 2,2-dimethylpropanal, and all ketones examined give only the metal-alkyl insertion products with the diphenyltitanacyclobutene. The results of all these studies are summarized in Table 1.

This procedure provides a simple synthesis of many difficultly accessible dienes from simple alkynes and ketones or aldehydes, and would appear to be quite general as long as very hindered substrates are avoided. We are continuing to study both the scope of this diene synthesis and the unusual selectivity of the insertion reactions, favoring metal-vinyl over metal-alkyl insertion in all but the most hindered cases.

## **References and Notes**

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- 5) Tanke, R. S.; Crabtree, R. H. Inorg. Chem. 1989, 28, 3444-7.
- 6) Stereochemistry assigned by spectral and reaction analogy with the E-2,3,5,5-tetramethyl-1,3-hexadiene obtained from thermolysis of 3a (vide infra). The synthesis of 2,3-dimethyl-1,3-pentadiene has been reported.<sup>A</sup> Frey, H. M.; Lamont, A. M.; Walsh, R. J. Chem. Soc. A 1971, 2642-6, Nazarov, I. N.; Mavrov, M. V. J. Gen. Chem. USSR 1959, 29, 1130-8. Other syntheses of this diene give inseparable mixtures of isomeric products: Titoya, L. F.; Fel'dylyum, V. Sh.; Moskvin, A. F.; Loshchilova, V. D.; Pankov, A. G. Neftekhimiya 1966, 6, 854-8 (Chem. Abstr. 1967, 66:85381k), Arai, A.; Ichikizaki, I. Bull. Chem. Soc. Jpn. 1962, 35, 45-51; Matida, S. J. Chem. Soc. Jpn. 1941, 62, 293-7 (Chem. Abstr. 1949, 37:4363<sup>7</sup>).
- 7) Less volatile dienes may be obtained in pure form by simple evaporation of solvent. Volatile dienes were isolated as solutions in benzene or toluene.
- 8) See, e.g., Craig, D.; Shipman, J. J.; Fowler, R. B. J. Am. Chem. Soc. 1961, 83, 2885-91.
- 9) Meinhart, J. D.; Grubbs, R. H. Bull. Chem. Soc. Jpn. 1988, 61, 171-80.
- 10) To a solution of 1.004 g diphenyltitanacyclobutene (2.71 mmol) in 10 mL toluene under nitrogen was added solid paraformaldehyde (0.265 g, 8.82 mmol, 3.2 equiv). The mixture was heated on a steam bath for 2.25 h, then cooled, reduced in volume to ca. 5 mL, and chromatographed in air through a 5" silica column, eluting with toluene. 2,3-Diphenylbutadiene (0.281 g, 1.36 mmol, 50.3%) eluted at the solvent front. <sup>1</sup>H NMR (C<sub>6</sub>D<sub>6</sub>): δ 5.287 (d, 2H, =CH), 5.439 (d, 2H, =CH), 6.85-7.10 (m, 10H, ArH); <sup>13</sup>C NMR (C<sub>6</sub>D<sub>6</sub>): δ 116.35 (=CH<sub>2</sub>), 127.78 (Ar), 127.82 (Ar), 128.48 (Ar), 140.54 (C=CH<sub>2</sub>), 150.40 (Ar). High resolution MS: Calcd for C<sub>16</sub>H<sub>14</sub>: 206.1095. Found: 206.1093.
- 11) Vinyl insertion product: <sup>1</sup>H NMR (C<sub>6</sub>D<sub>6</sub>):  $\delta$  1.15 (d, 3H, <sup>3</sup>J<sub>HH</sub> = 6.0 Hz, CH<sub>3</sub>), 1.42 (d, 1H, <sup>2</sup>J<sub>HH</sub> = 9.9 Hz, half of CH<sub>2</sub>), 4.41 (dd, 1H, <sup>2</sup>J<sub>HH</sub> = 9.9 Hz, <sup>5</sup>J<sub>HH</sub> = 4.0 Hz, half of CH<sub>2</sub>), 5.64 (m, 1H, <sup>3</sup>J<sub>HH</sub> = 6.0 Hz, <sup>5</sup>J<sub>HH</sub> = 4.0 Hz, CH), 5.828 (s, 5H, Cp), 5.833 (s, 5H, Cp), 7.03-7.28 (m, 10H, ArH); <sup>13</sup>C NMR (C<sub>6</sub>D<sub>6</sub>):  $\delta$  22.5 (CH<sub>3</sub>), 59.4 (CH<sub>2</sub>), 88.0 (C-O), 111.3 (Cp), 113.6 (Cp), 125.6 (Ar), 126.1 (Ar), 127.8 (Ar), 130.0 (Ar), 130.5 (Ar), 143.1 (Ar), 144.6 (Ar), 146.1 (CH<sub>2</sub>-C=<u>C</u>), 148.3 (CH<sub>2</sub>-<u>C</u>=C); one Ar not resolved. Alkyl insertion product: <sup>1</sup>H NMR (C<sub>6</sub>D<sub>6</sub>):  $\delta$  1.06 (d, 3H, <sup>3</sup>J<sub>HH</sub> = 6.0 Hz, CH<sub>3</sub>), 2.62 (dd, 1H, <sup>2</sup>J<sub>HH</sub> = 16.5 Hz, <sup>3</sup>J<sub>HH</sub> = 9.3 Hz, half of CH<sub>2</sub>), 2.71 (dd, 1H, <sup>2</sup>J<sub>HH</sub> = 16.5 Hz, <sup>3</sup>J<sub>HH</sub> = 3.2 Hz, half of CH<sub>2</sub>), 4.47-4.53 (m, 1H, <sup>3</sup>J<sub>HH</sub> = 9.3 Hz, <sup>3</sup>J<sub>HH</sub> = 6.0 Hz, <sup>3</sup>J<sub>HH</sub> = 3.2 Hz, CH), 5.59 (s, 5H, Cp), 5.98 (s, 5H, Cp), 6.88-7.40 (m, 10H, ArH); <sup>13</sup>C NMR (C<sub>6</sub>D<sub>6</sub>):  $\delta$  23.8 (CH<sub>3</sub>), 55.9 (CH<sub>2</sub>), 83.2 (C-O), 113.5 (Cp), 114.1 (Cp), 123.0 (Ar), 124.8 (Ar), 127.5 (Ar), 127.8 (Ar), 128.3 (Ar) 130.0 (Ar), 136.1 (Ti-C=<u>C</u>), 146.7 (Ar), 153.2 (Ar), 191.1 (Ti-<u>C</u>=C).

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