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Thermal degradation of some new 7-(4'-pyridyl)-indolizine derivatives

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Abstract: Thermal degradation behavior under nitrogen was investigated for some new 7-(4'-pyridyl)-indolizine derivatives by TG-FTIR and DTA thermal analysis. TG-DTG analysis showed a complex two-stage thermal degradation mechanism, conclusion that was also supported by DTA spectra. A comparative discussion on the degradation mechanism for the samples taken into study is presented, based on the structural similarities between samples. Time-resolved gas-phase FTIR analysis of the evolved gas was performed in order to obtain additional information on the degradation products in different stages.

Keywords: Thermal degradation; Indolizine derivatives; TG-FTIR, DTA.

Introduction

Indolizine is an aromatic bicyclic 10π-electron system and

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constitutional isomer of 1*H*-indole which due to its special electronic structure, has long drawn much theoretical interest.[1,2] Indolizine derivatives have been used as a key scaffold in the pharmaceutical industry due to the broad spectrum of biological activities associated with this privileged structure. Besides, indolizine derivatives have been actively investigated as anti-inflammatory,[3] antiviral,[4] analgesic[5] and antitumor[6] agents. All these make indolizines an important synthetic target in view of developing new pharmaceuticals for the treatment of cancer,[6] cardiovascular diseases,[3b,7] and HIV infections.[8] In addition, indolizine-bearing polycyclic compounds have been found to have long wavelength absorption and strong fluorescence in the visible region.[9] Considering these important properties and the steadily increasing importance of fluorophores in biolabeling and environmental trace analysis, the synthesis of these types of compounds has drawn great interest of chemists to develop new drugs, novel classes of fluorescent dyes or chemosensors.

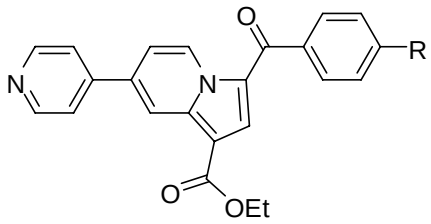
In the present paper, thermal degradation behavior under nitrogen was investigated for some new 7-(4'-pyridyl)-indolizine derivatives by TG-FTIR and DTA thermal analysis. Our study aims at characterization by thermal methods of these indolizine derivatives, noting that such investigation is not to be found in the literature for these substances. The purpose is to obtain information that we can use in future studies comprising thermal analysis of a novel class of calixarenes functionalized with these indolizine derivatives.

The characteristic features of the DTG and DTA thermal spectra was extracted, which afforded a comparative discussion on the degradation mechanism for the samples taken into study to be performed, based on the structural similarities between samples. In order to obtain additional information on the degradation products in different stages, time-resolved

gas-phase FTIR analysis of the evolved gaseous products was performed.

Results and discussions

The indolizine derivatives that were submitted to thermal analysis are of the form 1-ethylcarboxylate-3-(4-R-benzoyl)-7-(4'-pyridyl)-indolizine with different R substituents. Sample designation (from **a** to **d**) is as follows:



a. R = H
b. R = OMe
c. R = Me
d. R = Cl

The recorded thermograms are depicted in Figures 1-4.

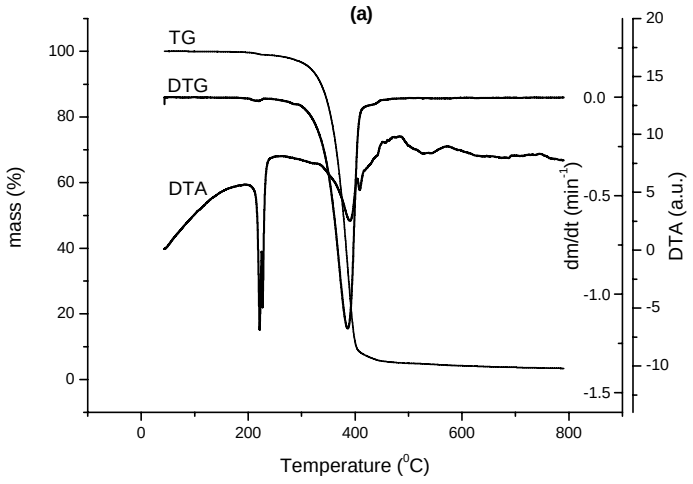


Figure 1. TG-DTG and DTA curves for sample (a).

