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Facile Formation of Unexpected [m,6,n]-tricyclic Spiranes *via* Intramolecular [3+2] Cyclization of Platinum-bound Pyrylium with Alkenes†

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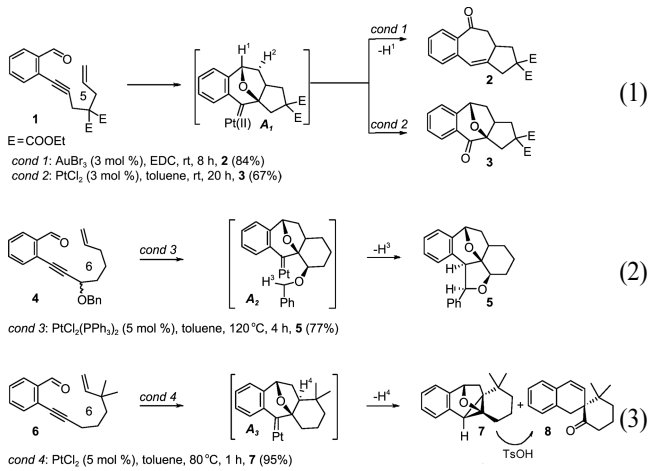
Enynals bearing an olefinic pendant were successfully cyclized *via* Huisgen-type [3+2] cycloaddition to the tetracyclic Pt-carbene complexes which would undergo insertion into a C-H bond of the β-position to afford the fused cyclopropane intermediates. Their tandem rearrangement afforded diverse types of spiranes depending on the tethered alkenes of the enynals.

Key Words : Cyclization, Platinum, Pyrylium ions, Carbene, Spirane

Introduction

The cycloaddition reaction is one of the most powerful synthetic tools for the construction of various cyclic compounds. In particular, the intramolecular metal-catalyzed cycloaddition is very attractive because it gives multicyclic compounds from acyclic substrates in one pot. Among the various strategies for diverse polycyclic skeletons, intramolecular metal-catalyzed [4+2 or 3+2] cycloadditions are well established strategy for the synthesis of carbo- and heterocyclic structures, which have been reported.[1] During the course of our scientific endeavors leading to a general and modular entry to polycyles, we reported a highly unique behavior of Pt-carbene complexes ***A***, formed *via* a Huisgen-type [3+2] cycloaddition between metal-bound pyrylium and a pendant alkene.[2] In the cases involving a five-membered ring formation in the 3rd cycle, we have reported Au-catalyzed cyclization of enynals (like **1**) to yield 2,3,10,10a-tetrahydrobenzo[*f*]azulen-9(1H)-ones (like **2**) *via* [3+2] cycloaddition followed by elimination of H^1 [Eq. (1)].[3] It is noted that elimination of H^2 from A_1 would result in sequential migration eventually to form the naphthalene derivative.[4] Surprisingly, Pt-catalyzed cyclization of **1** would also form A_1 *via* [3+2] cycloaddition with an alkene and eventually resulted in **3** as a major product, presumably *via* oxygenation of A_1.[5] During our synthesis of tricycles containing a six-membered ring in the 3rd cycle, we observed an unique insertion of the Pt-carbene intermediate A_2, derived from **4**, into the benzylic C-H of the δ-position to afford **5** [Eq. (2)].[6] The Pt-carbene A_3, without possessing such CH bond, resulted in insertion into the tertiary CH bond to form the cyclopropane ring like **7**.[7] Furthermore, heating the reaction solution of **6** or TsOH-catalyzed isomerization of the isolated **7** furnished **8** in high yield [Eq. (3)].8 It was worthwhile to note that the substrates like **6** with an aromatic anchor were successful in the present cyclopropanation of the Pt-carbene complex A_3.



(1)

(2)

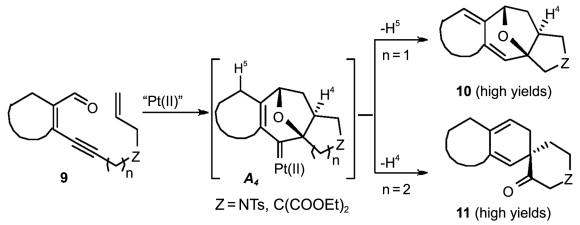
(3)

We have examined cycloalkene-based substrates **9** in order to extend the scope of the Pt-catalyzed cyclizations. Thus, we have found that H^5 in A_4 intermediate was involved in this sequence to furnish the eliminated products **10** (Scheme 1).[9] In Pt-catalyzed cyclization of 2-alkynylcycloalkenecarboxaldehydes **9a-g** with a remote olefinic tether (n=2 or larger), we found a catalytic method forming the corresponding [m,6,n]-tricyclic spiranes **11** in good to excellent yields.

