207. Concerning the Configuration of the Side Chain in the Antibiotic Pluramycin A

Preliminary Communication[1])

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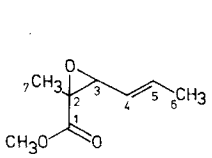
Summary

The configuration of the side chain in the antibiotic pluramycin A is shown to be *cis* for the olefin and *trans* for the epoxide (*cf.* **4**).

In the course of our investigation of epoxides we have recently synthesized the two diastereomeric methyl 2,3-epoxy-2-methyl-4-hexenoates **1** and **2** by *Darzens* condensation of methyl 2-chloropropionate and crotonaldehyde. The two stereoisomers were separated by column chromatography and the epoxide configuration was assigned from the ^{13}C-chemical shifts of the methyl group at C(2). These two compounds may serve as models for the assignment of the side chain configuration in the antibiotic pluramycin A (**3**) whose structure was recently published by *Kondo et al.* [1].

The configuration of the double bond in pluramycin was given as *trans*, the arguments being the 11 Hz vicinal coupling of the olefinic protons and the



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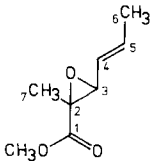

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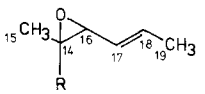

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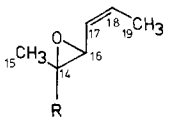

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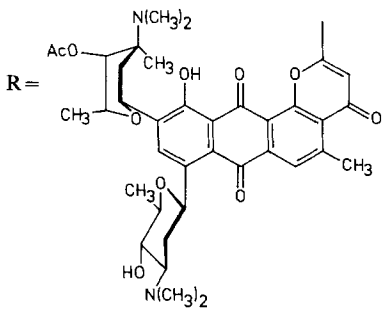

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[1]) A full paper will be published later.

Table. ^{13}C-*NMR. data*

	Carbon Atoms							
	C(1)	C(2)	C(3)	C(4)	C(5)	C(6)	C(7)	OCH_3
cis-Epoxide **1**	170.2 *s*	61.0 *s*	64.3 *d*	134.9 *d*	124.4 *d*	18.0 *qa*	19.2 *qa*	52.3 *qa*
trans-Epoxide **2**	171.5 *s*	59.1 *s*	62.1 *d*	134.7 *d*	124.0 *d*	18.1 *qa*	13.6 *qa*	52.5 *qa*
	C(14)	C(16)	C(17)[a])	C(18)[a])	C(19)	C(15)		
Pluramcyin A (**3**) [1]	60.3 *s*	61.7 *d*	123.3 *d*	134.1 *d*	14.4 *qa*	14.9 *qa*		

[a]) These two carbon atoms were obviously assigned incorrectly as can be seen by a comparison with *e.g.* 2-heptene [5].

2 Hz allylic coupling between the H–C(17) and the methyl protons at C(19). However, in disubstituted ethylenes, when the two substituents are carbon atoms, the vicinal coupling is known to be *ca.* 11 Hz for *cis*-protons and *ca.* 16 Hz for *trans*-protons [2]. The value reported by *Kondo et al.* thus clearly indicates a *cis*-olefin. This is further corroborated by the 15.5 Hz coupling found in the two *trans*-models **1** and **2**. The size of the allylic coupling cannot, however, be used for the determination of the geometry at the double bond in acyclic systems as was pointed out by *Barfield et al.* [3]. Additional support for a *cis*-double bond in pluramycin A comes from the ^{13}C-NMR. data (see the *Table*). The chemical shifts of the terminal methyl groups in the model compounds **1** and **2**, where the double bond is *trans*, are 18 ppm. *Kondo et al.*, on the other hand, found 14.4 ppm for the corresponding carbon atom in pluramycin A. The observed upfield shift clearly must be caused by the γ-effect of C(16) on C(19) due to the *cis*-geometry of the olefin in the antibiotic.

The configuration of the epoxide in pluramycin A was determined as *cis* from the NOE which was observed for the H–C(16) upon irradiation of the methyl protons at C(15) [1]. The chemical shift of the C(16) proton was given as 4.15 ppm; the resonances of the corresponding protons in the models are at 3.36 ppm for the *cis*-epoxide **1** and 3.63 ppm for the *trans*-isomer **2**. These values would rather suggest a *trans*-configuration for the pluramycin A epoxide. Again the ^{13}C-NMR. data give additional information. The chemical shift of the methyl group at C(14) was reported to be 14.9 ppm. Comparison with the models (see the Table) clearly is in favour of the *trans*-configuration. Similar values were found for 2,3-epoxy-2-methyl-butanoates: 13.3 ppm for the *trans*-isomer ('epoxytiglate') and 19.4 ppm for the *cis*-isomer ('epoxyangelicate') [4].

The conclusion, which can be drawn from the spectroscopic data of the antibiotic **3** [1] and our model compounds **1** and **2**, is that the configuration of the pluramycin A side chain is not that proposed by *Kondo et al.* but much more likely *cis* for the olefin and *trans* for the epoxide as shown in structure **4**.

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208. Reaction of Aminoalcohols with Butadiene Catalyzed by Palladium Complexes

Preliminary Communication

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Summary

The aminoalcohols **1**, react with 2 equivalents of butadiene in the presence of catalytic quantities of bis(acetylacetonato)palladium/triphenylphosphine to give exclusively the corresponding *N*-octadienyl aminoalcohols. In the presence of excess butadiene, subsequent *O*-octadienylation occurs only for *N*-octadienyliminodiethanol **2g**, affording the monoether **4g**. *O*-octadienylation of **2a–f** and **4g** can be effected by the addition of molar quantities of triethylamine to the reaction mixture.

The palladium or nickel catalyzed reaction of active hydrogen compounds with 1,3-butadiene has been reported for alcohols, amines, carboxylic acids, phenols, active methylene and methyne compounds, oximes, hydrazones and *Schiff* bases [1]. Generally, for the palladium catalyzed reaction, the major products are octadienyl derivatives of the active hydrogen compounds, with smaller amounts of the corresponding butenyl compounds.

The recent publication of two patents [2] [3] prompts us to report our own results on the palladium-catalyzed reaction of butadiene with a number of multifunctional active-hydrogen compounds, viz. alkanolamines. The reactions provide a highly selective synthetic route to a number of long chain tertiary amino alcohols that are useful intermediates for a variety of applications.