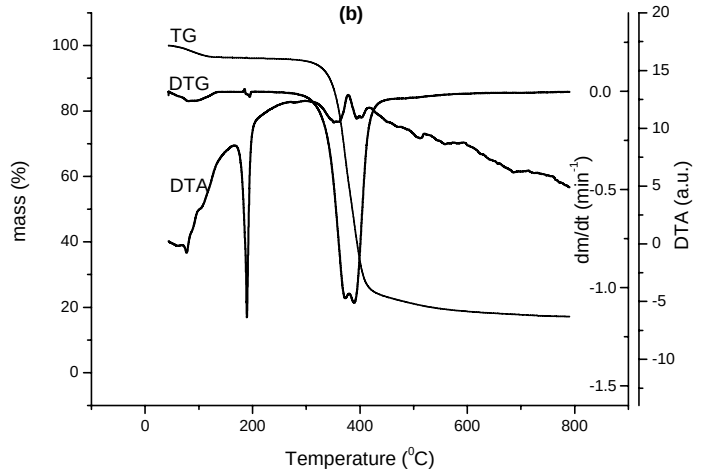


Figure 2. TG-DTG and DTA curves for sample (b).

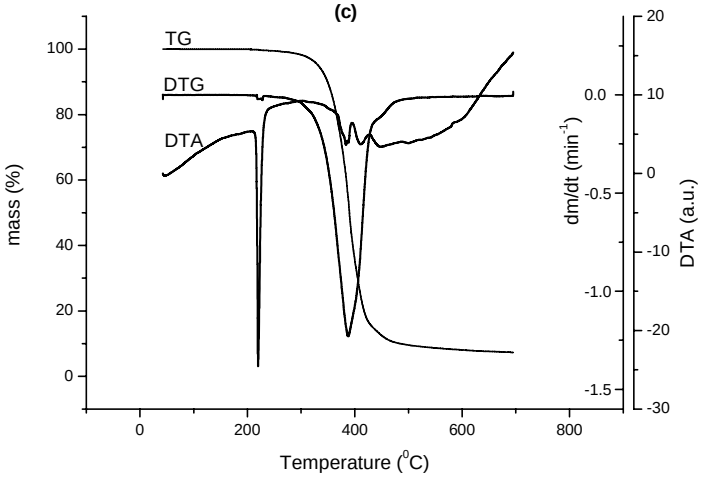


Figure 3. TG-DTG and DTA curves for sample (c).

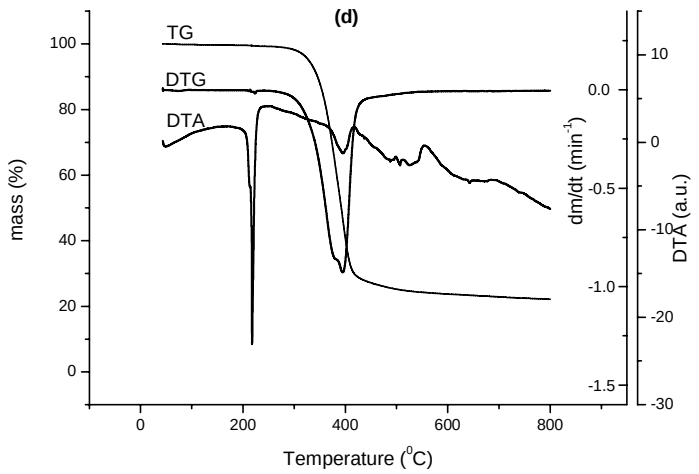


Figure 4. TG-DTG and DTA curves for sample (d).

As it can be seen, all samples exhibit two-stage thermal degradation under nitrogen.

The first stage is similar for all the samples, and occurs in the temperature interval 190-250 ^{0}C. Here the weight loss is very small (under 4% wt), yet the thermal effect is very high and endothermic, as it can be seen from DTA curves. As the temperature is rather high, and since prior to be submitted to thermal analysis the samples were thoroughly dried, elimination solvent traces is excluded. Noting also the magnitude of the endothermic effect, we attribute this first stage to a degradation reaction that occurs through molecular scission with formation of mostly nonvolatile compounds. Since all the samples behave similar, and so the different R groups have little to no effect on the temperature interval and weight loss in this stage, we conclude that the degradation process involves the main backbone of the molecules, where some weak bonds can be identified between the aromatic cycles. Additional support for this conclusion will be presented later in this section.

The second stage shows some differences between samples. While the temperature interval is quite similar (260-500 ^{0}C), as well as the characteristic temperature at DTG maximum (around 395 ^{0}C), weight losses are quite different (93% and 91% for samples (a) and (c), respectively 78% for both samples (b) and (d)). This observation correlates with the fact that DTG curves are almost identical for samples (a) and (c), while for samples (b) and (d) there is an inflexion point in the DTG curve at 382 ^{0}C. All samples show degradation residue, relatively small for samples (a) and (c) (3% and 6%, respectively), while quite large for samples (b) and (d) (19% and 21%, respectively).

These similarities between DTG curves for samples (b) and (d) suggest similar degradation mechanism, probably due to the similarities in the structure of R group, which contains electronegative atoms (O and Cl) in both samples. The same conclusion can be applied to samples (a) and (c), where R contains no heteroatom.

