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PALLADIUM-CATALYZED ASYMMETRIC CYCLIZATION OF METHYL (*E*)-OXO-9-PHENOXY-7-NONENOATE AND ITS ANALOGS

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Summary: Asymmetric cyclizations of methyl (*E*)-3-oxo-9-phenoxy-7-nonenoate (1) or methyl (*E*)-3-oxo-9-(methoxycarbonyl)oxy-7-nonenoate (4) without added base were carried out in the presence of a catalytic amount of palladium(II) acetate and chiral diphosphine as ligands. Allylic carbonate 4 reacted by use of $Pd(OAc)_2$-(*S*)-(*R*)-BPPFA at room temperature to give (*R*)-3-vinylcyclohexanone (3), after decarboxylation, in up to 48% e. e.

Palladium-catalyzed allylic alkylation by using resonance-stabilized enolate anions as nucleophiles is of current interest in organic syntheses.[1] Asymmetric induction in the chiral palladium-catalyzed allylic alkylation has also been reported.[2]

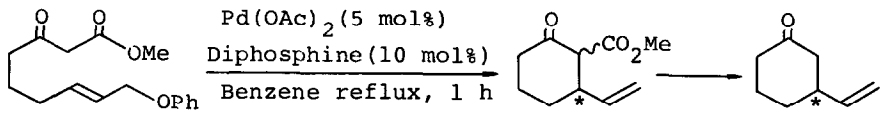
The intramolecular version of the reaction with methyl (*E*)-3-oxo-9-phenoxy-7-nonenoate (1) cleanly gives 2-methoxycarbonyl-3-vinylcyclohexanone (2) despite the problem of *O* vs. *C* alkylation in the case of the corresponding 8-phenoxy-6-octenoate.[3] The study aimed at preparing five- and six-membered, 2,3-disubstituted cycloalkanones by the palladium-catalyzed cyclization led us to investigate asymmetric cyclization of 1 using $Pd(OAc)_2$-chiral diphosphine as a catalyst.

Methyl (*E*)-3-oxo-9-phenoxy-7-nonenoate (1) was prepared from a butadiene telomer, (*E*)-2,7-octadienyl phenyl ether, by a reported procedure.[3] Asymmetric cyclization of 1 (0.30 g, 1.09 mmol) was carried out under nitrogen in the presence of $Pd(OAc)_2$ (5 mol%) and a chiral diphosphine (10 mol%) dissolved in dry benzene (3 mL, ca. 0.3 M solution) at reflux temperature for 1 h. Homogeneous red-brown solution was concentrated by evaporation and the residue was subjected to column chromatographic separation to give 2-methoxycarbonyl-3-vinylcyclohexanone (2)[4] in 60-80% yield. Since the latter compound is in keto-enol equilibrium and even contaminated always with a small amount of unknown product,[4] optical activity was examined with 3-vinylcyclohexanone (3) which was obtained by demethoxycarbonylation of 2 followed by Kugelrohr distillation. All results are summarized in Table 1.

Of five chiral chelating diphosphines employed, BPPFA in benzene solution was found to be the most effective for the catalytic asymmetric cyclization of 1 (entries 5 and 6 for duplication), the optical yield being at best 33% on the

basis of the estimated maximum rotation of 3 as described below. Dimethoxyethane as the solvent deteriorated both catalytic activity and optical yield (entry 7).

Table 1. Asymmetric Cyclization of Methyl (*E*)-3-Oxo-9-phenoxy-7-nonenoate (1) Catalyzed by $Pd(OAc)_2$-diphosphine

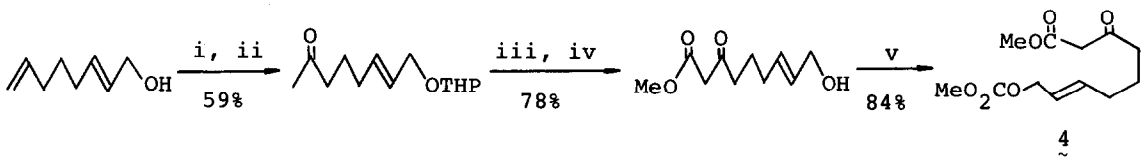


1 2 3

Entry	Diphosphine[a]	Yield of 2[b] (%)	Specific rotation of 3[c] deg. ($CHCl_3$)
1	(*R*,*R*)-DIOP	62	-2.26
2	(*S*,*S*)-BPPM	76	-3.45
3	(*S*,*S*)-CHIRAPHOS	50[d]	-4.32
4	(*R*)-(*S*)-PPFA[e]	74	-3.24
5	(*S*)-(*R*)-BPPFA	79	+6.40
6	(*S*)-(*R*)-BPPFA	72[f]	+6.81
7	(*S*)-(*R*)-BPPFA	58[g]	+4.00

a For abbreviations, see ref. 5).
b Isolated by column chromatography.
c Decarboxylation by alkaline hydrolysis and distillation.
d Starting material recovered (36%).
e Four equivalents to palladium(II) acetate.
f Optical rotation of 2: $[\alpha]_D^{25}$ +20.95° (*c* 2.11, $CHCl_3$).
g Dimethoxyethane as solvent; starting material recovered (13%).

We have found that allylic carbonates undergo oxidative addition with palladium catalysts much faster than allylic phenyl ethers.[6] Thus, the requisite methyl (*E*)-3-oxo-9-(methoxycarbonyl)oxy-7-nonenoate (4)[7] was prepared starting from another butadiene telomer in 39% overall yield as depicted in the Scheme.



