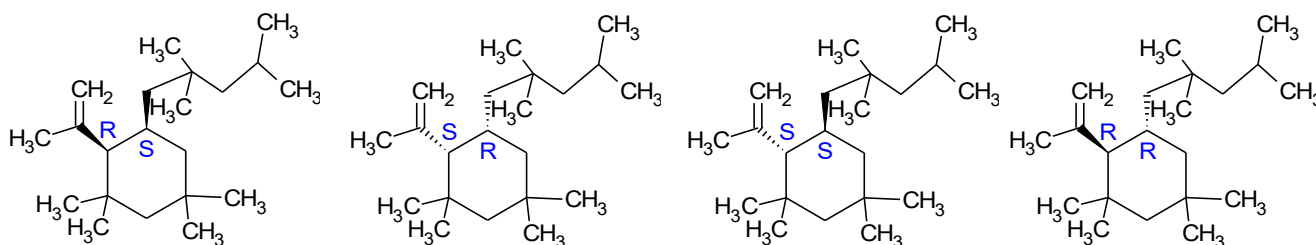


Optical isomers (diastereomers) of rubber oligomer C₂₁H₄₀

Rubber oligomer C₂₁H₄₀, CAS 2512216-71-4 (ASAS Labor GmbH, article no. ASAS-003) is a mixture of 2 pairs of diastereomers. The diastereomers are not separated using GC-MS on a DB-5 (or similar) column. The chromatographic peak appears symmetric without any signs of (even partial) separation. However, NMR experiments revealed the presence of a diastereomer mixture. In the ¹H-NMR spectrum, there is a pair of signals for the methylene group protons (4.55/4.65/4.85/5.0 ppm) [1]. The same is true for the ¹³C-NMR signals for the methylene group (112/116 ppm) [2].

The diastereomer CAS 114123-73-8 (named 1,1,5,5-tetramethyl-2-(1-methylethenyl)-3-methylethenyl-3-(2,2,4-trimethylpentyl)-,cis [3]) consists of the configuration (2*R*,3*S*) / (2*S*,3*R*), whereas the diastereomer CAS 114123-74-9 (named 1,1,5,5-tetramethyl-2-(1-methylethenyl)-3-methylethenyl-3-(2,2,4-trimethylpentyl)-,trans [4]) consists of configuration (2*S*,3*S*) / (2*R*,3*R*).



Cyclohexane, 1,1,5,5-tetramethyl-2-(1-methylethenyl)-3-methylethenyl-3-(2,2,4-trimethylpentyl)-,cis

CAS 114123-73-8

Pair of diastereomers with

absolute configuration (2*R*,3*S*) / (2*S*,3*R*)

Cyclohexane, 1,1,5,5-tetramethyl-2-(1-methylethenyl)-3-(2,2,4-trimethylpentyl)-,trans

CAS 114123-74-9

Pair of diastereomers with

absolute configuration (2*S*,3*S*) / (2*R*,3*R*)

There seems to be some confusion using the CAS numbers. Some suppliers offer rubber oligomer 3 (numbering of rubber oligomer C₂₁H₄₀ CAS 2512216-71-4 as used by companies like TLC), but state, it is CAS no. 114123-73-8 [5]. For the purified diastereomer CAS 114123-74-9, the common synonym is rubber oligomer 7 [6]. Sometimes, the CAS no's CAS 2512216-71-4, 114123-74-9 and 114123-73-8 are used synonymously. It has to be mentioned, that the usage of isolated diastereomers as analytical standards in E&L studies is of no benefit as they are not normally separated in GC-MS methods.

By the way, beside ASAS Labor GmbH, some other suppliers of rubber oligomer suppliers were mentioned above.

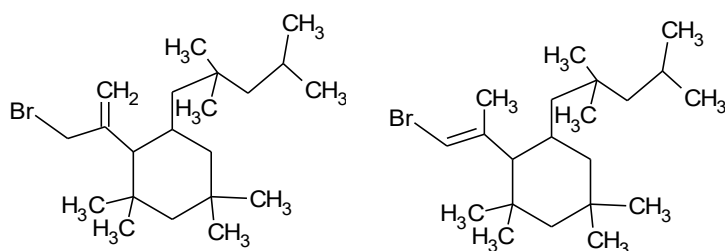
The citation „Another need that has been identified is to make available individual reference standards for extractables and leachables that may be commonly encountered but that are not commercially available (e.g., rubber oligomers) “given in the USP stimuli paper „Proposals for the Development, Composition, and Routine Use of System Suitability Standard Mixtures in Support of Chromatographic Screening for Organic Extractables and Leachables “ [7], sounds somewhat misleading, given the providers listed above.

