Tetrahedron Letters,Vol.29,No.51,pp 6745-6748,1988 0040-4039/88 $3.00 + .00
Printed in Great Britain Pergamon Press plc

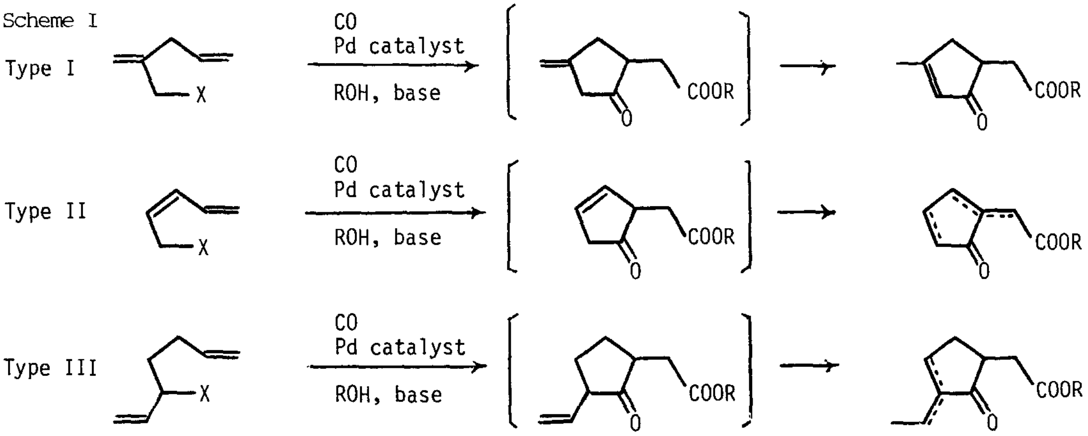
PALLADIUM-CATALYZED CYCLIC ACYLMETALATION OF ALLYLIC ELECTROPHILES AS A ROUTE TO CYCLOPENTENONE DERIVATIVES[1]

Ei-ichi Negishi,* Guangzhong Wu, and James M. Tour
Department of Chemistry, Purdue University, W. Lafayette, Indiana 47907, U.S.A.

SUMMARY: Treatment of allylic electrophiles containing an additional alkene moiety in a suitable position with CO, NEt_3, MeOH, and a catalytic amount of a Pd catalyst, e.g., $Cl_2Pd(PPh_3)_2$, can induce cyclic acylmetallation followed by carbonylative esterification to produce α-methoxycarbonylmethyl cyclopentenones.

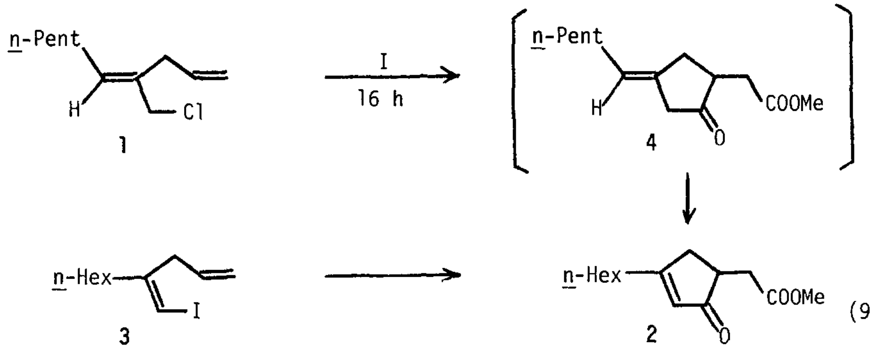
We have recently reported the synthesis of five- and six-membered cyclic ketones via a cyclic acylmetalation reaction of alkenyl and aryl halides catalyzed by palladium complexes.[2] Since allyl halides and related electrophiles are also known to undergo facile oxidative addition to Pd(0) complexes,[3] we sought their cyclic acylpalladation as an attractive and potentially more economical alternative. Three different types of cyclic acylpalladation for allyl derivatives are conceivable (Scheme I for the synthesis of cyclopentenones).

