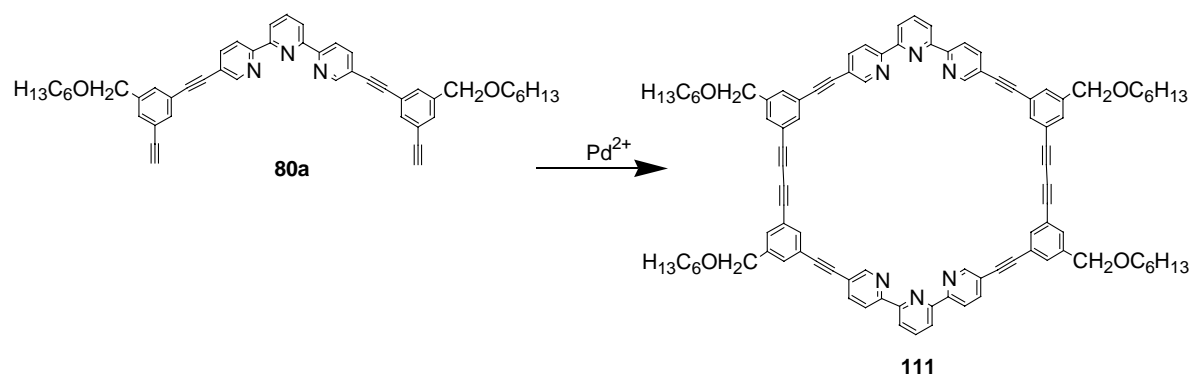## 4.5 A 50-membered cycle with two terpyridine units



*Scheme 46. 50-membered macrocycle **111** with two terpyridine units via oxidative Glaser coupling.*

With Lehmann's structure **26** (Scheme 11, p. 13) and the compounds **95a** and **110a** prepared here, a set of 34-, 46-, and 58-membered shape-persistent macrocycles with two terpyridine units and the same side chain pattern is available which allows a systematic investigation into the macrocycles' properties in relation to size. All these macrocycles were prepared by Sonogashira coupling of two differently functionalized precursors. A further member of this class, **111** with 50 ring atoms, is accessible by oxidative cyclodimerization of the single precursor **80a** (Scheme 46). Its synthesis therefore not only accomplishes the existing set of macrocycles by an additional size, but also explores the compatibility of the structures investigated here with the Glaser type alkynyl-alkynyl coupling.

