Tetrahedron Vol. 40, No. 10, pp. 1791 to 1793, 1984
Printed in Great Britain

0040-4020/84 $3.00 + .00

PALLADIUM(II) CATALYZED ALLYLIC REARRANGEMENT: STEREOSELECTIVE SYNTHESIS OF 2-SUBSTITUTED (E)-β-ACETOXY (OR BENZOYLOXY)ETHYLIDENECYCLOHEXANES

Y. TAMARU, Y. YAMADA, H. OCHIAI, E. NAKAJO and Z. YOSHIDA*
Department of Synthetic Chemistry, Kyoto University, Kyoto 606, Japan

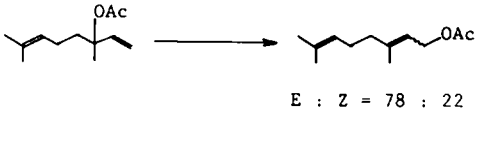
(*Received in Japan* 1 *July* 1983)

Abstract—Diastereomeric mixtures of 2-substituted 1-vinylcyclohexyl acetates (or benzoates) are rearranged stereoselectively to 2-substituted (E)-β-acetoxy(or benzoyloxy)ethylidenecyclohexanes by the catalysis of bis(acetonitrile)palladium(II) chloride. A mechanism related to the stereoselectivity and reactivity is discussed in terms of the conformational requirements in a transition state.

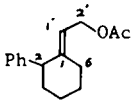
In other study, we needed 2-substituted (E)-β-hydroxyethylidenecycloalkanes in a stereochemically pure state.[1] Wittig reaction seems to be of no value for such purpose.[2] Indeed, despite considerable experimentation, we observed a moderate selectivity for the reaction of 2-methylcyclohexanone and triethyl phosphonacetate.[3] Fortunately, we have found that palladium(II) promotes rearrangement of 2-substituted 1-vinylcyclohexyl acetate (or benzoate) **1**, irrespective of cis, trans stereochemistry of **1**, to provide (E)-2-substituted β-acetoxy (or benzoyloxy)ethylidene cyclohexanes **2** selectively.[4] In this paper, we describe the scope and mechanism of this novel rearrangement.

RESULTS AND DISCUSSION

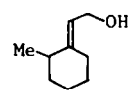
It is well documented that palladium(0) and (II) species promote Cope[5] and (polyhetero)Claisen rearrangements.[6] Rearrangement of allylic acetates was first developed by Overman *et al.*[7] An asymmetric 1,3-transposition in this rearrangement was noted by Grieco *et al.* and this propensity was succesfully applied to an enantioselective synthesis of a key intermediate for 12-hydroxyprostaglandins.[8] In general, however, the stereo-selectivity of this rearrangement is not high, especially in the reaction providing tri-substituted allylic acetates (e.g. eqn 1).



E : Z = 78 : 22 (1)



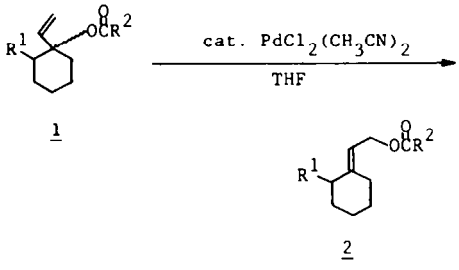
2 (R^1=Ph, R^2=Me)



3

In contrast, 2-substituted 1-vinylcyclohexyl acetates (or benzoates) **1** were found to rearrange to provide tri-substituted allylic acetates (or benzoates) **2** selectively.

Reactions were carried out in the presence of 4 or 8 mol% of bis(acetonitrile)palladium(II) chloride in THF at an ambient or at the THF reflux temperature. Results together with the reaction conditions are summarized in Table 1.



