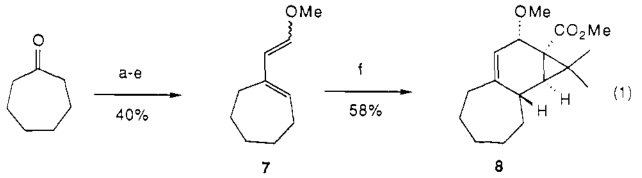
Scheme I[a]



[a] (a) Tf_2O, $(t\text{-}Bu)_2MeC_5H_5N$;[13] (b) CO, MeOH, $Pd(OAc)_2$, Et_3N, Ph_3P;[14] (c) Dibal; (d) Swern oxidation; (e) $Ph_3P^+CH_2OMe\ Cl^-$, *n*-BuLi; (f) **4**, 6 kbar.

diastereoselectivity can be achieved merely by proper selection of dienophile.[11] Additional examples of this process are delineated in Table I.

It is interesting to note that when similar cycloadditions are performed at ambient pressure, the dominant isomer is the same as that produced in the high-pressure experiments although the magnitude of the selectivity was diminished.[12] For example, (*E*)-1-(trimethylsilyloxy)-1,3-butadiene gave a 1:3 (exo:endo) mixture of cycloadducts when warmed with pyrazole **3a** at 50 °C, while **4** gave a 5:1 (exo:endo) mixture under the same conditions (cf. entries 2 and 6, Table I). This observation is suggestive that factors in addition to pressure effects are influencing the complementary stereoselectivity displayed by the two dienophiles. The stereochemical result in entry 4, Table I renders it unlikely that a purely steric argument can be advanced to rationalize the stereocomplementarity of **3a** and **4** since in most cases the most hindered dienophile substituent assumes an endo orientation in cycloadditions with cyclic dienes.[5a,b] Thus, in the absence of other factors, the pyrazole moiety is presumed to be more hindered than the carbomethoxy group. It is tempting to speculate that an unusual competitive secondary orbital interaction may be operative in these reactions. To the best of our knowledge this type of competition is without precedent. This phenomenon, if general, could be profitably exploited in numerous situations as a powerful stereochemical control element in organic synthesis.

To illustrate the synthetic utility of our methodology, a rapid, stereoselective assembly of a model for the BCD ring component of phorbol has been achieved. Readily available dienol ether **7** (2:1 [*E*:*Z*] mixture of geometrical isomers) was reacted with cyclopropene **4** (1 equiv, CH_2Cl_2, 6 kbar, 18 h) to provide tricycle **8** as a single diastereomer in 58% yield.[15] None of the minor *Z*-diene was observed to engage in cycloaddition in this case. This overall process efficiently controls the relative stereochemistry of four contiguous stereogenic centers (three have the correct phorbol orientation) while simultaneously elaborating three of the four rings comprising the tigliane carbon skeleton in a single operation. Application of this methodology to the total synthesis of phorbol and further examination of the unique stereochemical features of this chemistry are underway in our laboratory.

Acknowledgment. We thank the National Institutes of Health (CA-36543) for their generous financial support of this project and Dr. M. J. Heeg, W.S.U., for obtaining the X-ray of the pyrazole adduct of (*E*)-1-((3,5-dinitrobenzoyl)oxy)-1,3-butadiene.

Supplementary Material Available: IR, NMR, and MS data for the compounds discussed (4 pages). Ordering information is given on any current masthead page.

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(10) For recent examples of cycloadditions in which a single reagent adds with reversal of diastereoselectivity at high pressure; see: (a) Padwa, A.; Kline, D. N.; Norman, B. H. *Tetrahedron Lett.* **1988**, *29*, 265. (b) Bell, S. I.; Weinreb, S. M. *Ibid.* **1988**, *29*, 4233.

(11) The "endo" nature of the pyrazole adducts was established by single-crystal X-ray analysis of the pyrazole cycloadduct of (*E*)-1-((3,5-dinitrobenzoyl)oxy)-1,3-butadiene. Full details of this crystallographic analysis will appear in a separate publication.

(12) For a discussion of pressure-induced diastereoselectivity in the Diels-Alder reaction, see: Tietze, L. F.; Huebsch, T.; Voss, E.; Buback, M.; Tost, W. *J. Am. Chem. Soc.* **1988**, *110*, 4065 and references cited therein.

