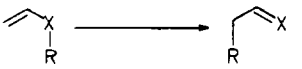
(14) Cf. Whitlock, H. W., Jr.; Smith, G. L. *J. Am. Chem. Soc.* **1967**, *89*, 3600.
(15) Muller, E.; Heischkeil; Bauer, M. *Justus Liebegs Ann. Chem.* **1964**, *677* 55.
(16) It should be emphasized that we cannot rule out the possibility that formylation of the aromatic ring might have occurred under the various reaction conditions but that other functionalities were perturbed. We can only state with certainty that in no case were we able to detect the presence of pretazettine (**2**) or its *O*-methyl ether (**19**), both of which were available to us through the courtesy of Professor P. Scheuer and Professor E. Furusawa of the University of Hawaii.
(17) The TLC (acetone) of the reaction mixture prior to the total consumation of **4a** indicated the presence of the mixed orthoformate **4e** which had been independently prepared and characterized by the reaction of **4a** with trimethylorthoformate and aluminum chloride at 100 °C. Following an aqueous workup, the TLC of the crude product showed only **20** and no trace of **4e**.
(18) Bailey, D. T. Ph.D. Thesis, Iowa State University, 1968.
(19) Sainsbury, M. "Rodd's Chemistry of Carbon Compounds", Coffey, S., Ed., Elsevier Scientific: Amsterdam, 1977; Vol. IV (B), p 165.
(20) Address correspondence to the Department of Chemistry, Yale University, New Haven, Conn. 06520.

Samuel Danishefsky,*[20] Joel Morris*[20]
George Mullen, Ronald Gammill
Department of Chemistry, University of Pittsburgh
Pittsburgh, Pennsylvania 15260
Received November 26, 1979

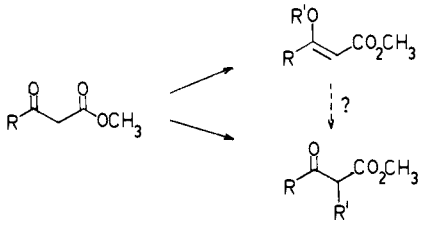
A 1,3-*O*- to -*C*-Alkyl Shift Catalyzed by Palladium

Sir:

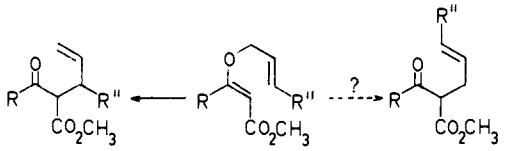
1,3-Alkyl shifts as in eq 1 represent a class of reactions that generally require rather stringent conditions to perform.[1] Such


(1)

a result stems from the requirement that, for an orbital symmetry allowed reaction, an inversion must accompany the 1,3 migration (either antarafacial with respect to the allyl unit or inversion at the migrating center) or the reaction must proceed via nonconcerted pathways. The classic contest between O and C alkylation with β-keto esters generates the need for a reac-

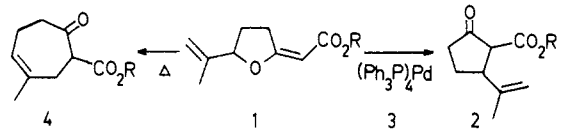


tion that would allow conversion of the O-alkylated product into the C-alkylated product. Only when R′ = allyl does such a reaction occur but with inversion of the allyl residue via a



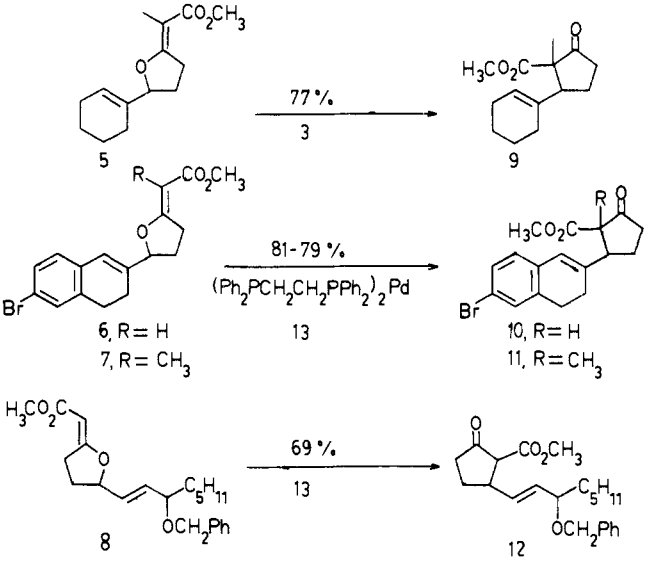
Claisen rearrangement.[2] We report herein that palladium(0) catalyzes a 1,3 shift with no allyl inversion which has led to a new cyclopentanone synthesis.

