Observations on the Unusual Stereochemistry of the Oxidative Cleavage of Palladium–Carbon Bonds

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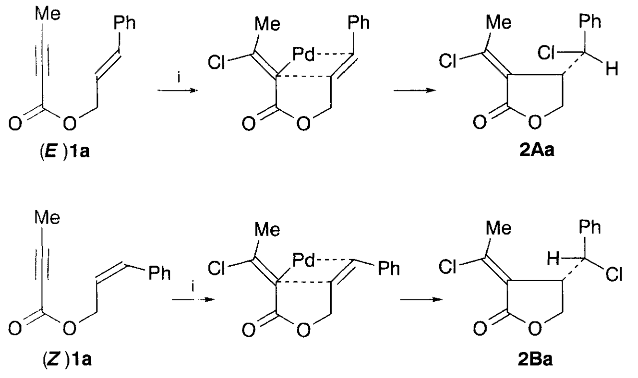
Oxidative cleavage of palladium–carbon bonds by $CuCl_2$ occurs with retention of configuration at the carbon atom in the palladium(II)-catalysed cyclization of allylic 2-alkynoates.

Oxidative cleavage of palladium–carbon σ bonds takes place in a number of palladium-catalysed oxidation reactions in the presence of nucleophiles.[1] The oxidizing agent usually weakens the palladium–carbon bonds, so that the palladium is turned into a good leaving group.[2] As a result, an organic end-product is formed by nucleophilic substitution.

$$R_1R_2CH\text{–}PdCl \xrightarrow[\text{oxidation}]{\text{Nu:}} R_1R_2CH\text{–}Nu + Pd^{II}$$

Although oxidative cleavage of palladium–carbon bonds has been studied extensively, the detailed mechanisms of these reactions are still unclear. The mechanism of the oxidative cleavage of carbon–palladium bonds by cupric chloride has been a matter of considerable speculation. In order to provide evidence for the mechanism of this reaction, the stereochemistry of such cleavage has been studied by several workers. According to the stereochemical results, this cleavage reaction has been proposed to proceed by reductive elimination,[3] a radical mechanism[4,5] or an ionic mechanism involving nucleophilic displacement at the carbon atom.[6,7a] Bäckvall observed that cupric chloride-induced cleavage of β-oxoalkyl–palladium bonds occurred with predominant inversion at the carbon atom in the presence of free chloride ion.[6] To the best of our knowledge, the only example that the oxidative cleavage of palladium–carbon bond by $CuCl_2$ occurred with retention of configuration is the $CuCl_2$-cleavage of the β-phenethyl–palladium bond,[8] in which carbonium character was important as revealed by the anchimeric assistance. Here we report the cleavage of palladium–carbon bonds by cupric chloride with predominant retention of configuration at the carbon atom, even in the presence of a large excess of chloride ion.



Scheme 1 *Reagents and conditions*: i, $CuCl_2$ (5 equiv.), LiCl (2 equiv.), $PdCl_2(PhCN)_2$, MeCN

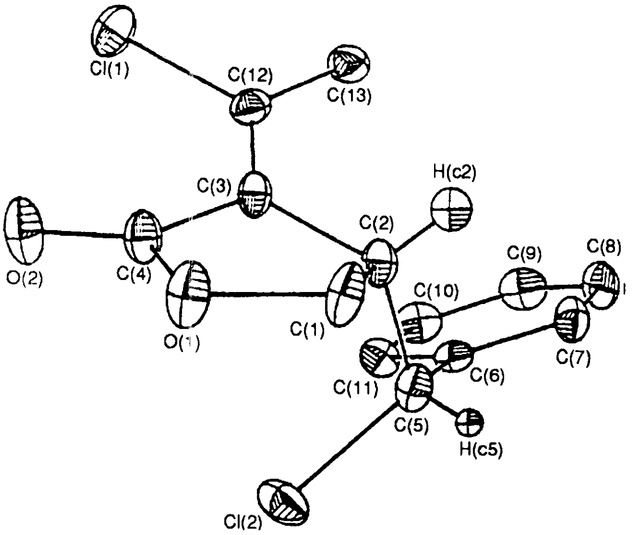
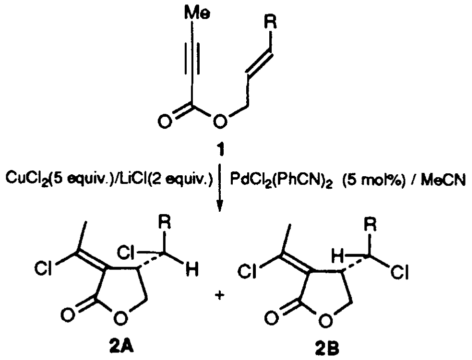