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(14) Ortar, G.; Cacchi, S.; Morera, E. *Tetrahedron Lett.* **1985**, *26*, 1109.

(15) All new compounds in this sequence display satisfactory spectral (IR, ^1H NMR, ^{13}C NMR) and high resolution mass spectral data.

The Palladium-Catalyzed Directed Aldol Reaction of Aldehydes with Ketone Enolates Generated by the Decarboxylation of Allyl β-Keto Carboxylates under Neutral Conditions

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During the last decade new methods have been developed for the directed aldol reaction to produce a desired cross aldol.[1] The success of these methods depends on how to generate enolates regioselectively. Regioselective formation of various metal enolates is now known. The generation of organotransition-metal enolates and their use in directed aldol reaction are attracting increasing interests. Particularly, in situ formation of Ti[2] and Zr[3] enolates and their reactions with aldehydes are well-known. However, stoichiometric amounts of these organometallic compounds are required. Recently aldol reactions catalyzed by Rh complexes involving Rh enolates have been reported.[4] In this communication, we wish to report the catalytic and directed cross aldol reaction based on the generation of the palladium enolates by the decarboxylation of allyl β-keto carboxylates under mild conditions. Concerning the chemistry of palladium enolates, formation of (oxo-π-allyl)palladium intermediates, which can be regarded as palladium enolates, by the reaction of silyl enol ethers with $Pd(OAc)_2$ was proposed.[5] Also reaction of Pd^0 complexes with α-halo carbonyl compounds affords palladium enolates.[6] But standard enolate reactions such as aldol reaction were not reported with these kinds of palladium enolates. Thus the chemistry of palladium enolates is virtually unexplored. We wish to present in this communication the aldol reaction as the first typical enolate reaction of palladium. The characteristic feature of our new method for aldol via the palladium enolates is that the reaction proceeds with a catalytic amount of palladium complex under neutral condition.

We have reported a series of palladium-catalyzed reactions of allyl β-keto carboxylates under neutral conditions via decarboxylation[7] followed by allylation,[8] dehydrogenation,[9] deacetoxylation,[10] and hydrogenolysis.[11] We assumed that the first step in these reactions is the formation of (π-allyl)palladium enolates [(oxo-π-allyl)(π-allyl)palladium complex **16** in Scheme I]. On the basis of this assumption, we investigated the possibility of aldol reaction of the palladium enolate. We carried out intramolecular reaction of allyl β-keto carboxylates having an aldehyde side chain and discovered a very smooth aldol reaction to give the β-ketols

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(2) Stille, J. R.; Grubbs, R. H. *J. Am. Chem. Soc.* **1983**, *105*, 1664-1665.

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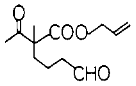
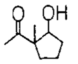
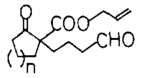
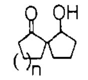
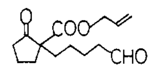
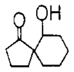
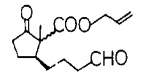
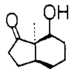
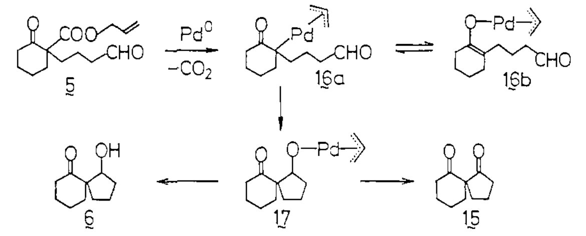
0002-7863/89/1511-4126$01.50/0

Table I. Pd-Catalyzed Intramolecular Aldol Reaction[a]

aldehyde		reaction		product[b]		
		temp (°C)	time (h)			yield (%)
	**1**	rt[d]	29		**2**	82 (1/5)
	**3** $n = 1$	40	4		**4**	90 (1/1)
	5 $n = 2$	rt[d]	40		**6**	69[c] (1/1)
	7 $n = 4$	rt[d]	30		**8**	77 (1/2)
	9 $n = 8$	65	40		**10**	85 (1/1)
	**11**	rt[d]	5		**12**	93 (1/1)
	**13a** trans	rt[d]	10		**14**	70 (1/4)
	13b cis	rt[d]	34			96 (1/4)

[a] $Pd(OAc)_2$, 5%; PPh_3, 10%; in acetonitrile. [b] The erythro/threo ratios are shown in parentheses. [c] The diketone **15** was obtained in 9% yield from **5**. [d] rt stands for room temperature.

