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Thermal decomposition and stability of quinoline compounds using thermogravimetry and differential scanning calorimetry

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Abstract

Thermal analysis, with DSC and TGA of fusion and decomposition processes of some quinoline compounds were carried out to determine their stability. The quinoline compounds are classified by the R_6 sustituent: NO_2, $NHCOCH_3$, H or OCH_3 and they have a variable substitution in position 1. Certain factors in the substitution (length of chain, chain branching and unsaturation) are not especially relevant to the physical stability. The compounds are very polar and the dipole–dipole forces give stability to the crystal. An increase in the physical stability is also observed with aromaticity and when halogens are present. An increase in the chemical stability, from the acetylamine group to the nitro group, is observed.

Keywords: Degradation process; Thermal analysis; Thermal decomposition; Quinolines

1. Introduction

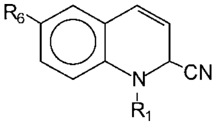
The application of thermal methods to organic compounds of potential pharmacological action can be of great use for determining their physical and chemical stability [1–5].

Predicting stability or instability at a very early stage of product development, such as immediately after the initial synthesis process, provides valuable information.

In the description of a degradation reaction of an organic compound, most compounds melt, decompose, sublimate or volatilize [6]. The decomposition can be accompanied by a superficial fusion or by the formation of liquid products in which the reagent is soluble. The reaction can take place simultaneously in the homogeneous phase as well as in the heterogeneous phase. Nevertheless, there is a tendency for decomposition to be more rapid in the homogeneous condition than in the heterogeneous condition.

2. Material

Asymmetric compounds of variable disubstitution have been selected; these structures are referable to a general formula that consists of an invariable matrix of quinoline structure on which a variable substitution is carried out in positions 1 and 6, with substituents of diverse nature. Compounds that carry both aromatic and aliphatic parts, of diverse polarity and geometry, and are distributed heterogeneously throughout the molecule, are obtained.



In the following series, the compounds are classified in terms of the R_6 substituent: series A: $R_6 = NO_2$; series B: $R_6 = NHCOCH_3$; series C: $R_6 = H$ and series D: $R_6 = OCH_3$.

3. Methodology

The calorimetric studies are carried out with a Perkin-Elmer, DSC-7, and thermogravimetric studies with a Perkin-Elmer, TGA-7.

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Calorimetric analyses are performed at 10 °C/min in aluminium capsules for volatiles of 10 μL, to find the T_{onset}, T_{max} and the enthalpy of fusion, ΔH_f. In some cases, the T_{onset}, T_{max} and ΔH of the exothermal degradation are calculated. The analyses are performed in high-pressure capsules, at 10 °C/min and under nitrogen atmosphere.

Thermogravimetric analyses are carried out at 10 °C/min (under air atmosphere with a gas flow of 40 mL/min). The $T_{initial}$, T_{onset} and T_{max}, as well as any associated weight loss, are calculated. Likewise, if the degradation process develops in several stages, the temperature at which the first stage finishes is calculated; this temperature is called $T_{1\text{–}2}$, and the associated weight loss is referred to as w_∞.

4. Results and discussion

Series A ($R_6 = NO_2$): the presence of halogens causes an increase in temperature and enthalpy of fusion. In addition, the chain length of the substituent in position 1 of the quinoline matrix influences compound physical stability. An increase in the chain length provokes decreases in the temperature, enthalpy of fusion, and physical stability of the compound. Unsaturation and the chain branching seem to be determinant factors (Table 1).

Series B ($R_6 = NHCOCH_3$): a decrease in the temperature and enthalpy of fusion occurs when the chain is lengthened. With regard to chain branching, the temperature and enthalpy of fusion values increase towards the linear compound (Table 2).

Series C ($R_6 = H$): the length of the chain and/or the branching result in an increase in the stability. Once again, the presence of halogens gives rise to products with high temperatures and enthalpies of fusion, meaning products that are physically more stable (Table 3).

Series D ($R_6 = OCH_3$): the influence exerted by the length of the chain is observed once more. When this length increases, the temperature and enthalpy of fusion values decrease. In addition, when branching of the chain in position 1 increases, so does the stability. The physical stability increases with aromaticity and presence of halogens (Table 4).

4.1. Conclusions regarding the physical stability

The previously mentioned factors (length of chain, branching and unsaturation) are not especially relevant. When the principal molecule of this group is structurally analyzed, it is observed that the compounds present an amide or carbamate group in position 1, which give the compounds

Table 1
Fusion and degradation processes of nitro-substituent quinoline compounds

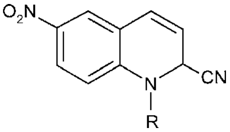
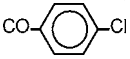
	Series A		
	Fusion process (DSC)		Degradation process (TGA)
R	T_{onset} (°C)	ΔH_f (J/g)	T_{onset} (°C)
$COOCH(CH_3)_2$	128.8	96.6	236.1
	157.3	75.4	218.4
$COOCH_2CH_2CH_2CH_3$	85.9	83.5	244.0
$COOCH_2CH_2CH_3$	99.0	87.0	237.7
$COOCH_2CH_2Br$	146.0	56.2	225.8
$COOCH_2CH_3$	118.0	99.2	227.0
$COOCH_2CH{=}CH_2$	110.5	94.2	220.1
$COOC(CH_3){=}CH_2$	116.2	92.1	231.6
$COCH_2CH_2Cl$	145.7	55.8	236.2
$COOCH_2CH(CH_3)_2$	115.6	93.8	251.9