1 **2** (2)

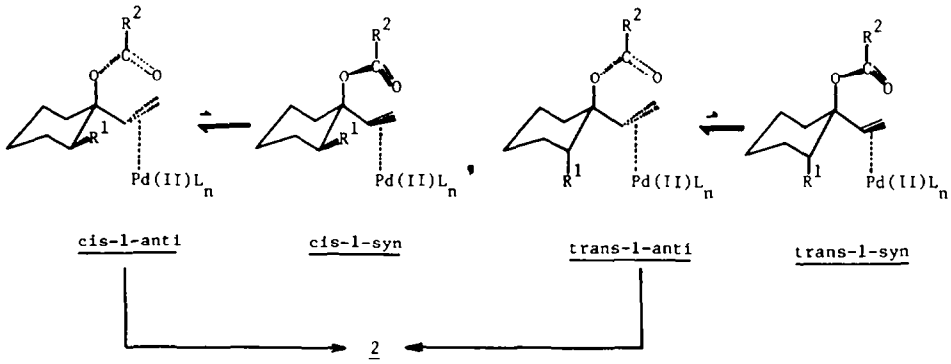
Generally the rearrangement of 1-vinylcyclohexyl acetates proceeds smoothly at room temperature. Benzoates showed somewhat lower reactivity compared with acetates. That is, the allylic acetate **1** ($R^1 = R^2$ = Me) attained completion at room temperature within 20 h, while the corresponding benzoate **1** (R^1 = Me, R^2 = Ph) reached only 12% conversion at room temperature after 14 h and for the completion of reaction were required the reflux temperature and an additional 4 mol% of a catalyst (eqn 2, entries 1 and 2 in Table 1). With similar ease 1-vinyl-2-phenylcyclopentyl benzoate was rearranged to provide the expected product in 60% isolated yield (room temperature for 24 h in the presence of 4 mol% of a catalyst). In contrast to these, 2-methyl substituted 1-vinylcyclooctyl and 1-vinylcyclododecyl benzoates were recovered unchanged even after a prolonged reaction time in the presence of 20 mol% of a catalyst (THF, reflux, 14 h).

The stereochemical course of the rearrangement was thoroughly investigated with the above mentioned acetate **1** (R^1=R^2=Me). Starting from *ca* 2 : 1 mixture of cis- and trans-isomers, the rearranged product consisted of the single isomer whose homogeneity was checked by means of VPC, ^{1}H and ^{13}C NMR spectra. The stereochemistry of newly formed tri-substituted double bond was determined to be E on the basis of a negligibly small europium (III)-induced paramagnetic shift of the methyl doublet of the corresponding allylic alcohol **3**, prepared by the alkaline hydrolysis (KOH/MeOH) of the acetate **2** (R^1=R^2=Me). Moreover the E-configuration of **2** (R^1=Ph, R^2=Me) was ascertained by the NOE

Table 1. Stereoselective rearrangement of allylic carboxylates catalyzed by palladium(II)

Entry	Starting Carboxylate 1		Catalyst	Temp.	Time	Conv.	Isolated Yield of 2
	R^1	R^2	(mol%)		(h)	(%)	(%)
1	Me	Me	4	r.t.	20	100	85.3
2	Me	Ph	8	reflux	5[a]	97.5	69.4
3	Et	Me	4	r.t.	21	84.8	80.2
4	"	"	"	reflux	3	100	71.6
5	i-Pr	Me	4	r.t.	47	100	92.5
6	Ph	Me	4	r.t.	45	100	96.2

(a) After the reaction at r.t. for 14 hours in the presence of 4 mol% of catalyst (12% conversion), the mixture was heated for 5 hours with additional 4 mol% of a catalyst.



Scheme 1.

experiments[9] (9.4 and 4.5% increase of an area intensity of C(2')H protons on irradiation at the equatorial and axial C(6)H protons, respectively, and 2.4% increase of an area intensity of C(1')H proton on irradiation of C(2)H proton. The homogeneity of other products listed in Table 1 and 2-phenyl-2'-benzoyloxethylidenecyclopentate was also ascertained by means of VPC, ^1H and ^{13}C NMR spectra and their E-stereochemistry was assigned by similar analogy.