So, this statement has to be bolded and underlined:

Analytical standards for butyl rubber oligomers are commercially available!

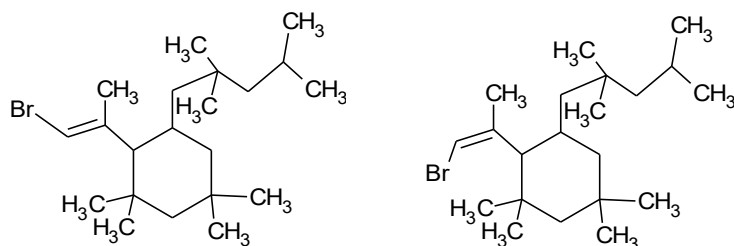
For the sake of completeness, some other types of isomer are mentioned below:

Structural isomers

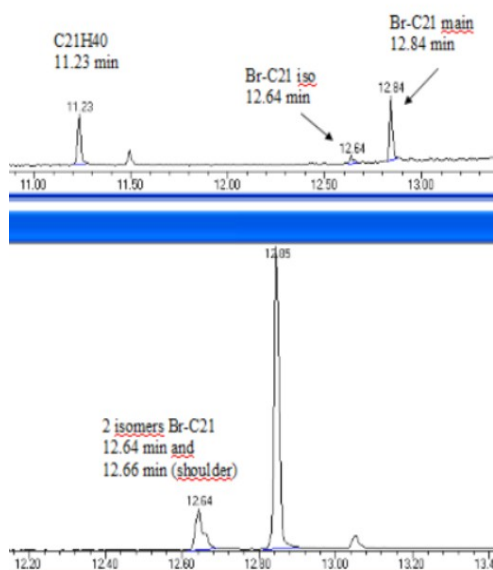


On the left side, the well known rubber oligomer C₂₁H₃₉Br, CAS 2518227-14-8, is depicted. A structural isomer that frequently occurs in bromobutyl rubber extracts is shown on the right and has the same formula. They differ in the position of the double bond, which is either in ally (left) or in vinyl (right) position. These isomers can be separated during GC-MS analysis, and they differ also in reactivity towards GSH (a surrogate for protein reactivity) [8].

Cis-trans isomers (or geometric isomers)



The prerequisite for this types of isomers is, that two non-identical groups are present on each double-bonded carbon atom. In contrast to rubber oligomer $C_{21}H_{39}Br$, CAS 2518227-14-8 with allylic structure, the bromine is directly connected to the double bond. Therefore, the vinyl structural isomer of $C_{21}H_{39}Br$ is further split into trans or E- (left picture) and cis or Z-isomers (right picture). The cis- and trans-isomer can be separated by GC-MS. An example of a chromatogram is given below:



The peak at 12.84 min is rubber oligomer $C_{21}H_{39}Br$, CAS 2518227-14-8
The peak at 11.23 min is rubber oligomer $C_{21}H_{40}$, CAS 2512216-71-4 (mixture of 2 pairs of diastereomers)

The 2 peaks at 12.64 and 12.66 min are the E- and Z-isomers of the vinyl analogue of rubber oligomer $C_{21}H_{39}Br$,

- [1] Spectral Service AG report ASL92927
- [2] Spectral Service AG report ASL203855
- [3] https://www.lookchem.com/CASDataBase_114123-73-8.htm
- [4] <https://www.lookchem.com/cas-114/114123-74-9.html>
- [5] <https://www.alfa-chemistry.com/product/rubber-oligomer-3-cas-114123-73-8-341671.html>
- [6] <https://tlcstandards.com/ProdDetail.aspx?ID=R-118007&name=RUBBER%20OLIGOMER>
- [7] DOI: https://doi.org/10.31003/USPNF_S203084_10101_01
- [8] <https://www.asas-labor.de/wp-content/uploads/2023/06/Br-C21-isomers-GSH-reactivity.pdf>