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[A0066]

Study of the Thermal Behavior of Azidohetarenes with Differential Scanning Calorimetry

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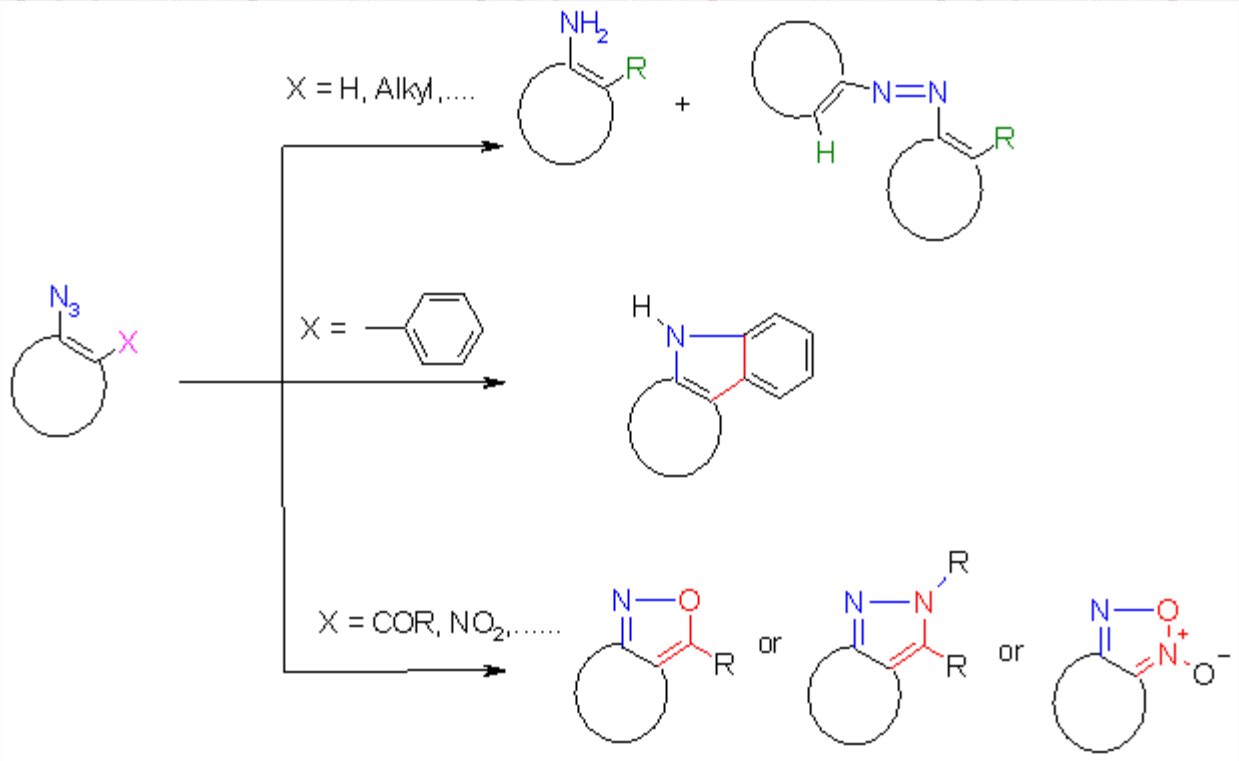
Contents:

1. General Aspects

Azidohetarenes have found large interest because of its reactive azido group which gives a number of reactions which can be used synthetically [1]. We have prepared previously a number of hetaryl azides [2] having reactive substituents such as phenyl-, acyl-, hydrazono- and nitro groups in *ortho*-position which were used as synthons for thermolytic induced heteroelectrocyclic ring closure reactions.

In this contribution we studied the thermal behavior of azidoarenes and azidohetarenes with and without reactive *ortho*-substituents to get insights in the thermal properties of these compounds which are interesting and important for thermal reactions.



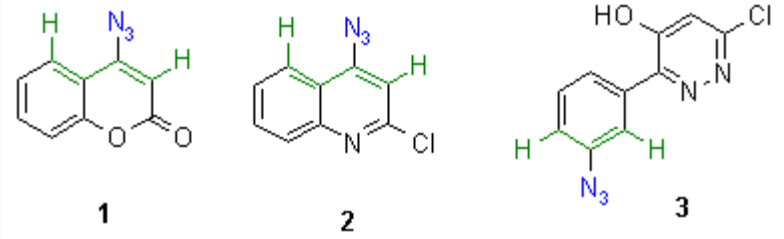
By means of **differential scanning calorimetry (DSC)** we obtained besides melting points (which are in many cases of interest because the purity can be better determined than with chromatographic methods) the temperature areas for reaction or decomposition [3]. This information is very valuable because it allows the synthetic chemist to plan the reaction conditions (e.g. to select suitable solvents and reaction temperatures which are high enough for a quick reaction, but below subsequent decomposition or rearrangement temperatures). Integration of the reaction and decomposition peak area gives information about the reaction enthalpy which in turn is a very important safety information. Together with the temperature it shows if and at which temperature a particular substance is an explosive, which is in azide chemistry of great value.