The stereoselectivity and reactivity of the present rearrangement may be explained as follows (Scheme 1). Due to a large steric demand of vinyl group coordinated by Pd(II), the vinyl group would strongly favor not only an equatorial orientation but also an anti-conformation with respect to R^1 substituent. And hence rearrangement may take place selectively through anti conformers (cis-**1**-anti, trans-**1**-anti) to give E-**2** stereoselectively.

The somewhat diminished reactivity of benzoates might be attributed to a low neucleophlicity of the carbonyl oxygen and a decreased population of an axial orientation of oxybenzoyl group.

EXPERIMENTAL

M.ps were determined in capillary tubes with a Buchi apparatus and not corrected. Unless otherwise indicated, short-path (bulb-to-bulb) distillations were carried out in a Kugelrohr apparatus. Microanalyses were performed by Microanalysis Center of Kyoto University. IR spectra were measured with JASCO A-102 Diffraction Grating Infrared Spectrophotometer. ^1H and ^{13}C NMR spectra were recorded with a JEOL JNM-PMX 60 and a JEOL FX-90 spectrometers, respectively. Mass spectra were measured either on a Hitachi Model RMU 6C instrument or on a JEOL D-300 instrument (high-resolution mass spectrometer).

Solvent and reagent. Tetrahydrofuran (THF) was dried over Na-benzophenone, distilled and kept under argon atmosphere. Bis-(acetonitrile)palladium chloride was prepared by the reported method.[10]

2-Substituted 1-vinylcycohexyl and 1-vinylcyclopentyl acetates and benzoates, **1**. 2-Phenyl-1-vinylcyclopentyl, 2-methyl-1-vinylcyclohexyl, 2-methyl-1-vinylcyclooctyl, and 2-methyl-1-vinylcyclododecyl benzoates were prepared by the following sequential reactions from the corresponding 2-substituted cycloalkanones ((i) vinyllithium,[11] THF–ether–pentane (4 : 1 : 1)/liq. N^2, −120°, (ii) benzoyl chloride, 0°). 2-Methyl-1-vinylcyclohexyl, 2-ethyl-1-vinylcyclohexyl, 2-isopropyl-1-vinylcyclohexyl, and 2-phenyl-1-vinylcyclohexyl acetates were prepared by the similar sequential reactions from the corresponding 2-substituted cycloalkanones ((i) vinylmagnesium bromide, THF, 0°, (ii) Ac_2O, 0°). When the acetylation was incomplete, the reaction mixture obtained above was treated with Ac_2O/Et_3N/4-dimethylaminopyridine (0.2 eq)).[12]

General procedure for the palladium(II) catalyzed rearrangement. Into argon-purged bis(acetonitrile)palladium chloride (0.08 mmol) was added a solution of allylic acetate **1** (2.0 mmol) in THF (10 ml). The clear solution was stirred at the temperature indicated in Table 1. The progress of reaction was monitored by means of VPC or TLC. After the

reaction had completed or ceased essentially, the solvent was distilled off under vacuum and the purification of the residue through column chromatography (silica gel, n-hexane–EtOAc gradient) gave spectroscopically pure materials **2** in the yields given in Table 1.

The spectral and analytical data of the new compounds are as follows.

(E)-2-Phenyl-2′-(benzoyloxy)ethylidenecyclopentane: b.p. 220° (0.3 mmHg); IR (neat film) 1718 (vs), 1270 (vs), 1110 (s), 710 (ms), 700 (m); ^{1}H NMR δ ($CDCl_3$) 1.49–2.37 (4H, m), 2.37–2.87 (2H, m), 4.84 (2H, d, J = 7.2 Hz), 5.00–5.45 (1H, m), 7.27 (5H, br.s), 7.14–7.67 (3H, m), 7.90–8.24 (2H, m); ^{13}C NMR δ ($CDCl_3$) 24.45, 29.56, 35.98, 51.80, 63.02, 116.81, 125.01, 126.05, 127.30, 128.15, 128.21, 129.47, 130.38, 132.59, 153.18, 166.40; mass spectrum, *m/e* (relative intensity) 292 (M^+, 0.14), 268 (18), 170 (100), 155 (58), 142 (100), 141 (100), 105 (100), 91 (40). (Found: C, 82.29; H, 6.97. Calc. for $C_{20}H_{20}O_2$: C. 82.16; H, 6.89%.)

