# USING PHYSICO-CHEMICAL DATA TO EVALUATE CMA'S OF SOME POLLUTANTS WHICH APPEAR AS INTERMEDIATES IN TRIAZOLOISOINDOLES SYNTHESIS

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**abstract:** The pollutant effect on the health exposed persons and on the environment, generally depends on the different factors: the most important is the extents concentration in the workplace atmosphere. Analyzing the recent procedures for triazoloisoindols synthesis we used the physical chemical data concerning some of intermediates after its purification, to calculate their CMA's (maximal admitted concentrations).

## Introduction

The ecotoxicology [1] is a new interdisciplinary science derived from ecology and toxicology. It has three complex objectives: 1) the foresight of the substances behavior in environment 2) the response of biological systems in their presence 3) the control of risk associated with emissions. In this work we concern on some problems related to the third objective of the ecotoxicology.

The pollutants effect on the health exposed persons and on the environment, generally, depends on the different factors: the most important is the extant concentration in the workplace atmosphere. [2] This in relation with other factors: the level of emission rate, the potential of accumulation in environment (or organism), the climatic conditions, the density of exposed population.

Felov firstly selected 38 physical-chemical properties (systematized in three classes), which have been used to obtain the characterization of risk limits for the industrial toxicants [3].

Now numerous companies and researchers are working on developing of the toxicology *in silico* (e.g. the computer based statistical methods of prediction) rather than the more conventionally *in vivo* or *in vitro* [4].

In this work we try to calculate CMA's (concentration maximal admitted[a], in $mg/m^3$) for the intermediates in new procedure [5] of triazoloisoindols from physical-chemical data.

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[a] or peak maximal admitted concentration. After Geneva established terminology CMA was abbreviated as TLV-C Threshold Limit Value-Ceiling. This value must not be exceeded at any time, otherwise the professional diseases appear [3].

Analele Universităţii din Bucureşti – Chimie, Anul XII (serie nouă), vol. I-II, pag. 279–284

The triazolisoindols are stable compounds with remarkable semiconductor properties used as analytical reactives pesticides [6].

## Calculation details

The physical chemical data of intermediates are done in Tables 2-3, and the computational requirements are described in footnote at Table 4.

## Results and discussions

Synthesis of 1H-[1,2]-[1,2,4] triazolo [3,4]-isoindols after is done in Fig.1.

After this schema it is possible to observe 4 distinct stages of synthesis. Each stage is developed within organic solvents with a high dielectric constant. In this synthesis exits 10 intermediates, which have been isolated with high yields in rapport with purified products. All isolated intermediates have been physical chemical chracterized [7] yields (s. Table 1), melting point (s. Table 2), molecular weight (s. Table 3), 1H RMN spectra. [7]

**Table 1. Reaction yields for purified products.**

| Compound | $R_1$ | $R_2$ | Yield (%) |
|---|---|---|---|
| Ia | $C_6H_5$-$CH_2$- | - | 70 |
| Ib | 4'-MeO-$C_6H_4$- | - | 86 |
| IIIa | $C_6H_5$-$CH_2$- | -H | 60 |
| IIIb | $C_6H_5$-$CH_2$- | -$CH_3$ | 75 |
| IIIc | $C_6H_5$-$CH_2$- | -$OCH_3$ | 47 |
| IIId | 4'-MeO-$C_6H_4$- | -H | 59 |
| Va | $C_6H_5$-$CH_2$- | -H | 68 |
| Vb | $C_6H_5$-$CH_2$- | -$CH_3$ | 62 |
| Vc | $C_6H_5$-$CH_2$- | -$OCH_3$ | 61 |
| Vd | 4'-MeO-$C_6H_4$- | -H | 77 |
| VIa | $C_6H_5$-$CH_2$- | -H | 76 |
| VIb | $C_6H_5$-$CH_2$- | -$CH_3$ | 75 |
| VIc | $C_6H_5$-$CH_2$- | -$OCH_3$ | 80 |
| VId | 4'-MeO-$C_6H_4$- | -H | 67 |

**Table 2. Determined melting points.**

| Compound | $R_1$ | $R_2$ | Melting point (°C) |
|---|---|---|---|
| Ia | $C_6H_5$-$CH_2$- | - | 53 |
| Ib | 4'-MeO-$C_6H_4$- | - | 84 |
| IIIa | $C_6H_5$-$CH_2$- | -H | 175 |
| IIIb | $C_6H_5$-$CH_2$- | -$CH_3$ | 155 |
| IIIc | $C_6H_5$-$CH_2$- | -$OCH_3$ | 160 |
| IIId | 4'-MeO-$C_6H_4$- | -H | 197 |
| Va | $C_6H_5$-$CH_2$- | -H | 97-98 |
| Vb | $C_6H_5$-$CH_2$- | -$CH_3$ | 101-102 |
| Vc | $C_6H_5$-$CH_2$- | -$OCH_3$ | 104-105 |
| Vd | 4'-MeO-$C_6H_4$- | -H | 109-110 |
| VIa | $C_6H_5$-$CH_2$- | -H | 225 |
| VIb | $C_6H_5$-$CH_2$- | -$CH_3$ | 235 |
| VIc | $C_6H_5$-$CH_2$- | -$OCH_3$ | 229 |
| VId | 4'-MeO-$C_6H_4$- | -H | 276 |