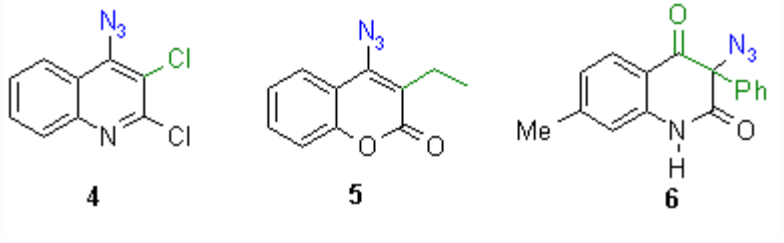
2. Decomposition of azidohetarenes without reactive *ortho*-substituents to nitrenes

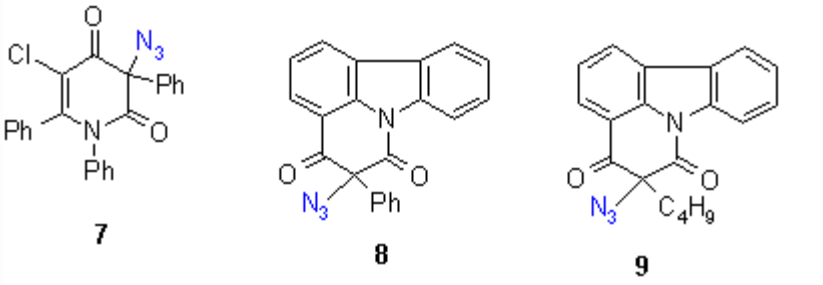
Azides are known to give on thermolysis singlet nitrenes (or by intersystem crossing triplet nitrenes) which react with hydrocarbon compounds to form e.g. a C-N bonding by C-H- insertion, or a N-N bonding by reaction with nucleophiles to give ring enlargements or amines. [1]. By dimerization e.g. the formation of colored azo compounds is observed.

Our interest in the thermal behavior of this type of compounds was directed mainly to melting and decomposition temperatures and enthalpies for safety hints. A further aspect was to get information for mechanistic studies, because we wanted to compare the thermal properties of nitrene reactions with reactions without nitrene intermediates. So we studied in the first series compounds having only hydrogens in ortho position (**1-3**), together with azides having chloro- and alkylsubstituents (**4, 5**). Compounds **6-9** have the azido group at a sp^3 carbon. The compounds were

obtained from the corresponding chloro compounds by the procedures described in earlier reports [2].