Fig. 1 X-Ray structure of **2Aa** obtained from cyclization of (*E*)-**1a**

Recently, we developed a cyclization reaction of allylic 2-alkynoates involving an oxidative cleavage step of the carbon–palladium bond.[9] In this reaction, when we used 3′-phenyl-2′(*Z*)- [and 2′(*E*)-]-propenyl 2-butynoates [(**Z**)-**1a** and (**E**)-**1a**] as model compounds, they afforded different diastereoisomers under the same cyclization conditions (Scheme 1).[9] That is to say, in our system, the oxidative cleavage of C–Pd bonds shows high stereoselectivity. But, because the configurations of the diastereoisomers could not be exactly assigned from their ^1H NMR spectra, they were tentatively assigned according to Bäckvall's results.[6a] For determining the stereochemistry of

Table 1 Cyclization of allylic 2-butynoates **1** catalysed by palladium(II)[a]



	1		Yield of products(%)[b]		
Entry	R	Configuration	2A	2B	Retention : inversion[c]
1	Ph	E[(*E*)-**1a**]	55 (**2Aa**)	0 (**2Ba**)	100 : 0 (**2Aa** : **2Ba**)
2[d]	Ph	E[(*E*)-**1a**]	52 (**2Aa**)	0 (**2Ba**)	100 : 0 (**2Aa** : **2Ba**)
3	Ph	Z[(*Z*)-**1a**]	7 (**2Aa**)	50 (**2Ba**)	88 : 12 (**2Ba** : **2Aa**)
4	Me	E[(*E*)-**1b**]	83 (**2Ab**)	0 (**2Bb**)	100 : 0 (**2Ab** : **2Bb**)
5	Me	Z[(*Z*)-**1b**]	40 (**2Ab**)	21 (**2Bb**)	34 : 66 (**2Bb** : **2Ab**)
6	Pr	E[(*E*)-**1c**]	72 (**2Ac**)	0 (**2Bc**)	100 : 0 (**2Ac** : **2Bc**)
7	Pr	T[(*Z*)-**1c**]	38 (**2Ac**)	19 (**2Bc**)	33 : 67 (**2Bc** : **2Ac**)

[a] Typical procedure: to a solution of (*E*)-**1a** (200 mg, 1.0 mmol), $CuCl_2$ (680 mg, 5.0 mmol) and LiCl (90 mg, 2.1 mmol) in MeCN was added $PdCl_2(PhCN)_2$ (20 mg, 0.053 mmol). The reaction was stirred, and monitored by TLC. After the reaction was complete, water (5 ml) was added, and the mixture was extracted with ethyl acetate and dried ($MgSO_4$). Preparative TLC on silica gel afforded the product **2Aa** in pure form. [b] Isolated yield. [c] Determined by 300 MHz ^1H NMR. [d] Reaction under Bäckvall's condition.[6a]

the reaction products, we obtained a single crystal of the product from (***E***)-**1a** (Fig. 1).† We were surprised to learn from the X-ray diffraction results that the stereochemistry of the oxidative cleavage in our cyclization reaction is in contrast to Bäckvall's results, *i.e.* in our system, the oxidative cleavage of C–Pd bonds by $CuCl_2$ occurred with predominant retention at the carbon atom, even in the presence of excess free chloride ion. Some papers reported that the use of less polar solvents favoured oxidative cleavage with retention of configuration at the carbon atom.[2,10] But in our case, even the reaction in strong polar solvent systems, similar to those described by Bäckvall,[6a] still afforded the retention product predominantly (Table 1, entry 2).

