perimentally, the Cu^{II}/K_2ZnF_4 system has a shorter lifetime (0.5 μs) and evidently less efficient emission than the cubic system (1.8 μs) while the related Cu^{II}/Ba_2ZnF_6 system, where the copper(II) is at a site of stronger tetragonal compression, showed no observable d-d emission. The ability of a six-coordinate copper(II) complex to fluoresce would seem to depend on a large (cubic) ligand field splitting at a site of near cubic symmetry as well as the absence of high energy accepting modes that act as a relaxation pathway.

Acknowledgment. We thank Dr. Hans Riesen for his assistance with some of the experiments.

Palladium-Catalyzed Cascade Carbometalation of Alkynes and Alkenes as an Efficient Route to Cyclic and Polycyclic Structures[1]

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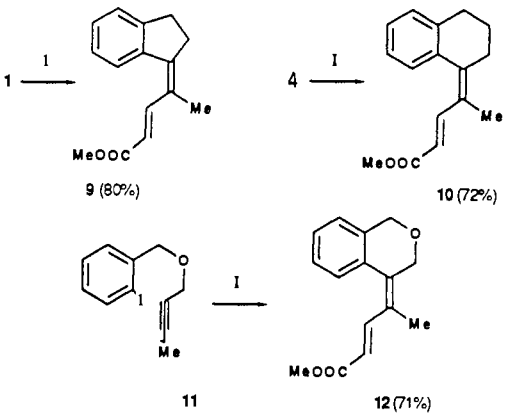
The Pd-catalyzed arylation and alkenylation of alkenes (the Heck reaction) have been widely used intermolecularly,[2] and their intramolecular versions are rapidly growing into a major new tool for the synthesis of heterocycles[2,3] and carbocycles.[4] On the other hand, the corresponding reaction of alkynes have not been extensively investigated.[5-8] Whereas alkene carbopalladation can be readily followed by dehydropalladation for recycling Pd complexes as catalysts, alkyne carbopalladation generally produces thermally stable alkenylpalladium species in a stoichiometric manner, requiring further transformations for recycling Pd complexes.

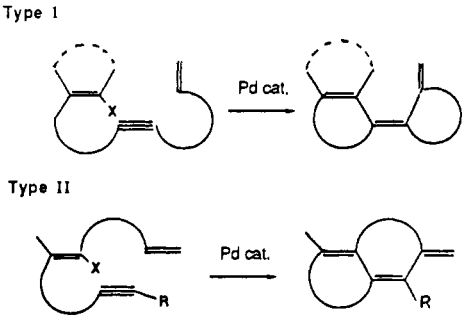
Our efforts to trap the alkenylpalladium species by carbonylation were only partially successful due to competitive carbonylation before carbopalladation. Thus, treatment of **1** with CO (600 psi), NEt_3 (1.5 equiv), MeOH (4 equiv), and 3 mol % of $Pd(PPh_3)_4$ in MeCN at 100 °C[9] gave a 60:40 mixture of **2** and **3** in 70% combined yield, while the reaction of **4** produced a 30:70 mixture of **5** and **6** in 60% combined yield. In neither case was the third expected product **7** or **8**[9] obtained. The formation of **2** and **5** was >95% stereoselective.

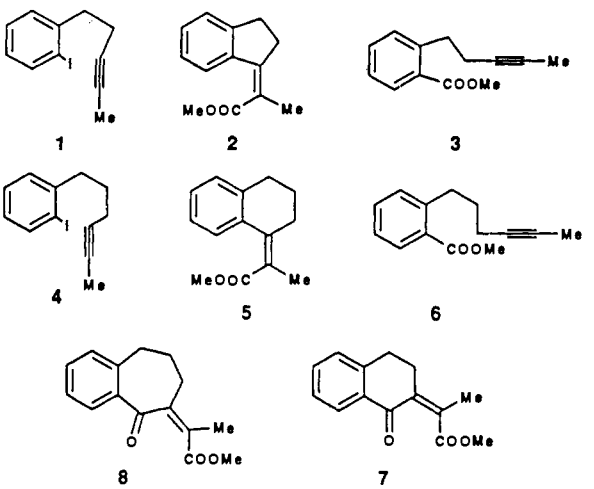
Scheme I[a]



[a] I = CH_2=CHCOOMe (1 equiv), NEt_3 (2 equiv), 3 mol % $Pd(PPh_3)_4$, MeCN reflux, 12 h.