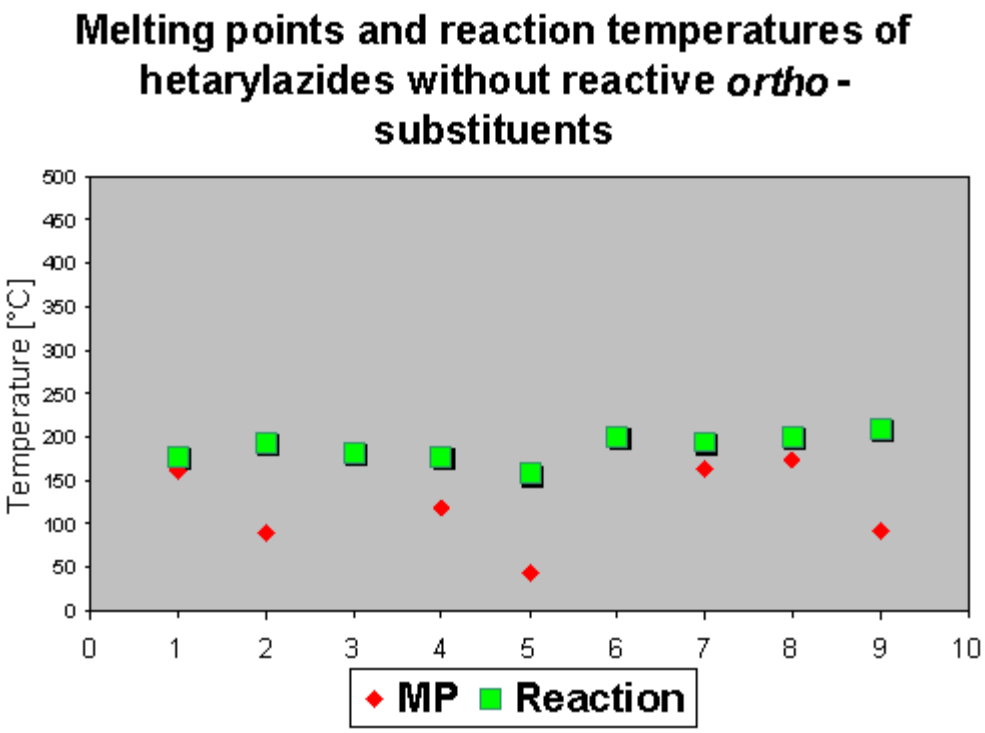






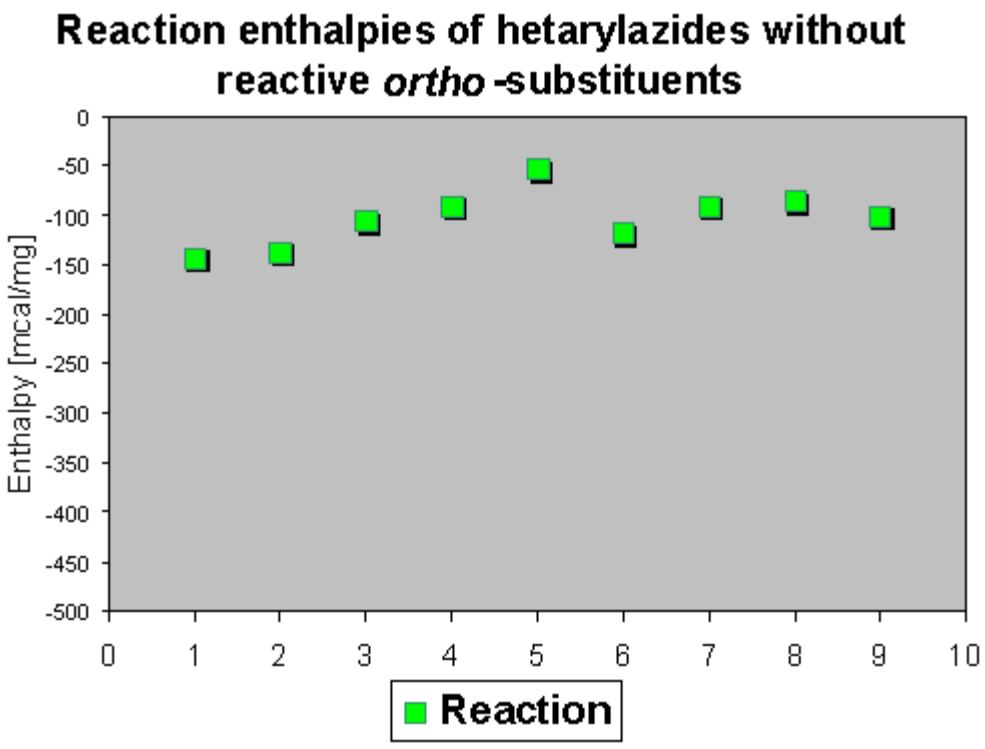
All these azides possess a structure which leads in the first step to a nitrene and gives then in inter- or intramolecular reaction with aromatic or aliphatic hydrocarbons amines, or dimerization products. The diagram of melting and reaction temperatures show that all these azides without reactive *ortho*-substituents have a rather uniform thermal behavior.

The reaction or decomposition temperatures were found between 150 and 200 ^{O}C. There is no hint that e.g. the ortho-ethyl group of **5** or the azido-1,3-dicarbonyl compounds **6-9** give reactions at significant lower temperatures.



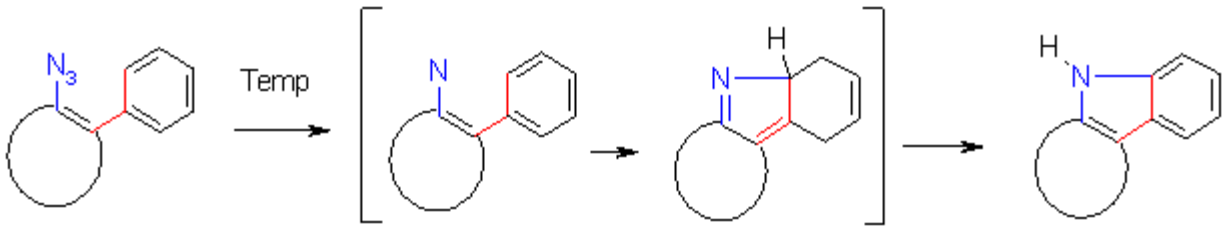
The values for the reaction enthalpy are in an average range between - 50 and - 150 mcal/mg, which means that

handling of these compounds bears no special danger.

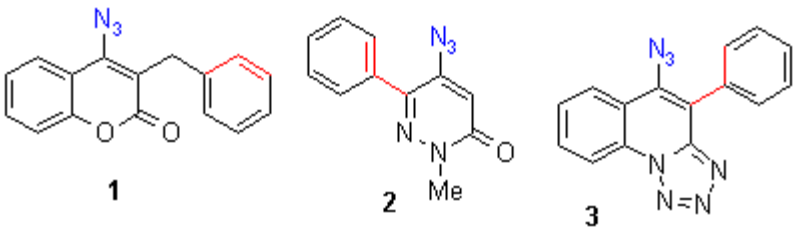


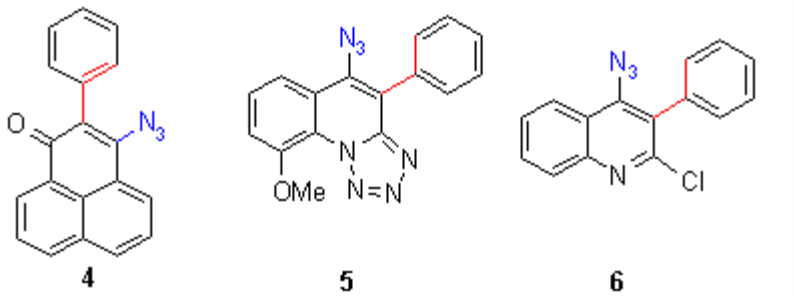
3. Decomposition of azidohetarenes with *ortho*-phenyl substituents to indoles

Thermolysis of azidohetarenes with ortho-phenyl groups is described to lead in the first step to hetaryl-nitrenes which cyclize by an electrocyclic reaction followed by a 1,5-hydrogen shift to give indolo-fused heterocycles [1]. This reaction sequence offers a simple way with high yields to this interesting class of compounds.



The azido compounds were obtained by the procedures described in earlier reports [2]. We could show that also azides with benzyl substituents such as compound **1** give in moderate yields the corresponding quinoline compounds. The phenyl compounds (**2-9**) react in good yields to indolofused heterocycles[2].