(E)-2-Methyl-2′-(benzoyloxy)ethylidenecyclohexane **2** (R^1=Me, R^2=Ph) (entry 2): b.p. 170° (0.6 mmHg); IR (neat film) 1720 (vs), 1605 (w), 1270 (vs), 1110 (s), 710 (s); ^{1}H NMR δ ($CDCl_3$) 1.06 (3H, d, J = 6.6 Hz), 1.23–2.90 (9H, m), 4.90 (2H, d, J = 7.0 Hz), 5.43 (1H, t, J = 7.0 Hz), 7.33–7.73 (3H, m), 7.93–8.30 (2H, m); ^{13}C NMR δ ($CDCl_3$) 18.29, 25.23, 28.00, 28.69, 36.45, 38.45, 61.20, 112.78, 128.08, 129.42, 130.50, 132.50, 150.54, 166.44; mass spectrum, *m/e* (relative intensity) 244 (M^+, 0.5), 122 (100), 107 (40), 105 (62), 93 (49). (Found: C, 78.37; H, 8.51. Calc. for $C_{16}H_{20}O_2$: C, 78.65; H, 8.25%.)

(E)-2-Ethyl-2′-(acetoxy)ethylidenecyclohexane **2** (R^1=Et, R^2=Me) (entries 3 and 4): b.p. 120° (4 mmHg); IR (neat film) 2950 (s), 1745 (vs), 1640 (br.w), 1450 (m), 1370 (m), 1245 (s), 1020 (m); ^{1}H NMR δ ($CDCl_3$), 0.84 (3H, t, J = 7.0 Hz), 1.06–2.80 (11H, m), 2.06 (3H, s), 4.62 (2H, d, J = 7.2 Hz), 5.28 (1H, t, J = 7.2 Hz); ^{13}C NMR δ ($CDCl_3$) 11.92, 20.91, 23.62, 24.54, 27.14, 28.12, 33.16, 46.22, 60.68, 114.37, 148.99, 170.83; mass spectrum, *m/e* (relative intensity) 196 (M^+, 0.2), 136 (98), 121 (36), 107 (100), 81 (35), 79 (38), 43 (59). (Found: C, 73.72; H, 10.21. Calc. for $C_{12}H_{20}O_2$: C, 73.43; H, 10.27%.)

(E)-2-Isopropyl-2′-(acetoxy)ethylidenecyclohexane **2** (R^1= i-Pr, R^2=Me) (entry 5): IR (neat film) 2930 (s), 1744 (vs), 1665 (w), 1450 (m), 1370 (m), 1230 (vs), 1022 (m), 955 (w); ^{1}H NMR δ ($CDCl_3$) 0.78 (3H, d, J = 6.8 Hz), 0.92 (3H, d, J = 6.0 Hz), 1.13–2.60 (10H, m), 2.05 (3H, s), 4.57 (2H, d, J = 7.0 Hz); ^{13}C NMR δ ($CDCl_3$) 20.29, 20.89, 21.46, 21.93, 26.01, 26.14, 28.00, 29.69, 52.40, 60.51, 115.94, 148.71, 170.82; mass spectrum, *m/e* (relative intensity) 210 (M^+, 0.02), 150 (72), 135 (45), 107 (100), 57 (53), 43 (21). (Found: C, 74.15; H, 10.75. Calc. for $C_{13}H_{22}O_2$: C, 74.24; H, 10.54%.)