Alkylidenetetrahydrofurans such as **1** undergo thermal rearrangement to cycloheptanones (e.g., **4**) as reported by



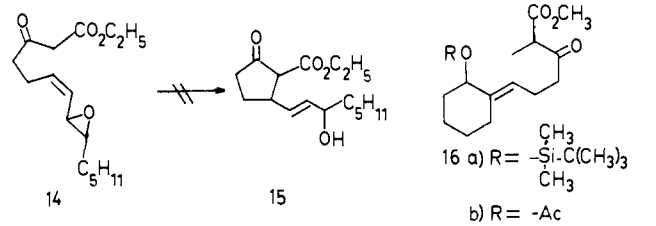
Rhoads.[3] On the other hand, subjection of **1** (R = C_2H_5) to 6 mol % of tetrakis(triphenylphosphine)palladium (**3**) in refluxing DME led to the cyclopentanone **2** (R = C_2H_5) whose spectral data compared excellently with those of an authentic sample of **2** (R = CH_3).[4] No trace of the cycloheptenone **4** was seen.

The generality of this 1,3 shift was explored with substrates **5–8**.[5,6] Isomerization of **5** to **9** with **3** as catalyst proceeded



smoothly in Me_2SO at 120 °C to give **9**[5,6,8] as a 1:1 *Z/E* mixture. Use of bis[1,2-bis(diphenylphosphino)ethane]palladium (**13**)[7] as the catalyst effected the reaction somewhat more rapidly. Performing the reaction with **3** as catalyst in DMF with the addition of anhydrous zinc chloride gave **9** in a *Z/E* ratio of 3.5:1. Interestingly, isomerizing **7** with **3** gave very poor results, whereas, using the diphos catalyst **13**, the reaction proceeded smoothly at 50 °C in Me_2SO to give **11**[5,6,8] in a 3.5:1 *Z/E* ratio. Use of pyridine-Me_2SO, acetonitrile, or DMF as solvent was somewhat less satisfactory and gave *Z/E* ratios of 2.7:1, 2:1, and 2:1, respectively. Replacing the methyl group in **7** by hydrogen, i.e., **6**, produced the isomerized product **10**[5,6] with a *Z/E* ratio of ~1:13. However, in this case, it was not possible to ascertain whether this was simply a result of equilibration of a kinetically formed product mixture. Isomerization of **8** with **13** as catalyst in dioxane gave the prostaglandin A_2 intermediate[9] **12**[5,6] in excellent yield.[10a] Use of catalyst **13** (3–6 mol %) in Me_2SO at 60 °C effected the rearrangement of **1** to **2** (R = C_2H_5) in 80% yield.

These results are especially interesting in light of the reported failure of **14** to cyclize to **15**.[9] We, too, failed in our



attempts to cyclize similar substrates—only the O-alkylated products were obtained. Indeed, treatment of **16b** with NaH or triethylamine and catalyst **3** led to O-alkylated product **5**. The alkylidene tetrahydrofuran **5** was best prepared by treatment of **16a** with 10 mol % ferric chloride in acetic anhydride[10b] (60%) at 0 °C and could then be isomerized with palladium(0) to the desired C-alkylated product **9**. Similarly, **19, 20,** and **22,** did not undergo C alkylation, but were converted in excellent yields into the O-alkylated precursors **6, 7,** and **8,** respectively, upon treatment with boron trifluoride etherate. Thus, this new reaction provides, in one class of substrates, a solution to the persistent problem of O vs. C al-