A large variety of different conditions for this coupling reaction exist, and many shape-persistent macrocycles published rest upon these reactions (ref. Chapter 3.1). Some authors describe attempts to optimize the reaction conditions, but there are no systematic studies available yet which would allow to select appropriate reaction conditions in a rational way.[141] Astonishing results still pose many questions. For example, Tobe isolated from a Glaser reaction not the expected macrocycle with hexagonal geometry, but its geometrically strained tetra- and octagonal analogs (for details, ref.[142]); from an attempt towards a macrocycle with four bipyridine units by cyclodimerization in a $CuCl/CuCl_2$ slurry in pyridine, Henze isolated only the open-chain dimer. Under different reaction conditions ($PdCl_2(PPh_3)_2/CuI$/piperidine/THF), he could detect the desired cyclodimer by MALDI-TOF.
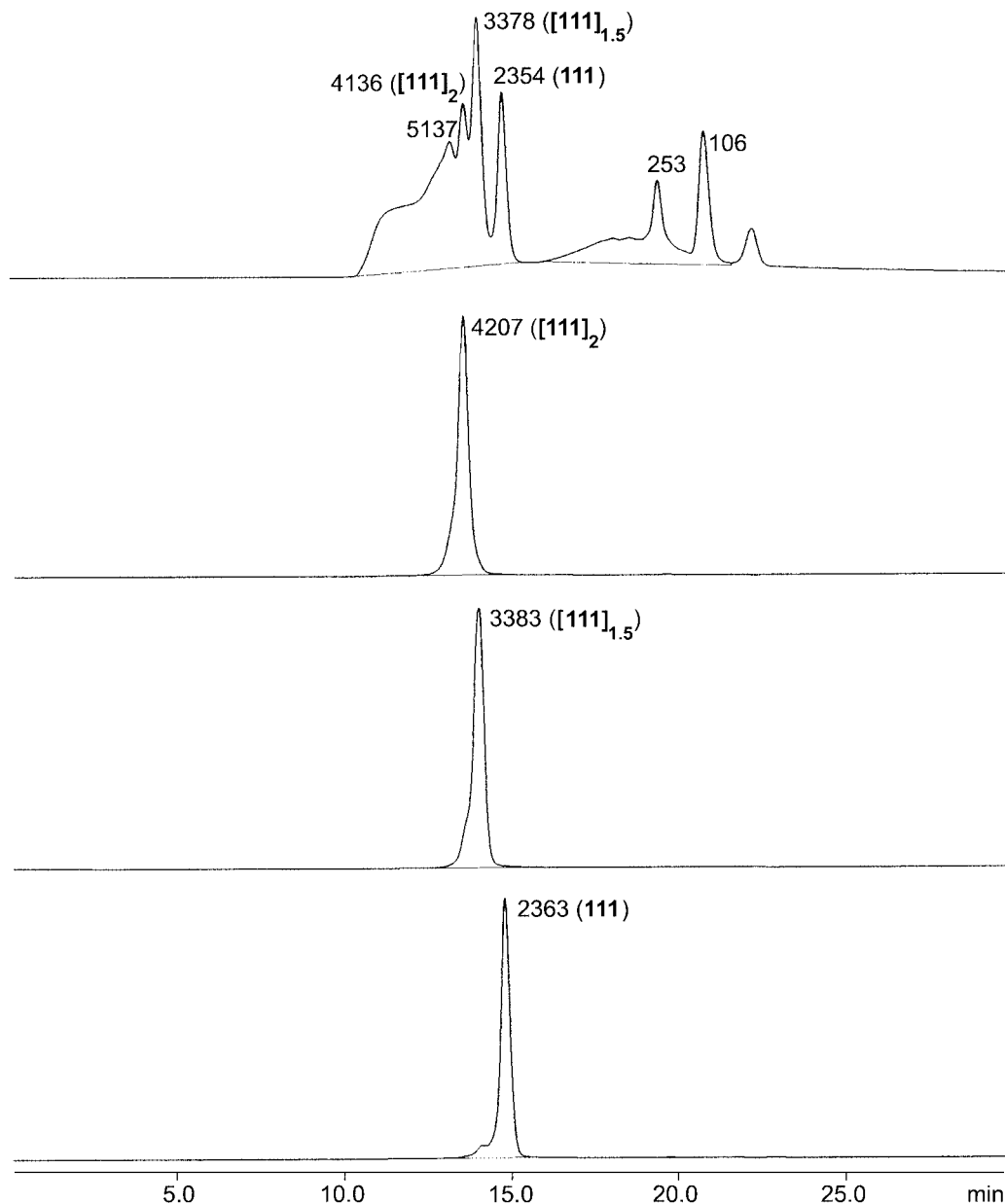
*Fig. 18. GPC traces (from top to bottom) of the raw product of the cyclization to 111, of isolated cyclic tetramer [111]₂, trimer [111]₁.₅ and the dimer 111. Ref. Scheme 46.*

Here, an attempt to cyclodimerize **80a** was done under the latter conditions. Under air, the catalysts $PdCl_2(PPh_3)_2$ and CuI were stirred in piperidine/THF 1:1 at room temperature. A solution of **80a** in THF was added via a syringe pump over a period of 3 days, and the reaction mixture was stirred for 3 more days. The GPC trace of the raw product after work-up showed at least three characteristic, sharp signals (Fig. 18). By preparative GPC, the corresponding compounds were isolated and assigned as the expected (dimeric) macrocycle **111** and its (tetrameric) double mass analog **[111]₂** - this is in analogy to the previously described cycles - and, additionally, the trimeric macrocycle **[111]₁.₅**, which can form here

due to the homocoupling reaction conditions. Again, **111** is extremely poorly soluble. As described for **110a** (Fig. 17), also here a precipitate formed during preparative GPC, which was enriched with cycle **111**. The low yield is therefore probably due to solubility reasons. This assumption is also backed by the observation, that the intensity of the signal of **111** in the raw product GPC is relatively low with respect to well soluble **[111]$_{1.5}$** and **[111]$_2$** (compare all other raw product GPCs shown); poorly soluble **111** may therefore be lost during work-up. This, however, is under the assumption, that the relative ratio of the cyclic oligomers formed in the reaction is really comparable to the other cases, which not necessarily needs to be the case [**111**: 23 % (GPC), 8 % (isolated); **[111]$_{1.5}$**: 19 % (GPC), 8 % (isolated), **[111]$_2$**: 12 % (GPC), 3 % (isolated)]. The yields according to GPC can only be interpreted relative to each other here and not quantitatively, as the raw product still contained a considerable amount of piperidine and could therefore not be weighed correctly.