Scheme I



We now report that both Type I and Type II cyclic acylpalladation reactions can indeed proceed as shown in Scheme I to produce the corresponding cyclopentenone derivatives. Typically, (E)-4-chloromethyl-1,4-decadiene(**1**) prepared from 2-octyn-1-ol via CuI-catalyzed allylmagnesiation[4] using allylmagnesium bromide in Et_2O followed by conversion of the resulting alcohol to the corresponding chloride,[5] was carbonylated (CO pressure, 600 psi) using a 45 mL stainless steel autoclave (Parr Instrument Co.) in 1:1 benzene-CH_3CN for 16 h at 100°C in the presence of NEt_3 (1.5 equiv), MeOH (4 equiv), and $Cl_2Pd(PPh_3)_2$ (0.05 equiv).[2b] The standard extractive workup followed by distillation provided a 90% yield of isomerically pure **2**: bp 105-110°C (0.1 mm Hg, Kugelrohr) (eq 1). This compound was identical with that prepared from (*Z*)-1-iodo-2-*n*-hexyl-1,4-pentadiene(**3**).[2b] Although the initially formed product must be **4**, all our attempts to detect this compound have failed. To examine the effects of the leaving group, several derivatives of (*E*)-2-allyl-2-nonyn-1-ol containing Cl, Br, OAc, OCO_2Me, $OPO(OEt)_2$, and OSO_2Me (**5a-5f**) were subjected to the above-described acylpalladation conditions. All six compounds reacted as expected and produced **6** in 88, 94, 42, 65, 76, and 82 yields, respectively (eq 2). The use of $Cl_2Pd(PEt_3)_2$ as a catalyst led to a 32% yield of **2** along with a 55% yield of a mixture of methyl 3-allyldecenoates. The use of *i*-PrOH(55%), *t*-BuOH(0%), and PhOH(98%) in place of MeOH gave the corresponding cyclized esters in the yields in parentheses, suggesting that alcohols of relatively low basicity e.g., MeOH and PhOH, are desirable. As indicated in eq 3, even a phenyl group in conjugation with the allylic olefin group, as in **7**, does not prevent the double bond migration, the only product from **7** being **8**. Additional substituents on the cyclopentenone ring can be accommodated as indicated by conversion of **9-11** into **12**, **13**, and **15**, respectively (eqs 4-6). However, some complications were also noted. Thus, **12**, obtained in 83% yield, was a 82/12 mixture of **12a** and **12b**. The formation of **13** (61% by GLC) was accompanied by that of **14** (33% by GLC). In the low-yield conversion of **11** into **15**, however, no other byproducts were detectable by GLC. The preparation of **9** and **10** was readily achieved via the above-mentioned CuI-catalyzed allylmagnesiation[4] using crotylmagnesium bromide and methyallylmagnesium bromide, respectively, while that of **11** involved the CuI-catalyzed allylmagnesiation of 2-butyn-1-ol, oxidation, addition of MeMgBr, conversion of the alcohol into the chloride.

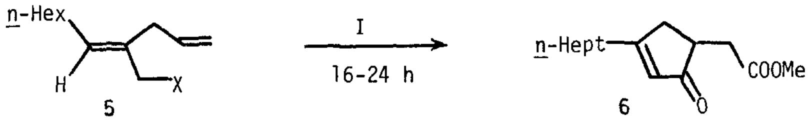
To probe the feasibility of Type II cyclic acylpalladation, **16** was prepared from 2-nonyn-1-ol via reduction with $LiAlH_4$-iodinolysis,[7] vinylation with vinylzinc bromide (3 equiv) and 5 mol % of $Cl_2Pd(PPh_3)_2$,[8] and conversion of the alcohol into the chloride.[5] Cyclic acylpalladation of **16** under the same conditions as above for 24 h indeed produced the expected product **17** in 50% yield along with very minor amounts (2-3% each) of **18** and **19** (eq 7). In the reaction of **20**, the product **21** was isomerically pure, although its yield was relatively low (eq 8). That Type II acylpalladation must require the cis configuration of the pentadienyl moiety was indicated by clean conversion of (*E*)-5-bromo-1,3-pentadiene(**22**) into the carbonylative esterification product **23** in 94% yield. Interestingly, **24** was converted into an 80:20 mixture of **25** formed via Type I acylpalladation and **26** formed via Type II acylpalladation in 62% overall yield. Unfortunately, our attempts to induce Type III cyclic acylpalladation using **27** as the substrate led to a mixture of unidentified products without producing the desired cyclization product in any significant (>5-10%) yield. Spectral data of the above mixture suggest that carbonylative esterification and elimination of **27** must have taken place as side reactions.



(1)

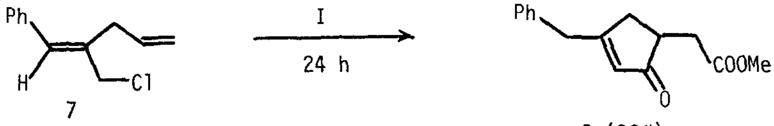
(90% from 1)

I = CO (600 psi), NEt_3 (1.5 x), MeOH (4 x), 5 mol % $Cl_2Pd(PPh_3)_2$, MeCN-PhH, 100°C.



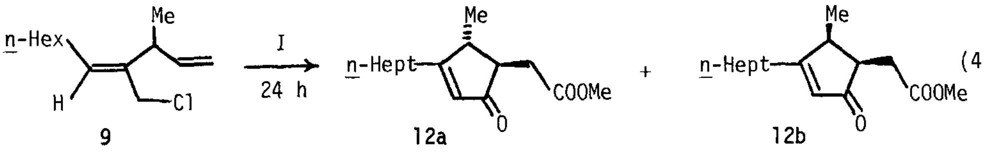
(2)

a: X = Cl (88%). b: X = Br (94%). c: X = OAc (42 %). d: X = OCO_2Me (65 %).
e: X = $OPO(OEt)_2$ (76 %). f: X = OSO_2Me (82%).