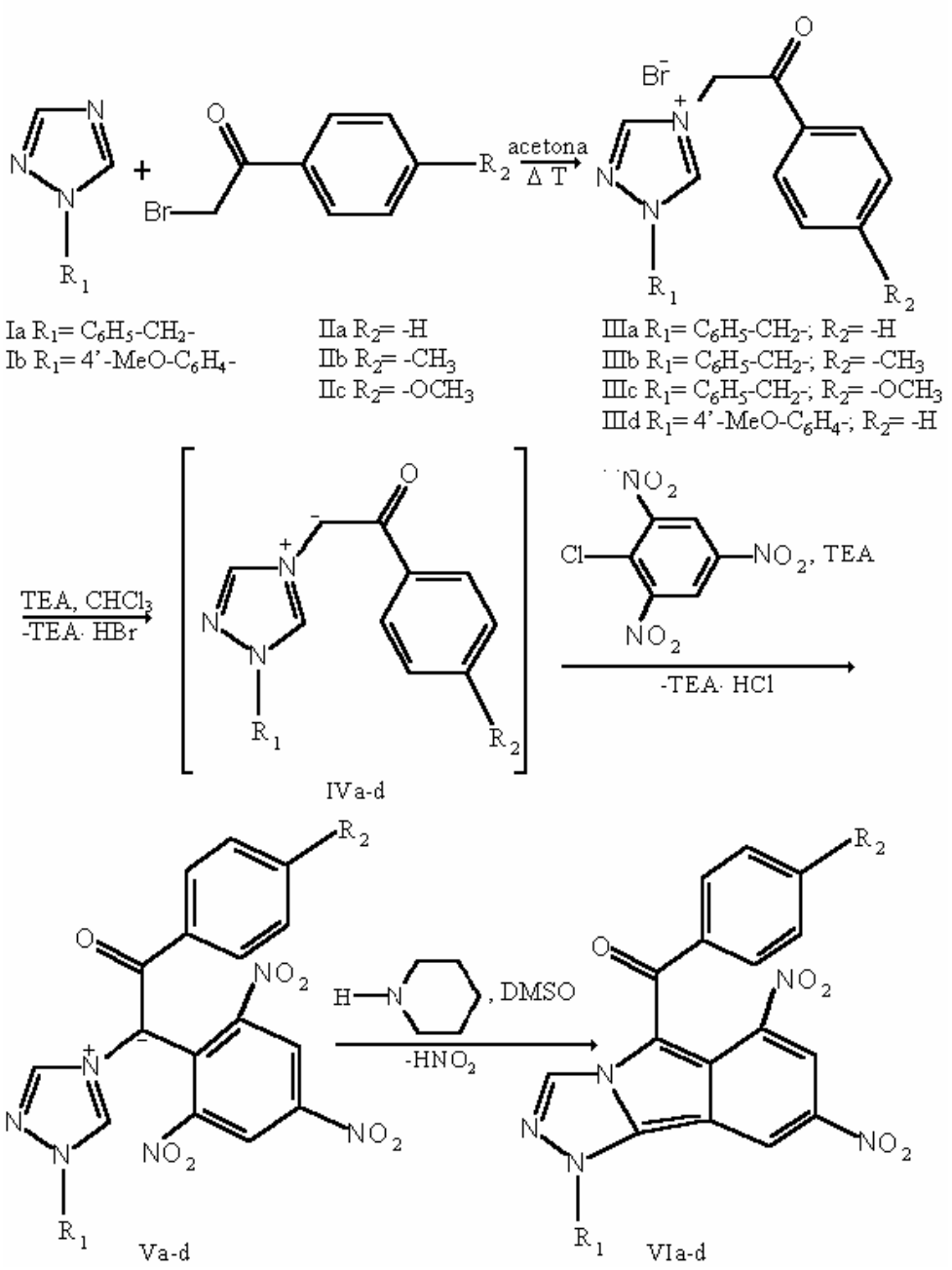
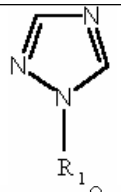
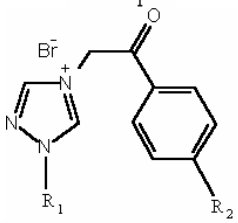
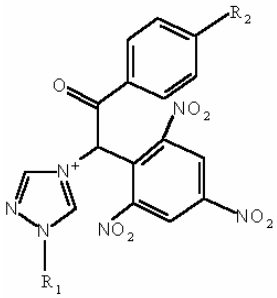
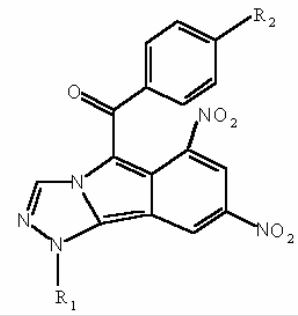



