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Correlation between structure and stability of nitronic acids and nitronic esters*

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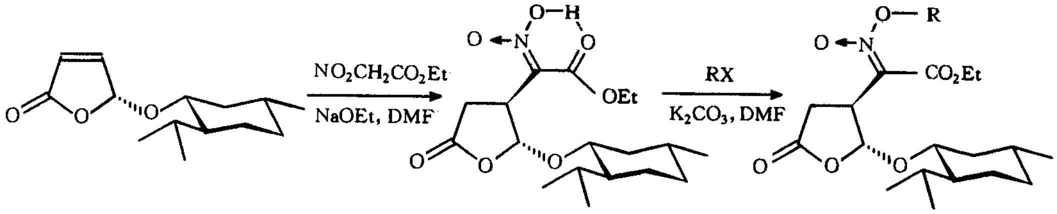
Abstract On the basis of investigation on structural characteristics and stability of more than one hundred nitronic acids and nitronic esters, an equilibrium theory of electronic effects in conjugated systems is put forward and the type of structures is classified. On that basis, an empirical rule for the correlation between structure and stability of nitronic acids and nitronic esters is proposed, which predicts that stable nitronic acids and nitronic esters should have the C type of structure that meets the matching principle of electronic effects.

Keywords: **nitronic acid, nitronic ester, stability, conjugative effect, hyperconjugative effect.**

Nitronic acids and nitronic esters are special species of organic compounds, whose striking property is instability[1—3]. Due to this reason, studies related to these species have progressed very slowly. Recently, we reported the synthesis of stable nitronic acid **I** and nitronic ester **II**[4—6] (fig. 1), and studied some of their chemical reactions[7]. Research on the structures of these new compounds led to some interesting and important findings[8,9]. Based on the studies of structure and stability of more than one hundred compounds, this paper for the first time discusses the correlation between structure and stability of nitronic acids and nitronic esters.



I **II**

R = CH_3, C_2H_5, C_3H_7, i-C_3H_7, C_4H_9, s-C_4H_9, c-C_5H_9, c-C_6H_{11}, C_8H_{17}, C_9H_{19}, $C_{12}H_{25}$, $C_{16}H_{33}$, $CH_2C_6H_5$, $CH_2CH{=}CH_2$

Fig. 1. Synthesis of nitronic acid **I** and nitronic ester **II**.

1 Discussion

1.1 Origin of the question

The first nitronic acid and nitronic ester were synthesized in 1893—1894 by Konowalow and Nef respectively[1]. In the past century, more than one hundred nitronic acids and nitronic esters have been obtained. They are reported to be unstable compounds with half lives at ambient

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temperature ranging from minutes to weeks and their decomposition products usually include oximes[1]. Although various nitronic acids and nitronic esters are synthesized, few of them claim to be sufficiently stable. Consequently, in 1964 Kornblum and Brown pointed out that there seemed to be no relationship between structure and stability of these species[10].

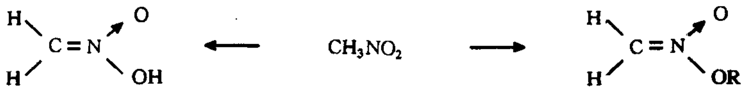
However, in contrast to previous results, nitronic acid **I** is observed to be quite stable in its crystalline state at ambient temperature, except decomposing at its melting point (146℃) and tautomerizing to its corresponding nitro form when left in a solution for a long period[5]. Although nitronic ester **II** can undergo α,β-elimination reaction in refluxing toluene[7], it is found to be stable enough in boiling water[6].

These anomalous results naturally lead to such questions: Why are nitronic acid **I** and nitronic ester **II** with the same structural characteristics so coincidentally different from their analogues to become very stable compounds? Whether are these characteristics suggesting the requisite factors that stable nitronic acids and nitronic esters must possess? Is there indeed a correlation between structure and stability of nitronic acids and nitronic esters?

1.2 Electronic effect of substituent

After studying the structural characteristics and stability of more than one hundred nitronic acids and nitronic esters reported so far, we have noticed that in most of these compounds, the nitronate groups $C{=}NO_2H(R)$ are bonded directly to some electron-withdrawing groups, such as NO_2, CN, $C{=}O$, CO_2R, Ar, $C{=}C$, etc. Interestingly, the nitronate groups $C{=}NO_2H(R)$ in the stable compounds **I** and **II** are also bonded directly to an electron-withdrawing group CO_2Et. At least from this point, something can be safely drawn that there might be a certain special relationship between stability and electronic effects of the substituents bonded directly to the nitronate group $C{=}NO_2H(R)$ of nitronic acids and nitronic esters. Therefore, as for the relationship between structure and stability of nitronic acids and nitronic esters, we think two primary conclusions can be obtained:

(i) In the structures of nitronic acids and nitronic esters, the nitronate group $C{=}NO_2H(R)$ is an extremely unstable subunit, namely there is little possibility that the nitronic acid and nitronic ester derived from nitromethane could exist (scheme 1).



