

RAPPORTO FINALE SUI RISULTATI DEL PROGETTO COMUNE DI RICERCA
FINAL REPORT ON RESULTS OF JOINT RESEARCH PROJECT

1. Accordo /Agreement CNR / ASM anni/ years2.....	
2. Titolo del progetto Design, sintesi e caratterizzazione di nuovi composti organometallici per NLO 2. Title of the project Design, synthesis and characterization of new organometallic compounds showing NLO activity	
Parole chiave (massimo 3) Complessi a basi di Schiff, leganti basati su tiosemicarbazide, ottica non lineare Key words (max. 3) Schiff base complexes, thiosemicarbazide-based ligands, nonlinear optics	
(solo per parte italiana) Area scientifica / Scientific area (tabella 1/ table1) 6 – Dipartimento Progettazione Molecolare	
3. Responsabili del progetto Project leaders	
Responsabile italiano Alessandra Forni	ASM project leader Yurii Chumakov
istituto di appartenenza Istituto di Scienze e Tecnologie Molecolari del CNR indirizzo via Golgi 19, 20133 Milano (Italy)	affiliation Institute of Applied Physics of the Academy of Sciences of Moldova address Academiei Str. 5, Chisinau (Moldovia)

4. Obiettivi del progetto

- 1) Design, sintesi e caratterizzazione di leganti basati su tiosemicarbazide, e determinazione della loro efficienza in NLO tramite misura in stato solido e calcoli teorici
- 2) Preparazione di composti organometallici con elevata risposta NLO
- 3) Investigazione delle relazioni struttura-proprietà sul composto organico solido acido p-aminobenzoico

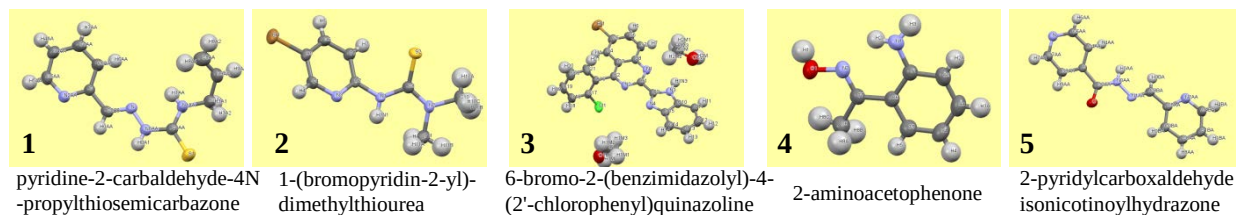
4. Aims of the project

- 1) Design, synthesis and characterization of thiosemicarbazide-based ligands, and determination of their NLO efficiency by solid-state measurements and theoretical calculations
- 2) Preparation of organometallic compounds with large NLO response
- 3) Structure-property relationship investigation on the multicomponent organic solid p-aminobenzoic acid

5. Risultati ottenuti per obiettivo (1 pagina)

1) Design, sintesi e caratterizzazione di leganti basati su tiosemicarbazide, e determinazione della loro efficienza NLO tramite misura in stato solido e calcoli teorici (vedi Punto 7. Prodotto 2)