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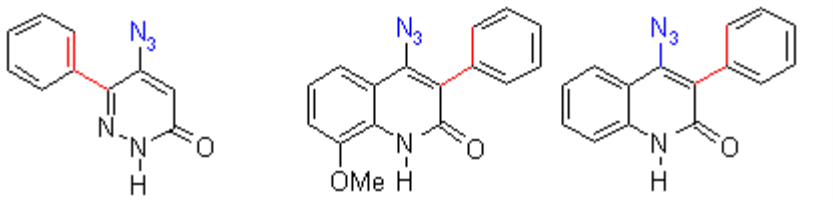
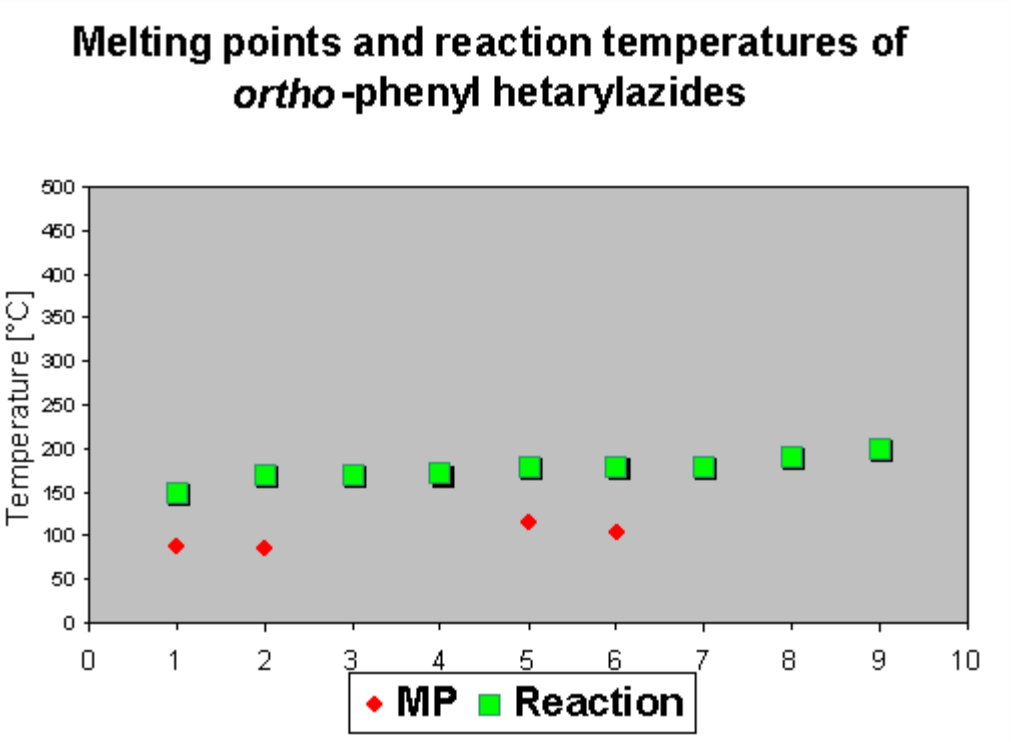


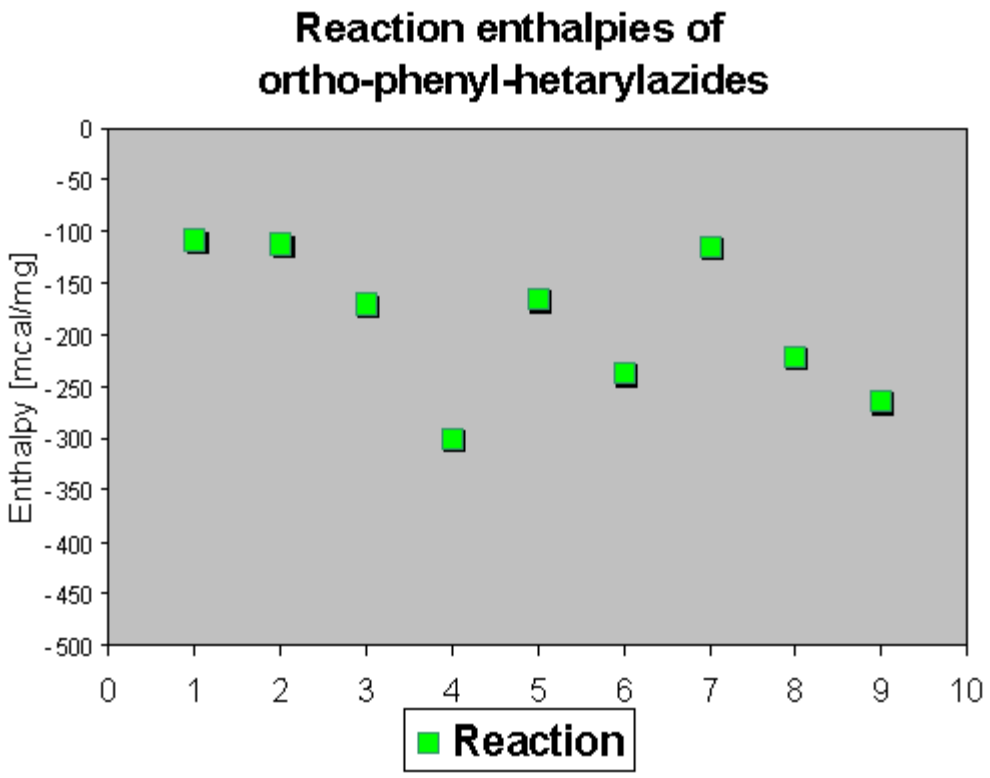
7 8 9

As the first step - similar to the compounds described in chapter 2 - a nitrene is described to be formed by thermolysis, which means that there should be no influence on the decomposition temperature. It was of interest to check if there is an influence visible of the *ortho*-phenyl group to the the reaction enthalpies.

Because of its reactivity, only a few compounds show a mp. The reaction temperature ranges again between 150 and 200 ^{o}C, which means that actually the **ortho-phenyl substituent does not change the initial reaction temperature**.



The reaction enthalpies of the azides **1-9** have rather different values between - 110 and - 300 mcal/mg. So this assay does not allow a general statement on further activation influence of the phenyl group, because substituent effects and the heterocyclic system seem to superimpose the effects of the phenyl group.

