Short Communications

On the Reaction of Epoxides with Trimethylchlorosilane

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The N-acetyl derivative of pimaricin, a polyene macrolide antibiotic containing an epoxy function, has been mass spectrometrically investigated as a persilyl derivative to distinguish between the molecular compositions $C_{33}H_{47}NO_{14}$[1] and $C_{33}H_{47}NO_{13}$[2,3] which differ by one hydroxyl group. The persilylated derivative was formed by reacting N-acetylpimaricin with a mixture of hexamethyldisilazane and trimethylchlorosilane in pyridine.[2] This solution is one of the more widely used silylating agents and it is commercially available as Trisil ®. The reactions of epoxides with silylating agents does not seem to have been studied extensively. Epoxides are known to react with pure trimethylchlorosilane by addition, forming the silyl ether of a chlorohydrin.[4] (Fig. 1). Pierce states[5] that "the epoxy group is more reactive than the primary hydroxyl group" under silylating conditions, apparently referring to the work of Romantsevich and Malinovskii.[6]

Although mass spectrometric as well as chemical evidence[2,3] seems to favour the $C_{33}H_{47}NO_{13}$ formula for pimaricin, we were disturbed by the conflict between the reported molecular formula for the persilyl derivative of N-acetylpimaricin and Pierce's statement concerning the high reactivity of the epoxy function when treated with silylating agents. We therefore felt it desirable to investigate the behaviour of some simple epoxides when treated with (a) pure trimethylchlorosilane (TMCS) and (b) Trisil ®. This was done in sealed glass tubes at 100 °C, and the progress of the reaction was followed by taking samples at different intervals and analysing them by GLC. All
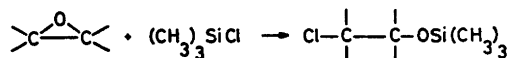

Fig. 1. The reaction between an epoxide and trimethylchlorosilane.

Table 1. The times needed for complete derivatisation of the various epoxides with TMCS and Trisil ® at 100 °C.

Epoxide	TMCS	Trisil
1,2-Epoxycyclohexane	2 h	2 h
1,2-Epoxycyclooctane	24 h	36 h
1,2-Epoxycyclododecane	16 h	150 h
trans-2,3-Epoxybutane	15 min	—
1,2-Epoxy-3,3,3-trichloropropane	24 h	24 h
1,2-Epoxydecane	5 min	16 h
(1,2-Epoxyethyl) benzene	150 h	16 h

epoxides investigated gave derivatives and their GLC retention times were in all cases longer than those of the original epoxides. The reactivity, however, varied considerably among the epoxides. The times for complete reaction for the various epoxides are listed in Table 1.

Exact mass determinations and the fragmentation patterns in the mass spectra of the derivatives (details of which will be discussed below) clearly show that the epoxides react with the silylating agents used by addition of the elements of trimethylchlorosilane over the epoxy function. Two products were formed when the epoxy ring could open in two ways.[7] The predominant product was always formed by opening at the primary carbon atom to give the silyl ether function on the secondary carbon atom and the chlorine atom added to the primary carbon atom (Fig. 2). The two silylation methods (a) and (b) gave the same product distribution, only differences in the reaction rates being observed. These rates are, however, in all cases lower than the normal reaction rate for a hydroxy function. The example chosen by Pierce[5] to illustrate the high reactivity of the epoxy function under silylating conditions in comparison to the reactivity of the hydroxyl function is evidently an exception from the general trend that we have observed. One difference was observed between the products obtained by the two different methods; the silyl ethers formed by pure trimethylchlorosilane were much more sensitive to hydrolysis than the same ethers formed with Trisil ®. The hydrolysed products showed up as new peaks in the gas chromatograms when the reaction tubes had been exposed to
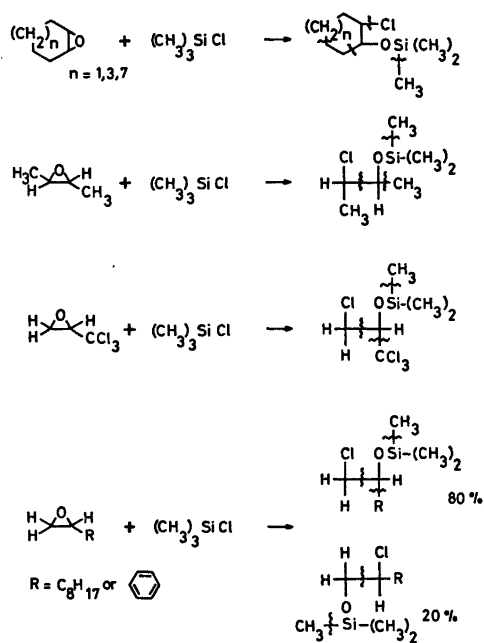
Fig. 2. Reaction schemes for the various epoxides with trimethylchlorosilane and prominent fragmentations in the mass spectra of the silyl ethers formed.

the atmosphere for a few hours. These new peaks had retention times that were shorter than that of the corresponding silyl ether but longer than that of the original epoxide. Mass spectra of these new compounds showed that they were the free chlorohydrins without the silyl ether group.

The epoxides were also treated with other silylating agents for comparison. Treatment with the second component in Trisil ®, pure hexamethyldisilazane, gave no reaction whatsoever. When epoxyclohexane was treated with bis(trimethylsilyl)trifluoroacetamide, BSTFA, and with trimethylsilylimidazole in pyridine, Trisil-Z ®, it was obvious that some kind of reaction occurred since the epoxide disappeared from the gas chromatogram, but the products formed could not be analysed by GLC and MS.