Table 2
Fusion and degradation processes of acetylamide-substituent quinoline compounds

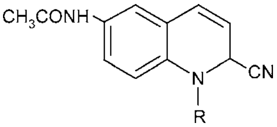
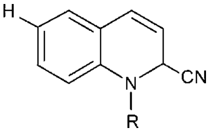
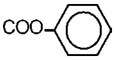
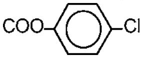
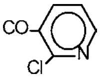
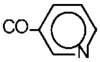
	Series B		
	Fusion process (DSC)		Degradation process (TGA)
R	T_{onset} (°C)	ΔH_f (J/g)	T_{onset} (°C)
$COOCH_2CH_2CH_3$	–	–	168.4
$COOCH_2CH(CH_3)_2$	131.4	63.3	173.1
$COCH(CH_3)_2$	104.2	42.3	178.7
$COOCH_2CH_2CH_2CH_3$	162.9	116.3	182.1
$COOCH_2CH_3$	168.0	122.8	160.6

Table 3
Fusion and degradation processes of hydrogen-substituent quinoline compounds

	Series C		
	Fusion process (DSC)		Degradation process (TGA)
R	T_{onset} (°C)	ΔH_f (J/g)	T_{onset} (°C)
$COOCH_2CH_3$	63.8	87.1	213.8
	125.8	114.1	209.4
$COOCH_2CH(CH_3)_2$	74.3	87.8	201.1
	151.0	119.7	213.2
	216.6	172.1	258.5
	139.3	118.7	180.1

great polarity and consequently, the dipole–dipole forces, give principal stability to the crystal.

An increase in physical stability is also observed with aromaticity, due to the electronic delocalization in the π orbitals of the aromatic ring that causes an additional intermolecular interaction. This increase also occurs when halogens (compounds with higher polarity and more intense dipole–dipole interactions) are present.

4.2. Chemical stability

Series A ($R_6 = NO_2$): the degradation temperature increases when the chain length of the substituent increases. With regard to chain branching, contradictory effects are observed. On the one hand, the degree of lateral substitution slightly decreases the degradation temperature. However, examples of just the opposite are observed; the degradation temperature increases with branching (Table 1).

Series B ($R_6 = NHCOCH_3$): an increase in the chain length of the sustituent gives stability to the molecule because it causes an increase in the temperatures of degradation (Table 2).

Series C ($R_6 = H$) and series D ($R_6 = OCH_3$): the aforementioned conclusions could also be done (Tables 3 and 4).

4.3. Chemical stability conclusions

Upon comparing the different series (Table 5), an ascending increase in the chemical stability from the acetylamine group to the nitro group, is observed. This could be due to the tendency of the groups to attempt to counteract the strong electron-withdrawing inducing effect of the cyano group in position 2, which produces general displacement of the π cloud along the axis, positions 2–6.

The nitro group with its high electron-withdrawing capability stabilizes the molecule. However, groups, such as

Table 4
Fusion and degradation processes of methoxy-substituent quinoline compounds

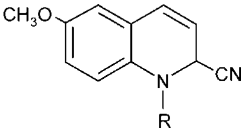
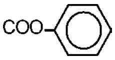
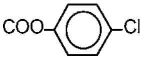
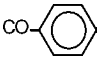
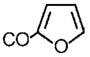
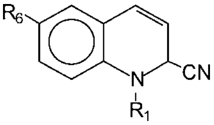
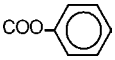
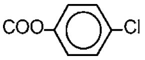
	Series D		
	Fusion process (DSC)		Degradation process (TGA)
R	T_{onset} (°C)	ΔH_f (J/g)	T_{onset} (°C)
$COOCH_2CH_3$	85.9	86.6	186.8
$COOCH_2CH_2CH_3$	66.7	57.3	193.7
	110.8	74.7	174.4
$COOCH_2CH(CH_3)_2$	73.2	85.4	198.1
	101.0	65.6	178.6
	122.8	79.6	173.0
	134.0	123.2	178.9

Table 5
Temperatures of degradation between series of quinoline compounds

	Comparison between series			
	Temperatures of degradation (TGA) (°C)			
R_1/R_6	NO_2	CH_3CONH	H	CH_3O
$COOCH_2CH_3$	227.0	160.6	213.8	186.8
$COOCH_2CH_2CH_3$	237.7	168.4	–	193.7
$COOCH_2CH_2CH_2CH_3$	244.0	182.1	–	–
$COOCH(CH_3)_2$	236.1	–	–	–
$COOCH_2CH(CH_3)_2$	251.9	173.1	201.1	198.1
	–	–	209.4	174.4
	236.2	–	213.2	178.6

OCH_3 or $NHCOCH_3$, do not stabilize due to their electron-releasing character.

While there appears to be a correlation with the thermal stability, the halogenated compounds present, contrary to that which is expected, a slightly lesser stability than the rest of the compounds in the group.

5. Conclusions

The asymmetric compounds studied present considerable polarity and therefore, dipole–dipole interactions confer stability to the crystal. In addition, aromaticity and electronic displacement in conjugated π orbitals also contribute substantially to crystalline cohesion. In this respect, the substitution in position 6 is fundamental and the presence of groups there, such as nitro, increases the stability considerably.

Strongly electron-withdrawing groups in position 6 of the quinoline ring confer stability to the molecule due to the fact that they counter the electron-withdrawing effect of the cyano group in position 2, producing displacement of the π cloud along the length of the axis positions 6–2, which leads to a more homogenous and balanced electron distribution.

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