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Note

Separation of isomeric β -lactam derivatives containing olefinic double bonds by chromatography on silica gel impregnated with silver nitrate*

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It has been known for many years that olefins form moderately stable π -complexes with silver ions¹. The bond between the olefinic ligand and the metal ion is believed to be formed by electron donation by the double bond to the vacant *s*-orbital of the silver ion, followed by donation of *d*-electrons from the metal ion to the anti-bonding orbitals of the olefins¹⁻³. The stability of these complexes depend on steric, electronic and strain effects^{1,4}.

This ability to form complexes has been used by several investigators for the selective separation of compounds containing olefinic double bonds by column, thin-layer and gas chromatography with stationary phases impregnated with silver nitrate^{2,5-8}.

In the course of our work with poly- β -amides containing reactive double bonds, problems arose in the separation of isomeric mono- β -lactams containing olefinic double bonds. These lactams, which are not mentioned in the literature, were synthesized from 4-vinylcyclohexene and N-chlorosulphonyl isocyanate⁹. The mixture of the N-chlorosulphonyl derivatives of the β -lactams was reduced and fractionally distilled in order to separate the unreacted 4-vinylcyclohexene from the mixture of mono- β -lactams, which was then submitted to chromatography.

EXPERIMENTAL

For thin-layer chromatography, chromatographic plates of silica gel 6060 (Eastman Kodak, Rochester, N.Y., U.S.A.) were employed. After impregnation with a 20% (w/v) solution of silver nitrate, the plates were dried at approximately 100° in order to activate the silica. The mixture of isomeric β -propiolactam derivatives was chromatographed using ethyl acetate as eluent and the dark spots were developed by exposure to sunlight or to iodine vapour.

The packing material for column chromatography was prepared by mixing 250 g of silica gel, 70-325 mesh (E. Merck, Darmstadt, G.F.R.) with 230 ml of a 38% (w/v) solution of silver nitrate. After being well homogenized, the slurry was

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dried in a vacuum oven at 80° for 32 h. This material was then packed into a glass column (60 × 4.7 cm I.D.) wrapped with aluminium foil so as to prevent reduction of the silver nitrate by light. In each batch separation, the amounts of silica gel and the mixture of β -lactams were 20 g and 1 g, respectively, and ethyl acetate was used as eluent. For collection of the eluate, an automatic fraction collector (Technicon, Tarrytown, N.Y., U.S.A.) was used and fractions of approximately 15 ml were collected at the rate of 2 ml/min. The refractive indices of the effluent solutions were measured in an Abbe refractometer (Bausch & Lomb, Model 3L) at 25°.

RESULTS AND DISCUSSION

Several investigators have shown that olefinic compounds containing more than one double bond, whether conjugated or not, react with N-chlorosulphonyl isocyanate to give monolactams¹⁰⁻¹⁴. With 4-vinylcyclohexene, disregarding the possibilities of conformational and optical isomerism, eight isomers are possible: two monolactams derived from the vinyl double bond, two monolactams derived from the double bond in the ring and four dilactams derived from the monolactams. The possibility of there being dilactams in the product obtained after removal of the unreacted 4-vinylcyclohexene by vacuum distillation was readily disproved by mass spectroscopy of the product, the molecular ion appearing at exactly m/e 151.

The presence of more than one type of monolactam in the product was shown by NMR spectroscopy in carbon tetrachloride. The spectrum of the mixture (Fig. 1a) shows a predominance of the lactam that resonates at 7.8 ppm over that which resonates at 7.4 ppm. As it is claimed that olefins of the type $RCH = CH_2$ are more reactive towards N-chlorosulphonyl isocyanate than those of the $RHC = CHR$ type¹⁵, one might expect that the 7.8 ppm peak is due to the lactam formed on the vinyl double bond while that at 7.4 ppm corresponds to a lactam formed on the cyclohexene ring.

The separation of the lactams by column chromatography on silica gel impregnated with silver nitrate is shown in Fig. 2. After removal of the solvent, the first lactam to be eluted from the column was distilled (b.p. 118-120°/0.1 mm Hg; n_D^{25} 1.5102) and characterized as 4-(3-cyclohexenyl)-2-azetidinone by elemental analysis (calculated: C = 71.5, H = 8.6, N = 9.2%; found: C = 71.0, H = 8.8, N = 9.1%), IR (bands at 3240, 1750, 1650 and 760 cm^{-1}), NMR (Fig. 1b) and mass spectroscopy (fragments at m/e 151 and 109). Similarly, the second product to be eluted from the column was distilled (b.p. 120-125°/0.7 mm Hg; n_D^{25} 1.5107) and characterized as a monolactam by elemental analysis (calculated: C = 71.5, H = 8.6, N = 9.2%; found: C = 70.8, H = 8.6, N = 9.2%) and mass spectroscopy (m/e 151). However, although the NMR (Fig. 1c) and IR spectra (bands at 1640, 990 and 910 cm^{-1}) show the presence of a vinyl double bond, it was impossible, by the methods employed, to establish if the product consisted of a mixture or only one of the compounds with the structures represented in Fig. 2.