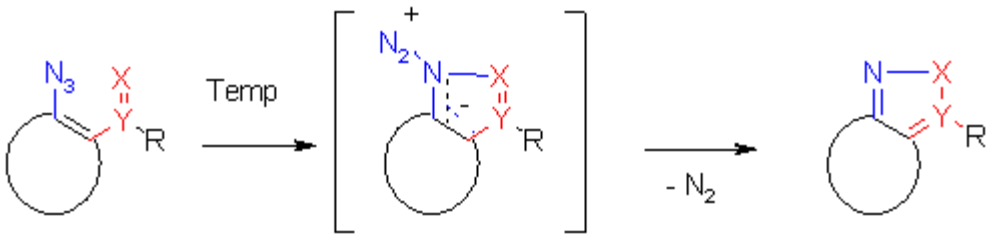


The rather high enthalpy values beyond - 200 mcal/mg in some of the compounds give hints that **this class of compounds must be carefully handled** - especially if large scales are thermolyzed.

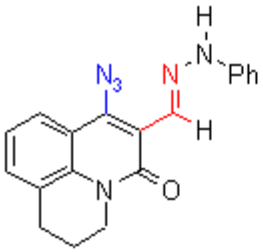
4. Decomposition of azidohetarenes with reactive *ortho*-substituents to isoxazoles, pyrazoles and furoxanes

Ring closure reactions of an azido group with ortho-acyl groups has been described to proceed not via a nitrene mechanism [1], but a heteroelectrocyclic (or pseudopericyclic) mechanism is postulated [4] involving as the first step a cyclization followed in a second step by loss of nitrogen. As reaction products isoxazoles, pyrazoles or furoxanes are obtained, which offers a simple approach to this interesting class of compounds. This reported reaction sequence means that - in contrast to the 2 preceeding chapters - the first reaction step (and also the reaction temperature) involves the attack of the azide as an electrophile at the negative carbonyl oxygen of the acyl group.

It was of interest whether this mechanism is visible in the reaction temperature by lower temperatures, or if the first activation step needs a similar activation energy as been found in the preceeding chapters.



The compounds were obtained by the procedures described in earlier reports [2].



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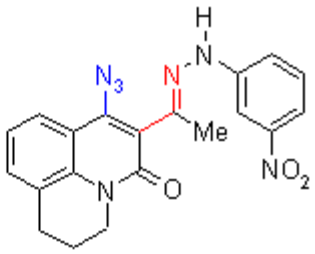

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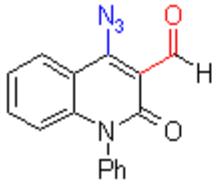

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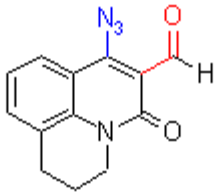

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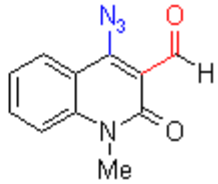

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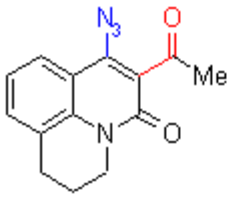

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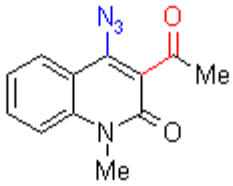

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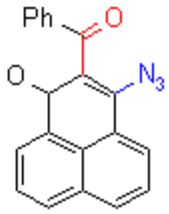

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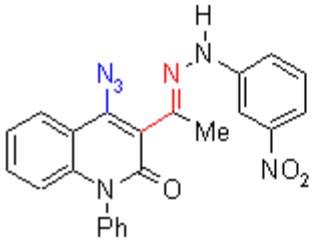

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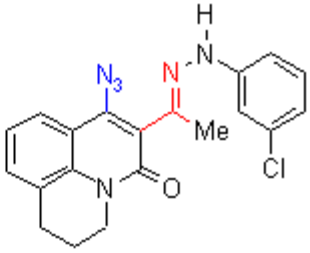

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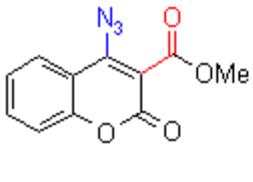

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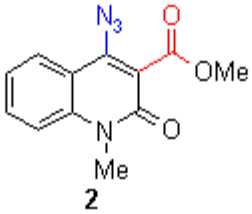

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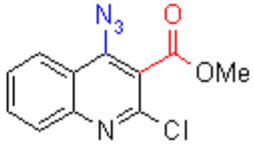

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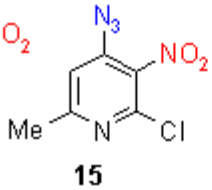

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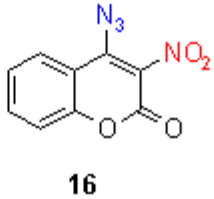

