Published in final edited form as:
Chem Commun (Camb). 2013 June 4; 49(44): 5046–5048. doi:10.1039/c3cc41699b.

Catalytic platinum-initiated cation-olefin reactions with alkene terminating groups†

Joseph G. Sokol[a], **Nikki A. Cochrane**[a], **Jennifer J. Becker**[b], and **Michel R. Gagné**[a,*]

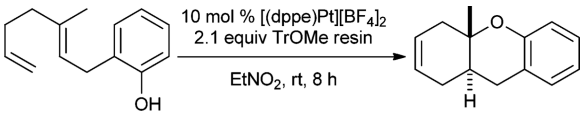
[a] Department of Chemistry, University of North Carolina at Chapel Hill, Chapel Hill, North Carolina 27599-3290, USA.

[b] U.S. Army Research Office, P.O. Box 23322, Research Triangle Park, North Carolina 27709, USA

Abstract

A series of phosphine–Pt^{2+}-catalysts is reported, which enable the oxidative cascade cyclization of poly-alkene substrates. When the terminus is appropriately arranged and a catalyst reoxidation mediator is included, several polycyclic all carbon skeletons can be obtained. In one example, a chiral P_2Pt^{+2} catalyst provides up to 79% ee.

The cation-olefin cascade cyclization of polyenes with a terminating alkene are considerably more difficult than the analogous cyclization containing a protic terminus (OH, NH, *etc.*),[1] *e.g.* eqn (1).[2] Terminating group effects on cyclization efficiency have been long known and pioneers like Johnson,[3] van Tamelen[4] and Corey[5] used these effects to benefit in the development of increasingly efficient synthetic methodologies.[6] Thus far, catalytic methodologies, especially those able to exercise absolute stereocontrol have been unable to overcome the challenge of a simple alkene terminating group.[5,7] H-bond activation of terminating OH groups by a base leads to a nearly barrierless cascade (once in the correct conformation), which additionally benefits from an enhanced thermodynamic driving force.[8] Since alkene termini do not become acidic until the cation is nearly fully formed, H-bond assistance is lost in these cases and higher energy intermediates are required with a concominant decrease in cyclization rate. Enzymatic cyclizations can overcome these inherent features by the strategic positioning of bases or arenes for stabilizing cation-π interactions,[9] but fully synthetic versions must rely on other means.

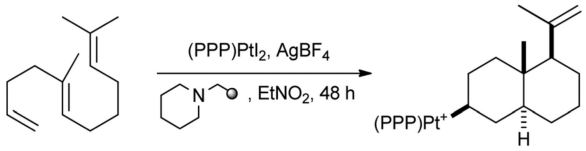


(1)

We have recently reported that electrophilic (triphos)Pt-dications can indeed initiate the cation-olefin cascade cyclization of all-alkene substrates,[10] though rates suffered considerably *versus* analogs with protic termini (*e.g.* eqn (2)). In this contribution we extend these initial observations, which were stoichiometric in Pt(II), to ligand–metal combinations that are amenable to catalysis and with chiral ligand variants, asymmetric catalysis.

† Electronic supplementary information (ESI) available: Synthesis and characterization of all compounds.

* mgagne@unc.edu.

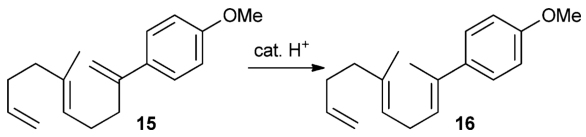


(2)

Our earliest studies sought to simply apply the conditions optimized for reactions like eqn (1), but these led to poor rates and conversions that eventually ceased prior to complete consumption of starting material. Based on unpublished observations that show slow hydride abstraction to be the cause of catalyst deactivation, optimization efforts sought to improve the hydride abstraction step of the proposed mechanism by the addition of Ph_3C^+ (Tr^+) to the catalyst formulation (Scheme 1). Under these conditions improved conversions were possible. These conditions were utilized to search for beneficial ligand effects. A screen of common diphosphine ligands showed that BINAP provides a catalyst capable of generating 81% **2** at 90% conversion; the mass balance were minor amounts of unidentified isomeric products.