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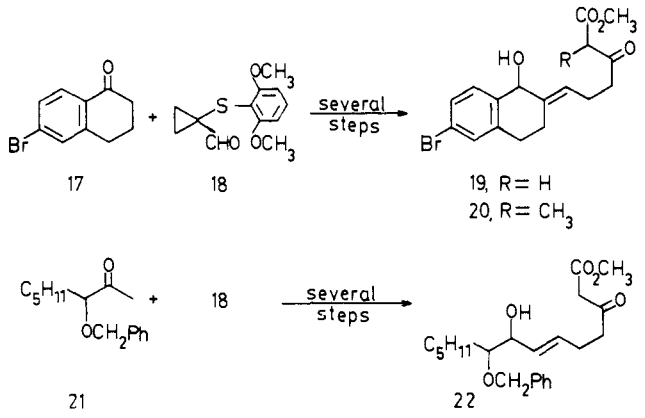
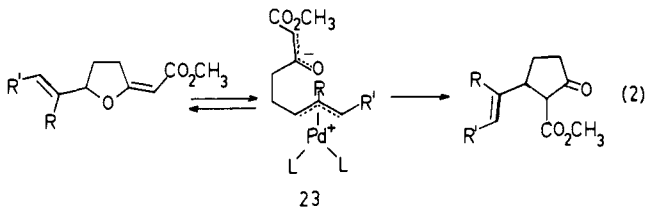


kylation of β-keto esters. The fact that **19, 20,** and **22** are readily available from the ketones **17** and **21** using a new conjunctive reagent **18**[11] makes this 1,3 shift a lynchpin in a new cyclopentanone synthesis. The formation of **10, 11,** and **12** illustrate applications of this new methodology in prostaglandin[9] and steroid synthesis.

The mechanism of this 1,3 shift can be thought to involve an oxidative addition of the allyl ether to palladium(0) as in eq 2 to form a zwitterion **23.**[12] This intermediate collapses by



C alkylation to form the observed product. The regiochemistry of the collapse is quite interesting in that a five-membered-ring product is observed, even in the case of R′ = H where seven-membered-ring formation could have proceeded by attack at the less hindered carbon of the allyl unit.[13] These results stand in stark contrast to cyclizations to form lactones in which the larger of the two possible ring sizes dominates even when an eight-membered ring results rather than a six.[14] Applications and additional mechanistic studies into this metal-catalyzed 1,3 shift are underway.[15] This new reaction illustrates an ability of a transition metal to change the normal rules of reactivity of an organic system.

Acknowledgment. We thank the National Science Foundation and the General Medical Sciences Institute of the National Institutes of Health for the generous support of our programs.

