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Palladium(II)- and mercury(II)-catalyzed rearrangements of propargyl acetates

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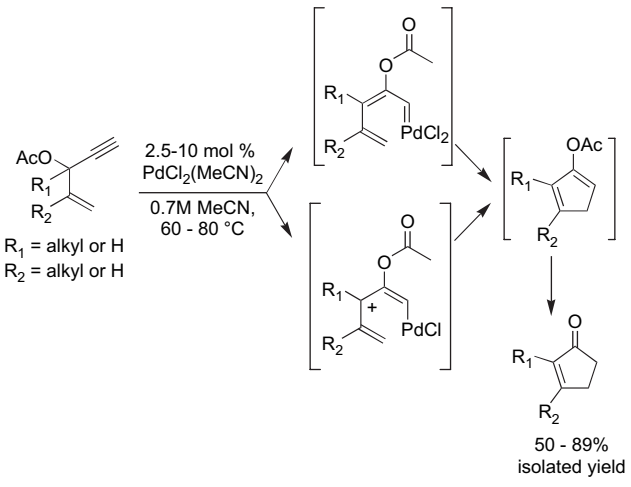
Abstract—The scope and utility of the metal-catalyzed rearrangement of propargyl acetates first reported by Rautenstrauch were expanded. Treatment of a series of appropriate acetate substrates with Pd(II)- and Hg(II)-catalysts afforded synthetically useful fused 5,6-bicyclic-1,4-cyclopentadienyl acetates and 2-cyclopentenones. It was found that the substituents at the terminal alkynyl and alkenyl positions of the acetate substrate had a significant impact on the outcome of the reaction.

1. Introduction

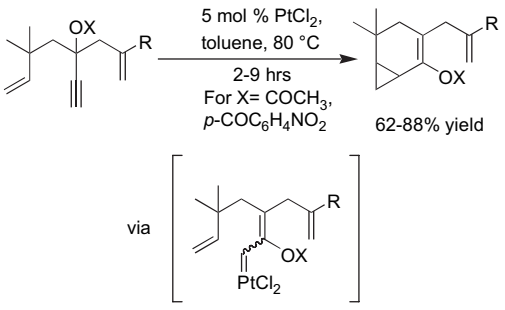
In 1984, Rautenstrauch reported a unique Pd(II)-mediated rearrangement of 1-ethynyl-2-propenyl acetates to give 1,4-cyclopentadienyl acetates, which were cleaved in situ to 2-cyclopentenones (Scheme 1).[1] It was proposed that coordination of the Pd(II) species to the alkyne effects 1,2-acetoxy migration to give a metal carbene species that is in equilibrium with a pentadienyl cation. Both intermediates can undergo cyclization and ester cleavage to generate the cyclopentenone products. The study described the optimization of reaction conditions and the rearrangement results for five different substrates.



Scheme 1. Rautenstrauch rearrangement of propargyl acetates.

This rearrangement came to our attention because one of the potential mechanisms proposed for the reaction was a 4π-electrocyclization, with generation of the pentadienyl cation intermediate via an unusual reaction pathway. In contrast to the usual Lewis or Bronsted acid-promoted Nazarov electrocyclization, the oxypalladation creates a transient vinyl palladium species at one of the carbon termini involved in the putative electrocyclization. The ability to place the catalyst so close to the site of bond formation led us to wonder whether enantioselectivity could be controlled using chiral palladium(II) complexes.[2,3] Several studies that appeared during the course of our work (vide infra) have prompted us to report our findings.[4]

In 2002, Fensterbank and co-workers reported the $PtCl_2$-catalyzed tandem rearrangement/cyclopropanation of dienynes to give fused bicyclic cyclopropanes (see Eq. 1).[5] The reaction mechanism proposed involved a metal carbene intermediate generated through 1,2-acetoxy migration, similar to the reaction pathway proposed by Rautenstrauch in 1984 for palladium(II). Sarpong and co-workers have also reported platinum(II)-catalyzed pentannulation reactions of propargylic esters involving the putative formation of metal carbene intermediates by a similar pathway.[6]



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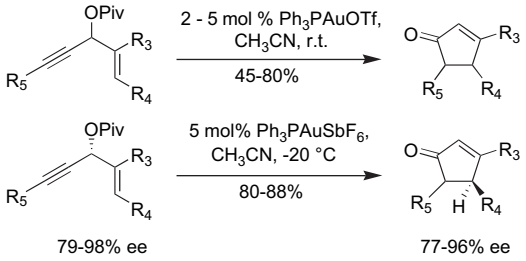
Ruthenium-[7] and gold-catalyzed reactions[8] involving 1,2-acetoxy migration have also been reported. Recently, Toste and co-workers reported a gold(I)-catalyzed transformation of propargylic pivaloates to 2-cyclopentenones (Eq. 2).[9] Significantly, a high degree of chirality transfer was observed for reactions of chiral substrates (Eq. 3). Computational studies focused on Toste's work indicate that reactions that occur with chirality transfer proceed through helical, pentadienyl cationic intermediates.[10]



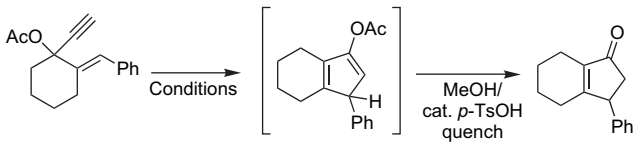
2. Results

Initial studies focused on extending the limited scope of Rautenstrauch's pioneering work. In one of his five cases, an unusual cyclopentenone fused to a macrocycle was generated. This result suggested that it should be possible to achieve the synthesis of fused bicyclic ring systems with an improved protocol. Furthermore, the introduction of substituents at the terminal alkenyl and alkynyl positions should lead to new arrays of substitution.

Thus, substrates **7a–d** were synthesized as shown in Scheme 2. Ketones **1** and **2** were subjected to both conditions **A** and **B**, leading to the formation of substituted propargyl alcohols **3–6**. Reactions of ketones with lithiated ethyl propiolate led to alkynoates, while reactions with lithiated trimethylsilylacetylene ultimately led to terminal alkynes. The resulting tertiary alcohols were acetylated under standard conditions to give the desired propargyl acetates **7a–d** in moderate to good yields. Purified **7a** could only be attained by recrystallization, as efforts at column chromatography resulted in quantitative conversion to allylic acetate **9** (entry 2, Table 2) via a known allylic rearrangement process.[11]

Optimized conditions for the rearrangement of **7a** to **8a** were established after extensive experimentation (Table 1). Temperature was found to be a key variable in this study. Increasing

Table 1. Optimization of the reaction conditions

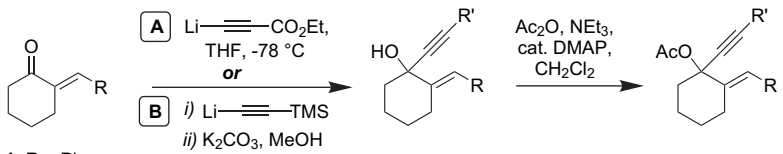


Entry[a]	Catalyst	Temp (°C)	Time (min)	Yield[b] (%)
1	5 mol % $Cl_2Pd(PhCN)_2$	70	40	44[c]
2	5 mol % $Cl_2Pd(MeCN)_2$	60	15	68
3	10 mol % $Cl_2Pd(PPh_3)_2$	60	960	[d]
4	5 mol % $PdCl_2$	60→70	20	17
5	15 mol % $PdCl_2$	65	30	71
6	*5 mol % $PdCl_2$*	*60*	*15*	*92*
7	5 mol % $PdCl_2$	rt	360	67
8	5 mol % $PdCl_2$	60→75	120	[e]
9	5 mol % $Pd(OAc)_2$	60	15	21

[a] Reactions were run in MeCN (0.7 M) unless otherwise specified.
[b] Yields indicate isolated product formed upon quenching the reaction with MeOH, cat. *p*-TsOH.
[c] AcOH (1 equiv) was added.
[d] Reaction run in DCE; starting material was recovered.
[e] Reaction run in DCE; crude NMR showed 1:1 mixture of starting material/enol ether.