A second round of optimization on the BINAP-based catalyst, paying particular attention to the seemingly key hydride abstraction step was undertaken. In addition to TrOMe, the 4-methoxy variant, resin based versions of both and recently reported acetal-based variants were tested.[11] While dimethoxy methane (and benzaldehyde) function well with protic terminators, they led to reaction rates that were half that of TrOMe. The use of TrOMe plus an equimolar quantity (to Pt) of $TrBF_4$ ensured that the putative $P_2Pt–H^+$ intermediate reacted with at least a 2-fold excess of Tr^+. More than any other modification of the reaction conditions, extra Tr^+ was most beneficial. Increasing $TrBF_4$ up to a 5-fold excess (*vs.* Pt) was optimum and 100% conversion of **1** was possible (Table 1).[12]

With a set of reaction conditions capable of efficiently converting **1** to **2** (90%) in hand, a survey of alternative poly-ene structures was undertaken (Table 2). Tetra-ene **3** efficiently generated a single stereoisomer of **4** as the predominant product of the oxidative cyclization (entry 1). Previous studies have shown[7] that the nucleophilicity of the terminating alkene[13] is a good predictor of the reaction time. Poly-ene substrates with more nucleophilic terminating alkenes were thus tested, though their cyclizations met with mixed success. Some cyclized effectively (*e.g.* entry 2) while others displayed more complex behavior. The styrene terminated **5** proved to be an excellent substrate, providing a product whose mass balance was 90% bicyclic diene **6**. In contrast, the *para*-methoxy substituted variant, **15**, preferentially isomerizes to the tri-substituted (and unreactive) alkene **16** (eqn (3)).



(3)

The low selectivities for the dihydronaphthyl substrates **9** and **11** are due to a series of side reactions (Scheme 2), including direct oxidization by Tr^+/TrOMe of the dihydro naphthyl to a naphthyl analog, which was surprisingly unreactive to follow up cyclization. Compounds **10** and **12** were also prone to rearrangement under the acidic conditions. This rearrangement could be accelerated by the deliberate addition of acid ($MeSO_3H$). Aryl terminating groups

have provided mixed success with other cyclization techniques.[14] In the present case, **13** provided numerous side products, despite having the stoichiometric cyclizations with (PPP)Pt^{+2} being selective for a single product.[15]

The clean conversion of **5** to diene **6** suggests that the putative carbenium ion intermediate **A** may generate the product under kinetic or thermodynamic control. DFT calculations[16] on the decalin (deplatinated) products indicated that the observed product was favored by 4.0 kcal mol^{-1} over its alternative styrene isomer. Attempts to manipulate the direction of this elimination through methyl substitutions on the carbon skeleton were unsuccessful. When the 8,8-dimethyl analog of **5** was examined (Scheme 3), no reaction was observed, either with the standard P_2Pt^{+2} or the (triphos)Pt^{+2} initiators. An analysis of the low energy conformers of 8,8-Me_2-**5** suggested that gem-dimethyl groups deconjugate the styrene and thus reduce its nucleophilicity and the concomitant stability of the benzyl cation intermediate.[17]

The ability to catalyze the cation-olefin cyclization under the control of a P_2Pt^{+2}-catalyst suggests the reasonableness of enantioselective variants. As shown in Table 3, the optimum conditions could be ported to catalysts carrying chiral diphosphine ligands. As before,[18] the xylyl-PHANEPHOS derived catalyst provided the optimum enantioselectivities (79% ee), though xylyl-BINAP gave a reasonable compromise between conversion and % ee.

As described herein, the significant challenge of an ionic catalyst-controlled cascade-cyclization of poly-enes can at least partially be solved using P_2Pt^{+2} catalysts. Key to the methodology development has been the realization that fast hydride abstraction from a key Pt–H intermediate is key to catalytic efficiency. To our knowledge these represent a first for a catalytic cascade cyclization of polyenes containing alkene terminating groups. Proof-of-principle enantioselective results are also reported.

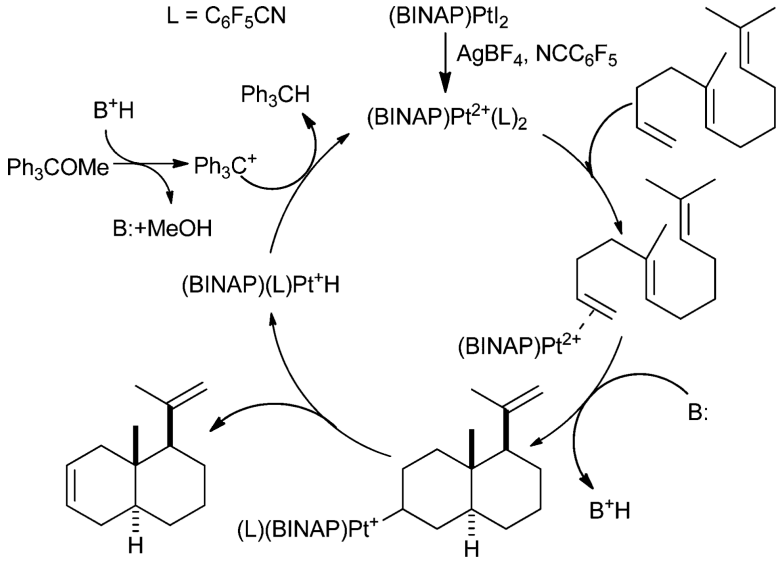
Supplementary Material

Refer to Web version on PubMed Central for supplementary material.