Scheme II





In view of the above results, we were pleased to find that treatment of **1** and **4** with methyl acrylate (1 equiv) in refluxing MeCN for 12 h in the presence of 3 mol % $Pd(PPh_3)_4$ and NEt_3 (2 equiv) afforded **9** and **10** in 80 and 72% yields, respectively, without contamination by the noncyclized cinnamate esters. The stereoisomeric purities of **9** and **10** were >98 and >95%, respectively. Similarly **11** gave >98% pure **12** in 71% yield. Prolonged reaction times must be avoided, since they led to lower stereoselectivity figures. Throughout this investigation, the ste-

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(5) Maitlis, P. M. *The Organic Chemistry of Palladium*; Academic Press: New York, 1971; Vol. II.

(6) For arene-forming reactions similar to those described in ref 5 that are mostly stoichiometric in Pd, see: Wu, G.; Geib, S. J.; Rheingold, A. L.; Heck, R. F. *J. Org. Chem.* **1988**, *53*, 3238 and earlier references cited therein.

(7) For catalytic carbopalladation of alkynes followed by hydrogenolysis, see: (a) Arcadi, A.; Cacchi, S.; Marinelli, F. *Tetrahedron* **1985**, *41*, 5121. (b) Burns, B.; Grigg, R.; Sridharan, V.; Worakun, T. *Tetrahedron Lett.* **1988**, *29*, 4325.

(8) After completion of this study, a paper describing a cascade carbopalladation involving enynes in a different context was published [Trost, B. M.; Lee, D. C. *J. Am. Chem. Soc.* **1988**, *110*, 7255].

(9) Tour, J. M.; Negishi, E. *J. Am. Chem. Soc.* **1985**, *107*, 8289.

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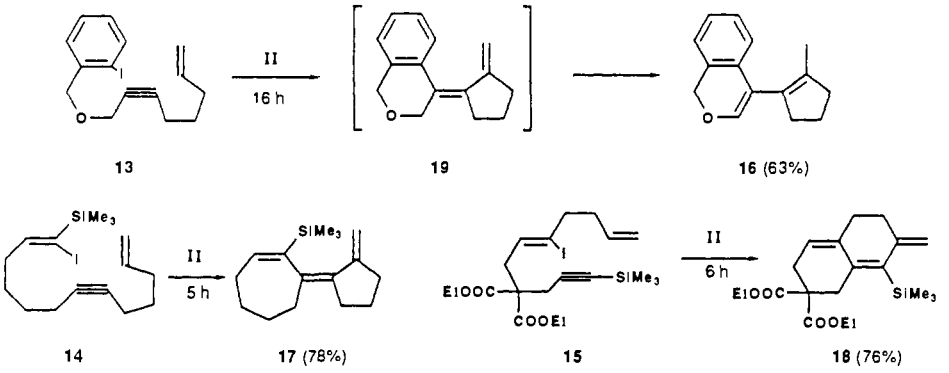
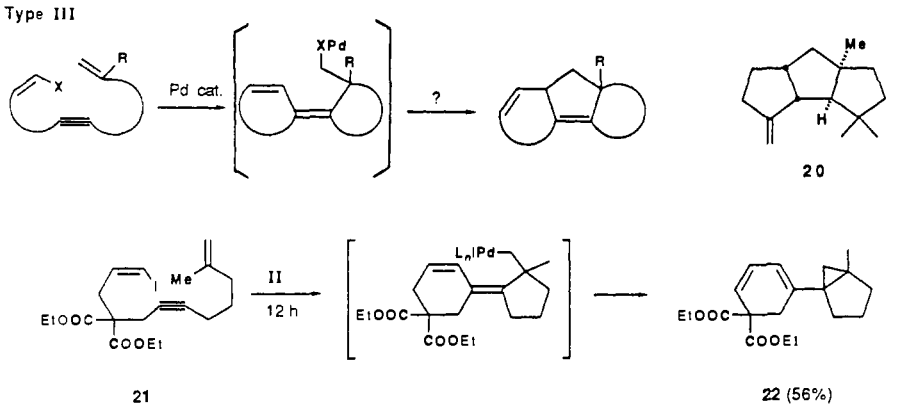
Scheme III[a]



[a] II = 3 mol % $Pd(PPh_3)_4$, NEt_3 (2 equiv), MeCN, reflux.