(E)-2-Phenyl-2′-(acetoxy)ethylidenecyclohexane **2** (R^1= Ph, R^2=Me) (entry 6): IR (neat film) 3030 (vw), 2930 (ms), 1738 (vs), 1664 (br.m), 1605 (w), 1370 (m), 1230 (vs), 1020 (m), 695 (ms); ^{1}H NMR δ ($CDCl_3$) 1.20–2.10 (7H, m), 1.98 (3H, s), 2.62 (1H, br.d, J = 14 Hz), 3.32 (1H, br.t, J = 14 Hz), 4.57 (2H, d, J = 6.8 Hz), 4.83 (1H, t, J = 6.8 Hz), 7.09–7.44 (5H, m); ^{13}C NMR δ ($CDCl_3$) 20.81, 25.70, 27.70, 29.08, 33.64, 50.45, 60.60, 116.81, 126.05, 128.04, 128.38, 142.47, 148.88, 170.73; mass spectrum, *m/e* (relative intensity) 184 (M^+-60, 100), 169 (16), 142 (47), 141 (51), 91 (10). (Found: C, 78.42; H, 8.32. Calc. for $C_{16}H_{20}O_2$: C, 78.65; H, 8.25%.)

REFERENCES

[1a]Y. Tamaru, M. Kagotani, R. Suzuki and Z. Yoshida, *J. Org. Chem.* **46**, 3374 (1981); [1b]Y. Tamaru, Y. Yamada, M. Kagotani, H. Ochiai, E. Nakajo, R. Suzuki, and Z. Yoshida, *J. Org. Chem.* **48**, 4669 (1983).

[2a]P. M. Wovkulich and M. R. Uskokovic, *J. Org. Chem.* **47**, 1600, (1982); [b]C. Sreekumar, P. D. Kevin and W. C. Still, *Ibid.* **45**, 4260 (1980) and Ref. cited therein.

[3a]H. Hauth, D. Stauffacher, P. Niklaus and A. Melera, *Helv. Chim. Acta* **48**, 1087 (1965); [b]E. G. Buggiolini, J. A. Iacobelli, B. M. Hennessy and M. R. Uskokovic, *J. Am. Chem. Soc.* **104**, 2945 (1982).

[4]The allylic migration of acetoxy group was also noted in the course of acetylation of 2-methyl-1-vinylcyclohexanol to give 2-methyl-(2′-acetoxy)ethylidenecyclohexane in 27.3% yield. But the stereochemistry of the double bond was not specified: J. D. Billimoria, *J. Chem. Soc.* 2626 (1953).

[5a]R. Hamilton, T. R. B. Mitchell and J. J. Rooney, *J. Chem. Soc. Chem. Commun.* 456 (1981); [b]L. E. Overman and F. M. Knoll, *J. Am. Chem. Soc.* **102**, 865 (1980).

[6a]Y. Yamada, K. Mukai, H. Yoshioka, Y. Tamaru and Z. Yoshida, *Tetrahedron Letters* 5015 (1979); [b]Y. Tamaru, Z. Yoshida, Y. Yamada, K. Mukai and H. Yoshioka, *J. Org. Chem.* **48**, 1293 (1983); [c]Y. Tamaru, M. Kagotani and Z. Yoshida, *J. Org. Chem.* **45**, 5221 (1980); [d]*Idem*, *Tetrahedron Letters* **22**, 4245 (1981).

[7a]L. E. Overman and F. M. Knoll, *Tetrahedron Letters* 321 (1979); [b]*Idem*, *J. Am. Chem. Soc.* **102**, 865 (1980).

[8a]P. A. Grieco, T. Takigawa, S. L. Bongers and H. Tanaka, *J. Am. Chem. Soc.* **102**, 7587 (1980); [b]P. A. Grieco, P. Tuthill and H. L. Sham, *J. Org. Chem.* **46**, 5005 (1981).

[9]A. Gaudemer, *Steroechemistry* (Edited by H. B. Kagan), Vol. 1. Georg Thieme Verlag, Stuttgart (1977).

[10]J. R. Doyle, P. E. Slade and H. B. Jonassen, *Inorg. Synth.* **6**, 218 (1960).

[11]D. Seebach, *Tetrahedron Letters* 4839 (1967).

[12]S. E. Chillous, D. J. Hart and D. K. Hutchinson, *J. Org. Chem.* **47**, 5418 (1982).