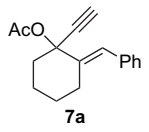
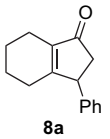
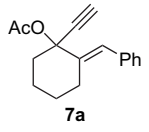
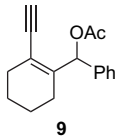
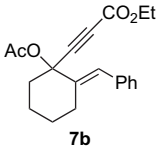
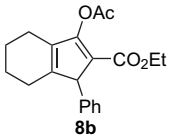
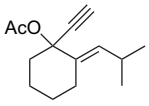
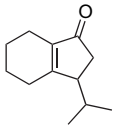
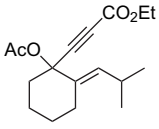
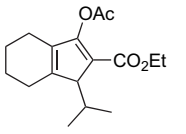
the temperature from 60 to 70 °C in acetonitrile in the presence of $PdCl_2$ correlated with a substantial decrease in isolated yield (entries 4–6). The reaction did proceed in a sluggish manner at room temperature, albeit in lower yield (entry 7). Other Pd(II) complexes (entries 1–3 and 9) and solvents (entries 3 and 8) gave inferior results in comparison to $PdCl_2$ in acetonitrile. The optimal conditions found were treatment of **7a** in acetonitrile with 5 mol % $PdCl_2$ for 15 min at 60 °C, which afforded **8a** in 92% isolated yield upon *p*-TsOH/MeOH quench and silica gel chromatography (entry 6).[12]

With optimized conditions in hand,[13] propargyl acetates **7b–d** were subjected to the reaction conditions (Table 2). The reaction tolerated various substituents at the unsaturated positions, leading to the formation of fused 5,6-bicyclic compounds **8b–d** in moderate to excellent yields. The efficiency of the reaction was largely dependent on substitution patterns at the terminal alkenyl and alkynyl moieties. The alkyl cases were more sluggish in comparison to the phenyl cases (entries 1 vs 4; 3 vs 5). Reactions with alkynyl esters led to the isolation of stabilized enol acetates in excellent yields (entries 3 and 5). Reaction times and yields for alkynoates were similar to those of their terminal alkyne analogs (entries 1 vs 3; 4 vs 5).



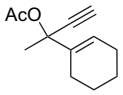
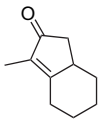
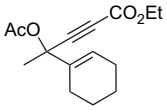
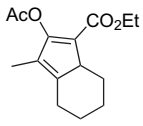
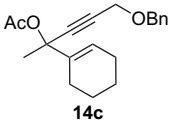
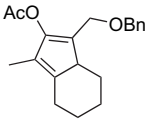
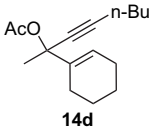
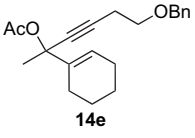
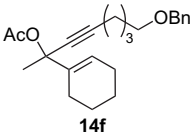
Scheme 2. Synthesis of propargylic acetates **7a–d**.

Table 2. Rearrangement of propargyl acetates **7a–d**

Entry	Acetate	Time (min)	Product[a]	Yield[b] (%)
1	 **7a**	15	 **8a**	92[c]
2	 **7a**	1	 **9**	>99[d]
3	 **7b**	15	 **8b**	97[e]
4	 **7c**	50	 **8c**	57[e]
5	 **7d**	45	 **8d**	60[e]

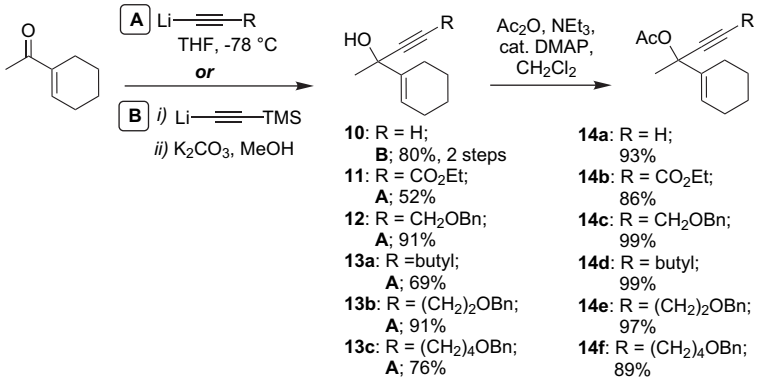
[a] In cases where ketone is the product, yield refers to the product formed after quenching the reaction with MeOH, cat. *p*-TsOH.
[b] Higher catalyst loadings (10 mol %) were sometimes required to drive the reaction to completion.
[c] Conditions: 5 mol % $PdCl_2$, MeCN (0.7 M), 60 °C.
[d] Conditions: silica gel, rt.
[e] Conditions: 10 mol % $PdCl_2$, MeCN (0.7 M), 60 °C.

Table 3. Rearrangement of propargyl acetates **14a–f**

Entry	Acetate	Time (min)	Product[a]	Yield[b] (%)
1	 **14a**	35	 **15a**	56[c]
2	 **14b**	35	 **15b**	88[c]
3	 **14c**	5	 **15c**	64[d]
4	 **14d**	5	—	[d,e]
5	 **14e**	5	—	[d,e]
6	 **14f**	5	—	[d,e]

[a] Compound **15a** formed from quenching the reaction with MeOH, cat. *p*-TsOH.
[b] Higher catalyst loadings (10–20 mol %) were required to drive the reaction to completion in certain cases.
[c] Conditions: 10 mol % $PdCl_2$, MeCN (0.7 M), 60 °C.
[d] Conditions: 20 mol % $PdCl_2$, MeCN (0.7 M), 60 °C.
[e] Reaction yielded predominantly starting material+complex mixture that appeared to contain target enol acetate.

In an effort to broaden the scope of the reaction, another class of substrates expected to deliver a different type of fused 5,6-bicyclic system was examined. As shown in Scheme 3, propargyl acetates **14a–f** were synthesized in good yields according to the routes used in the synthesis of **7a–d** and then subjected to the rearrangement conditions (Table 3). Substrates **14a** and **14b** cyclized smoothly to give products ketone **15a** and enol acetate **15b**,[14] respectively, in moderate to excellent yields (entries 1 and 2). A search for other substituents that would accelerate and/or facilitate the reaction led us to study the cyclization of **14c–f**. Propargyl acetate **14c**, when treated with 20 mol % $PdCl_2$ in acetonitrile at 60 °C, underwent complete conversion in 5 min to deliver enol acetate **15c**, which was isolated in 64% yield. In contrast, reactions of butyl-substituted analog **14d** and benzyloxy derivatives **14e** and **14f** afforded complex



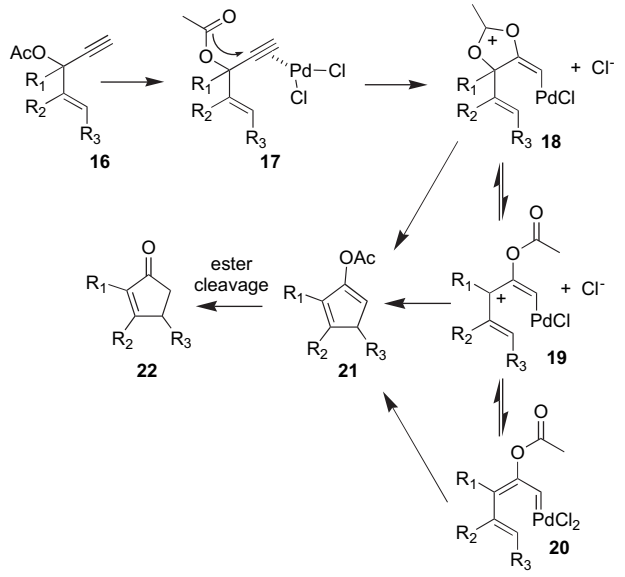
Scheme 3. Synthesis of propargylic acetates **14a–f**.

mixtures containing significant amounts of starting material.[15]

Unfortunately, the chiral cationic palladium(II) complexes we tested were not effective catalysts for the rearrangement,[16] so this strategy did not appear to be viable for the development of a catalytic, enantioselective variant of the reaction.