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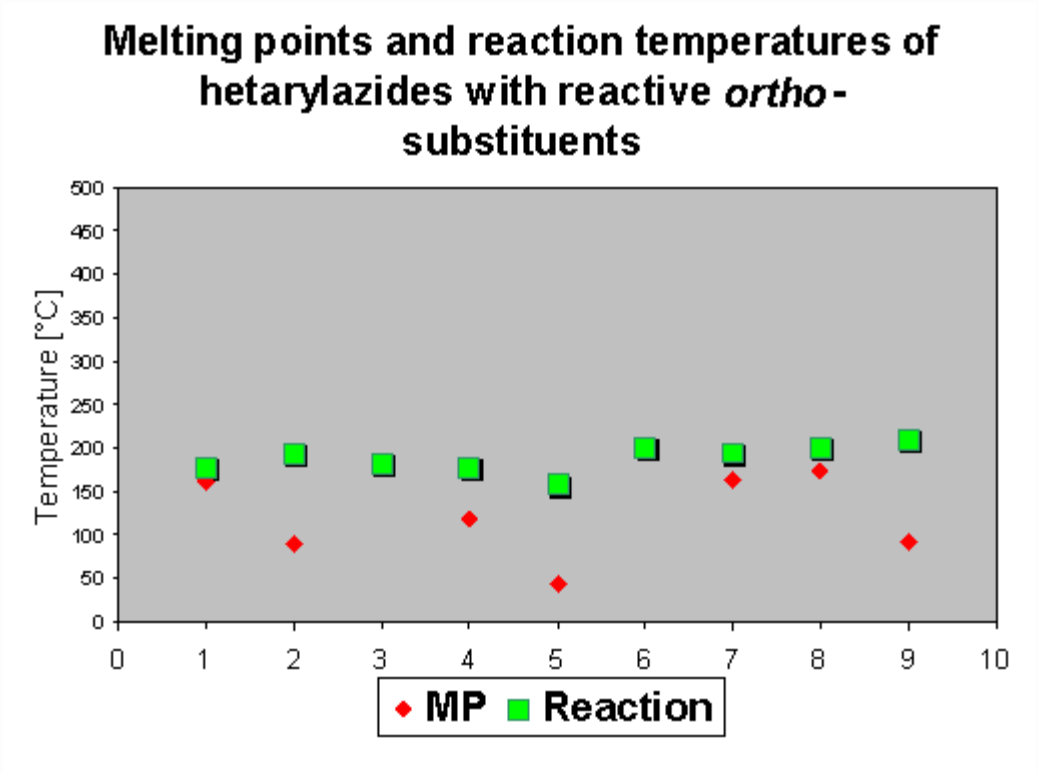
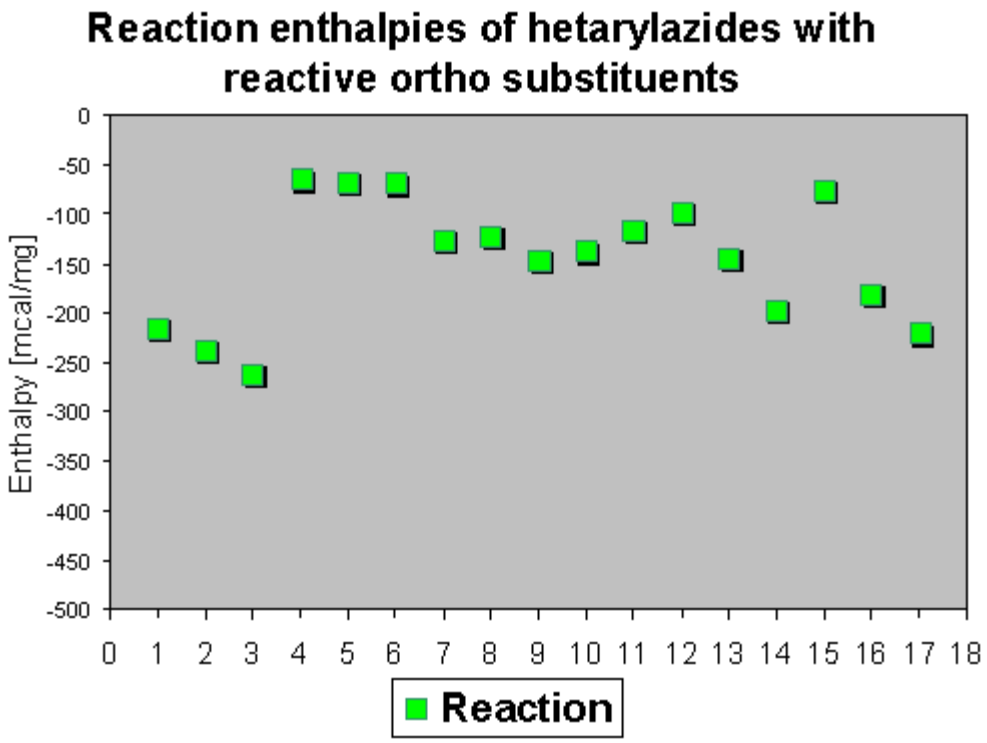
None of the investigated aldehydes (**4-6**) and ketones (**7-9**) show a mp, because the reactive substituent causes a quick reaction at rather low temperatures of 120 - 160 ^{O}C, which means that in this case the reaction temperature

was lowered for about 30°C. Analogous esters (**1-3**) have all a mp, the reaction temperatures are similar to the preceeding compounds in chapter 2 and 3 between 150-180 °C. Azidohetarenes with ortho-hydrazono substituents (**10-13**) have no mp and cyclize between 130-180 °C by thermolysis to give a five-membered pyrazolo ring (and not a sixmembered triazino ring) [2]. Ortho-nitroazides (**14-17**) have again no mp and give between 110 and 190 °C the fivemembered furoxanes (oxadiazolo-3-oxides) [2].