Result and Discussion

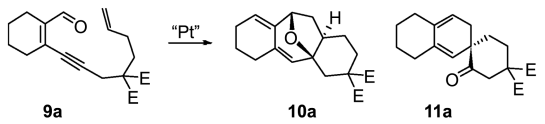
We examined the reaction of substrate **9a** in the presence of Pt catalysts under a variety of conditions (Table 1). First of all, the reaction of **9a** with $PtCl_2(PPh_3)_2$ as the catalyst proceeded well under reflux in toluene to furnish products **10a** and **11a** in 80% and 10% yields, respectively (entry 7). When **9a** was treated with $PtCl_2(PPh_3)_2$ at 80 °C in 1,2-dichloroethane (EDC) for 12 h, **10a** was formed as a major product (entry 8). Several conditions were tested to optimize the reaction efficacy. This reaction was also successful in other solvents, such as *p*-dioxane (entry 9), and other

†This paper is dedicated to Professor Eun Lee on the occasion of his honourable retirement.



Scheme 1. Pt-catalyzed reaction of non aromatic substrate **9**.

Table 1. Platinium-Catalyzed Reaction of Enynal **9a**



Entry	Catalysts (5 mol%)	Solvent	Temp (°C) time (h)	Products[b] (% yield)[c]
1	$PtCl_2$	toluene	120,1	**11a** (72)
2	$PtCl_2$	toluene	80,1	**11a** (91)
3	$PtCl_2$	EDC	60,5	**11a** (25)
4	$PtCl_2$	CH_3CN	80,12	**11a** (20)
5	$PtCl_2$	*p*-dioxane	80,12	**11a** (55)
6	$PtCl_2(PPh^3)^2$	toluene	100,24	**10a** (70), **11a** (15)
7	$PtCl_2(PPh^3)^2$	toluene	120,12	**10a** (80), **11a** (10)
8	$PtCl_2(PPh^3)^2$	EDC	80,12	**10a** (43)
9	$PtCl_2(PPh^3)^2$	*p*-dioxane	120,18	**10a** (63), **11a** (15)

[a]Reaction condition: The reaction was carried out with **9a** in the presence of 10 mol % of the Pt catalyst under the given conditions. [b]E = COOEt. [c]EDC = 1,2-dichloroethane. [d]Isolated yields.

conditions, such as 100 °C, 24h (entry 6). Surprisingly, when **9a** was treated with $PtCl_2$ at 120 °C in toluene for 1h, an unexpected product **11a** was isolated in 72% yield without forming product **10a** (entry 1). The $PtCl_2$ catalyst showed selective reactivity of Pt-carbene complex ***B4*** which would undergo insertion into a C-H^5 bond of the β-position to afford **11a** in high yield. This reaction was also working in other solvents such as 1,2-dichloroethane (EDC), CH_3CN, and *p*-dioxane (entries 3-5). Finally, we could optimize this reaction by decreasing temperature, where **11a** was isolated in 91% yield (entry 2).

Various substrates were subjected to optimized reactions for the formation of **11a** to explore the scope and limitation of this process (Figure 1).

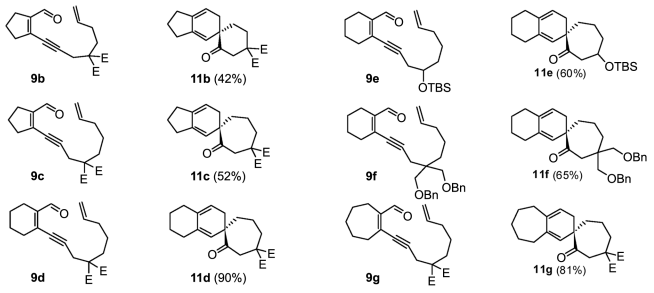
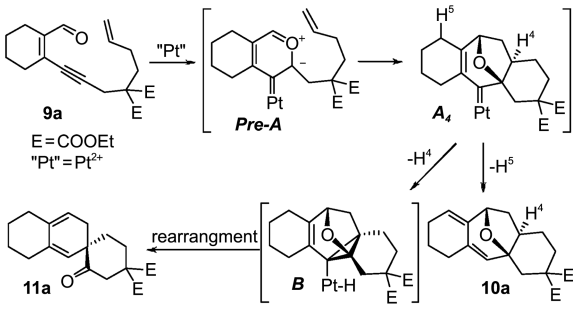


Figure 1. Products **11** of Platinum-catalyzed cyclization, and the corresponding substrates **9.** E = COOEt, TBS = *tert*-butyldimethylsilyl, Bn = benzyl



Scheme 2. A possible mechanism for the formation of **10a** and **11a**

Mechanistically, intermediates ***pre-A*** would undergo [3+2] cycloaddition with a pendent double bond to form the Pt-carbene complex ***A4*** (Scheme 2). While any basic species, even solvent molecules, could abstract H^5 from ***A4*** followed by deprotonation to give the product **10a**, Pt-carbene complex ***A4***, increasing the number of carbon tethers, would be more facile to insert into the tertiary C-H^4 bond to form the fused cyclopropane intermediates ***B*** followed by tandem rearrangement to result in spirane **11a**.

