Riga Technical University
Faculty of Material Science and Applied Chemistry

ABSTRACTS
of the

Riga Technical University
53rd International Scientific Conference

Dedicated to the 150th Anniversary and
The 1st Congress of World Engineers
and Riga Polytechnical Institute / RTU Alumni

Section:
Material Science and Applied Chemistry
October 11–12, 2012, Riga, Latvia

RTU Publishing House
Riga 2012

Riga Technical University 53rd International Scientific Conference dedicated to the 150th anniversary and
The 1st Congress of World Engineers and Riga Polytechnical Institute / RTU Alumni

Condensation of Malonanilic Acids with Aromatic Aldehydes

Inese Mierina, Agnese Stikute and Mara Jure (*Riga Technical University*)

Keywords **– malonanilic acids, aldol condensation, cinnamanilides, 4-hydroxy-1*H*-quinolin-2-ones**

I. Introduction

Cinnamic acid derivatives – amides and esters – demonstrate wide range of biological activity, among them antioxidant and antiradical activities deserve attention. Most often these compounds are synthesized by acylation of the aniline with activated derivatives of cinnamic acid; the disadvantage of such strategy is necessity of protecting groups when the aniline or cinnamic acid contains free hydroxyl or amino group. Less common, but more attractive appears condensation of malonanilic acid and aromatic aldehyde [1, 2]. The aim of our work was to find appropriate conditions for the synthesis of cinnamanilides **1** from malonanilic acids **2** and aromatic aldehydes **3** by Knoevenagel-Doebner condensation.

II. Results and Discussion

According to the literature [1] the condensation of malonanilic acids **2** and aromatic aldehydes **3** proceeds in pyridine in the presence of β-alanine under reflux providing exclusively cinnamanilides **1**. Unfortunately, we observed fast decarboxylation of monoamides **2** forming acylated anilines **4** under these conditions; due to this the yield of Knoevenagel condensation in some cases was even only 30%.

In order to optimize synthesis of cinnamanilides **1**, we studied reaction of 2-[(4-methoxyphenyl)carbamoyl]acetic acid (**2A**) with vanillin (**3A**) at different conditions. When the reaction was carried out in pyridine, the change of base (β-alanine, guanidine and piperidine) did not affect its course – decarboxylation product **4A** was the main compound in the crude mixture of products; the condensation was little preferred in the presence of guanidine and piperidine in comparison with β-alanine.

We varied solvents using those with high boiling point - over 100°C. When mixture of reagents was refluxed in acetic acid, duration of reaction was the same as in pyridine: decarboxylation of malonanilic acid **2A** occurred and the crude product contained only 13% of cinnamanilide **1A**. The reaction was more successful when it was carried out at 75°C – the decarboxylation of raw material **2A** did not happen and we obtained product of aldol condensation **5A**. In water decarboxylation of compound **2A** did not take place, but the Knoevenagel condensation proceeded slowly; when the reaction was carried out in pyridine or water at temperature ~75°C, the reaction did not take place at all.

When the reaction of vanillin (**3A**) and malonanilic acid **2A** was carried out in trifluoroacetic acid, we were able to synthesize 4-hydroxy-1*H*-quinolin-2-one **6A** just in one step; when reagents were allowed to react in different solvents at room temperature (~20°C), condensation did not proceed at all.

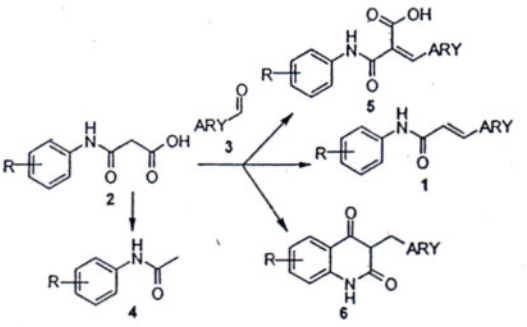

TABLE I

CONDENSATION OF COMPOUNDS **2A** WITH **3A**

No	Conditions of reaction[a]			Products[b]			
	Solvent	Duration	Temp., °C	Comp. **1A**, %	Comp. **4A**, %	Comp. **5A**, %	Comp. **6A**, %
1.	Acetic acid	2 h 25 min	118	13	68	0	0
2.	Acetic acid	> 9 h	75	0	0	97	0
3.	Pyridine	3 h 15 min	116	6	47	0	0
4.	Water	4 h 5 min	100	6	0	0	0
5.	Trifluoroacetic acid	10 h 40 min	72	0	0	0	96
6.	Ethanol	9 h 5 min	78	27	59	0	0

[a]condensation was carried out in the presence of 10 mol-% of guanidine; [b]amount of compounds **1**, **4-6** in the crude product was detected with HPLC.

III. Conclusions

Above described examples demonstrate, that the condensation of malonanilic acids **2** and aldehydes **3** strongly depends on the conditions of reaction: their variation opens way to the synthesis of different products. Undesirable decarboxylation of both starting malonanilic acids and products of aldol condensation can be prevented if reaction is carried out at lower temperature (~75°C) in polar solvents.

To the best of our knowledge for the first time derivative of 4-hydroxy-1*H*-quinolin-2-one was obtained by condensation of malonanilic acid and aromatic aldehyde in trifluoroacetic acid under reflux.

IV. References

[1] **Kamat, S. P., Parab., J. S.** A Simple two-step Synthesis of Avenanthramides, constituents of Oats (*Avena Satina L*). *Indian Journal of Chemistry*, 2007, vol. 46B, pp. 2074-2078.

[2] **Ittyerah, P. I., Pandya, K. C.** Condensation of Malonanilic Acid with Aldehydes. Part IV. With *o*-, *m*- and *p*-methoxybenzaldehydes: the influence of a Hydroxyl-group. *Proceedings Mathematical Sciences*, 1941, vol. 13, 461-466.

[3] **Lee-Manison, A. M., Price, R. K., Strain, J. J. *et al.*** *In vitro* Antioxidant Activity and Antigenotoxic Effects of Avenanthramides and related Compounds. *Journal of Agricultural and Food Chemistry*, 2009, vol. 57, 10619-10624.

Acknowledgment: This work has been supported by the European Social Fund within the project «Support for the implementation of doctoral studies at Riga Technical University»