References and Notes

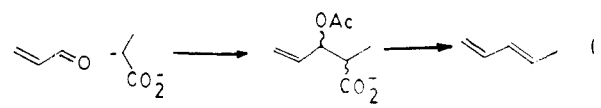
(1) For recent studies and leading reference in alkoxide-promoted 1,3 shifts see: Thies, R. W.; Seitz, E. P. *J. Org. Chem.* **1978,** *43,* 1050. Wilson, S. R.; Misra, R. N. *Ibid.* **1978,** *43,* 4903.
(2) For a review, see Rhoads, S. J.; Raulins, N. R. *Org. React.* **1975,** *22,* 1.
(3) Rhoads, S. J.; Watson, J. M. *J. Am. Chem. Soc.* **1971,** *93,* 5813. Demole, E.; Enggish, P. *Chem. Commun.* **1969,** 264.
(4) Trost, B. M.; Vladuchick, W. C. *J. Org. Chem.* **1979,** *44,* 148.
(5) This compound has been fully characterized by spectral means and elemental analysis and/or elemental composition by high resolution mass spectroscopy.
(6) Selected spectral data are as follows. **8:** IR ($CHCl_3$) 1700, 1640 cm^{-1}; NMR (270 MHz) δ 0.87 (t, *J* = 6 Hz, 3 H), 1.16–1.92 (m, 9 H), 2.27 (m, 1 H), 3.02 (m, 1 H), 3.29 (dddd, *J* = 18.5, 9, 4.5, 1.5 Hz, 1 H), 3.67 (s, 3 H), 3.77 (m, 1 H), 4.35 (d, *J* = 12 Hz, 1 H), 4.56 (two d, *J* = 12 Hz, 1 H), 4.86 (m, 1 H), 5.35 (br s, 1 H), 5.67 (m, 2 H), 7.30 (br s, 5 H); mol wt calcd for $C_{22}H_{30}O_4$ 358.2144, found 358.2144. **5:** IR (CCl_4) 1700, 1635 cm^{-1}; NMR (CCl_4) δ 1.3–1.7 (m, 4 H), 1.62 (t, *J* = 1 Hz, 3 H), 1.7–2.1 (m, 6 H), 2.5–3.3 (m, 2 H), 3.51 (s, 3 H), 4.5 (br t, *J* = 7 Hz, 1 H), 5.55 (br m, 1 H), Anal. ($C_{14}H_{20}O_3$) C, H, mol wt. **6:** IR (CCl_4) 1695, 1635, 1590, 1555 cm^{-1}, NMR (270 MHz, CCl_4) δ 1.88–2.35 (m, 4 H), 2.81 (t, *J* = 8 Hz, 2 H), 3.05 (m, 1 H), 3.33 (dddd, *J* = 17.5, 8.7, 4.5, 1.5 Hz, 1 H), 3.68 (s, 3 H), 4.95 (t, *J* = 7.2 Hz, 1 H), 5.39 (t, *J* = 1.5 Hz, 1 H), 6.41 (br s, 1 H), 6.90 (d, *J* = 8 Hz, 1 H), 7.26 (m, 2 H). Anal. ($C_{17}H_{17}BrO_3$) C, H. **7:** IR (CCl_4) 1700, 1638, 1595, 1485 cm^{-1}; NMR (270 MHz, $CDCl_3$) δ 1.88 (t, *J* = 1.5 Hz, 3 H), 1.93 (m, 1 H), 2.25 (m, 3 H), 2.81 (t, *J* = 8.2 Hz, 2 H), 3.01 (m, 1 H), 3.26 (dddq, *J* = 18, 9, 5, 1.5 Hz, 1 H), 3.70 (s, 3 H), 4.93 (t, *J* = 7.5 Hz, 1 H), 6.39 (s, 1 H), 6.90 (d, *J* = 7.7 Hz, 1 H), 7.27 (m, 2 H). Anal. ($C_{18}H_{19}BrO_3$) C, H, mol wt. **12:** IR ($CHCl_3$) 1755, 1725, 1655 cm^{-1}; NMR (270 MHz, $CDCl_3$) δ 0.87 (t, *J* = 6 Hz, 3 H), 1.16–1.79 (m, 8 H), 2.09 (m, 4 H), 3.02 and 3.00 (two d, *J* = 11 Hz, 1 H), 3.24 (m, 1 H), 3.70 (m, 1 H), 3.75 and 3.74 (two s, 3 H), 4.28–4.56 (m, 2 H), 5.50 (dd, *J* = 15, 7.5 Hz, 1 H), 5.63 (dd, *J* = 15, 6.7 Hz, 1 H), 7.31 (m, 5 H); mol wt calcd for $C_{22}H_{30}O_4$ 358.2144, found 358.2154. (*E*)-**9:** IR ($CDCl_3$); 1760, 1740 cm^{-1}; NMR (270 MHz, $CDCl_3$) δ 1.04 (s, 3 H), 1.45–2.47 (m, 9 H), 2.47–2.88 (m, 2 H), 3.27 (m, 1 H), 3.73 (s, 3 H), 5.50 (br s, 1 H); ^{13}C NMR (15 MHz, C_6D_6) δ 13.7 (q), 22.7, 22.9, 23.1, 25.5, 29.1, 37.4, 51.7, 52.0, 59.3, 123.1, 135.4, 173.3, 213.3; mol wt calcd for $C_{14}H_{20}O_3$ 236.1412, found 236.1412. (*Z*)-**9:** IR ($CDCl_3$) 1760, 1740 cm^{-1}; NMR (270 MHz, $CDCl_3$) δ 1.38 (s, 3 H), 1.48–2.71 (m, 12 H), 3.61 (s, 3 H), 5.55 (m, 1 H); ^{13}C NMR (C_6D_6) δ 20.5 (q), 22.7, 23.4, 23.9, 25.7, 28.9, 37.6, 51.2, 56.3, 59.8, 123.5, 135.7, 171.0, 214.0; mol wt found 236.1415. (*E*)- + (*Z*)-**11:** IR (CCl_4) 1755, 1735, 1640, 1590, 1470 cm^{-1}; NMR (270 MHz, C_6D_6) 1.03 (s, 1 H, *E* isomer), 1.40 (s, 2 H, *Z* isomer), 1.5–2.40 (m, 9 H), 3.08 (s, 2 H), 3.34 (s, 1 H), 5.90 (br s, 0.33 H), 6.05 (br s, 067 H), 6.55 (d, *J* = 7.5 Hz, 0.67 H), 6.57 (d, *J* = 7.5 Hz, 0.33 H), 7.08 (d, *J* = 7.5 Hz, 1 H), 7.15 (m, 1 H); ^{13}C NMR (C_6D_6) δ 14 (q), 20 (q), 24, 27, 27.7, 28, 37, 51, 52, 56, 60, 121, 123, 124, 128, 131, 133, 137, 140, 170, 204, 208, 213; mol wt calcd for $C_{18}H_{19}{}^{79}BrO_3$ 362.0518, found 362.0516. (*E*)- + (*Z*)-**10:** IR ($CDCl_3$) 1765, 1725, 1655, 1590, 1480 cm^{-1}; NMR (270 MHz, $CDCl_3$) δ 1.7–1.9 (m, 1 H), 2.3–2.6 (m, 5 H), 2.80 (t, *J* = 8 Hz, 2 H), 3.26 (d, *J* = 11.5 Hz, 1 H), 3.39 (td, *J* = 11.5, 6.2 Hz, 1 H), 3.69 (s, 0.21 H), 3.76 (s, 2.79 H), 6.14 (br s, 0.07 H), 6.28 (br s, 0.93 H), 6.88 (d, *J* = 7.5 Hz, 1 H), 7.25 (m, 2 H); ^{13}C NMR (C_6D_6) δ 25, 26, 28, 38, 48, 52, 59, 120, 122, 127.5, 130, 133, 137, 141, 169, 209. Anal. ($C_{17}H_{17}BrO_3$): C, H, Br, mol wt.
(7) This catalyst was prepared in an analogous manner to the preparation of tetrakis(triphenylphosphine)palladium. See Coulson, D. R. *Inorg. Synth.* **1974,** *13,* 121.
(8) *Z*:*E* ratio established from the chemical shifts of the angular methyl group (see ref 6).
(9) Martel, J.; Toromanoff, E.; Mathieu, J.; Nomine, G. *Tetrahedron Lett.* **1972,** 1491. Martel, J.; Blade-Font, A.; Marie, C.; Vivat, M.; Toromanoff, E.; Buendia, J. *Bull Chem. Soc. Fr.* **1978,** Part II, 131.
(10) (a) For this run, addition of *O,N*-bis(trimethylsilyl)acetamide avoided concommitant decarbomethoxylation. (b) Most recent work in a related series showed 10 mol % ferric chloride in methylene chloride at 0 °C to be superior to the conditions reported herein.
(11) Jungheim, L. N. Ph.D. Thesis, University of Wisconsin—Madison, 1979.
(12) For a review, see Trost, B. M. *Tetrahedron* **1977,** *33,* 2615; *Pure Appl. Chem.* **1979,** *51,* 787. Compare addition to allyl phenyl ethers (Takahashi, K.; Miyaki, A.; Hata, G. *Bull. Chem. Soc. Jpn.* **1972,** 230) and to vinyl carbonates (Trost, B. M.; Masse, G., unpublished work in these laboratories). These substrates can be considered vinylogous carbonates.
(13) In the rearrangement of **6** on large scale, a byproduct isolated in <5% yield was tentatively assigned the structure of the seven-membered-ring product.
(14) Trost, B. M.; Verhoeven, T. R. *J. Am. Chem. Soc.* **1979,** *101,* 1595.
(15) For a related independent investigation, see: Balavoine, G.; Guibe, F. *Tetrahedron Lett.* **1979,** 3949. Belavoine, G.; Bram, G.; Guibe, F. *Nouv. J. Chim.* **1978,** *2,* 207.

Barry M. Trost,* Thomas A. Runge, Louis N. Jungheim
Samuel M. McElvain Laboratories of Organic Chemistry
Department of Chemistry, University of Wisconsin—Madison
Madison, Wisconsin 53706
Received October 12, 1979

A New Diene Synthesis via Organopalladium Chemistry

Sir:

Approaches to dienes via carbonyl olefination procedures usually lead to stereoisomeric mixtures. We report here that a new palladium catalyzed decarboxylative elimination of the adducts from enals and carboxylate enolates, a prototype for transition metal catalyzed fragmentation reactions, can lead to a highly stereocontrolled diene synthesis from erythro-threo mixtures as outlined in eq 1. This new fragmentation reaction



has also generated a cyclohexadiene synthesis in conjunction with Diels–Alder reactions. Application of this method to a synthesis of the insect sex pheromones bombykol[1] and codlemone[2] is also reported. We believe that this study represents the first case of activation of a substrate for loss of CO_2 by palladium catalysts.

Reported methods[3-5] that effect the elimination of β-hydroxycarboxylic acids to olefins do so with high stereospeci-

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