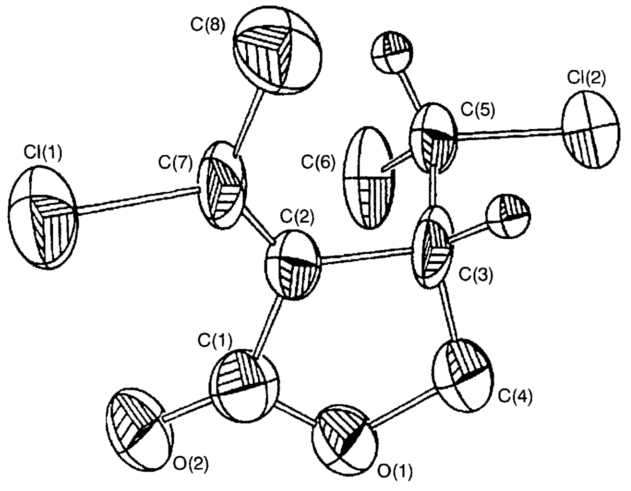
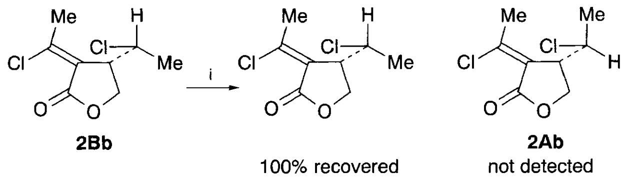
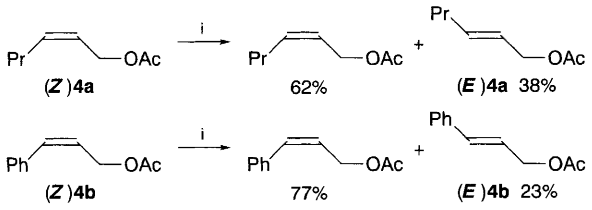


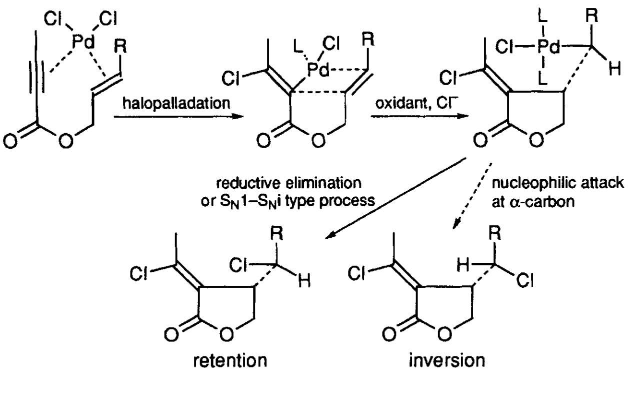
Fig. 2 X-Ray structure of **2Ab** obtained from cyclization of (*E*)-**1b**



Scheme 2 *Reagents and conditions*: i, $CuCl_2$ (5 equiv.), LiCl (2 equiv.), $PdCl_2(PhCN)_2$ (5 mol%), MeCN, 24 h



Scheme 3 *Reagents and conditions*: i, $CuCl_2$ (5 equiv.), LiCl (2 equiv.), $PdCl_2(PhCN)_2$ (5 mol%), MeCN, 44 h



Scheme 4

For such an unusual stereochemical result, we suspected that the phenyl group caused the oxidative cleavage to occur with unusual stereoselectivity. To study the generality of the stereochemistry of the oxidative cleavage of C–Pd bonds by $CuCl_2$, we chose alkyl groups (methyl and propyl) instead of the phenyl group. Under the same cyclization conditions (***E***)-**1b** and (***E***)-**1c** also afforded a single diastereoisomer in good yields (entries 4, 6), and an X-ray diffraction study (Fig. 2)‡ of the product obtained from (***E***)-**1b** showed that the oxidative cleavage had also taken place with retention of configuration at the carbon atom. But the cyclization of (**Z**)-**1b** and (**Z**)-**1c** afforded mixtures of the diastereoisomers, the inversion products (**2Ab** and **2Ac**) were also obtained in considerable ratios. A control experiment showed that **2Bb** was stable under the reaction conditions and did not rearrange to **2Ab** (Scheme 2).