Scheme 1

(ii) Stable or relatively stable nitronic acids or nitronic esters can exist, and their stability depends on the electronic effects of the substituents bonded directly to the nitronate group $C{=}NO_2H(R)$.

It is well known that electronic effects of substituents in a molecule can remarkably affect or even change the physical or chemical properties of a certain substance. For example, $(CH_3)_3COH$ is a typical alcohol, while $CF_3(CH_3)_2COH$ is acidic enough to give carbonic acid when treated with carbonate salts; $(CH_3)_3N$ is a typical base, while $(CF_3)_3N$ has no basicity; CCl_3CHO can form stable hydrate with water, a weak nucleophile, while ordinary aldehydes are hard to form hydrates. Obviously, these anomalous phenomena result from the strong electronic effects of the fluorine and chloride atoms[11].

1.3 Type of structure

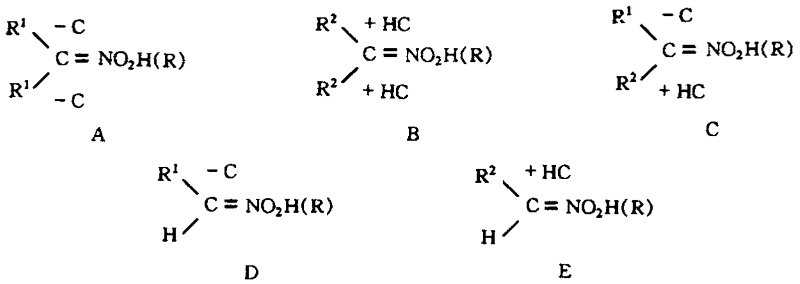
In the structure of nitronic acid or nitronic ester, the substituents bonded directly to the nitronate group $C{=}NO_2H(R)$ can be roughly divided into three types: (i) Electron-withdrawing groups, $R^1 = NO_2$, $C{=}O$, CO_2R, CO_2NH_2, $ArSO_2$, Ar, $C{=}C$, $N{=}N$. (ii) Electron-donating groups, R^2 = alkyls or alkyls substituted by R^1. (iii) Hydrogen atom, H.

It is already known that electron-withdrawing conjugative effects ($-$C) of electron-withdrawing groups and electron-donating hyperconjugative effects ($+$HC) of electron-donating groups can approximately be placed in the following sequences with decreasing intensities[12]:

$-$C effects of R^1: $NO_2 > C{=}O > SO_2 > CO_2R > CH > C_6H_5 > CH{=}CH_2$;

$+$HC effects of R^2: $CH_3 > CH_2R > CHR_2 > CR_3$.

So, there could be only five types (A—E) of structures made up of these three types of substituents as shown in scheme 2.



Scheme 2

1.4 An empirical rule

Apparently, nitronic acid **I** and nitronic ester **II** belong to the C type of structure. According to this fact as well as the two primary conclusions mentioned above, we propose an empirical rule for the correlation between structure and stability of nitronic acids and nitronic esters:

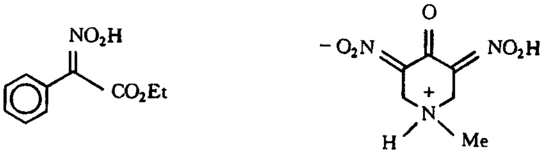
(i) Of the two substituents bonded directly to the nitronate group $C{=}NO_2H(R)$ in the structure of a nitronic acid or a nitronic ester, one should be an electron-withdrawing group R^1 with $-$C effect, the other should be an electron-donating group R^2 with $+$HC effect. Only when the electronic effects of the interacting groups R^1 and R^2 of opposite properties reach a certain equilibrium in their jointly formed conjugated system, should the molecule's internal energy be lowered, which enables the molecule to be stable enough. Therefore, only C type of nitronic acids and nitronic esters are expected to be stable compounds.

(ii) If the two substituents belong to the same type, they would make a unitary contribution to the conjugated system. This should result in the destruction of the equilibrium formed by the interacting electronic effects. Under this circumstance, the molecule's internal energy would be raised with stability being lowered. Therefore, A and B types of nitronic acids and nitronic esters are expected to be unstable compounds.

(iii) Compared to other substituents, the electronic effect of hydrogen atom can be regarded to be null[12]. So, if one of the two substituents is a hydrogen atom, the electronic effects in the conjugated system would largely be dependent upon the property of the other substituent. Thus, the situation is similar to that of rule (ii). Therefore, D and E types of nitronic acids and nitronic esters are expected to be unstable compounds.