3. Discussion

While the mechanism is not fully understood, a scheme depicting several possibilities is shown below (Scheme 4). Coordination of the palladium(II) species to the electron-rich alkyne effects 1,2-acetoxy migration to give cationic intermediate **18**, which can also exist as the pentadienyl cation **19** or palladium carbene **20**. Both the intermediates **19** and **20** can then undergo cyclization to give 1,4-cyclopentadienyl acetate **21**, which upon ester cleavage would give the 2-cyclopentenone species **22**.



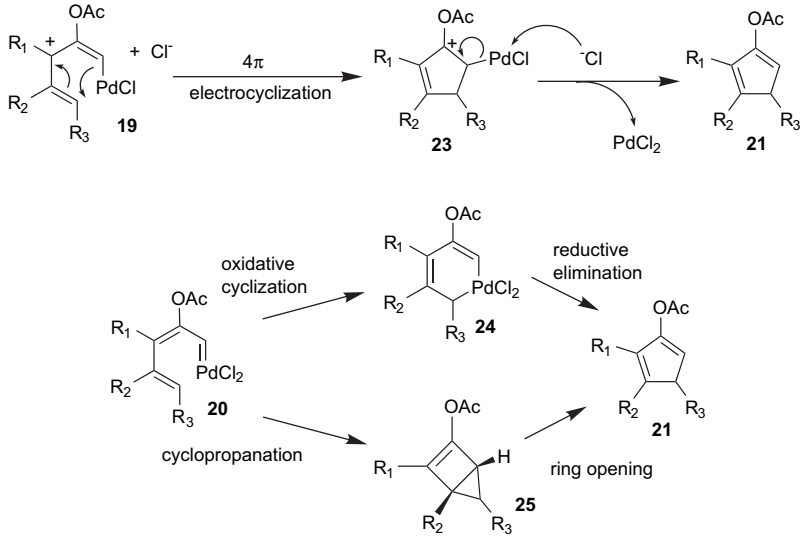
Scheme 4. General mechanistic scheme.

A more detailed view of the cyclization step is depicted in Scheme 5. 4π-Conrotatory electrocyclization of polarized pentadienyl cation **19** (Nazarov cyclization)[17] would give stabilized allylic cation **23**, which upon elimination of the palladium moiety would afford the desired product **21** and the regenerated Pd(II) catalyst.[18] If palladium carbene **20** is the reactive intermediate, then a few different pathways to enol acetate **21** exist. Oxidative cyclization of **20** to give palladium(IV) intermediate **24** followed by reductive elimination would lead to the desired species, as originally proposed by Rautenstrauch. Another feasible pathway involves intramolecular cyclopropanation of carbene **20** to give fused [2.1.0] bicyclic intermediate **25**, which upon ring opening would yield enol acetate **21**. Since both the carbene-based routes to enol acetate **21** invoke high-energy intermediates **24** and **25**, the 4π-electrocyclic mechanism is widely accepted.[10]

Three factors that appear to contribute to reactivity trends are outlined below.

(1) *Electron-withdrawing ability of the alkyne*. Rearrangement of alkynoate **14b** occurred more efficiently than the rearrangement of either terminal or alkyl-substituted substrates **14a** and **14d–f**. This outcome can be rationalized in terms of the electronic and coordinative properties of the ester moiety. The electron-withdrawing nature of the ester in conjunction with its ability to direct coordination of the palladium(II) species to the alkyne likely promotes the 1,2-acetoxy shift, thereby facilitating the cyclization (Fig. 1, A).

(2) *Coordinative ability of the propargylic substituent*. The rearrangement of substrate **14c**, which bears a benzyloxy group at the propargylic position, was greatly accelerated in comparison to the rearrangement of **14d**, **14e**, and **14f**, which have only alkyl substitution at the propargylic position (Table 3). The benzyloxy group of **14c** might be able to direct the catalyst to the alkyne as proposed for alkynoates (Fig. 1, B). The unique positioning of both the ester carbonyl and benzyloxy functionalities adjacent to the alkyne terminus appears to be vital to the



Scheme 5. Proposed mechanisms for the formation of enol acetate **21**.

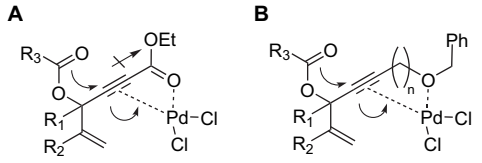
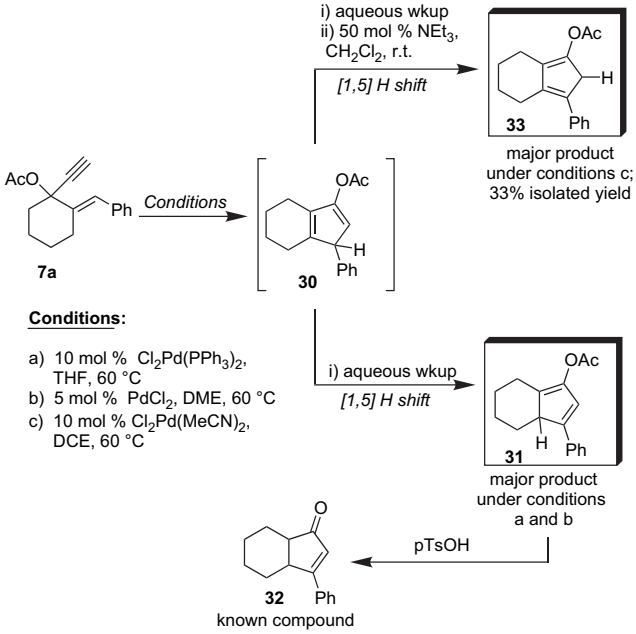


Figure 1. Esters and benzyloxy groups may promote 1,2-acetoxy migration.

efficiency of the 1,2-acetoxy migration. Formation of a reactive Pd(II)–oxygen–alkyne complex appears optimal for **14c**, where the length of the carbon tether n=1 (entry 3, Table 3). Surprisingly, when n=2, the reaction was extremely slow (entry 5). It is possible that the five-membered Pd(II) chelate derived from **14e** is too stable to allow catalyst turnover. Extension of the tether to n=4 (**14f**) would require the formation of an unlikely seven-membered chelate, and might be expected to behave like simple alkyl substrate **14d**. This prediction appeared to be consistent with our experimental results (entries 4 and 6).

(3) *Impact of substituents at the alkene terminus*. Substitution at the terminal position of the alkene also had a significant effect on the outcome of the reaction. Sluggish reactions and lower yields of rearrangements were observed for substrates **7c** and **7d**, in comparison to the reactions of **7a** and **7b** (Table 2). This can be ascribed to either an electronic effect or steric factors in the transition state of the cyclization step (Scheme 6). It is possible that an aromatic substituent in the R position would better stabilize the developing positive charge α to the R group relative to alkyl, facilitating the desired cyclization pathway and minimizing unwanted side reactions. Alternatively, steric interactions between the R group and vinyl palladium group in the transition state **28** would be expected to be greater for R=isopropyl than for the more planar R=phenyl, which could affect the rate of conrotatory 4π-electrocyclization of pentadienyl cation **27**. Therefore, either electronic or steric factors could account for the observed differences in reaction efficiency evident in Table 2.