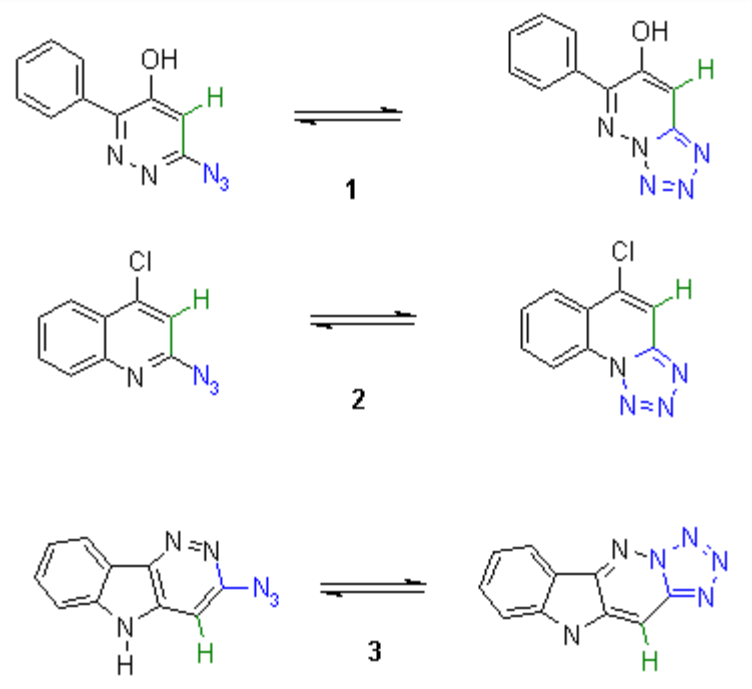
The reaction enthalpies of the acyl compounds **4-9** are between - 70 and - 150 mcal/mg, the reaction enthalpies of the esters **1-3** range between - 50 and - 240 mcal/mg. It can be found that methyl esters have high enthalpy values (between -200 and - 260), whereas ethyl esters (not shown in the diagram) range between -50 and - 160 mcal/mg. The enthalpy values of the hydrazono compounds **10-13** range between 100-140 °C. The enthalpy values of ortho-nitroazides (**14-17**) are between - 50 and - 200 mcal/mg. So this assay does again not allow a general statement on further activation influence of the reactive ortho group, because different group and substituent effects seem to superimpose the effects of the reactive ortho group.

The rather high enthalpy values - beyond - 200 mcal/mg - of some compounds give hints that **this class of compounds must be handled carefully** - especially if such azides are thermolyzed in large scales.



5. Azido-tetrazolo tautomers

Heterocyclic azides in the ortho-position of ring nitrogens are known to exist in a high percentage as the corresponding tetrazolo tautomers [5, 2e, 2f, 2m]. In this assay the thermal behavior of azides was investigated, which are known to exist mainly in the tetrazolo form. It was of interest if these tetrazoles could react at higher temperatures in its azido form and if the reaction or decomposition temperatures are in the same region as found for azidohetarenes.



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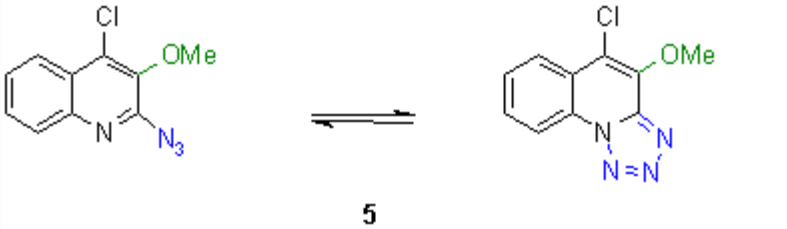

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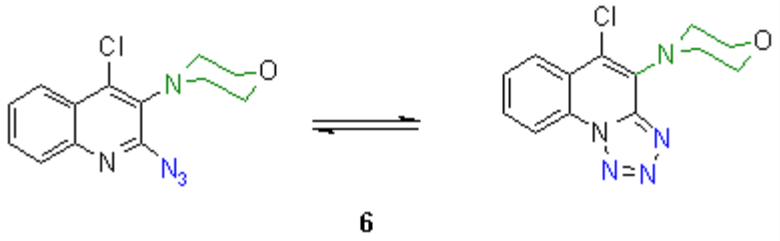