Sono stati preparati diversi leganti basati su tiosemicarbazidi da utilizzare per la sintesi di composti organometallici con elevata attività NLO. I composti sono stati sintetizzati dal gruppo di ricerca ASM, che ha anche provveduto a determinarne la struttura tramite raggi X. Dei composti sintetizzati, quelli che presentano impaccamento non-centrosimmetrico sono stati sottoposti allo studio NLO da parte del partner CNR. L'efficienza relativa di generazione di seconda armonica (SHG) di una decina di composti è stata testata tramite tecnica Kurtz and Perry su polveri, utilizzando come riferimento sia urea che KH_2PO_4 (KDP) e operando a 1907 e 1064 nm. Il composto più promettente è risultato essere il derivato **1** (vedi Figura sotto), che mostra a 1907 nm un'efficienza SHG $I(2\omega)$ circa 1.5 volte quella dell'urea. Altri leganti che hanno fornito una risposta diversa da zero sono i composti **2** [$0.25 \times I(2\omega)_{\text{urea}, 1907\text{nm}}$ e $0.6 \times I(2\omega)_{\text{KDP}, 1064\text{nm}}$], **3** [$0.5 \times I(2\omega)_{\text{KDP}, 1064\text{nm}}$], **4** [$0.3 \times I(2\omega)_{\text{KDP}, 1064\text{nm}}$] e **5** [$0.1 \times I(2\omega)_{\text{urea}, 1907\text{nm}}$]. Tutti questi leganti sono stati investigati dal team italiano tramite tecniche quantomeccaniche. Per il composto **1** si è confermata una discreta iperpolarizzabilità ($\beta_\lambda = 40 \times 10^{-30}$ esu, dove $\lambda = 1907$ nm, a livello CAM-B3LYP/6-311++G(d,p)), oltre che un moderato momento di dipolo ($\mu = 5.7$ D a livello B3LYP/6-311++G(d,p)). D'altra parte, si è ottenuta una risposta elevata per il composto quasi apolare **3** allo stesso livello di teoria ($\beta_\lambda = 92 \times 10^{-30}$ esu), indicando un allineamento inefficace delle molecole nel cristallo, tale da impedire un incremento della risposta NLO da parte del materiale. Attualmente sono in corso misure sperimentali sul composto **3** in soluzione al fine di determinarne la risposta NLO intrinseca molecolare. Ulteriori studi teorici verranno effettuati sul composto **3** per razionalizzarne l'elevata iperpolarizzabilità.



2) Preparazione di composti organometallici con elevate risposta NLO (vedi Punto 7. Prodotto 3).

Il passo successivo della ricerca è stato la sintesi di complessi organometallici utilizzando come leganti i migliori candidati ottenuti nella precedente analisi. L'utilizzo del composto **1** ha consentito finora di ottenere solo complessi di rame centrosimmetrici, rendendo necessario effettuare le misure in soluzione tramite la tecnica EFISH. Tuttavia, misure preliminari hanno mostrato che i composti sono scarsamente solubili, impedendo di ottenere risultati attendibili delle proprietà NLO. Sono stati ottenuti nel frattempo altri complessi basati su derivati di tiosemicarbazide, che cristallizzano in gruppi spaziali non-centrosimmetrici. Le misure della loro risposta SHG in stato solido sono ancora in corso e verranno terminate entro la fine del progetto bilaterale.

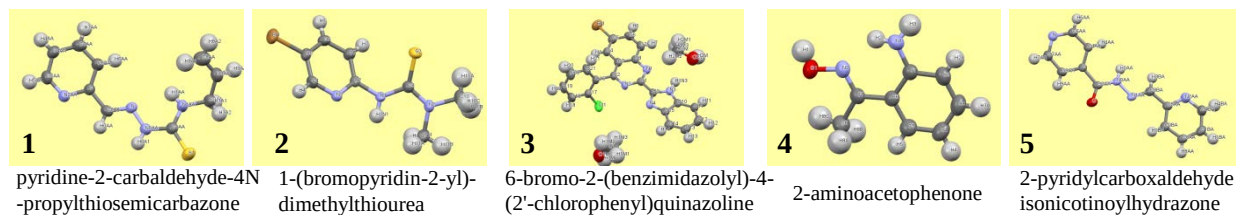
3) Investigazione delle relazioni struttura-proprietà sul composto organico solido acido *p*-aminobenzoico (vedi Punto 7. Prodotto 1).

Sono stati condotti anche degli studi su un composto organico, l'acido *p*-aminobenzoico (*p*ABA), e sul suo sale con 2-hydroxyethylamine (HEA), che costituiscono dei candidati promettenti per NLO grazie alle loro proprietà spettroscopiche. A causa delle somiglianze strutturali di *p*ABA con la molecola di auxina, questo composto e il suo sale sono stati caratterizzati e testati dal team moldavo, in collaborazione con un gruppo di ricerca rumeno, per attività auxina e anti-auxina. Il team italiano ha valutato i possibili modi di legame di *p*ABA alla proteina TR1, il recettore dell'auxina, tramite docking e calcoli QM/MM. I risultati di questo studio, comprendenti sintesi, calcoli teorici, analisi cristallografica, studi in vitro per determinare l'attività biologica e la fitotossicità del sale HEA-*p*ABA, sono stati pubblicati su una rivista internazionale ISI.