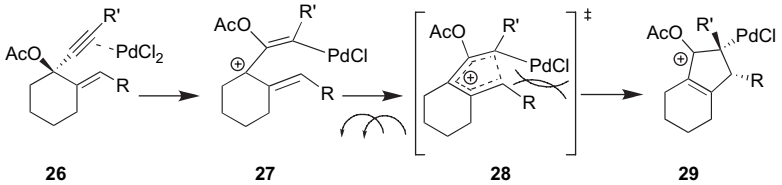
The unique reactivity patterns of enol acetate **30** were uncovered during purification and while screening reaction conditions. During some experiments, enol acetate **30** underwent unexpected further rearrangements to give alternative cyclopentadienes (Scheme 7). When substrate **7a** was treated with $Cl_2Pd(PPh_3)$ in THF or $PdCl_2$ in dimethoxyethane at 60 °C, enol acetate **31**[19] was the major product. Its structure was confirmed by treatment with *p*-TsOH, which gave the known unsaturated ketone **32**.[20] Furthermore, during purification of enol acetate **30** via triethylamine-deactivated silica gel chromatography, a third enol acetate **33** was generated. We believed that triethylamine was mediating the rearrangement and therefore sought reaction conditions that would allow for the exclusive formation of **33** from pure enol acetate **30**. Indeed, treatment of **7a** with 10 mol % $Cl_2Pd(MeCN)_2$ in DCE at 60 °C afforded acetate **30** with only trace amounts of ketone **8a**. Enol acetate **30** could then be converted to conjugated enol acetate **33** after aqueous workup in the presence of 50 mol % NEt_3 in CH_2Cl_2 at room temperature. Enol acetates **33** and **31** are both thought to arise from [1,5] hydride shifts of enol acetate **30**.[21]



Scheme 7. [1,5] Hydride shifts of enol acetate **30**.

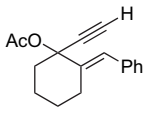
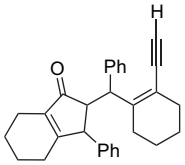
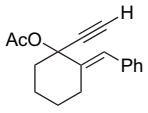
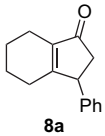
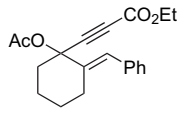
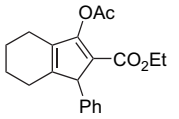
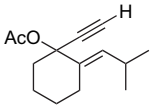
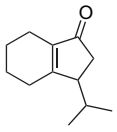
Since the scope of the rearrangement was found to be limited in experiments with palladium(II) catalysts, we began to consider alternatives. Mercury(II) species have a long history of effectiveness in oxymercuration reactions with alkenes and alkynes,[22] and recently it has been reported that mercury(II) complexes can catalyze intramolecular cyclizations of carboxylates[23] and polyenes.[24] The mechanistic similarity to the Pd(II)-mediated 1,2-acetoxy shifts led us to wonder whether catalysis of the Rautenstrauch rearrangement could be achieved with mercury(II) salts.

Indeed, treatment of propargyl acetates **7a–c** with 5 mol % $HgCl_2$ did effect the rearrangement under mild conditions (Table 4). To our surprise, treatment of **7a** with 5 mol % $HgCl_2$ in MeCN gave exclusively the dimer **34** as a 1.3:1 mixture of diastereomers (entry 1).[25] This product was apparently the result of a mercuric chloride-promoted S_N2' reaction between the desired product enol acetate **30** and a molecule of the starting material. Fortunately, when



Scheme 6. Steric interactions at the alkene terminus.

Table 4. Reactions catalyzed by $HgCl_2$

Entry	Acetate	Time (h)	Product	Yield (%)
1	 **7a**	1	 **34**	88[a,b]
2	 **7a**	1.5	 **8a**	>99[c]
3	 **7b**	2	 **8b**	>99[b]
4	 **7c**	1.5	 **8c**	44[c]

[a] Yield reflects mixture of 1.3:1 ratio of diastereomers.
[b] Conditions: 5 mol % $HgCl_2$, MeCN, rt.
[c] Conditions: 5 mol % $HgCl_2$, CH_2Cl_2, rt, then *p*-TsOH, MeOH.

dichloromethane was used as solvent instead of acetonitrile, the monomer was obtained in quantitative yield (entry 2). Monomer product **8b** was also obtained in quantitative yield from the alkynyl ester **7b** in the presence of 5 mol % $HgCl_2$ in acetonitrile. In this case, the stability of the enol acetate product **8b** probably suppresses the mercuric chloride-mediated dimerization event. The rearrangement of propargyl acetate **7c** to **8c** was also carried out in the presence of 5 mol % $HgCl_2$ and CH_2Cl_2 at room temperature, but the isolated yield (44%) proved to be lower than the palladium(II)-catalyzed reaction (entry 4).

4. Conclusions

In summary, we have successfully extended the scope and utility of the palladium(II)-catalyzed rearrangement of 1-ethynyl-2-propenyl acetates first reported by Rautenstrauch in 1984. Our methodology resulted in the novel synthesis of synthetically useful fused 5,6-bicyclic-1,4-cyclopentadienyl acetates and 2-cyclopentenones via treatment of various substituted propargyl acetates with Pd(II) and Hg(II) catalysts. Although our results are consistent with a Nazarov-type mechanism, a mechanism involving a palladium carbene intermediate cannot be ruled out. The unexpected reactivity of some substrates and enol acetate products hindered our efforts at further generalizing the reaction. We were, however, successful in elucidating the interesting reactivity of enol acetate **30**, which rearranged via [1,5] H shifts to give enol acetates **31** and **33** under specific reaction conditions.

The substituents at the terminal positions of both the alkyne and the alkene had a strong impact on the outcome of the reaction. Substrates with ester substituents at the alkyne terminus rearranged smoothly to give relatively stable enol acetate products, as compared to those with alkyl substituents, which exhibited poor reactivity. Aryl substituents on the alkene terminus gave better results than alkyl substituents. Thus, alkene substituents, able to stabilize the pentadienyl cation intermediate, may improve reactivity. Conversely, nonbonding interactions between the terminal substituent and the internally situated vinyl palladium may hinder reactivity. Lastly, electron-withdrawing substituents at the propargyl position (i.e., either carboethoxy (**14b**) or benzyloxy (**14c**)) seem to improve the reactivity. While it is likely that the 1,2-acetoxy migration is more favorable in a substrate with an electron deficient alkyne, it is also possible that the oxygen lone pairs at the propargylic position improve the ability of these substrates to complex the Pd(II) catalyst.

5. Experimental

5.1. General

Reactions were done in oven-dried glassware under an argon atmosphere unless otherwise noted. Acetonitrile, tetrahydrofuran, dichloromethane, 1,2-dichloroethane, and diethyl ether were purchased from Fisher or VWR and dispensed using the Glass Contour solvent purification system. Reactions were heated in a mineral oil bath using an IKA Werke RCT basic magnetic stirrer/hot plate, and the temperature was monitored with an ETS-D4 fuzzy IKA Werke digital thermometer. TLC visualization was done with UV light and/or potassium permanganate, *p*-anisaldehyde, or ceric ammonium molybdate solution followed by heating. Column chromatography was performed on EM Science silica gel 60 (230–400 mesh). ^1H NMR and ^{13}C NMR spectra were collected on a Bruker Amax 400, Avance 400, or Avance 500 MHz spectrometer at ambient temperature. Chemical shifts δ are reported in parts per million (ppm) relative to tetramethylsilane. Multiplicity is abbreviated as follows: s (singlet), d (doublet), t (triplet), q (quartet), qn (quintet), m (multiplet), dd (doublet of doublets), dt (doublet of triplets), qd (quartet of doublets), qt (quartet of triplets), br (broad). High resolution mass spectra were done on a ThermoFinnigan MAT 95XL at the Chemistry Instrumentation Center of the University of Buffalo. Infrared spectra were recorded on an 8400S Shimadzu FTIR spectrometer.

$PdCl_2$ was purchased from Strem Chemicals and stored on the benchtop. $Cl_2Pd(MeCN)_2$ was prepared according to a literature procedure and stored in a desiccator. $Pd(TFA)_2$ was purchased from Aldrich and stored in a desiccator. $[MeCN]_4Pd(BF_4)_2$ was purchased from Aldrich and stored in an argon-filled glovebox. NEt_3 and diisopropylamine were distilled from calcium hydride and stored under argon. *n*-Butyl lithium in hexanes was purchased from Aldrich and stored in a refrigerator.