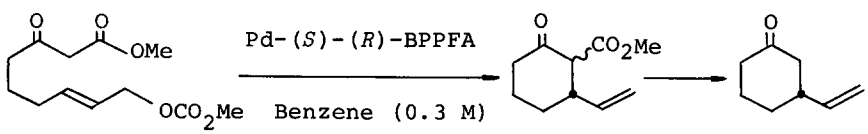
4

Scheme

i, DHP/acid/CH_2Cl_2 ii, $PdCl_2$-Cu_2Cl_2/O_2/aq DMF iii, $(MeO)_2CO$/NaH/PhH
iv, p-TsOH/MeOH v, $ClCO_2Me$/Pyridine/PhH

Catalytic asymmetric cyclization of 4 was carried out under similar conditions to those in Entry 5 of Table 1 but at much lower reaction temperature. Evolution of carbon dioxide took place smoothly and the resulting methoxide ion acted principally as a base to conduct intramolecular allylic alkylation. Table 2 indicates that reaction temperature affects significantly the degree of asymmetric induction in the cyclization to give (*R*)-3-vinylcyclohexanone (3), after decarboxylation, in up to 48% e. e.

Table 2. Asymmetric Cyclization of Methyl (*E*)-3-Oxo-9-(methoxycarbonyl)oxy-7-nonenoate (4) Catalyzed by $Pd(OAc)_2$ — (*S*)-(*R*)-BPPFA



4 2 (*R*)-3, $[\alpha]_{D\,max}^{25}$ +20.6°

Reaction Conditions		Yield of 2[a]	Specific Rotation of 3	Optical Yield
Temp(°C)	Time(h)	(%)	deg. ($CHCl_3$)	(% e. e.)
50	0.2	77	+8.51	41
30	0.7	83	+9.86	48
10	2.5	82	+9.14	44

a Isolated yield: Methyl (*E*)-3-oxo-9-methoxy-7-nonenoate as by-product in 3-5% yield.

Partially active (*R*)-3 ($[\alpha]_D^{25}$ +8.51° (*c* 0.94, $CHCl_3$)) was hydrogenated on 5% $Pd/BaSO_4$ under normal pressure of hydrogen to give (*R*)-3-ethylcyclohexanone (5), $[\alpha]_D^{25}$ +6.76° (EtOH). The maximum rotation of (*R*)-5, $[\alpha]_{D\,max}^{25}$ +16.4° (*c* 1, EtOH), is given by Prelog and his coworker.[8] Therefore, the estimated maximum rotation of (*R*)-3 should be $[\alpha]_{D\,max}^{25}$ +20.60° (± 0.6°)($CHCl_3$). Optical yields herein are based on this value.

Although the present catalytic asymmetric cyclizations of 1 and 4 to give 2 are not necessarily of potential synthetic use, these are the first examples of chiral palladium-catalyzed, intramolecular allylic alkylations with ease. Asymmetric cyclizations of allylic carbonates homologous to 4 to prepare 2,3-disubstituted cyclopentanones are in progress.

We are grateful to Professor V. Prelog for informing us of the optical rotation of (*R*)-3-ethylcyclohexanone. This work was supported by a Grant for Basic Chemical Research (1981) administered by Japan Society for Promotion of Sciences .

References and Notes

1) a) J. Tsuji, Pure & Appl. Chem., 54, 197 (1982), and references cited therein.
b) B. M. Trost, Tetrahedron, 33, 2615 (1977).

2) B. M. Trost and P. E. Strege, J. Am. Chem. Soc., 99, 1649 (1977).

3) J. Tsuji, Y. Kobayashi, H. Kataoka, and T. Takahashi, Tetrahedron Lett., 21, 1475 (1980).

4) Product 2: NMR ($CDCl_3$, TMS) δ 1.65 (m, 4 H), 2.24 (m, 3 H), 3.17-3.37 (diffused), 3.70 (s, 3 H), 4.7-6.1 (m, 3 H), and 12.44 ppm (s).
TLC (20% EtOAc-Hexane) R_f 0.65 (keto form), 0.52 (unknown), and 0.32 (enol form).

5) DIOP: 2,3-*O*-Isopropylidene-2,3-dihydroxy-1,4-bis(diphenylphosphino)butane.
BPPM: *N*-*t*-Butoxycarbonyl-2-(diphenylphosphino)ethyl-4-diphenylphosphinopyrrolidine.
CHIRAPHOS: 2,3-Bis(diphenylphosphino)butane.
PPFA: *N*,*N*-Dimethyl-1-[2-(diphenylphosphino)ferrocenyl]ethylamine.
BPPFA: *N*,*N*-Dimethyl-1-[1',2-bis(diphenylphosphino)ferrocenyl]ethylamine.

6) We thank Dr. I. Shimizu of this laboratory for valuable suggestion in this respect. There is one precedent of allylic alkylation using cyclic allylic carbonate; B. M. Trost and T. A. Runge, J. Am. Chem. Soc., 103, 7550 (1981).

7) Analytically pure 4: NMR ($CDCl_3$, TMS) δ 1.5-2.2 (m, 4 H), 2.53 (t, 2 H), 3.40 (s, 1 H), 3.70 (s, 3 H), 3.74 (s, 3 H), 4.53 (d, 2 H), and 5.67 ppm (m, 2 H).
IR (neat) 1750, 1745, and 1715 cm^{-1} ($\nu_{C=O}$)

8) P. Good, PhD thesis (ETH 6571).

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