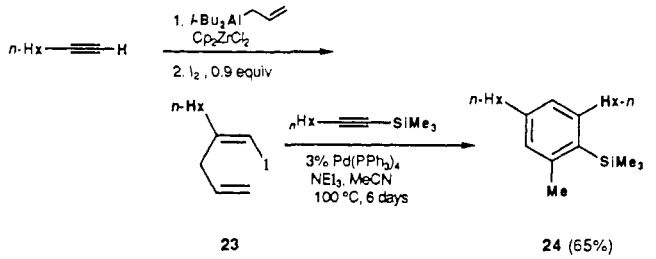
Scheme IV



reochemical assignments were made based on a combination of ^1H and ^{13}C NMR as well as ^1H 2D NOESY NMR.

Having achieved the intramolecular–intermolecular cascade carbopalladation described above, we then considered the intramolecular–intramolecular cascade carbopalladation of the following two types. A similar cascade involving alkenes was recently reported by Overman.[10] As indicated by the high yield conversions of **13–15** into **16–18**, respectively, both types of transformations are eminently feasible. Specifically, **13** was prepared from *o*-iodobenzyl alcohol via bromination with PBr_3–pyridine and etherification with the sodium salt of 7-octen-2-yn-1-ol in 75% overall yield and was then treated with 3 mol % $Pd(PPh_3)_4$ and NEt_3 (2 equiv) in refluxing MeCN (condition II) for 16 h to give isomerically pure double cyclization product **16** in 63% yield (81% by GLC). Since the expected initial product is **19**, complete isomerization of the two double bonds must have taken place before completion of the cyclization reaction. On the other hand, the original regiochemistry is largely retained in the conversion of **14** into **17** in 78% yield under the same condition over 5 h. The *Z* stereochemistry of **14** is essential to observing the desired cyclization, since its *E* isomer did not give **17** at all even after 24 h under the same reaction conditions. The same reaction of **15** gave **18** in 76% yield as a >90% pure compound. Thus, the extent of double bond isomerization including aromatization is minimal, although the isolated product turned out to be relatively unstable. It is important to note that, unlike radical cyclization reactions,[11] not only five- and six-membered rings but also seven-membered rings are accessible by this method. In principle, type II sequence can be extended to achieve a series of three of more carbometalation reactions. Such possibilities are under current investigation.

Scheme V



We have also briefly explored an intriguing possibility of extending type I process to achieve the third carbopalladation as a potentially attractive route to tricyclic compounds such as capnellene[12] (**20**). As a test system, **21** was prepared and subjected to the standard reaction condition II. Interestingly, the major monomeric cyclization product produced in 56% yield was **22**. A minor unidentified but apparently isomeric product was also obtained in 14% yield. Evidently, the presumed bicyclization intermediate underwent the third carbopalladation with the proximal double bond which leads to the formation of an energetically favorable allylpalladium species that can dehydropalladate to give **22**.

In addition to the intra–inter and intra–intra cascades presented above, it is also feasible to achieve inter–intra cascade carbopalladation processes as exemplified by the following regioselective conversion of **23**[13] into a highly substituted benzene derivative **24**[14] in 65% yield (83% by GLC).

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(14) Its regiochemistry was unequivocally established by its treatment with CF_3COOH, which cleanly produced 3,5-di-*n*-hexyltoluene in 80% yield.

Acknowledgment. We thank the National institutes of Health (GM 36792) for support.

Supplementary Material Available: Spectral data (IR, MS, ^1H NMR, and ^{13}C NMR) for compounds **1–6**, **9**, **10**, **12–18**, **21**, **22**, and **24** (4 pages). Ordering information is given on any current masthead page.

Novel Stereospecific Silyl Group Transfer Reactions: Practical Routes to the Prostaglandins

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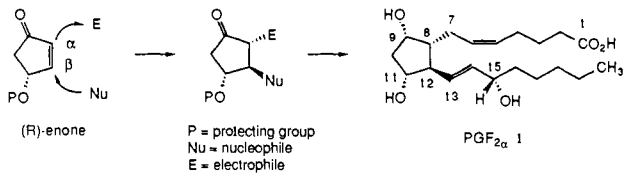
The notion of synthesizing prostaglandins by dialkylation of an α,β-unsaturated ketone goes back to the early days of the field.[1] The first success in a fully functionalized setting was realized by Stork and Isobe.[2] Major advances in conciseness and efficiency have been introduced by Noyori,[3,4] Johnson,[5] and Corey.[6]

While there have been countless variations, a common theme is apparent. Addition of a nucleophilic version of the C_{13}–C_{20} ("lower-chain") to C_{12} generates a C_8–C_9 enolate which is trapped with an electrophile suitable for construction of the C_7–C_1 ("upper") chain. In these schemes, the R enantiomer is employed. The stereochemical rationale of this method is that the organometallic nucleophile (Nu) attacks anti to the OP group and the electrophile attacks C_8 anti to the "lower" chain installed at C_{12}. The proper configuration at C_{15} is achieved either from the use of a suitable educt[7] or by reduction of the C_{15} ketone.[7,8] The general outlines of the previous three-component strategy are implied in Scheme I, where $PGF_{2\alpha}$ is the goal system.