The mass spectra of the silylated epoxides all display weak molecular-ion peaks in contrast to the M − 15 peaks which are prominent. Both peaks display a P + 2 peak of about 30 % intensity which is the typical isotope pattern for an ion containing one chlorine atom. This statement is obviously not valid for 1,2-epoxy-3,3,3-epoxypropane. The strong peak at M − 15 is characteristic for the mass spectra of all silyl ethers and represents one way of α-cleavage to lose one of the methyl groups in the tri-

methylsilyl group (Fig. 2). The two other ways of α-cleavage also give rise to ions that are observed in the different spectra.

In the silylated epoxides of the alicyclic compounds the ring opening by α-cleavage is followed by the expulsion of one or more ethylene units. Prominent peaks corresponding to the carbocyclic skeleton of these molecules are also present. The loss of chlorine or hydrogen chloride from the molecular ions, as well as from the M − 15 ions, gives peaks lacking the chlorine isotope pattern in all observed spectra.

The unsymmetrical epoxides can give two different derivatives. This is observed for (1,2-epoxyethyl) benzene (styrene oxide) and 1,2-epoxydecane while 1,2-epoxy-3,3,3-trichloropropane gives just one product. The mass spectrum of the latter derivative displays prominent peaks at M − 15, M − CH_2Cl and M − CCl_3, all representing α-cleavage in the structure where the epoxide ring has opened in the normal way at the primary carbon atom (Fig. 2). For (1,2-epoxyethyl) benzene, as well as 1,2-epoxydecane, two products are observed in the gas chromatogram after silylation. Mass spectra were recorded for both compounds in each case, and the spectra displayed molecular ions at the same mass number but different fragmentation patterns indicating that the two components were isomers. The more abundant isomers gave mass spectra with strong peaks at M − 15 and M − CH_2Cl which corresponds to α-cleavage in the silyl ether originating from epoxide-ring opening at the primary carbon atom (Fig. 2). The mass spectra of the less abundant isomers are dominated by strong peaks at 103 mu. This ion is formed by α-cleavage to give $CH_2OSi(CH_3)_3^+$ which is typical of the mass spectra of the isomers formed by abnormal epoxide-ring opening at the secondary carbon atom. The exact mass of the strong M − 15 peak in the mass spectrum of silylated 1,2-epoxydecane was determined to be 249.1447 while the calculated value for $C_{13}H_{29}ClOSi − CH_3 = C_{12}H_{26}ClOSi$ is 249.1441. This together with the fragmentation patterns in the recorded spectra proves that the reaction taking place when the epoxides are treated with trimethylchlorosilane is an addition over the epoxy function.

Experimental. GLC analyses were performed on a Perkin-Elmer Modell 900 Gas Chromatograph equipped with 2 m × 3 mm steel columns with 3 % SE-30 on 80/110 mesh Chromosorb W AW DMCS as the stationary phase. Combined GLC-MS measurements were performed on an LKB 9000 instrument and exact mass determinations were obtained with an AEI 902 instrument at the Department of Medical Biochemistry, University of Göteborg. All the investigated epoxides except 1,2-epoxydecane were commercially available and were used without further purification after having been found pure by GLC analysis. 1,2-Epoxydecane was prepared using the method of Prileschajev.[6]

Trisil ®, trimethylchlorosilane, and hexamethyldisilazane were purchased from Pierce Chemical Company, Rockford, Illinois.

Preparation of derivatives The epoxides were derivatised in the following way with pure trimethylchlorosilane or Trisil ® (trimethylchlorosilane-hexamethyldisilazane in pyridine). Mixtures of 25 μl of the epoxide and 0.2 ml of trimethylchlorosilane (or 1 ml of Trisil ®) were kept in sealed glass tubes at 100 °C for different time intervals. The tube was then cooled and opened, and the reaction mixture was transferred to a micro round flask and the volatile components were removed under vacuum. Dry pentane (2 ml) was added and solid by-products were separated by centrifugation. The clear pentane solution was concentrated under vacuum and the oily residue was directly used for GlC and MS analysis.

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Nitrodiphenyl Ethers from 1,2- or 1,4-Dinitrobenzenes and Copper in Pyridine

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Copper and copper salts have been used in a variety of organic reactions, including Ullmann's biaryl and diaryl ether syntheses [1-3] and various copper-promoted arylations.[3,4]

Symmetrical dinitrophenyl ethers are formed when 1,2- or 1,4-dinitrobenzenes are treated with copper in boiling pyridine [Reaction (1)].
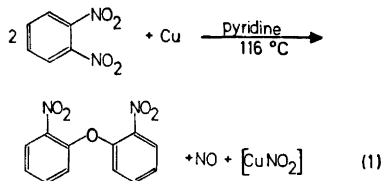
1,2-Dinitrobenzene gave bis(2-nitrophenyl) ether (*1*) (65 %), and 1,4-dinitrobenzene bis(4-nitrophenyl) ether (77 %). Some 2-nitrophenol (*2*) or 4-nitrophenol, respectively, was also obtained.

Various copper compounds were tried (Table 1). Copper(0) was found to be most suitable. Both copper and copper(I) oxide dissolved during the reactions. The molar ratio of copper to 1,2-dinitrobenzene in reaction 1 was varied from 0.5 to 5. The yields of *1* and *2* were essentially the same in all cases. We believe the stoichiometric ratio to be 0.5 (*cf.* Scheme 1). A lower ratio gave lower yields and longer reaction times. Reaction 1 can be carried out in the presence of glacial acetic acid or water with essentially unchanged yields.

Table 1. Yields of products from reaction 1 with different copper sources.

Copper compound	*1*/%	*2*/%
Cu	65	19
Cu$_2$O	25	38
CuO	0	9
None	0	8

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