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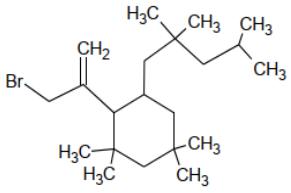
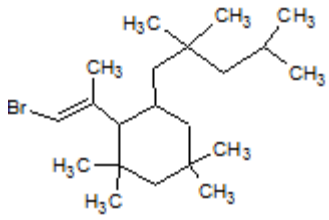
Protein-reactivity of rubber oligomer C21H39Br isomers

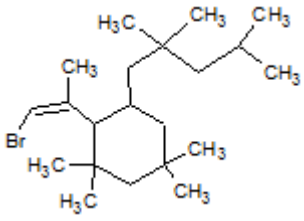
We recently described the structure of isomers of the rubber oligomer C21H39Br.
In contrast to the main compound C21H39Br (CAS 2518227-14-8), with the bromine in allyl position, the isomers consist of the E-and Z-form of the vinyl analog.



C21H39Br (allyl)



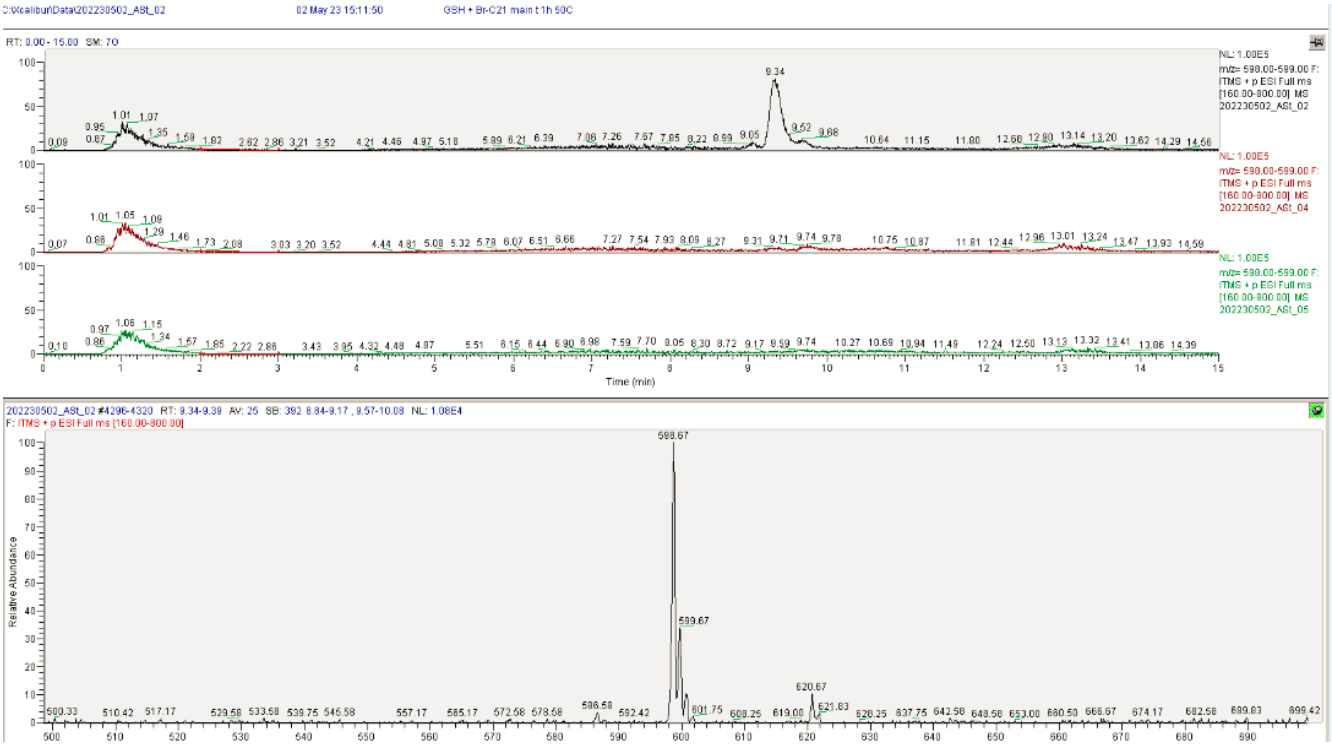
C21H39Br E-isomer (vinyl)



C21H39Br Z-isomer (vinyl)

The main compound C21H39Br is an alkylating agent, which reacts with glutathione (GSH) [1].
GSH-depletion and adduct formation is a measure to determine protein reactivity [2].

C21H39Br main compound and the E- and Z-isomers of the vinyl analog were treated with glutathione.
Whereas the main compound was reactive, the isomers didn't form GSH-adducts.



LC-MS chromatograms of GSH + C21H39Br main compound (top), GSH + C21H39Br Z-isomer (middle) and GSH + E-isomer (bottom). LC-MS spectrum of GSH-adduct of C21H39Br main compound (peak at 9.3 min).

The experimental results fit with theoretical consideration. The bromine in ally position is activated, but bromine in vinyl position not.

The results indicate, that the C21H39Br main isomer and the vinyl isomers have different protein reactivity and that toxicological evaluations or derived PDE for the main isomer might be an overestimation of risk for the isomers.

[1] R. Haep et.al. *Pharm.Ind.* 2018, *80* (1), 104-144
[2] OECD QSAR Toolbox v.4.1 Implementation AOP workflow in Toolbox: Skin Sensitization
https://www.oecd.org/env/ehs/risk-assessment/Tutorial_
11_TB%204.1_Implementation%20of%20AOP%20workf
low%20in%20Toolbox%20SS.pdf