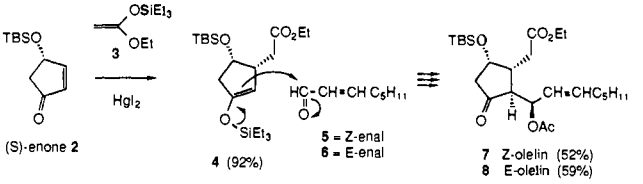
In this paper we disclose a new strategy wherein the C_{12}–C_{13} bond is established from an electrophilic version of C_{13}, and the C_8–C_7 bond is fashioned from a nucleophilic version of C_7. As will be seen, this method has significant advantages in terms of simplicity of building blocks and reactions. Either isomer at C_{15} becomes readily available by stereochemical communication.[9]

The success of the route arises from the confluence of several rather interesting findings. The first is that a group transfer reaction of (*S*)-enone **2** (vide infra) with the silylketeneacetal derivative **3** occurs cis to the OTBS group to produce the specific enolate equivalent **4**.[10,11] This compound reacts with (*Z*)-[12a] or (*E*)-octenal[12b] (**5** and **6**, respectively) under catalysis by $TiCl_4$ to produce the C_{12}–C_{13} syn aldol products.[13,14] In each case, the aldehyde has entered trans to the carbethoxymethyl group at C_8. In each instance, the aldol process involves a second group transfer reaction of the triethylsilyl (TES) unit. Each aldehyde attacks trans to the resident group at C_8, and a syn C_{12}–C_{13} siloxyaldol system is produced in an essentially stereospecific reaction. In each instance selective cleavage of the TES function is achieved with maintenance of the OTBS group.[15] For the product derived

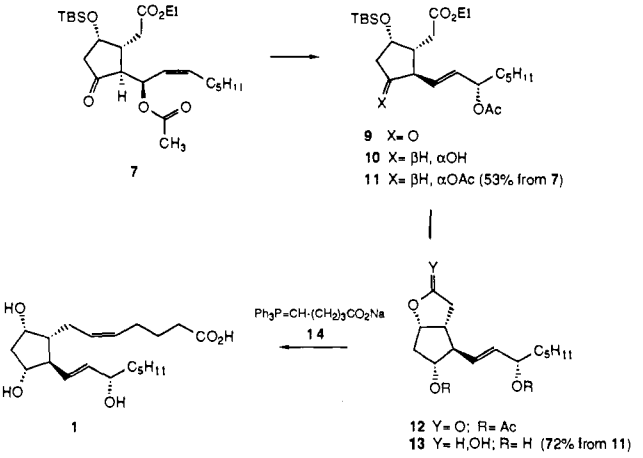
Scheme I



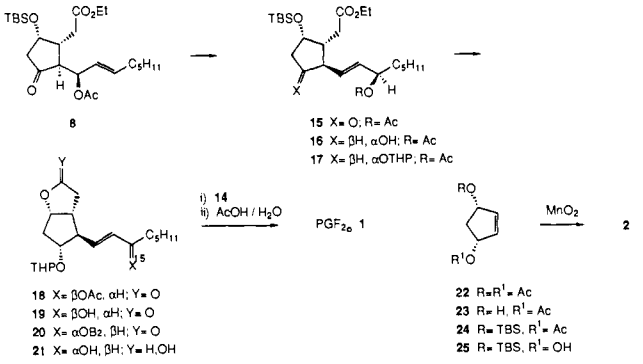
Scheme II



Scheme III



Scheme IV



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(10) This phenomenon which awaits full explanation is restricted to Lewis acid catalyzed additions (as opposed to cuprate additions which occur anti to the OTBS group). It has also been extended to $TiCl_4$ mediated addition of allyltrimethylsilane to **2** (Chow, K. Yale University unpublished results). For similar results using 4-OTBS cyclohexenone, see: a) Danishefsky, S. J.; Simoneau, B. *Pure Appl. Chem.* **1988**, *60*, 1555. b) Danishefsky, S. J.; Simoneau, B. *J. Am. Chem. Soc.* **1989**, 0000.

(11) All new compounds were characterized by ^1H NMR, IR, mass spectrometry, HRMS, and/or elemental analyses.

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