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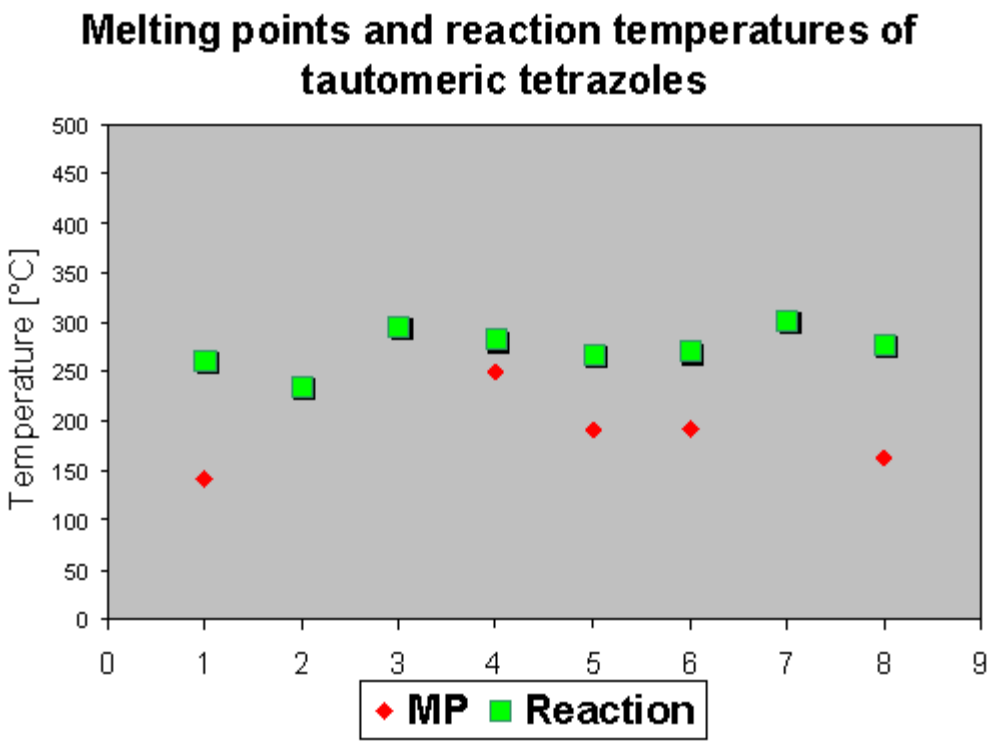
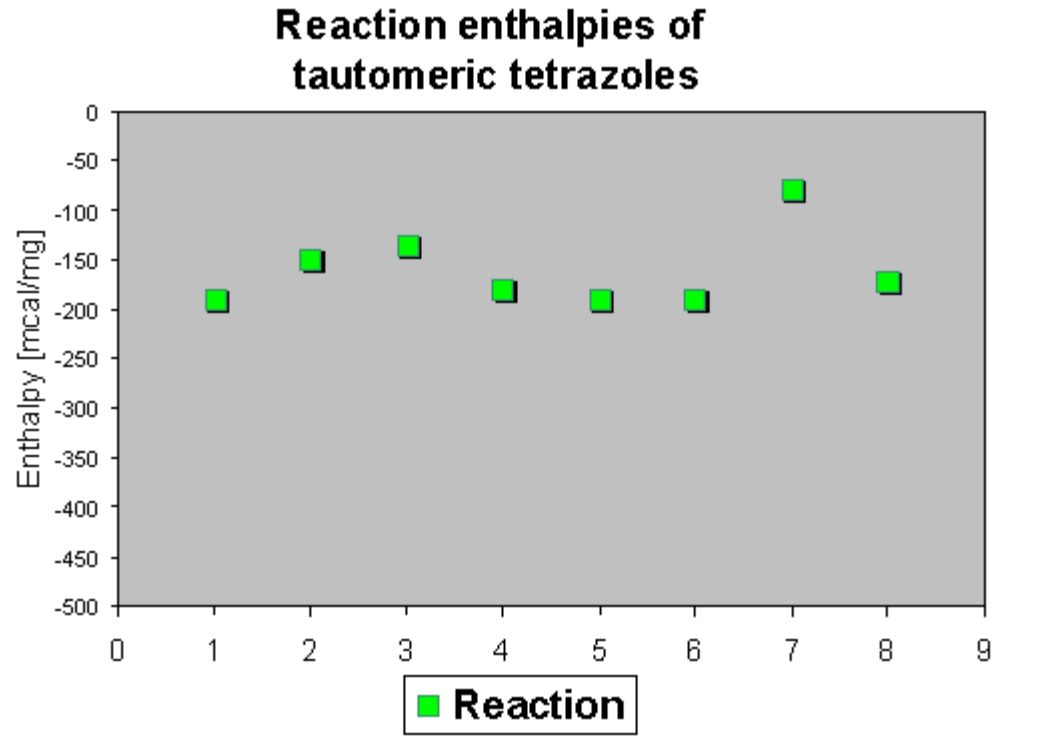
The reaction temperatures of tetrazolo-hetarenes were generally found at significantly higher values, between 220-330 ^{o}C. Preparative investigations revealed that **no defined reaction products were found**, e.g. the corresponding indoles from **7** and **8** [6].



The reaction enthalpies are in the average range between - 70 and - 180 mcal/mg, but synthetic assays [6] reveal only decomposition reactions, which could not used for preparative purposes.



The findings in the tetrazolo field show that tetrazoles which do not show any azido moiety cannot be used as masked azides. There could not be found any useable synthetic reaction, a result which is also supported by the findings when we tried to reduce the tetrazolo moiety to amines in analogy to azides. In all cases the tetrazolo moiety remained unchanged [2] except when a *Staudinger reaction* [5]was used cleaving the tetrazole with triphenylphosphane.

6. Conclusion

The DSC diagrams show that the **decomposition of hetarylazides** occurs generally between 80 and 200 ^{o}C, and the influence of an reactive ortho group is rather small - it does not exceed more than 30 ^{o}C.

The **enthalpies** which range between - 50 and - 300 mcal/mg show that reactive ortho groups increase in some cases (depending on further substituent influences) the values which should be interpreted as a safety hint, because on scaling up a reaction this can produce explosions. It is not possible to obtain reliable data for general mechanistic statements because there are substituent effects which superimpose the different reaction enthalpies. Exact statements are restricted exactly to one particular system.

7. Experimental

General preparation of the azides used in this work:
The preparations isare described in detail in ref. [2]. A standard procedure starts from either the corresponding chloro- or tosyloxy compounds, which were reacted with sodium azide in dimethylformamide or N-methylpyrrolidone at temperatures between 0 - 80 ^{o}C. After the reaction, the reaction mixture was poured onto ice, and the solid which precipitated was collected by filtration.

Measurements:
The differential scanning calorimetry experiments were performed with a Rheometric Scientific DSC-Plus instrument with the DSC software V5.42. The DSC plots were recorded between 25 - 500 ^{o}C, with a heating rate of 2-10 ^{o}C/min, and 1.5-3 mg compound in sealed aluminium crucibles (11 bar).

8. Acknowledgement

This work was supported by the FWF (Österreichischer Fonds zur Förderung der wissenschaftlichen Forschung) project No. P 10785-CHE .

9. References

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