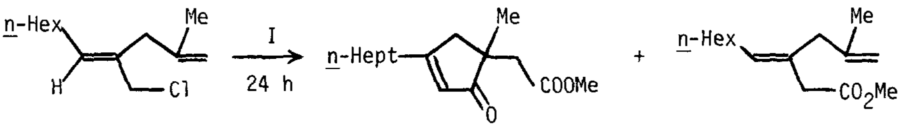
8 (93%)

(3)



(4)

12a + 12b = 83%. 12a/12b = 88/12

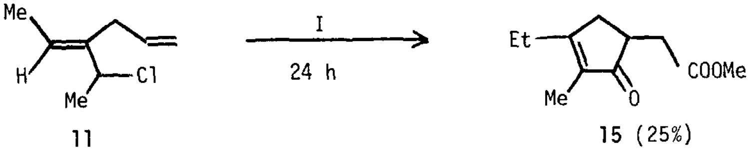


10

13 (54%)

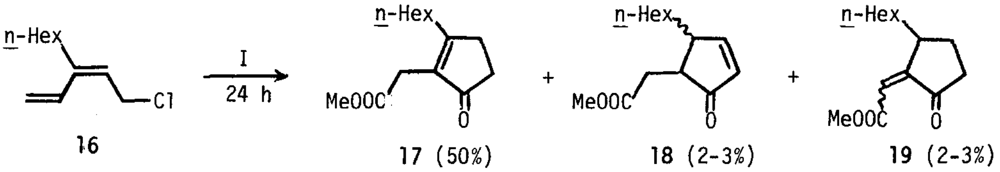
14 (33%)

(5)

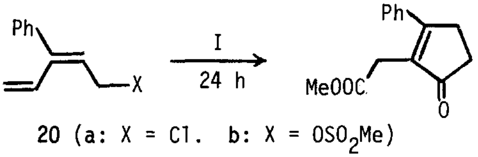


15 (25%)

(6)

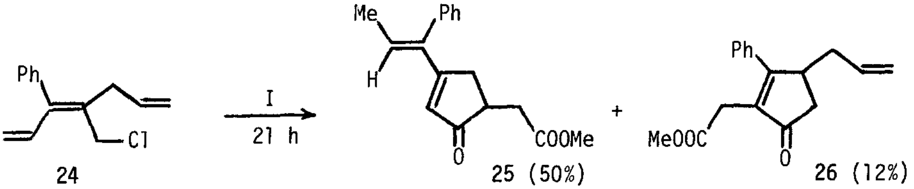


(7)



21 (33% from **20a** and 39% from **20b**) (8)

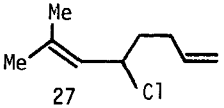
20 (a: X = Cl. b: X = OSO_2Me)



(9)

22

23



27

Acknowledgments. We thank the National Institutes of Health (GM 36792) for support. We also thank Dr. C. Jones for technical assistance in obtaining some NMR spectra.

References and Notes

(1) Metal-Promoted Cyclization. 23. Part 22. Negishi, E.; Nguyen, T.; O'Connor, B.; Evans, J. M.; Silveira, A., Jr. Heterocycles, submitted.

(2) (a) Negishi, E.; Miller, J. A. J. Am. Chem. Soc. **1983**, 105, 6761. (b) Tour, J. M.; Negishi, E. J. Am. Chem. Soc. **1985**, 107, 8289. (c) Negishi, E.; Tour, J. M. Tetrahedron Lett. **1986**, 27, 4869. (d) Negishi, E.; Sawada, H.; Tour, J. M.; Wei, Y. J. Org. Chem. **1988**, 53, 913.

(3) For a review, see Collman, J. P.; Hegedus, L. S.; Norton, J. R.; Finke, R. G. Principles and Applications of Organotransition Metal Chemistry, University Science Books, Mill Valley, CA, 1987.

(4) Duboudin, J. G.; Jousseaume, B. J. Organomet. Chem. **1979**, 168, 1.

(5) Corey, E. J.; Kim, C. U.; Takeda, M. Tetrahedron Lett. **1972**, 4339.

(6) All isolated cyclized products have yielded satisfactory spectral data including high resolution mass spectra.

(7) Corey, E. J.; Katzenellenbogen, J. A.; Posner, G. H. J. Am. Chem. Soc. **1967**, 89, 4245.

(8) Negishi, E.; Takahashi, T.; Baba, S.; Van Horn, D. E.; Okukado, N.; Luo, F. T. J. Am. Chem. Soc. **1987**, 109, 2393.

(Received in USA 31 August 1988)