Some isomerization of the *Z*-configuration of the carbon–carbon double bond in the starting material during the reaction might be expected, to test such a speculation, 2(*Z*)-hexenyl acetate [(**Z**)-**4a**] and 3-phenyl-2(*Z*)-propenyl acetate [(**Z**)-**4b**] were chose as model compounds to study the isomerization. Under the same cyclization conditions after 44 h, about 38% of (**Z**)-**4a** isomerized to (***E***)-**4a** (Scheme 3), while for (**Z**)-**4b**, only 23% isomerized after 44 h (Scheme 3), implying that under our cyclization conditions isomerization of the *Z*-olefin did occur and isomerization of the alkyl-substituted *Z*-olefin was faster than that of the phenyl-substituted *Z*-olefin. From the isomerization results, it was suggested that (**Z**)-**1b** and (**Z**)-**1c** would isomerize during the reaction. Thus the products formed from the cyclization of (**Z**)-**1b** and (**Z**)-**1c** might contain some cyclization product of (***E***)-**1b** [and (***E***)-**1c**] which was formed *in situ* by the isomerization of the (*Z*)-C=C bond to an (*E*)-C=C bond, *i.e.* from (**Z**)-**1b** to (***E***)-**1b** [and from (**Z**)-**1c** to (***E***)-**1c**]. Thus, we claim that although cyclization of (**Z**)-**1b** and (**Z**)-**1c** afforded mixtures of pairs of diastereoisomers, the oxidative cleavage of C–Pd bonds by $CuCl_2$ still took place *via* reductive elimination or S_N1–S_Ni type process[11] with retention at the carbon atom stereoselectivity (Scheme 4).

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Footnotes

† *Crystal data* for **2Aa**: $C_{13}H_{12}O_2Cl_2$, M_w = 271.2, monoclinic, space group $P2_1/a$, a = 13.914(3), b = 6.398(3), c = 14.004(3) Å, β = 96.69(2)°, V = 1238.2(7) Å^3, Z = 4, $F(000)$ = 560.0, λ = 1.5418 Å (Cu-Kα), μ = 44.48 cm^{-1}. Crystal size 0.1 × 0.1 × 0.3 mm. Intensity data were collected at 20 °C. Cell parameters defined by 24 reflections with $24 < 2\theta < 46°$. 1645 unique reflections measured with $2\theta_{max}$ = 120°. Two standard reflections monitored every 100 reflections, no significant variation found. Structure was determined by direct methods. All non-hydrogen atoms positioned and anisotropic thermal parameters refined for 1608 observed reflections with $F > 4.0\sigma(F)$ by full-matrix least squares analysis, R = 0.077.

‡ *Crystal data* for **2Ab**: $C_8H_{10}O_2Cl_2$, M_w = 209.1, monoclinic, space group $P2_1/n$, a = 6.402(5), b = 10.834(9), c = 13.774(8) Å, β = 99.80(5)°, V = 941.4(8) Å^3, Z = 4, $F(000)$ = 432.0, λ = 1.5418 Å (Cu-Kα), μ = 56.8 cm^{-1}. Crystal size 0.4 × 0.4 × 0.1 mm. Intensity data were collected at 18 °C. Cell parameters defined by 25 reflections with $20 < 2\theta < 30°$. 1012 unique reflections measured with $2\theta_{max}$ = 120°. Two standard reflections monitored every 120 reflections, no significant variation found. Structure was determined by direct methods. All non-hydrogen atoms positioned and anisotropic thermal parameters refined for 974 observed reflections with $F > 4.0\sigma(F)$ by full-matrix least-squares analysis R = 0.078.

All calculations performed on a micro VAX II computer with programs SHELXS-76 and SHELXS-86. Atomic coordinates, bond lengths and angles, and thermal parameters have been deposited at the

Cambridge Crystallographic Data Centre. See Information for Authors, Issue No. 1.

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