5. Achieved results (one page)

1) Design, synthesis and characterization of thiosemicarbazide-based ligands, and determination of their NLO efficiency by solid-state measurements and theoretical calculations (see 7. Product 2).

We have first prepared a series of potential ligands suitable for obtaining organometallic compounds with large NLO activity. The compounds have been synthesized by the Moldovian team, which also provided their X-ray structural characterization. Among the synthesized compounds, those showing non-centrosymmetrical packing have been then submitted to NLO investigation by the Italian team. The relative second harmonic generation (SHG) efficiency of about ten samples was tested by Kurtz and Perry powder technique, using both urea and KH_2PO_4 (KDP) as reference and operating at both 1907 and 1064 nm. The most promising compound was the thiosemicarbazide derivative **1** (see Figure below), showing an SHG efficiency $I(2\omega)$ about 1.5 times that of urea at 1907 nm. Other ligands showing a non-zero response were compounds **2** [$0.25 \times I(2\omega)_{\text{urea}, 1907\text{nm}}$ and $0.6 \times I(2\omega)_{\text{KDP}, 1064\text{nm}}$], **3** [$0.5 \times I(2\omega)_{\text{KDP}, 1064\text{nm}}$], **4** [$0.3 \times I(2\omega)_{\text{KDP}, 1064\text{nm}}$] and **5** [$0.1 \times I(2\omega)_{\text{urea}, 1907\text{nm}}$]. All these ligands have been also investigated by the Italian team using Quantum-Chemical techniques. Compound **1** was confirmed to possess a fair hyperpolarizability ($\beta_\lambda = 40 \times 10^{-30}$ esu, with $\lambda=1907$ nm, at CAM-B3LYP/6-311++G** level), together with a moderate dipole moment ($\mu = 5.7$ D at B3LYP/6-311++G** level). Interestingly, for the almost apolar compound **3** a quite larger β_λ has been obtained at the same level of theory (92×10^{-30} esu), indicating an ineffective alignment of the molecules in the crystal, preventing the enhancement of the NLO response from the bulk. Experimental measurements on compound **3** in solution to determine its intrinsic NLO response are in progress, together with theoretical studies aimed at rationalizing its high hyperpolarizability.



2) Preparation of organometallic compounds with large NLO response (see 7. Product 3).

The next step of our research was the preparation of organometallic complexes with large NLO response using as ligands the best candidates as resulted from our previous analysis. Using compound **1**, only centrosymmetrical copper complexes have been obtained up to now, making necessary to perform NLO measurements in solution using the solution-phase direct current electric-field-induced second harmonic (EFISH) generation technique. Preliminary measurements indicated that the complexes are scarcely soluble preventing us from obtaining reliable results. Other copper complexes based on thiosemicarbazide derivatives, packing in non-centrosymmetrical space groups, have been recently obtained. The measurements of their SHG response in solid state are in progress and will be concluded within the end of the bilateral project.

3) Structure-property relationship investigation on the multicomponent organic solid *p*-aminobenzoic acid (see 7. Product 1).

Attention has been also focused on an organic compound, *p*-aminobenzoic acid (*p*ABA), and its salt with 2-hydroxyethylamine (HEA), which could be considered a promising candidate for NLO owing to its spectroscopic properties. Due to its structural similarities with classical auxin molecules, this compound has been fully characterized and tested for auxin and anti-auxin activity by the Moldavian team, in collaboration with a Romanian research group. In this study, the Italian team has evaluated the possible binding modes of *p*ABA to the TR1 protein, the auxin's receptor, by docking experiments and by Quantum Mechanics/Molecular Mechanics (QM/MM) calculations. The results of the present investigation, including synthesis, theoretical calculations, crystallographic investigation, and an in vitro study determining the biological activity and phytotoxicity of 2-hydroxyethylammonium *p*-aminobenzoate (HEA-*p*ABA), have been recently published on an international ISI journal.