5.2. General procedures for the preparation of 1-ethynyl-2-propenyl alcohols 3–6, 10–13c

5.2.1. Terminal alkynes 3, 5, 10. To a stirred solution of TMS acetylene (2.0 equiv) in THF (1.5 M) at −60 °C was

added *n*-BuLi (1.6 M in hexanes, 2.0 equiv) dropwise. After stirring for 30 min at this temperature, the solution was cooled to −78 °C and ketones **1**, **2**, or 1-acetyl cyclohexene (1 equiv) was added dropwise either neat or in solution (1.3 M). The reaction was allowed to warm slowly to −50→−40 °C, and progress was monitored by TLC. Upon completion or near-completion, the reaction mixture was quenched with water and allowed to warm to room temperature. The solution was then diluted with ether, and the aqueous and organic layers were separated. The aqueous layer was washed with ether (2×), and the combined organic portions were washed with brine (1×). The combined organic extracts were then dried with anhydrous magnesium sulfate and concentrated in vacuo. Silica gel chromatography (7/1 hexanes/ethyl acetates) afforded pure TMS-alkyne products as precursors to the terminal alkyne alcohols **3**, **5**, and **10**. The TMS-alkyne precursor to **10** was purified by simply washing the crude material with 7/1 hexanes/ethyl acetate. The TMS-alkyne derivatives were then dissolved in MeOH (0.3 M), treated with anhydrous K_2CO_3 (2.0 equiv), and stirred at room temperature until judged complete by TLC. The reaction mixture was concentrated in vacuo and redissolved in ether. Water was added to the organic phase, and the layers were separated. The aqueous layer was washed with ether (2×), and the combined organic portions were washed with water (1×) and brine (1×). The combined organic extracts were then dried with anhydrous magnesium sulfate and concentrated in vacuo to afford pure propargylic alcohols **5** and **10**. Silica gel chromatography (3/1 hexane/ethyl acetate) was used to obtain pure **3**.

5.2.2. Ethyl propiolates 4, 6, 11. To a stirred solution of ethyl propiolate (2.5 equiv) in THF (1.7 M) at −78 °C was added *n*-BuLi (1.6 M in hexanes, 2.5 equiv) dropwise. After stirring for 10 min at −78 °C, ketones **1**, **2**, or 1-acetyl cyclohexene (1 equiv) was added dropwise either neat or in solution (1.3 M). The reaction mixture was stirred at −78 °C until judged complete by TLC. The solution was then quenched with saturated NH_4Cl and diluted with ether. The organic and aqueous phases were separated, and the aqueous layer was washed with ether (2×). The combined organic extracts were then dried with anhydrous magnesium sulfate and concentrated in vacuo. Silica gel chromatography afforded clean ethyl propiolates **4**, **6**, and **11** in excellent yields.

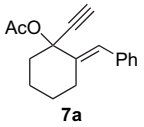
5.2.3. Alkyl-substituted alkynes 12, 13a–c. To a stirred solution of benzyl-protected yn-ol or 1-hexyne (1.5 equiv) in THF (1.2 M) at −78 °C was added *n*-BuLi (1.6 M in hexanes, 1.5 equiv) dropwise, and the resulting solution was warmed to −60 °C. After stirring for 1 h at −60 °C, the solution was cooled back down to −78 °C and 1-acetyl cyclohexene (1.0 equiv) was added dropwise. The reaction mixture was then allowed to warm slowly to −40 °C. Upon completion or near-completion of the reaction as judged by TLC, the solution was quenched with saturated NH_4Cl and diluted with ether. The organic and aqueous phases were separated, and the aqueous layer was washed with ether (2×). The combined organic extracts were then dried with anhydrous magnesium sulfate and concentrated in vacuo. Silica gel chromatography (gradient systems) afforded clean alkyl-substituted alkynes **12**, **13a–c** in excellent yields.

5.3. Representative procedure for the synthesis of propargyl ester substrates 7a–d, 14a–f from tertiary alcohols

To a solution of **4** (0.74 g, 2.6 mmol) in CH_2Cl_2 (5.2 mL) was added Ac_2O (0.37 mL, 3.9 mmol, 1.5 equiv), NEt_3 (1.4 mL, 10.4 mmol, 4.0 equiv), and several crystals of DMAP. The resulting solution was stirred overnight at room temperature. Upon completion of the reaction as judged by TLC, the solution was then quenched with saturated ammonium chloride (aq) and the solvent was removed in vacuo. The resulting oil was diluted with ether and the aqueous layer was separated. After washing the aqueous layer with ether (2×), the organics were combined and washed with saturated (aq) ammonium chloride (2×), water (5–7×), saturated (aq) $NaHCO_3$ (2×), and brine (1×). The combined organic extracts were then dried with anhydrous $MgSO_4$ and concentrated in vacuo. Silica gel chromatography (3/1 hexanes/ethyl acetate) afforded acetate **7b** (0.75 g, 89% yield) as a light yellow oil. Crude acetate **7a** was recrystallized with 10/1 hexanes/MeOH and washed with ice-cold hexanes (silica gel chromatography was avoided as it promoted quantitative allylic rearrangement). Acetates **14a**, **c–f** were used following aqueous workup without further purification.

5.3.1. Spectroscopic data for propargyl acetates.

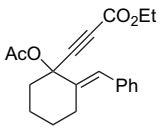
5.3.1.1. Propargyl acetate 7a.



7a

^{1}H NMR (500 MHz, $CDCl_3$): δ 7.35–7.32 (m, 2H), 7.25–7.21 (m, 3H), 7.11 (s, 1H), 2.82 (s, 1H), 2.71 (dt, J=13.5, 4.5 Hz, 1H), 2.45 (dt, J=13.5, 4.5 Hz, 1H), 2.24–2.04 (m, 5H), 1.83–1.67 (m, 3H), 1.50 (m, 1H); ^{13}C NMR (100 MHz, $CDCl_3$): δ 168.7, 138.5, 137.3, 128.9, 128.1, 126.7, 125.8, 82.0, 77.7, 76.8, 40.2, 27.1, 25.2, 21.81, 21.77; IR (neat, cm^{-1}) 3285, 3022, 2935, 2860, 2116, 1747, 1493, 1445, 1366, 1227; HRMS (EI$^+$): calculated for $C_{17}H_{18}O_2$ (M^+): 254.1301, found: 254.1311.

5.3.1.2. Propargyl acetate 7b.

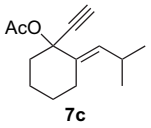


7b

^{1}H NMR (500 MHz, $CDCl_3$): δ 7.35–7.32 (m, 2H), 7.26–7.22 (m, 3H), 7.01 (s, 1H), 4.24 (q, J=7 Hz, 2H), 2.65 (dt, J=14, 4.5 Hz, 1H), 2.38 (dt, J=14, 4.5 Hz, 1H), 2.22–2.10 (m, 5H), 1.84–1.66 (m, 3H), 1.51 (m, 1H), 1.31 (t, J=7 Hz, 3H); ^{13}C NMR (100 MHz, $CDCl_3$): δ 168.3, 153.2, 137.3, 136.7, 128.7, 128.0, 126.7, 126.3, 84.6, 80.1, 76.8, 62.0, 39.4, 26.8, 25.1, 21.6, 21.3, 13.9; IR (neat, cm^{-1}) 3080, 3055, 3022, 2980, 2937, 2860, 2239, 1751,

1709, 1599, 1445, 1367, 1254, 1221; HRMS (EI$^+$): calculated for $C_{20}H_{22}O_4$ (M^+): 326.1513, found: 326.1524.

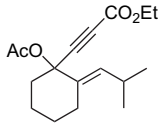
5.3.1.3. Propargyl acetate 7c.