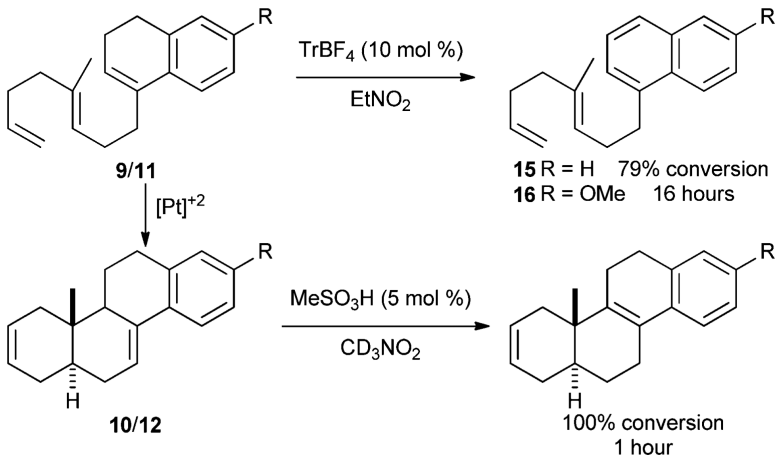
Notes and references

1. Pradal A, Chen Q, Faudot dit Bel P, Toullec PY, Michelet V. Synlett. 2012:74–79.Cannon JS, Olson AC, Overman LE, Solomon NS. J. Org. Chem. 2012; 77:1961–1973. [PubMed: 22316285] Sakakura A, Sakuma M, Ishihara K. Org. Lett. 2011; 13:3130–3133. [PubMed: 21591803] Toullec PY, Blarre T, Michelet V. Org. Lett. 2009; 11:2888–2891. [PubMed: 19480435] Liskin DV, Sibbald PA, Rosewall CF, Michael FE. J. Org. Chem. 2010; 75:6294–6296. [PubMed: 20738146] Surendra K, Corey EJ. J. Am. Chem. Soc. 2008; 130:8865–8869. [PubMed: 18597440] Nakamura S, Ishihara K, Yamamoto H. J. Am. Chem. Soc. 2000; 122:8131–8140.
2. Koh JH, Gagné MR. Angew. Chem., Int. Ed. 2004; 43:3459–3461.Koh JH, Mascarenhas C, Gagné MR. Tetrahedron. 2004; 60:7405–7410.
3. Johnson WS, Daub GW, Lyle TA, Niwa M. J. Am. Chem. Soc. 1980; 102:7800–7802.Johnson WS, Bunes LA. J. Am. Chem. Soc. 1976; 98:5597–5602.Carney RL, Johnson WS. J. Am. Chem. Soc. 1974; 96:2549–2556.Johnson WS. Acc. Chem. Res. 1967; 1:1–8.
4. Van Tamelen EE, Hwu JR. J. Am. Chem. Soc. 1983; 105:2490–2491.Van Tamelen EE. Acc. Chem. Res. 1975; 8:152–158.
5. Surendra K, Corey EJ. J. Am. Chem. Soc. 2012; 134:11992–11994. [PubMed: 22780430] Surendra K, Qiu W, Corey EJ. J. Am. Chem. Soc. 2011; 133:9724–9726. [PubMed: 21644499]
6. Kotora M, Hessler F, Eignerová B. Eur. J. Org. Chem. 2012:29–42.Yoder RA, Johnston JN. Chem. Rev. 2005; 105:4730–4756. [PubMed: 16351060] Bartlett, PA. Asymmetric Synthesis. Morrison, JD., editor. Vol. 3. Academic Press; New York: 1984. p. 341-454.