Conclusion

Enynals **9** bearing an olefinic pendant were successfully cyclized *via* Huisgen-type [3+2] cycloaddition to the tetracyclic Pt-carbene complex ***A*** which would undergo insertion into a C-H bond of the β-position to afford the fused cyclopropane intermediates and their tandem rearrangement afforded diverse types of spiranes **11** in good to excellent yields. This convenient methodology can be an useful route to organic chemists for easy access to spirocycle unit such as an effective building block in complex organic synthesis.

Experimental

General Procedures. In a 5 mL new test tube, enynals **9a-g** (0.10 mmol), $PtCl_2$ (10 mol%), and dried solvent (0.5 mL) were charged at 0. The reaction mixture was kept under argon atmosphere and stirred for 1 to 24 h in a preheated oil bath (60-120) by monitoring the reactions by TLC periodically. Upon completion, the solvent was removed under vacuum and the crude products were subjected for flash column chromatography to afford the pure products **10a** and **11a-g.**

Spectroscopic Data of Compounds 10a and 11a-g.

10a: IR (NaCl, cm^{-1}) 1739, 1673, 1598; ^1H NMR (400 MHz, $CDCl_3$) δ 5.47 (s, 1H), 5.38 (s 1H), 4.51 (t, *J* = 4.8 Hz, 1H), 4.32-4.06 (m, 4H), 2.78 (dd, *J* = 15.0, 1.4 Hz, 1H), 2.31 (dd, *J* = 13.2, 2.0 Hz, 1H), 2.24-2.16 (m, 3H), 2.09-1.99 (m, 3H), 1.79-1.77 (t, *J* = 4.4 Hz, 2H), 1.71-1.54 (m, 4H), 1.47-1.40 (m, 1H), 1.23 (t, *J* = 7.0 Hz, 6H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 172.98, 170.94, 139.06, 131.96, 129.11, 119.77, 79.27, 77.45, 61.66, 61.18, 52.01, 43.78, 40.08, 36.09, 30.04, 28.98, 28.01, 25.16, 22.79, 14.21, 14.17.

11a: IR (NaCl, cm^{-1}) 3470, 2935, 2864, 1730, 1447, 1367, 1299, 1251, 1211, 1152; ^1H NMR (400 MHz, $CDCl_3$) δ 5.43

(s, 1H), 5.40 (s, 1H), 4.23-4.15 (m, 4H), 2.95 (d, J = 14.8 Hz, 1H), 2.76 (d, J = 14.4 Hz, 1H), 2.31-2.20 (m, 6H), 2.02 (dd, J = 16.8, 4.8 Hz, 1H), 1.83-1.77 (m, 1H), 1.73-1.66 (m, 1H), 1.61-1.46 (m, 4H), 1.27-1.22 (m, 6H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 208.63, 170.84, 170.70, 136.98, 134.02, 121.94, 118.81, 62.20, 62.13, 57.99, 48.81, 42.42, 32.04, 31.60, 31.38, 30.96, 26.65, 24.86, 24.77, 14.35, 14.33.

11b: IR (NaCl, cm^{-1}) 3470, 2979, 1730, 1446, 1367, 1299, 1249, 1209, 1094; ^{1}H NMR (400 MHz, $CDCl_3$) δ 5.49 (s, 1H), 5.43 (s, 1H), 4.23-4.16 (m, 4H), 2.94 (t, J = 14.4 Hz, 1H), 2.78-2.69 (m, 2H), 2.78-2.69 (m, 2H), 2.34-2.23 (m, 6H), 2.11 (td, J = 17.6, 2.4 Hz, 1H), 1.84-1.64 (m, 5H), 1.27-1.22 (m, 6H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 208.68, 170.81, 170.71, 142.58, 138.69, 116.99 114.70, 62.18, 62.13, 57.92, 49.78, 42.40, 33.17, 32.51, 31.66, 31.02, 26.28, 25.24, 14.34.

