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Note

tert.-Butyldimethylsilylation of ethyl 3-bromo-2-hydroxyiminopropanoate and analysis of the products by gas chromatography–mass spectrometry

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The *tert.*-butyldimethylsilyl group is widely used as both a synthetic protecting group and as a derivative for gas chromatography (GC). The conventional method for formation of this derivative is to use a mixture of *tert.*-butyldimethylchlorosilane (TBDMCS), dimethylformamide (DMF) and imidazole as originally reported by Corey and Venkateswarlu[1]. This method has several disadvantages as recently discussed by Mawhinney and Madson[2]. When used as a derivatization method for GC and GC–mass spectrometry (MS) the disadvantages quoted are its ineffectiveness in silylating thiols, primary and secondary amines and slightly hindered hydroxyl groups; the fact that imidazole is an acid scavenger that interferes with the quantitative silylation of carboxylated compounds and that the derivative yield is diminished due to the necessary extraction step. The use of N-methyl-N-(*tert.*-butyldimethylsilyl) trifluoroacetamide (MTBSTFA) to overcome these problems was described and the usefulness of this derivatising reagent has recently been demonstrated by Baxan and Knapp[3] in the derivatization of 6-ketoprostaglandin $F_{1\alpha}$ for GC–MS.

Recently we required a GC method for the analysis of ethyl 3-bromo-2-hydroxyiminopropanoate (I) a useful synthetic reagent.

$$\begin{array}{l} BrCH_2CCOOCH_2CH_3 \\ \quad\quad\| \\ \quad\quad NOH \end{array} \qquad \text{(I)}$$

Initial attempts at silylation with BSA–pyridine failed to give a useful derivative. Whilst trying other silylation procedures we attempted to form the *tert.*-butyldimethylsilyl derivative using the method of Corey and Venkateswarlu[1]. These results and subsequent *tert.*-butyldimethylsilylation reactions are reported below.

EXPERIMENTAL

Apparatus

The GC–MS system used was a Pye Unicam 104 gas chromatograph coupled to a VG 70-70 mass spectrometer.

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Chromatographic conditions

The column was a 25 × 0.33 m I.D. BP1 capillary column held at 100°C for 2 min then temperature programmed to 290°C at 6°C/min. A split injection technique was used with helium as carrier gas.

Derivatization

The method of Corey and Venkateswarlu[1] involved making up a stock solution containing 200 mg TBDMCS, 200 mg imidazole in 300 μl DMF. 20 mg of ethyl 3-bromo-2-hydroxyiminopropanoate was dissolved in 1 ml of the stock solution and left to stand at room temperature for 30 min. 2 ml distilled water were then added, the solution shaken and 2 ml ethyl acetate added. The tube was shaken and then left to stand. The ethyl acetate layer was removed and 1-μl quantities were injected into the gas chromatograph. The *tert.*-butyldimethylsilylation method using MTBSTFA involved mixing 20 mg of ethyl 3-bromo-2-hydroxyiminopropanoate, 800 μl DMF and 200 μl MTBSTFA. After standing at room temperature for 30 min 2 ml DMF were added and 1-μl quantities injected into the gas chromatograph.