(iv) In the C type of structure, only substituent with moderate $-C$ effect and substituent with weak $+HC$ effect are matching, does their compensating contribution to the conjugate system enable the interacting electronic effects to reach a certain equilibrium. Under this situation, the molecule has the lowest internal energy so as to be the most stable. This means that in compounds **I** and **II**, methine and carbethoxy are the best matching and the conjugate system formed by them and the nitronate group $C{=}NO_2H(R)$ has the lowest internal energy.

It should be noted that this empirical rule neglects the influences caused by the alkyl R in nitronic esters and *cis-trans* configuration of the nitronate group $C{=}NO_2H(R)$, because a lot of facts have demonstrated that the former has little impact on the molecule's stability[1,5], while the latter only has a small impact[10,13]. In addition, the excellent stability of nitronic acid **I** probably has nothing to do with its intramolecular hydrogen bonding, since both of the following two nitronic acids have conditions or subunits to form intramolecular hydrogen bondings; however, they only have a half life of several days (scheme 3).



Scheme 3

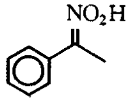
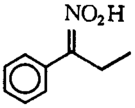
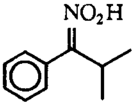
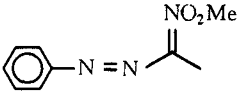
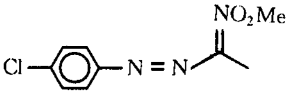
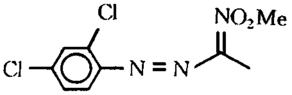
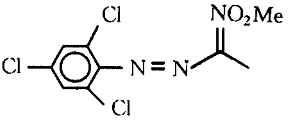
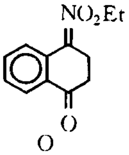
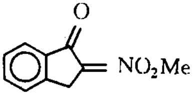
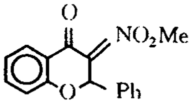
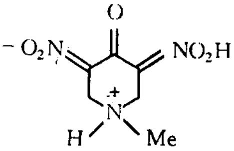
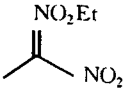
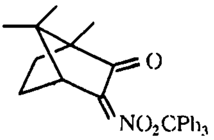
Of all the known nitronic acids and nitronic esters[1], the majority (90%) possess A, B, D and E types of structures. In fact, as the empirical rule points out, they are all unstable compounds. Only thirteen nitronic acids and nitronic esters have the C type structure (table 1). Because of their discrepancy to rule (iv), most of them fail to become stable compounds. It is noteworthy that the structural characteristics of compound **13** nearly meet the requirements of the empirical rule. The carbonyl of approximately moderate $-C$ effect and the methine of weak $+HC$ effect are roughly matching, which is expected to have a good stabilization for the nitronate group $C{=}NO_2H(R)$. Actually, compound **13** is indeed relatively stable. When being heated in toluene to 125℃, it isomerized into an oxaziran compound in 33% yield[14] rather than underwent notable decomposition reaction, which reveals its relative stability and is exactly consistent with the prediction of the empirical rule.

Since nitronic acid **I** is a derivative of ethyl nitroacetate, we have attempted to synthesize stable nitronic esters from ethyl nitroacetate. Therefore, in the presence of K_2CO_3 and DMF, ethyl nitroacetate was treated with benzyl chloride and benzyl bromide respectively, but no nitronic esters were produced. Surprisingly, it was found that the former afforded thermodynamically controlled *O*-alkylated product while the latter furnished kinetically controlled *C*-alkylated product[15]. This result does not look so strange at present. Because, although ethyl nitroacetate has the structural characteristics similar to those of nitronic acid **I**, it would produce D type of nitronic esters. According to the empirical rule, they are unable to survive.

2 Conclusion

According to the fundamental principle in chemistry that property depends on structure, we think there should be a correlation between structure and stability of nitronic acids and nitonic esters. On the basis of investigation on structure and stability of more than one hundred compounds, we propose an empirical rule for the correlation between structure and stability of nitronic acids and nitronic esters, which not only satisfactorily interprets the previous experimental facts,

Table 1 Nitronic acids and nitronic esters with the C type of structure[a]

Number	Formula	mp/℃	Half life
1		45	minutes
2		–	minutes
3		54	hours
4		72	hours
5		112	–
6		111	–
7		90	–
8		–	minutes
9		132	–
10		–	–
11		119	days
2		decomposition	hours
13		152	–

[a] Half life: an approximate time needed by the decomposition process of half of the pure sample.

but also predicts that stable nitronic acids and nitronic esters should have the C type structure that meets the matching principle of electronic effects.

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