11c: IR (NaCl, cm^{-1}) 3514, 2938, 2870, 1731, 1446, 1367, 1314, 1248, 1201, 1177; ^{1}H NMR (400 MHz, $CDCl_3$) δ 5.45 (s, 1H), 5.34 (s, 1H), 4.26-4.13 (m, 4H), 3.32 (d, J = 11.6 Hz, 1H), 2.98 (d, J = 11.6 Hz, 1H), 2.85-2.79 (m, 1H), 2.34-2.20 (m, 5H), 2.03 (td, J = 17.6, 2.0 Hz, 1H), 1.87-1.60 (m, 7H), 1.26 (td, J = 7.2, 5.8 Hz, 6H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 209.77, 171.56, 170.90, 142.74, 138.71, 117.50, 115.52, 62.05, 61.89, 55.38, 53.57, 42.51, 37.17, 36.06, 32.47, 31.65, 31.00, 25.27, 20.87, 14.33.

11d: IR (NaCl, cm^{-1}) 3470, 2981, 2935, 2862, 1732, 1707, 1449, 1367, 1249, 1201; ^{1}H NMR (400 MHz, $CDCl_3$) δ 5.41 (s, 1H), 5.31 (s, 1H), 4.25-4.15 (m, 4H), 3.31 (d, J = 12 Hz, 1H), 2.96 (d, J = 12 Hz, 1H), 2.68-2.62 (m, 1H), 2.26-2.15 (m, 5H), 1.98-1.86 (m, 2H), 1.72-1.71 (m, 3H), 1.58-1.50 (m, 5H), 1.28-1.23 (m, 6H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 209.70, 171.55, 170.94, 137.11, 133.98, 122.51, 119.76, 62.03, 61.89, 55.19, 52.56, 42.39, 36.36, 35.87, 31.56, 31.53, 30.93, 24.86, 24.78, 20.83, 14.32.

11e: IR (NaCl, cm^{-1}) 2929, 2856, 1709, 1471, 1461, 1434, 1376, 1360, 1252, 1078; ^{1}H NMR (400 MHz, $CDCl_3$) δ 5.41 (s, 1H), 5.28 (s, 1H), 3.88-3.81 (m, 1H), 3.02 (t, J = 10.2 Hz, 1H), 2.75 (d, J = 16.4 Hz, 1H), 2.55 (dd, J = 12, 2.8 Hz, 1H), 2.23 (s, 4H), 1.89-1.50 (m, 10H), 1.17-1.11 (m, 1H), 0.88 (s, 9H), 0.07(d, J = 6.4 Hz, 6H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 211.34, 136.19, 133.58, 122.94, 119.80, 70.83, 52.22, 49.75, 40.23, 35.38, 31.50, 31.33, 30.91, 26.15, 24.87, 24.80, 19.35, 18.45, -4.53.

11f: IR (NaCl, cm^{-1}) 3062, 3029, 2928, 2857, 1687, 1495, 1452, 1363, 1099, 1027; ^{1}H NMR (400 MHz, $CDCl_3$) δ7.32-7.27 (m, 10H), 5.38 (s, 1H), 5.32 (s, 1H), 4.54-4.44 (m, 4H), 3.37-3.29 (m, 4H), 2.74 (d, J = 11.6 Hz, 1H), 2.67-2.62 (m, 1H), 2.45 (d, J = 11.6 Hz, 1H), 2.24-2.19 (m, 6H), 1.95-1.91 (m, 2H), 1.75-1.34 (m, 7H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 213.10, 139.15, 139.08, 136.06, 134.05, 128.61, 128.56, 127.78, 127.71, 127.65, 123.35, 119.62, 74.46, 73.55, 73.50, 73.29, 52.39, 42.76, 41.28, 36.76, 33.75, 31.99, 31.56, 31.00, 24.94, 24.87, 19.63.

11g: IR (NaCl, cm^{-1}) 3471, 2980, 2923, 2851, 1732, 1708, 1451, 1367, 1249, 1200; ^{1}H NMR (400 MHz, $CDCl_3$) δ 5.46 (t, J = 4.0 Hz, 1H), 5.36 (s, 1H), 4.24-4.15 (m, 4H), 3.32 (d, J = 12.0 Hz, 1H), 2.96 (d, J = 12.0 Hz, 1H), 2.70 (dd, J = 17.2, 4.0 Hz, 1H), 2.23-2.19 (m, 6H), 1.95 (dd, J = 17.2, 4.4 Hz, 1H), 1.89-1.85 (m, 1H), 1.83-1.78 (m, 1H), 1.76-1.52 (m, 8H), 1.26 (dd, J = 6.4, 7.2 Hz, 6H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 209.74, 171.57, 170.91, 141.57, 138.32, 123.24, 121.01, 62.05, 61.90, 55.27, 52.79, 42.39, 36.53, 35.97, 35.91, 35.76, 31.74, 31.53, 30.81, 20.74, 14.32.

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