6. Prodotti del progetto / Results obtained	
	n./no.
Pubblicaz. scient. su riviste internaz./ scientific publications on international reviews con IF 3.534 (2013)	1
Pubblicaz. in atti congressi internaz./ publications in international congress proceedings	
Pubblicazioni in atti congressi nazionali / publications in national congress proceedings	2
Pubblicazione libri nazionali / Publication of national books	
Pubblicazione libri internazionali / Publication of international books	
Altre pubblicazioni / other publications	
Brevetti / Patents	
Prototipi / Prototypes	
Strumentazione / Equipment and /or Devices	
Programmi software / Software	
Banche dati / Data bases	
Protocolli / Protocols	
Nuovi Materiali / New Materials	
Nuovi processi / New processes	
Cataloghi/inventari/repertori / Catalogues/Inventories	
Atlanti/Carte/Mappe / Atlases/Charts/Maps	
Progetti di ricerca / Reserch project	
Trasferimento innovazioni / Knowledge transfer	
Laboratori congiunti / Joint laboratories	
Alta formazione / Training	
Altro / Other	

7. Informazioni dettagliate sui risultati indicati sub 6

Pubblicazioni scientifiche su riviste internazionali/ scientific publications on international reviews:

- 1) M. E. Crisan, P. Bourosh, M. E. Maffei, **A. Forni**, **S. Pieraccini**, M. Sironi, **Y. M. Chumakov**

Synthesis, Crystal Structure and Biological Activity of 2-Hydroxyethylammonium Salt of p-Aminobenzoic Acid

PLOS ONE 2014, 9, 101892_1-10

Abstract: p-Aminobenzoic acid (pABA) plays important roles in a wide variety of metabolic processes. Herein we report the synthesis, theoretical calculations, crystallographic investigation, and in vitro determination of the biological activity and phytotoxicity of the pABA salt, 2-hydroxyethylammonium p-aminobenzoate (HEA-pABA). The ability of neutral and anionic forms of pABA to interact with TIR1 pocket was investigated by calculation of molecular electrostatic potential maps on the accessible surface area, docking experiments, Molecular Dynamics and Quantum Mechanics/Molecular Mechanics calculations. The docking study of the folate precursor pABA, its anionic form and natural auxin (indole-3-acetic acid, IAA) with the auxin receptor TIR1 revealed a similar binding mode in the active site. The phytotoxic evaluation of HEA-pABA, pABA and 2-hydroxyethylamine (HEA) was performed on the model plant *Arabidopsis thaliana* ecotype Col 0 at five different concentrations. HEA-pABA and pABA acted as potential auxin-like regulators of root development in *Arabidopsis thaliana* (0.1 and 0.2 mM) and displayed an agravitropic root response at high concentration (2 mM). This study suggests that HEApABA and pABA might be considered as potential new regulators of plant growth.

Funding: This work was partially supported by the Bilateral Project Academy of Sciences of Moldova - National Research Council of Italy 2013–2014

Pubblicazioni in atti congressi nazionali/ publications in national congress proceedings:

- 2) **Yu. Chumakov**, **E. Melnic**, P. Petrenko, T. Codita, V. Tsapkov, A. Gulea, **A. Forni**, E. Cariati, **E. Lucenti**

The structural features study of 3-(5-bromopyridin-2-yl)-1,1-dimethylthiourea
The International Conference dedicated to the 55th anniversary from the foundation of the Institute of Chemistry of the Academy of Sciences of Moldova.

May 28 - 30, 2014, Chisinau, Moldova, **P060**, p.111

Abstract: It is now widely accepted that organic materials might be valuable for use in certain NLO applications [1]. In this connection we report here the crystal structure of 3-(5-bromopyridin-2-yl)-1,1-dimethylthiourea (**I**), which crystallizes in the orthorhombic **polar space group Fdd2** ($a = 20.809(1)$, $b = 36.959(2)$, $c = 5.462(4)$ Å, $V = 4200.3(5)$ Å³). In the crystal, **I** forms dimers where molecules are linked with each other via N1-H1...N3 hydrogen bonds (Fig. 1): H1...N3 2.39, N1...N3 3.119 Å, N1-H1...N3 150°. Owing to the non-centrosymmetric space group of **I**, its nonlinear optical response was evaluated in the solid state through the Kurtz-Perry technique. The SHG response for the studied compound is of the same order of magnitude of that of urea.