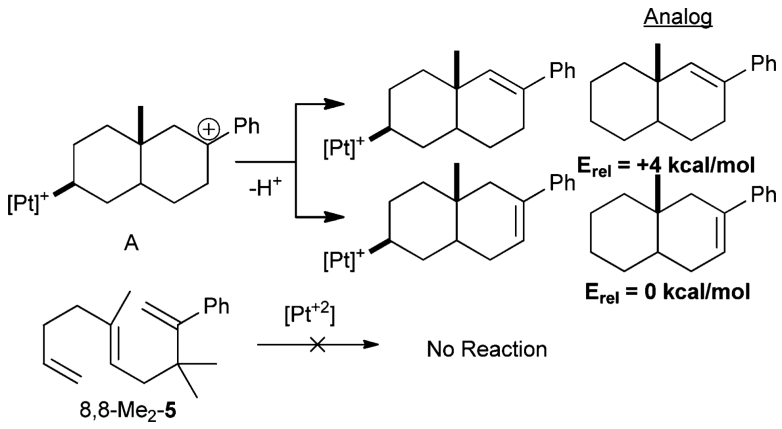
7. Godeau J, Fontaine-Vive F, Antoniotti S, Duñach E. Chem.–Eur. J. 2012; 18:16815–16822. [PubMed: 23143886] Vece V, Hassen KBH, Antoniotti S, Duñach E. Tetrahedron Lett. 2012; 53:5102–5105.Takao H, Wakabayashi A, Takahashi K, Imagawa H, Sugihara T, Nishizawa M. Tetrahedron Lett. 2004; 45:1079–1082.
8. Nowroozi-Isfahani T, Musaev DG, Morokuma K, Gagné MR. Organometallics. 2007; 26:2540–2549.Jenson C, Jorgensen WL. J. Am. Chem. Soc. 1997; 119:10846–10854.Metivier P, Gushurst AJ, Jorgensen WL. J. Org. Chem. 1987; 52:3724–3738.
9. Christianson DW. Chem. Rev. 2006; 106:3412–3442. [PubMed: 16895335] Rajamani R, Gao J. J. Am. Chem. Soc. 2003; 125:12768–12781. [PubMed: 14558824] Hoshino T, Sato T. Chem. Commun. 2002:291–301.Wendt KU, Schulz GE, Corey EJ, Liu DR. Angew. Chem., Int. Ed. 2000; 39:2812–2833.
10. Sokol JG, Korapala CS, White PS, Becker JJ, Gagné MR. Angew. Chem., Int. Ed. 2011; 50:5658–5661.
11. Cochrane NA, Brookhart MS, Gagné MR. Organometallics. 2011; 30:2457–2460. [PubMed: 21572581]
12. Screens of AgX (X = PF_6, SbF_6, OTf) and modified nitriles (tBuCN and 3,5-$(CF_3)_2C_6H_3CN$) revealed few significant effects on rate or conversion (see ESI†). The nitrile acts as a labile ligand and is capable of filling open coordination sites.
13. Mayr H, Kempf B, Ofial AR. Acc. Chem. Res. 2003; 36:66–77. [PubMed: 12534306]
14. Li B, Lai Y-C, Zhao Y, Wong Y-H, Shen Z-L, Loh T-P. Angew. Chem., Int. Ed. 2012; 51:10619–10623.Schafroth MA, Sarlah D, Krautwald S, Carreira EM. J. Am. Chem. Soc. 2012; 134:20276–20278. [PubMed: 23193947] Surendra K, Corey EJ. J. Am. Chem. Soc. 2008; 130:8865–8869. [PubMed: 18597440] Imagawa H, Iyenaga T, Nishizawa M. Org. Lett. 2005; 7:451–453. [PubMed: 15673262]
15. Kumazawa K, Ishihara K, Yamamoto H. Org. Lett. 2004; 6:2551–2554. [PubMed: 15255688] Ishihara K, Ishibashi H, Yamamoto H. J. Am. Chem. Soc. 2001; 123:1505–1506.
16. DFT B3LYP/6-31G* calculations on the deplatinated analogs, MacSpartan 2008 calculations; energies were uncorrected.
17. Cucciolito ME, D'Amora A, Vitagliano A. Organometallics. 2010; 29:5878–5884.Cucciolito ME, D'Amora A, Tuzi A, Vitagliano A. Organometallics. 2007; 26:5216–5223.Liu C, Bender CF, Han X, Widenhoefer RA. Chem. Commun. 2007:3607–3618.Wang X, Widenhoefer RA. Chem. Commun. 2004:660–661.
18. Mullen CA, Campbell AN, Gagné MR. Angew. Chem., Int. Ed. 2008; 47:6011–6014.



Scheme 1.
Proposed mechanism.



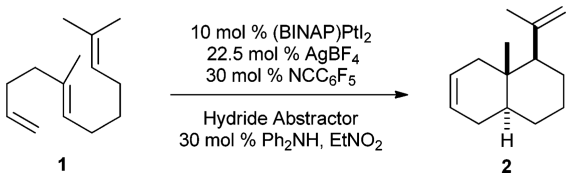
Scheme 2.
Side reactions of dihydronaphthyl substrate and product.



