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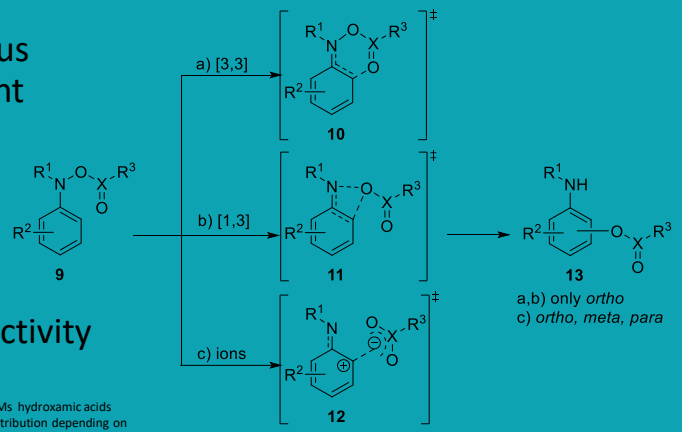
Rearrangements of N-aryl hydroxamic acid methanesulfonates („Towards novel and valuable organic substances“)

Q1: Scientific question

Known from literature: various intramolecular rearrangement mechanisms

Hydroxamic acids of general structure **9** can react by three different mechanisms: Sigmatropic rearrangement, where all bonds are rearranged simultaneously, is possible via a six-membered cyclic transit state **10** or via a four-membered cyclic transit state **11**, heterolytic dissociation of the N-O bond leads to the ionic transition state **12** (path c)

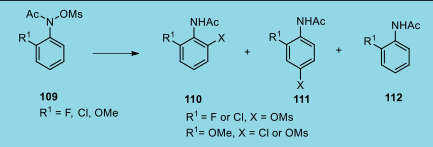
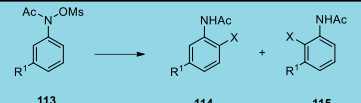
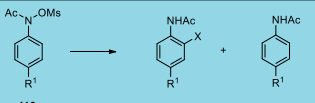


Rearrangement mechanisms

Research question: regioselectivity of OMs group

The aim of this work was to study the intramolecular rearrangement of N-aryl-OMs hydroxamic acids Main focus was on the regioselectivity of OMs group migration and product distribution depending on the substituent on benzene ring (electron acceptor groups (Cl and F), as well as electron donor groups (OMe and NHAc) were selected as substituents)

Q3: Data Analysis & Results

Ortho-substituted derivatives	
Meta-substituted derivatives	
Para-substituted derivatives	

Q2: Methodology

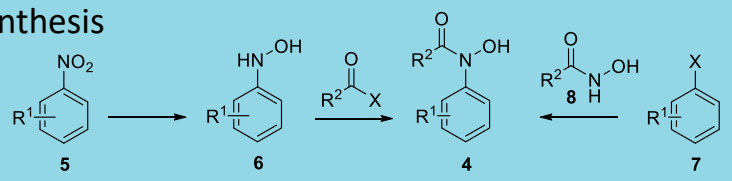
Reaction conditions:

1.Hydroxamic acid synthesis

Various approaches for the synthesis of *N*-arylhydroxamic acids **4** are known from the literature:

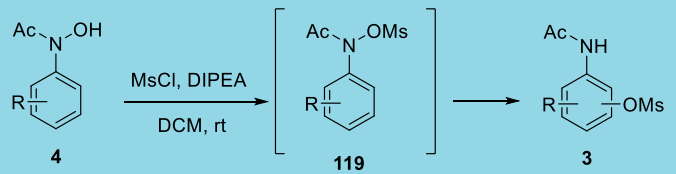
- selective partial reduction of nitroaromatics **5** to *N*-aryl hydroxylamine **6** and its subsequent acylation
- direct coupling of the electrophilic aromate **7** with the prefunctionalized hydroxylamide **8** (transition metal catalysis is necessary to achieve efficient C-N coupling

The reduction and subsequent acylation procedure was chosen for the synthesis of the studied compounds



2.Methanesulfonation

Hydroxamic acids **4** were subjected to methanesulfonylation: to a solution of hydroxamic acid **4** in anhydrous DCM was added MsCl and DIPEA. The reaction mixture was stirred at room temperature and monitored by HPLC/MS. *O*-mesylated intermediate **119** could not be detected, as it rapidly rearranged to C-mesylated product **3**. After the consumption of starting material, the reaction product(s) were purified by a column chromatography, or in same case by a semipreparative-HPLC. All products were characterized by NMR spectroscopy.

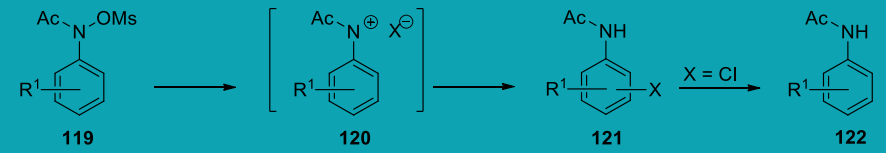


R = F, Cl, OMe, NHAc

Q4: Interpretation & Conclusions

Ionic rearrangement mechanism in *ortho* or *para* position

Based on all available experimental data, the rearrangement mechanism of studied compounds can be deduced. Everything points to an ionic mechanism, when in situ formed methanesulfonate **119** dissociates into ionic intermediate **120**.



R^1 = Cl, F, NHAc, OMe
X = OMs, Cl

Applications: valuable starting materials for organic synthesis, pharmacochemistry, biochemistry and materials chemistry