According to the literature, an increase in the number of substituents on the olefinic double bond decreases the stability of its silver ion complex; for example, cyclic terpenes, with terminal or exocyclic double bonds, form more stable silver ion complexes than those with internal double bonds¹⁶. Likewise, the silver ion complex of cyclohexene is less stable than that of 1-hexene⁴. In fact, the lactam with the

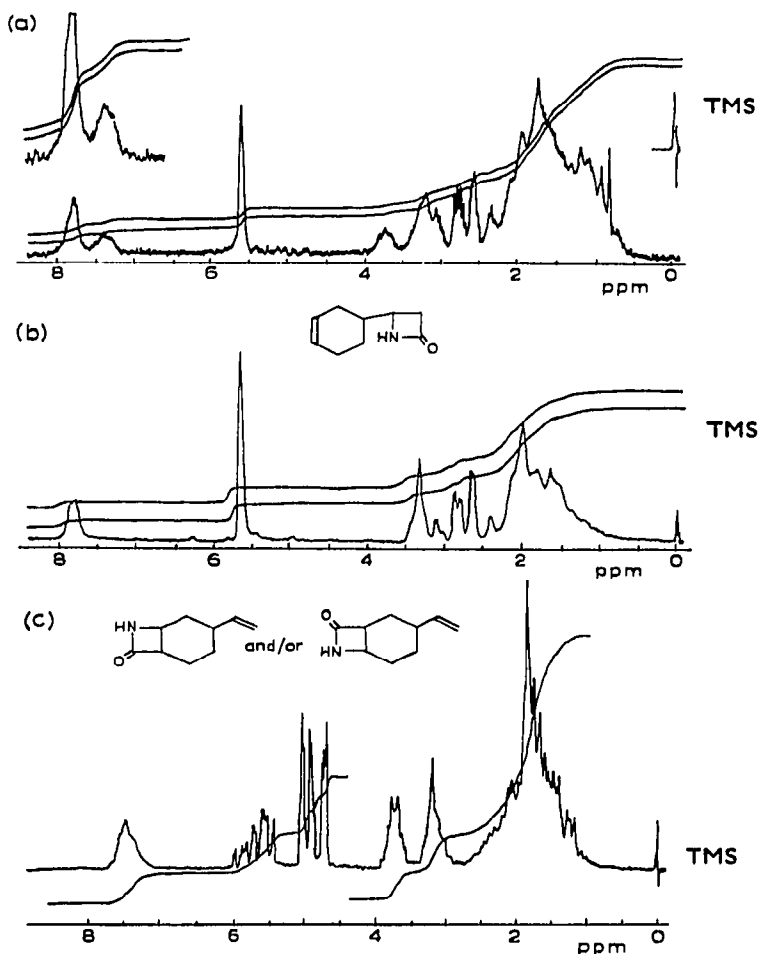


Fig. 1. NMR spectra in carbon tetrachloride at 60 mHz. (a), Mixture of β -lactams before fractionation; (b) 4-(3-cyclohexenyl)-2-azetidinone; (c) β -lactams with pendant vinyl groups.

smaller retention volume, for which the silver ion complex should be less stable, is the one in which the cyclohexene ring remained intact, that is, 4-(3-cyclohexenyl)-2-azetidinone.

It is important to notice that the ratio of the 4-(3-cyclohexenyl)-2-azetidinone to the product in the second fraction, as determined by column chromatography (2.6:1), is in very good agreement with that obtained by NMR spectroscopy (2.4:1) as the ratio of the areas under the peaks at 7.8 and 7.4 ppm.

In conclusion, the method described is potentially useful for the separation of other classes of compounds containing olefinic double bonds.

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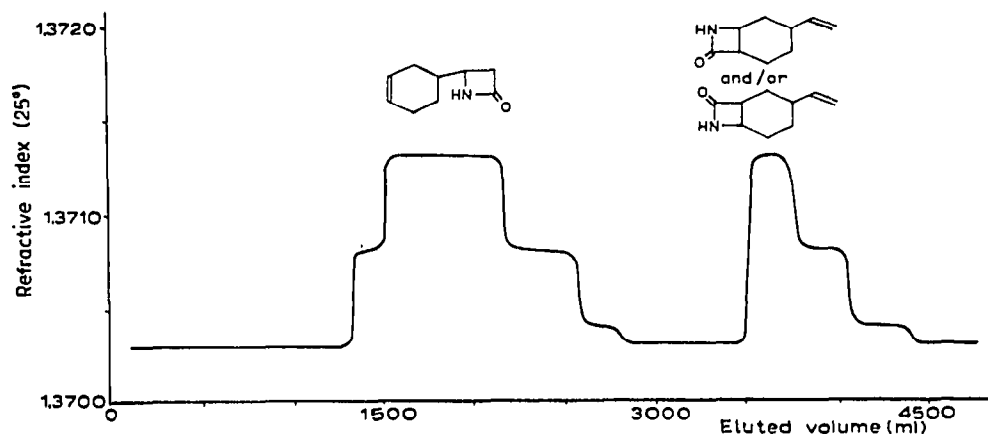


Fig. 2. Separation of the mixture of β -lactams by column chromatography in silica gel impregnated with silver nitrate. Eluent, ethyl acetate; elution rate, 2 ml/min.

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