This research has been performed in the framework of the International Moldavian-Italian Project 13.820.05.04/ItF.

1. Papagni, A.; Maiorana, S.; Del Buttero, P.; Perdicchia, D.; Cariati, F.; Cariati, E.; Marcolli, W. Eur. J. Org. Chem. 2002, 1380–1384.

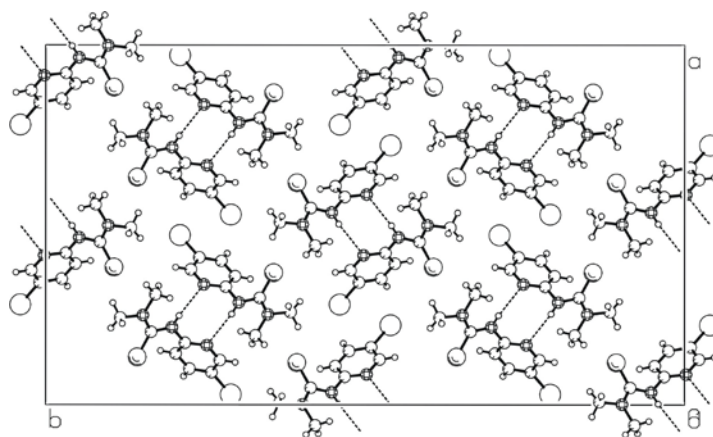


Figure 1. Fragment of crystal packing of **I**.

- 3) **Yu. Chumakov, E. Melnic, P. Petrenko, F. Julea, V. Tsapkov, A. Gulea, A. Forni, E. Cariati, E. Lucenti**

Crystal structure of bis{2-methyl-4-[(methylcarbamothioyl)hydrazono](phenyl)methyl}-2-phenylpyrazolidin-3-ono}nichel dimethylformamide solvate

The International Conference dedicated to the 55th anniversary from the foundation of the Institute of Chemistry of the Academy of Sciences of Moldova

May 28-30, 2014, Chisinau, Moldova, **P059**, p.110.

Abstract: It is known that thiosemicarbazide and its derivatives form stable coordination compounds with virtually all transition metals. Many of these compounds are biologically active, a property that allows their use as a base for selective microbiological culture media and makes them promising for applications as disinfectants and antiseptics. In many cases, the biological activity of drugs is correlated with their composition. Therefore, the synthesis and investigation of new biometal complexes with different ligands are of both scientific and practical interest. In this study we report on the crystal structure of bis{2-methyl-4-[(methylcarbamothioyl)hydrazono](phenyl)methyl}-2-phenylpyrazolidin-3-ono}nichel dimethylformamide solvate (**I**). The studied compound crystallizes in the monoclinic polar space group C2 ($a = 19.001(2)$, $b = 10.135(5)$, $c = 15.1635(1)$ Å, $\beta = 127.58(1)^\circ$, $V = 2314.2(3)$ Å³). The Ni atom adopts the octahedral molecular geometry with distances of Ni-O, Ni-N, Ni-S equal to 2.036(4), 2.053(3) and 2.428(2) Å, respectively (Fig. 1). Owing to the non-centrosymmetric space group of **I**, its nonlinear optical response was evaluated in solution by the electric-field-induced second harmonic generation method and in the solid state through the Kurtz-Perry technique.

This research has been performed in the framework of the International Moldavian-Italian Project 13.820.05.04/ItF.