Scheme I. Aldol Condensation via Pd Enolate



as shown in Table I. The reaction is highly chemoselective and almost no competitive reactions such as allylation, dehydrogenation, or hydrogenolysis was observed. For example, treatment of the allyl acetoacetate derivative **1** having the butanal side chain at the α-carbon with palladium complex (5 mol % of $Pd(OAc)_2$ and 10 mol % of triphenylphosphine) at room temperature in acetonitrile for 4 h gave a diastereomeric mixture of the cyclopentanol derivative **2** (erythro **2a**/threo **2b** = 1/5) in 82% yield. Similarly, other five- and six-membered spiro-aldol compounds **4**, **6**, **8**, **10**, and **12** were obtained in good yields. When the butanal side chain was introduced at the β-carbon of α-methyl-α-((allyloxy)carbonyl)cyclopentanone, 9-methylbicyclo[4.3.0]nonan-8-on-1-ols **14a,b** were obtained as expected. Both stereoisomers of the β-keto esters **13a** and **13b** were cyclized to form the cis ring junction exclusively.[12] The diastereomeric ratio of **14a**(erythro)/**14b**(threo) was almost 20/80 in both cases. The palladium enolate is insensitive to water, and similar results were obtained by the reactions of **1** and **11** carried out in dry and wet (10% H_2O) acetonitrile or THF.

As shown in Scheme I, the formation of the palladium enolates (**16a** or **16b**) is responsible for the aldol reaction. But there remains ambiguity particularly about how the catalytic species of Pd is regenerated from the palladium alkoxide **17** formed by the aldol reaction at the last step of the catalytic cycle. We expected the formation of the diketone **15** by the elimination of β-hydrogen as a reasonable reaction path.[13] Actually in one case we obtained spiro[4.5]decane-1,6-dione (**15**) from **5**, but it was a minor product (9%).

The attempted intermolecular aldol reaction was competitive with the allylation reaction. The reaction of allyl 2-methylacetoacetate (1 mmol) with hexanol (3 mmol) gave the aldol product (54%) and the allylated ketone (23%).

In summary, we could, for the first time, demonstrate the aldol reaction as a convincing enolate reaction of palladium. The characteristic features of this reaction are as follows. 1. It is possible to generate regioselectivity the palladium enolate of unsymmetrical ketones by the decarboxylation of β-keto esters. 2. The reaction proceeds under completely neutral conditions by using the palladium-phosphine complex only in a catalytic amount. 3. The reaction is particularly suitable for the intramolecular reaction.

Acknowledgment. We thank the Analysis Center of our university for ^1H and ^{13}C NMR and HRMS measurements.

Supplementary Material Available: Experimental data for compounds **2**, **4**, **6**, **8**, **10**, and **12** consisting of ^1H NMR, ^{13}C NMR, IR, HRMS(EI), and R_f (6 pages). Ordering information is given on any current masthead page.

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(12) NOEs between the angular methyl and proton in both **14a** and **14b** were observed (4.3% and 3.2%) indicating that the both rings are cis fused.

(13) Ketones were obtained from similar intermediates in the Pd-catalyzed oxidation of alcohols via allyl carbonates. Tsuji, J.; Minami, I.; Shimizu, I. *Tetrahedron Lett.* **1984**, *25*, 2791-2792.

γ-Silicon Effects on 2-Norbornyl Cations

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The effects of trimethylsilyl groups on carbocations have been studied extensively over the past decade. α-Silyl substitution at a positively charged carbon is destabilizing relative to methyl but stabilizing relative to hydrogen.[1] A β-silyl group strongly accelerates solvolysis, particularly if oriented antiperiplanar to the leaving group.[2] Recently evidence was adduced that γ-Me_3Si groups stabilize carbocations and the transition states for their formation through the "W" conformation.[3,4] With very few exceptions,[5,6] Me_3Si probes have not been applied to the notorious

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0002-7863/89/1511-4127$01.50/0