DTA curves also suggest complex degradation mechanism for all samples in stage II, and the small thermal effect associated to large mass loss requires further investigation.

In order to obtain additional information on the degradation products in different stages, time-resolved gas-phase FTIR analysis of the evolved gas was performed. The results for sample (a) are depicted below. The main signals appear at 772, 1600, 2361 and 2988 cm^{-1}, and we have yet to identify the gas species evolved. The 772 cm $^{-1}$ signal appears at around 200 ^{0}C (first degradation stage) and is attributed to the deformation vibrations of the quinoid ring[10]; still, further investigation on the mechanism of formation of such structures during thermal degradation is required. The strong signal at 2361 cm^{-1} is attributed to CO_2 and appears at around 400 ^{0}C,

corresponding to the second degradation stage.

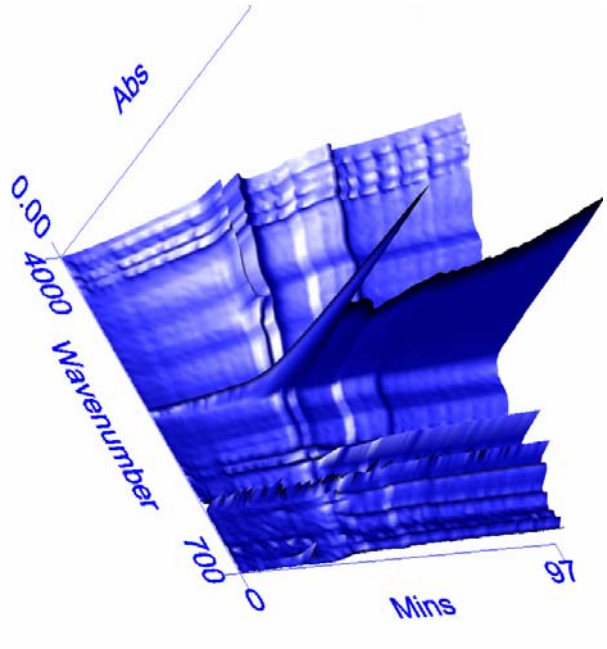
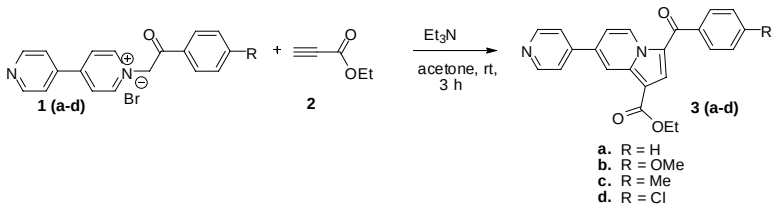


Figure 5. Time resolved FTIR analysis of the evolved gaseous products for sample (a).

Experimental

1-ethylcarboxylate-3-(4-R-benzoyl)-7-(4'-pyridyl)-indolizines used in thermal degradation study were synthesized in our laboratory, using analytical grade reagents. Pyridinium monoquaternary salts derivatives from 4,4'-bipyridine[11] were used as a starting material for monoindolizine synthesis. Thus, 1-(2-oxoethyl)pyridinium bromides are deprotonated by triethylamine to give *in situ* the resonance stabilized pyridinium ylide, an allyl-type 1,3-dipole, that readily undergoes a 1,3-dipolar cycloaddition with **2** to give the indolizines **3**, as a consequence of oxidative aromatization of dihydroindolizine intermediates (Scheme 1).[12]



Scheme 1

DTA and TG-DTG analysis were carried out on a Diamond Pyris TG-DTA thermobalance (Perkin-Elmer) under nitrogen flow. Temperature and heat flow calibration were done with Perkin-Elmer calibration reference materials. Thermograms and DTA spectra were recorded simultaneously, at a heating rate of 10 K/min, sample mass 10 mg, temperature interval 40-800 ^{0}C. Evolved gas analysis (EGA) was performed by coupled time-resolved gas-phase FTIR (Perkin-Elmer FTIR module).

Conclusions

TG-DTG and DTA analysis of the thermal degradation of the 7-pyridyl indolizine derivatives showed two degradation stages for all the samples: the first one, highly endothermic, comprises small mass losses, while the second one indicated complex mechanism and involves large mass losses. Samples (a) and (c) demonstrated similar degradation mechanism, and the same conclusion was valid for samples (b) and (d). These similarities were explained by similar structure of the R group in the two sample classes, respectively. Time-resolved FTIR analysis of the evolved gaseous degradation products suggested the formation of some quinoid-type structure of volatile products in the first stage, while in the second stage a mixture of gases is obtained, of which CO_2 was identified.

Acknowledgements

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