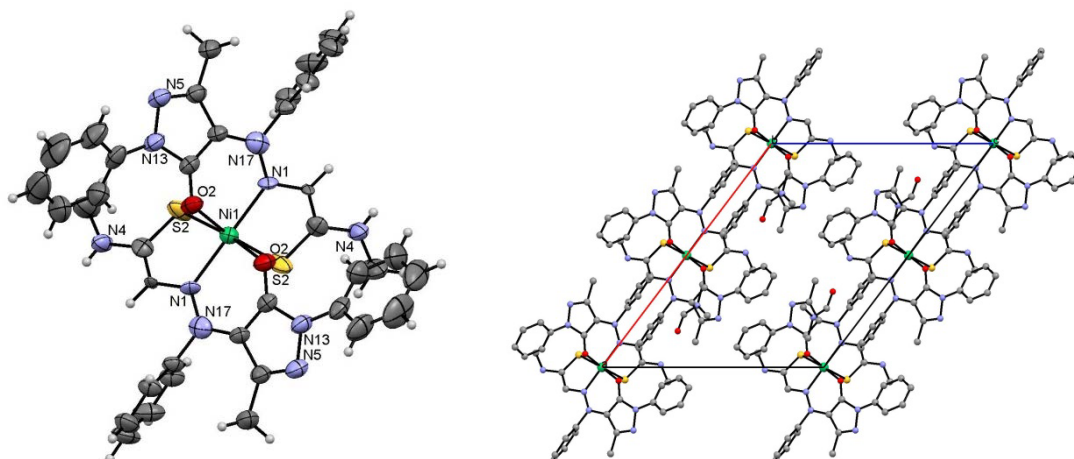


Figure 1. The crystal structure of **I** and fragment of its packing.

8. Formazione di giovani ricercatori Training of young researchers

The project has involved the participation of < 35-years-old researchers including structured (Stefano Pieraccini from Italian side and Elena Melnic from Moldovian side) and non-structured personnel (PhD and Master Degree students). They have actively participated to all activities implied in the project, increasing their knowledge and competences in advanced sectors of scientific research related to the development of materials for nonlinear optics. They have been also involved in all meetings between the research partners, directly or indirectly *via* Internet, giving a valuable contribution to the development of the project.

9. Motivazione degli sviluppi della collaborazione negli anni successivi

(eventuali estensione ad altri paesi, collaborazioni multilaterali, contratti nazionali o internazionali)
Il presente progetto ha consentito di instaurare una stretta collaborazione fra i partner coinvolti e di ottenere risultati significativi a livello internazionale (vedi Punto 6. Prodotti del progetto). Tuttavia, la collaborazione è ancora agli inizi poiché finora sono stati testati solo pochi composti per quanto riguarda le proprietà NLO. Si intende estendere la classe di composti esaminati a materiali organometallici ibridi con marcate proprietà luminescenti per la produzione di materiali multifunzionali con applicazioni in optoelettronica. Il progetto verrà esteso ad altri paesi tra cui la Romania (già coinvolta nel presente progetto) e gli USA.

9. Reasons for cooperative project developments in the following years, if any

(extension to other countries, multilateral collaboration, national or international contracts)

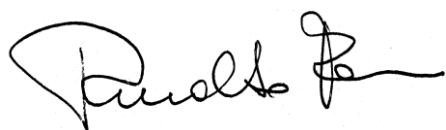
The present project has allowed to establish a consolidated collaboration between the involved partners and to obtain significant results at international level (see Section 6. Obtained results). However, the collaboration is still at its infancy, because only a few compounds have been tested as far as their NLO properties are concerned. We intend to extend the class of examined compounds to hybrid Metal-Organic Materials with pronounced luminescent properties for the fabrication of new multi-functional materials with applications in optoelectronics. The project will encompass researchers from other countries including Romania (already involved in the present project) and USA.



(firma del responsabile italiano del progetto)



(signature of the ASM project leader)
(anche fax)



(firma del direttore)

date:

26 settembre 2014

TABELLA 1

1 – Dipartimento Terra e Ambiente	7 – Dipartimento Materiali e Dispositivi
2 – Dipartimento Energia e Trasporti	8 – Dipartimento Sistemi di Produzione
3 – Dipartimento Agroalimentare	9 – Dipartimento Tecnologie dell'Informazione e delle Comunicazioni
4 – Dipartimento Medicina	10 – Dipartimento Identità Culturale
5 – Dipartimento Scienze della Vita	11 – Dipartimento Patrimonio Culturale
6 – Dipartimento Progettazione Molecolare	