Fig. 1: *1H-[1,2,4]triazolo[3,4-a]isoindols synthesis by intramolecular condensation of disubstituted carbanion ylide*

**Table 3. Molecular weights.**

| Compound | Molecular formula | $R_1$ | $R_2$ | M – Molecular weight |
|---|---|---|---|---|
| Ia |  | $C_6H_5$-$CH_2$- | - | 159 |
| Ib | | 4'-MeO-$C_6H_4$- | - | 175 |
| IIIa |  | $C_6H_5$-$CH_2$- | -H | 277/357 |
| IIIb | | $C_6H_5$-$CH_2$- | -$CH_3$ | 291/ 371 |
| IIIc | | $C_6H_5$-$CH_2$- | -$OCH_3$ | 307/ 387 |
| IIId | | 4'-MeO-$C_6H_4$- | -H | 293/ 373 |
| Va |  | $C_6H_5$-$CH_2$- | -H | 488 |
| Vb | | $C_6H_5$-$CH_2$- | -$CH_3$ | 502 |
| Vc | | $C_6H_5$-$CH_2$- | -$OCH_3$ | 518 |
| Vd | | 4'-MeO-$C_6H_4$- | -H | 504 |
| VIa |  | $C_6H_5$-$CH_2$- | -H | 442 |
| VIb | | $C_6H_5$-$CH_2$- | -$CH_3$ | 456 |
| VIc | | $C_6H_5$-$CH_2$- | -$OCH_3$ | 472 |
| VId | | 4'-MeO-$C_6H_4$- | -H | 458 |

For prediction of CMA's of triazolisoindols synthesis intermediates we preferred the logarithmic relation:

$$\log CMA = -1.2 - 0.012 m.p. + \log M \quad (1)$$

Where m.p. –melting point (in °C); M – molecular weight

This relation may be used for prediction of CMA ($mg/m^3$) for organic compounds with: -100 °C < m.p. < 180 °C and 30 < M < 300.

From examination of data from Table 3 results that only for the first six intermediates it is possible (for volatility reasons [8]) to use this type of equation to predict CMA's.

From examination of firstly calculated values of CMA's (s. Table 4) for these 6 intermediates in triazole isoindols synthesis we can observe the followings:

→ Compound Ib which has a radical more polarizable and heavy than compound Ia has a CMA value more reduced (e.g. it correspond to a greater risk);

→ In the series of intermediates IIIa-IIId the most reduced value of CMA (the greater risk) corresponds to compound IIId with asymmetric substitution (R1=4'MeO-$C_6H_4$, $R_2$=H).

**Table 4. Calculated log CMA values.**

| Compound | $R_1$ | $R_2$ | Log CMA* |
|---|---|---|---|
| Ia | $C_6H_5$-$CH_2$- | - | 0.365 |
| Ib | 4'-MeO-$C_6H_4$- | - | 0.035 |
| IIIa | $C_6H_5$-$CH_2$- | -H | 0.869 |
| IIIb | $C_6H_5$-$CH_2$- | -$CH_3$ | 0.591 |
| IIIc | $C_6H_5$-$CH_2$- | -$OCH_3$ | 0.632 |
| IIId | 4'-MeO-$C_6H_4$- | -H | 1.097 |

Thus we can repeat the assertion from ecotoxicology [1]: "the increase of molecular complexity of the pollutant is parallel with increasing of its toxicity".

It is perhaps "an impossible dream that computation will eradicate the need for real life toxicity testing"[4] but the progress that has been made in recent years is allowing the fundamental properties of a wide range of compounds from pollutants to pharmaceuticals, to be determined with increasing reliability.

## Conclusions

1. Analysis of synthesis procedure of triazoloisoindols and characterization of the isolated intermediates has allowed the computation of CMA's for 6 members of series.

2. The greater risk corresponds to intermediate IIId with the asymmetric substitution.

## Acknowledgement

This work is partially supported by a fellowship in France at University of Littoral, Dunkerque of Ioana Stanculescu and by GRANT 33618/2002 of Romanian National Council of Research in High Education.

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