Scheme 3.
Cation intermediate for the conversion of **5** to **6**.

Table 1

Screen of hydride abstraction agents



1 **2**

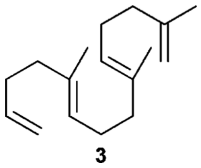
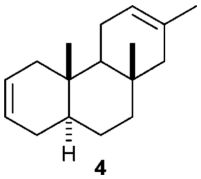
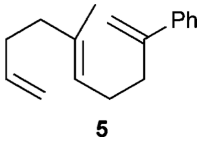
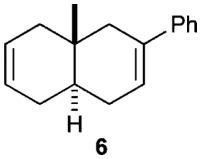
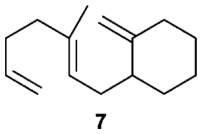
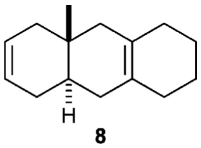
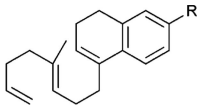
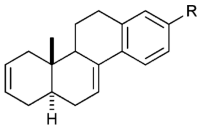
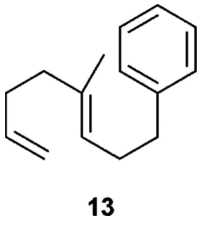
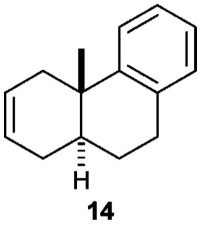
Entry	Hydride abstractor	2[a] (%)
1	200% TrOMe	17
2	300% TrOMe resin	14
3	200% 2(4-Meo)TrOMe	7
4	300% (4-MeO)TrOMe resin	8
5	200% TrOMe, 10% $TrBF_4$	44
6	160% TrOMe, 20% $TrBF_4$	65
7	100% TrOMe, 50% $TrBF_4$	90[b]
8	160% $(MeO)_2CH_2$, 10% $[Ph_2NH_2][BF_4]$	18

[a]Determined by GC analysis. Remainder is unreacted **1**.

[b]15% Isolated yield.

Table 2

Polyene cyclizations catalyzed by (BINAP)Pt^{2+}

Entry[a]	Substrate	Product	Time[b] (h)	Conversion[c] (isolated yield)
1	 **3**	 **4**	36	89[d] (14)
2	 **5**	 **6**	36	90[d] (19)
3	 **7**	 **8**	16	33[e] (9)
				
4	**9** R = H	**10**	24	50[f] (5)
5	**11** R = OMe	**12**	8	55[f] (5)
6	 **13**	 **14**	16	32[g] (4)

[a]Reaction conditions: 100 μmol substrate, 10 μmol (BINAP)PtI_2, 22.5 μmol $AgBF_4$, 30 μmol NCC_6F_5, 30 μmol Ph_2NH, 100 μmol TrOMe, 50 μmol $TrBF_4$, and 0.6 mL $EtNO_2$.

[b]Reaction time determined by consumption of starting material (GC analysis).

[c]GC conversions report mass balance of desired product relative to all other isomers and starting material. Spectroscopically pure (≥95%) products could be obtained, though difficulties in hydrocarbon separation considerably lowered the isolated yields.

[d]Mass balance composed of a single undetermined product isomer.

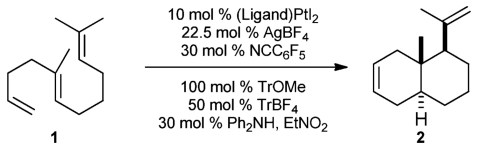
[e]Mass balance composed of 3 products from side reactivity between starting material and Tr^+ in a 2.1: 1 : 1.9 ratio.

[f]Mass balance composed of corresponding naphthyl product **15/16.**

[g]Mass balance composed of 5 monocyclized product isomers in a 1.3 : 2.1 : 1.3 : 1 : 2.2 ratio.

Table 3

Effect of ligand on enantioselectivity



Entry	Ligand	Conversion[a] (%)	% ee[b]
1[c]	(*R*)-xylyl-PHANEPHOS	44	79
2	(*R*)-xylyl-MeO-BINAP	80	68
3	(*R*)-xylyl-BINAP	87	67
4	(*R*)-SEGPHOS	90	44

[a] Mass balance composed of unreacted starting material.

[b] Determined by chiral GC.

[c] The absolute configuration of **2** is predicted to be as shown by analogy to previously reported work.[18]