7c

^{1}H NMR (400 MHz, $CDCl_3$): δ 5.78 (d, J=9.2 Hz, 1H), 2.73 (s, 1H), 2.55 (m, 1H), 2.45 (dt, J=14, 4.8 Hz, 1H), 2.35 (dt, J=14, 4.8 Hz, 1H), 2.08–2.03 (m, 4H), 1.88 (m, 1H), 1.68 (m, 3H), 1.39 (m, 1H), 0.98 (m, 6H); ^{13}C NMR (100 MHz, $CDCl_3$): δ 168.4, 133.3, 133.2, 82.0, 77.6, 76.1, 40.0, 27.0, 26.4, 24.7, 23.1, 22.9, 21.7, 21.6; IR (neat, cm^{-1}) 3286, 3267, 2959, 2935, 2866, 1749, 1464, 1445, 1366, 1229; HRMS (EI$^+$): calculated for $C_{14}H_{19}O_2$ (M^+): 219.1380, found: 219.1377.

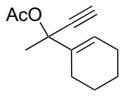
5.3.1.4. Propargyl acetate 7d.



7d

^{1}H NMR (400 MHz, $CDCl_3$): δ 5.68 (d, J=9.1 Hz, 1H), 4.22 (q, J=7.1 Hz, 2H), 2.53 (m, 1H), 2.42 (m, 1H), 2.27 (m, 1H), 2.07–1.97 (m, 5H), 1.71–1.67 (m, 3H), 1.41 (m, 1H), 1.30 (t, J=7.1 Hz, 3H), 0.97 (m, 6H); ^{13}C NMR (100 MHz, $CDCl_3$): δ 168.2, 153.3, 1133.8, 132.2, 85.2, 79.7, 61.8, 39.2, 26.8, 26.5, 24.7, 23.0, 22.8, 21.7, 21.4, 13.9; IR (neat, cm^{-1}) 2959, 2935, 2866, 2239, 1751, 1715, 1464, 1447, 1367, 1259, 1223; HRMS (ES$^+$): calculated for $C_{17}H_{24}O_4Na$ (M+Na)$^+$: 315.1567, found: 315.1577.

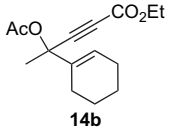
5.3.1.5. Propargyl acetate 14a.



14a

^{1}H NMR (400 MHz, $CDCl_3$): δ 6.08 (m, 1H), 2.63 (s, 1H), 2.13–2.02 (m, 6H), 1.93 (m, 1H), 1.67–1.51 (m, 7H); ^{13}C NMR (100 MHz, $CDCl_3$): δ 168.8, 136.8, 123.7, 83.2, 76.8, 74.4, 27.8, 25.0, 23.4, 22.7, 22.0, 21.7; IR (neat, cm^{-1}) 3262, 2990, 2931, 2858, 2120, 1748, 1447, 1437, 1366, 1236; HRMS (EI$^+$): calculated for $C_{12}H_{16}O_2$ (M^+): 192.1145, found: 192.1148.

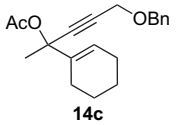
5.3.1.6. Propargyl acetate 14b.



14b

^{1}H NMR (400 MHz, $CDCl_3$): δ 6.05 (m, 1H), 4.22 (q, J=8 Hz, 2H), 2.13–2.02 (m, 6H), 1.92 (m, 1H), 1.72–1.56 (m, 7H), 1.30 (t, J=8 Hz, 3H); ^{13}C NMR (100 MHz, $CDCl_3$): δ 168.6, 153.5, 135.9, 124.6, 86.1, 78.3, 76.0, 62.0, 27.0, 25.0, 23.5, 22.6, 21.9, 21.5, 14.0; IR (neat, cm^{-1}) 2989, 2935, 2860, 2839, 2245, 1749, 1713, 1447, 1367, 1259, 1229; HRMS (EI$^+$): calculated for $C_{15}H_{20}O_4$ (M^+): 264.1356, found: 264.1363.

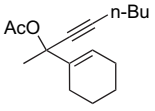
5.3.1.7. Propargyl acetate 14c.



14c

^{1}H NMR (400 MHz, $CDCl_3$): δ 7.38–7.27 (m, 5H), 6.07 (m, 1H), 4.62 (s, 2H), 4.26 (s, 2H), 2.16–1.95 (m, 7H), 1.70–1.53 (m, 7H); ^{13}C NMR (100 MHz, $CDCl_3$): δ 168.8, 137.5, 137.1, 128.4, 128.2, 127.8, 123.6, 86.3, 82.3, 77.1, 71.3, 57.4, 27.8, 25.0, 23.6, 22.7, 22.0, 21.8; IR (neat, cm^{-1}) 3062, 3030, 2990, 2932, 2856, 1747, 1497, 1454, 1366, 1238; HRMS (EI$^+$): calculated for $C_{20}H_{24}O_3$ (M^+): 312.1720, found: 312.1720.

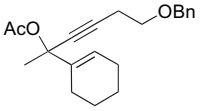
5.3.1.8. Propargyl acetate 14d.



14d

^{1}H NMR (500 MHz, $CDCl_3$): δ 6.04 (m, 1H), 2.24 (t, J=7.5 Hz, 2H), 2.16–1.91 (m, 7H), 1.66–1.39 (m, 11H), 0.90 (t, J=7.5 Hz, 3H); ^{13}C NMR (100 MHz, $CDCl_3$): δ 168.8, 137.8, 123.0, 86.7, 79.7, 77.6, 30.7, 28.1, 25.0, 23.5, 22.8, 22.0, 21.9, 21.8, 18.5, 13.6; IR (neat, cm^{-1}) 2988, 2954, 2931, 2860, 2839, 2241, 1747, 1680, 1447, 1366, 1236; HRMS (EI$^+$): calculated for $C_{16}H_{24}O_2$ (M^+): 248.1771, found: 248.1772.

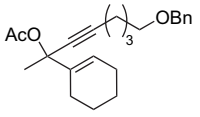
5.3.1.9. Propargyl acetate 14e.



14e

^{1}H NMR (400 MHz, $CDCl_3$): δ 7.34–7.26 (m, 5H), 6.04 (m, 1H), 4.55 (s, 2H), 3.61 (t, J=7.2 Hz, 2H), 2.58 (t, J=7.2 Hz, 2H), 2.10–1.90 (m, 7H), 1.66–1.54 (m, 7H); ^{13}C NMR (100 MHz, $CDCl_3$): δ 168.8, 138.3, 137.6, 128.4, 127.6, 123.2, 83.6, 80.8, 77.5, 72.9, 68.5, 28.0, 25.0, 23.5, 22.8, 22.1, 21.8, 20.3; IR (neat, cm^{-1}) 3062, 3029, 2988, 2931, 2857, 2246, 1746, 1496, 1453, 1437, 1364, 1238; HRMS (ES$^+$): calculated for $C_{21}H_{26}O_3Na$ (M+Na)$^+$: 349.1774, found: 349.1764.

5.3.1.10. Propargyl acetate 14f.



14f

^{1}H NMR (400 MHz, $CDCl_3$): δ 7.36–7.27 (m, 5H), 6.04 (m, 1H), 4.50 (s, 2H), 3.50 (t, J=6.4 Hz, 2H), 2.28 (t, J=7.2 Hz,

2H), 2.17–1.90 (m, 7H), 1.76–1.51 (m, 11H); ^{13}C NMR (100 MHz, $CDCl_3$): δ 168.8, 138.6, 137.8, 128.3, 127.6, 127.5, 123.1, 86.6, 80.0, 77.6, 72.8, 69.8, 28.8, 28.1, 25.4, 25.0, 23.6, 22.8, 22.1, 21.9, 18.6; IR (neat, cm^{-1}) 3087, 3062, 3029, 2932, 2857, 2793, 2242, 1742, 1453, 1365, 1236; HRMS (ES^+): calculated for $C_{23}H_{30}O_3Na$ $(M+Na)^+$: 377.2087, found: 377.2088.