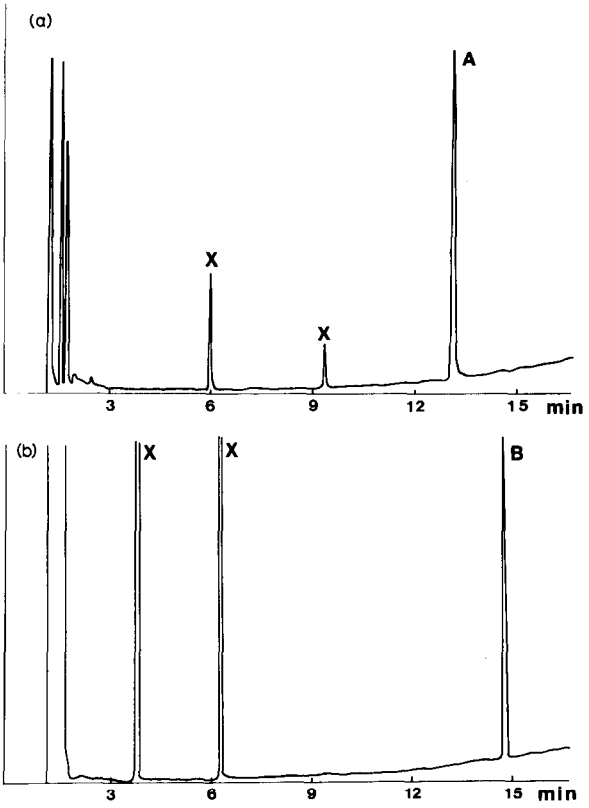

Fig. 1. Total ion-current chromatograms. (a) Reaction of ethyl 3-bromo-2-hydroxyiminopropanoate with TBDMCS, (b) reaction of ethyl 3-bromo-2-hydroxyiminopropanoate with MTBSTFA. Peaks: A = *tert.*-butyldimethylsilyl derivative of 3-chloro-2-hydroxyiminopropanoate, B = *tert.*-butyldimethylsilyl derivative of 3-bromo-2-hydroxyiminopropanoate, X = GC peaks also observed in derivatisation blanks.

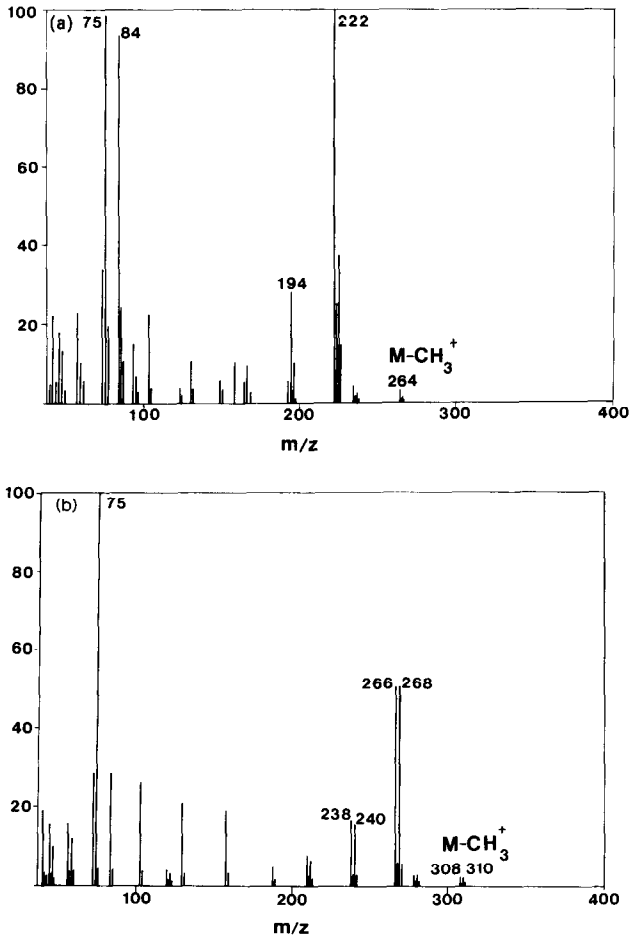

Fig. 2. Electron-impact mass spectra. (a) Peak A of Fig. 1a; (b) peak B of Fig. 1b.

RESULTS

GC of the reaction product of TBDMCS, DMF, imidazole with ethyl 3-bromo-2-hydroxyiminopropanoate indicated that one major derivative has been formed (Fig. 1a). GC–MS of this reaction product was performed and the electron-impact mass spectrum from this derivative is shown in Fig. 2a. It is obvious from this spectrum that halogen substitution has occurred and that the major reaction product was the *tert.*-butyldimethylsilyl derivative of 3-chloro-2-hydroxyiminopropanoate. This is formed by chloride-ion displacement with TBDMCS being the source of the chloride ions.

Derivatization using MTBSTFA also gave only one major derivative (Fig. 1b). The electron-impact mass spectrum of this indicated that the expected *tert.*-butyldimethylsilyl derivative of I had been formed (Fig. 2b).

CONCLUSION

The bromine atom in ethyl 3-bromo-2-hydroxyiminopropanoate is particularly labile and it is thus not surprising that chlorine substitution occurs during *tert.*-butyldimethylsilylation. One of the impurities for which the GC method was being used to detect was ethyl 3-chloro-2-hydroxyiminopropanoate and thus these observations are significant and illustrate another distinct advantage for using MTBSTFA for *tert.*-butyldimethylsilylation rather than the method of Corey and Venkateswarlu.

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