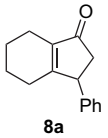
5.4. Representative procedure for Pd(II)-catalyzed rearrangement of propargyl acetates

$PdCl_2$ (4 mg, 0.02 mmol) was added to a solution of propargyl acetate **7a** (0.100 g, 0.39 mmol) in MeCN (0.6 mL), and the solution was heated to 60 °C (*≤62 °C!*) until TLC indicated complete consumption of the starting material (15 min in this case). The reaction was then cooled to room temperature and quenched with either a catalytic amount of *p*-TsOH·H_2O and MeOH, or water (reactions with non-terminal olefin substrates). After stirring the mixture for 5–10 min, ether and water were added and the aqueous layer was washed with ether (3×). The organics were combined, washed with brine (1×), dried with anhydrous $MgSO_4$, and concentrated in vacuo. Silica gel chromatography (4/1 hexanes/ethyl acetate) afforded ketone **8a** (77 mg, 92%) as a yellow oil. Cat. $HgCl_2$ reactions were carried out in the same fashion at room temperature.

5.4.1. Synthesis of enol acetate 33 from propargyl acetate 7a. To a stirred solution of **7a** (50 mg, 0.2 mmol) in dichloroethane (0.4 mL) was added $Cl_2Pd(MeCN)_2$ (5 mg, 0.02 mmol, 0.1 equiv), and the resulting mixture was then stirred at 60 °C for 12 min. The mixture was then quenched with water and the resulting aqueous layer was washed with ether (2×). The combined organics were washed with brine (1×), dried with anhydrous $MgSO_4$, and concentrated in vacuo. The crude material was redissolved in CH_2Cl_2 (1–2 mL), NEt_3 (14 μL, 0.1 mmol, 0.5 equiv) was added, and the mixture was stirred until TLC indicated total consumption of the enol acetate starting material (5–15 min). The reaction mixture was then concentrated in vacuo, and purification by alumina chromatography (hexane with minimal methylene chloride for solubility → 97.5/2.5 hexanes/ethyl acetate) afforded enol acetate **33** (17 mg, 34%) as a light yellow solid.

5.4.2. Spectroscopic data for rearranged products.

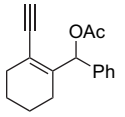
5.4.2.1. Unsaturated ketone 8a.



8a

^{1}H NMR (400 MHz, $CDCl_3$): δ 7.32–7.22 (m, 3H), 7.08 (m, 2H), 3.82 (m, 1H), 2.88 (dd, *J*=18.9, 6.9 Hz, 1H), 2.37–1.98 (m, 5H), 1.65 (m, 4H); ^{13}C NMR (100 MHz, $CDCl_3$): δ 207.9, 174.9, 141.8, 139.1, 128.8, 127.1, 126.7, 47.9, 44.8, 26.3, 22.0, 21.5, 20.0; IR (neat, cm^{-1}) 3026, 2930, 2858, 1697, 1647, 1601, 1493, 1454, 1389, 1277, 1244; HRMS (EI^+): calculated for $C_{15}H_{16}O$ (M^+): 212.1196, found: 212.1200.

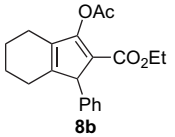
5.4.2.2. Allyl acetate 9.



9

^{1}H NMR (500 MHz, $CDCl_3$): δ 7.41–7.26 (m, 5H), 7.14 (s, 1H), 3.27 (s, 1H), 2.32–2.17 (m, 6H), 1.92 (m, 1H), 1.63–1.49 (m, 4H); ^{13}C NMR (100 MHz, $CDCl_3$): δ 169.5, 143.9, 139.2, 128.3, 127.4, 125.4, 117.9, 83.0, 81.4, 76.1, 30.1, 23.3, 22.0, 21.7, 21.0; IR (neat, cm^{-1}) 3283, 3061, 3030, 2934, 2860, 2839, 2091, 1495, 1450, 1435, 1369, 1232; HRMS (EI^+): calculated for $C_{17}H_{18}O_2$ (M^+): 254.1301, found: 254.1310.

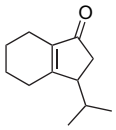
5.4.2.3. Enol acetate 8b.



8b

^{1}H NMR (400 MHz, $CDCl_3$): δ 7.26–7.05 (m, 5H), 4.26 (br s, 1H), 4.011 (m, 2H), 2.33, (s, 3H), 2.18–2.11 (m, 3H), 1.89 (m, 1H), 1.68–1.57 (m, 4H), 1.06 (t, *J*=7.1 Hz, 3H); ^{13}C NMR (100 MHz, $CDCl_3$): δ 167.5, 162.1, 160.2, 152.9, 136.9, 134.2, 128.3, 127.7, 126.5, 122.1, 59.3, 56.6, 24.0, 22.2, 21.8, 20.8, 20.5, 13.9; IR (neat, cm^{-1}) 3059, 3026, 2980, 2934, 2858, 2833, 1771, 1697, 1645, 1574, 1493, 1437, 1394, 1369, 1339, 1288; HRMS (EI^+): calculated for $C_{20}H_{22}O_4$ (M^+): 326.1513, found: 326.1520.

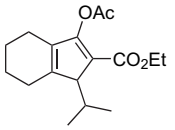
5.4.2.4. Unsaturated ketone 8c.



8c

^{1}H NMR (400 MHz, $CDCl_3$): δ 2.74 (br s, 1H), 2.31–2.10 (m, 7H), 1.76–1.58 (m, 4H), 0.98 (d, *J*=6.9 Hz, 3H), 0.62 (d, *J*=6.9 Hz, 3H); ^{13}C NMR (100 MHz, $CDCl_3$): δ 208.3, 175.3, 139.2, 47.3, 35.4, 27.6, 26.5, 22.1, 21.6, 21.2, 19.8, 15.0; IR (neat, cm^{-1}) 2954, 2932, 2870, 1697, 1647, 1391, 1277; HRMS (EI^+): calculated for $C_{12}H_{18}O$ (M^+): 178.1352, found: 178.1357.

5.4.2.5. Enol acetate 8d.

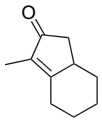


8d

^{1}H NMR (400 MHz, $CDCl_3$): δ 4.14 (m, 2H), 3.24 (br s, 1H), 2.60 (m, 1H), 2.33–2.27 (m, 5H), 2.17–2.05 (m, 2H), 1.77 (m, 2H), 1.58 (m, 2H), 1.27 (t, *J*=7.1 Hz, 3H), 1.08 (d,

J=6.9 Hz, 3H), 0.69 (d, J=6.9 Hz, 3H); ^{13}C NMR (100 MHz, $CDCl_3$): δ 167.5, 162.8, 159.0, 151.3, 135.0, 120.0, 59.4, 56.9, 28.0, 27.1, 22.5, 21.8, 20.8, 20.6, 20.5, 17.0, 14.2; IR (neat, cm^{-1}) 2933, 1772, 1695, 1571, 1458, 1383, 1371, 1321, 1288, 1261, 1232; HRMS (EI$^+$): calculated for $C_{17}H_{24}O_3Na$ (M+Na)$^+$: 315.1567, found: 315.1560.

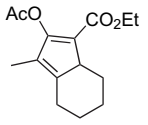
5.4.2.6. Unsaturated ketone 15a.



15a

^{1}H NMR (400 MHz, $CDCl_3$): δ 2.83 (m, 1H), 2.53 (m, 2H), 2.14–1.83 (m, 5H), 1.68 (s, 3H), 1.50 (qt, J=13.2, 3.2 Hz, 1H), 1.30 (qt, J=13.2, 3.6 Hz, 1H), 1.04 (qd, J=12, 3.2 Hz, 1H); ^{13}C NMR (100 MHz, $CDCl_3$): δ 209.0, 175.8, 132.5, 41.3, 40.2, 35.0, 28.6, 26.6, 25.5, 7.5; IR (neat, cm^{-1}) 2930, 2855, 1699, 1652, 1446, 1410, 1382, 1356, 1320, 1298; HRMS (EI$^+$): calculated for $C_{10}H_{14}O$ (M$^+$): 150.1039, found: 150.1038.

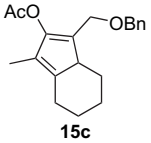
5.4.2.7. Enol acetate 15b.



15b

^{1}H NMR (400 MHz, $CDCl_3$): δ 4.17 (m, 2H), 2.96 (ddd, J=12, 5.9, 0.9 Hz, 1H), 2.74–2.67 (m, 2H), 2.30 (s, 3H), 2.10 (m, 1H), 2.00–1.96 (m, 1H), 1.81–1.73 (m, 4H), 1.47 (qt, J=13.2, 3.2 Hz, 1H), 1.27–1.12 (m, 4H), 0.91 (qd, J=12.9, 3.4 Hz, 1H); ^{13}C NMR (100 MHz, $CDCl_3$): δ 167.7, 162.6, 160.0, 152.7, 127.1, 120.8, 59.3, 49.3, 32.4, 28.2, 26.6, 25.0, 20.6, 14.3, 8.5; IR (neat, cm^{-1}) 2978, 2933, 2856, 1772, 1695, 1396, 1447, 1396, 1371, 1360, 1345, 1259, 1247, 1226; HRMS (EI$^+$): calculated for $C_{15}H_{20}O_4$ (M$^+$): 264.1356, found: 264.1368.

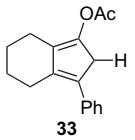
5.4.2.8. Enol acetate 15c.



15c

^{1}H NMR (400 MHz, $CDCl_3$): δ 7.39–7.25 (m, 5H), 4.43 (m, 2H), 4.15 (m, 2H), 2.75–2.64 (m, 2H), 2.38 (m, 1H), 2.19 (s, 3H), 2.09–1.78 (m, 3H), 1.71 (s, 3H), 1.43 (dt, J=13.2, 3.2 Hz, 1H), 1.17 (qt, J=13.2, 3.2 Hz, 1H), 0.88 (qd, J=11.2, 3.2 Hz, 1H); ^{13}C NMR (100 MHz, $CDCl_3$): δ 169.0, 150.1, 144.9, 138.6, 128.3, 127.8, 127.4, 126.6, 125.6, 71.2, 62.0, 48.9, 31.4, 28.3, 26.1, 25.4, 20.5, 9.2; IR (neat, cm^{-1}) 3086, 3063, 3030, 2928, 2852, 1762, 1663, 1609, 1497, 1445, 1367, 1329, 1294, 1205; HRMS (ES$^+$): calculated for $C_{20}H_{24}O_3Na$ (M+Na)$^+$: 335.1618, found: 335.1621.

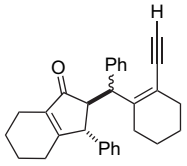
5.4.2.9. Enol acetate 33.



33

^{1}H NMR (400 MHz, C_6D_6): δ 7.38–7.28 (m, 4H), 7.17 (m, 1H), 3.67 (m, 2H), 2.56 (m, 2H), 2.45 (m, 2H), 1.84 (s, 3H), 1.49–1.38 (m, 4H); ^{13}C NMR (100 MHz, $CDCl_3$): δ 168.8, 146.8, 138.0, 137.0, 130.1, 128.3, 127.9, 126.8, 125.5, 40.4, 27.0, 23.6, 22.29, 22.26, 20.9; IR (neat, cm^{-1}) 3053, 3025, 2932, 2856, 1758, 1734, 1710, 1649, 1493, 1445, 1368, 1250, 1236, 1209; HRMS (EI$^+$): calculated for $C_{17}H_{18}O_2$ (M$^+$): 254.1301, found: 254.1302.

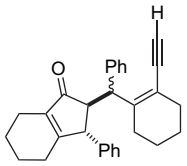
5.4.2.10. Dimer product (higher R_f spot) 34.



34

^{1}H NMR (400 MHz, $CDCl_3$): δ 7.23–7.11 (m, 8H), 6.75 (m, 2H), 4.42 (d, J=12 Hz, 1H), 3.32 (br s, 1H), 3.02 (m, 2H), 2.36–1.40 (m, 16H); ^{13}C NMR (100 MHz, $CDCl_3$): δ 207.7, 172.4, 147.1, 141.8, 141.4, 137.9, 128.5, 128.0, 127.4, 126.7, 126.5, 115.1, 84.9, 79.2, 55.6, 55.3, 54.3, 30.2, 26.4, 24.8, 22.2, 22.1, 22.0, 21.6, 20.0; IR (neat, cm^{-1}) 3302, 3250, 3084, 3059, 3026, 2932, 2858, 2085, 1699, 1649, 1599, 1492, 1450, 1434, 1391, 1275, 1246; HRMS (EI$^+$): calculated for $C_{30}H_{30}O$ (M$^+$): 406.2291, found: 406.2294.

5.4.2.11. Dimer product (lower R_f spot) 34.



34

^{1}H NMR (400 MHz, $CDCl_3$): δ 7.34–7.10 (m, 10H), 4.57 (d, J=11.6 Hz, 1H), 3.71 (br s, 1H), 3.19 (dd, J=11.6, 2.4 Hz, 1H), 3.14 (s, 1H), 2.27–1.01 (m, 16H); ^{13}C NMR (100 MHz, $CDCl_3$): δ 207.5, 172.5, 148.3, 141.8, 140.3, 138.0, 128.8, 128.6, 127.8, 127.7, 126.9, 126.3, 115.1, 84.6, 80.4, 54.8, 54.0, 52.3, 30.2, 26.2, 24.7, 22.3, 21.8, 21.6, 21.5, 20.1; IR (neat, cm^{-1}) 3302, 3059, 3026, 2932, 2858, 2087, 1699, 1651, 1601, 1493, 1452, 1389, 1275, 1244; HRMS (EI$^+$): calculated for $C_{30}H_{30}O$ (M$^+$): 406.2291, found: 406.2299.

Acknowledgements

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of the Chemistry Instrumentation Center at the University of Buffalo) for performing HRMS analysis.

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13. For most other substrates, $\geq$10% $PdCl_2$ was optimal.
14. ^{1}H NMR shows similar peaks to that of a structurally-related 2-ethoxycyclopentadiene: Hatanaka, M.; Himeda, Y.; Imashiro, R.; Tanaka, Y.; Ueda, I. *J. Org. Chem.* **1994**, *59*, 111.
15. Longer reaction times or higher catalyst loadings led to complex mixtures minus starting material. Crude NMR indicated that some cyclized product was likely formed, but it could not be isolated free of other compounds.
16. Classes of palladium(II) complexes examined: Pd(II)–bisoxazolines (trifluoroacetate and tetrafluoroborate derivatives); see: (a) Uozumi, Y.; Kato, K.; Hayashi, T. *J. Am. Chem. Soc.* **1997**, *119*, 5063; (b) Uozumi, Y.; Kato, K.; Hayashi, T. *J. Org. Chem.* **1998**, *63*, 5071; (c) Kato, K.; Tanaka, M.; Yamamoto, Y.; Akita, H. *Tetrahedron Lett.* **2002**, *43*, 1511 and Pd(II)–BINAP (tetrafluoroborate derivative). In most experiments, no cyclization was observed. Instead, the reaction produced a mixture of uncyclized products. Pd(II) chloride–bisoxazoline complex did promote the rearrangement of **7a**, but isolated product **8a** was racemic.
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18. A reviewer correctly pointed out that intermediate **20** could cyclize to give **23**. This can also be viewed as a 4π-electrocyclization if a (zwitterionic) resonance form of the carbene is considered.
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25. COSY data in conjunction with ^{1}H NMR *J* values for each diastereomer indicate a trans-relationship between the cyclopentenone stereocenters.