UNIVERSIDADE FEDERAL FLUMINENSE
INSTITUTO DE QUÍMICA
DEPARTAMENTO DE QUÍMICA ORGÂNICA
PROGRAMA DE PÓS-GRADUAÇÃO EM QUÍMICA

"Síntese de Pequenas Moléculas para Importantes Alvos Biológicos"

Prof. Fernando de Carvalho da Silva

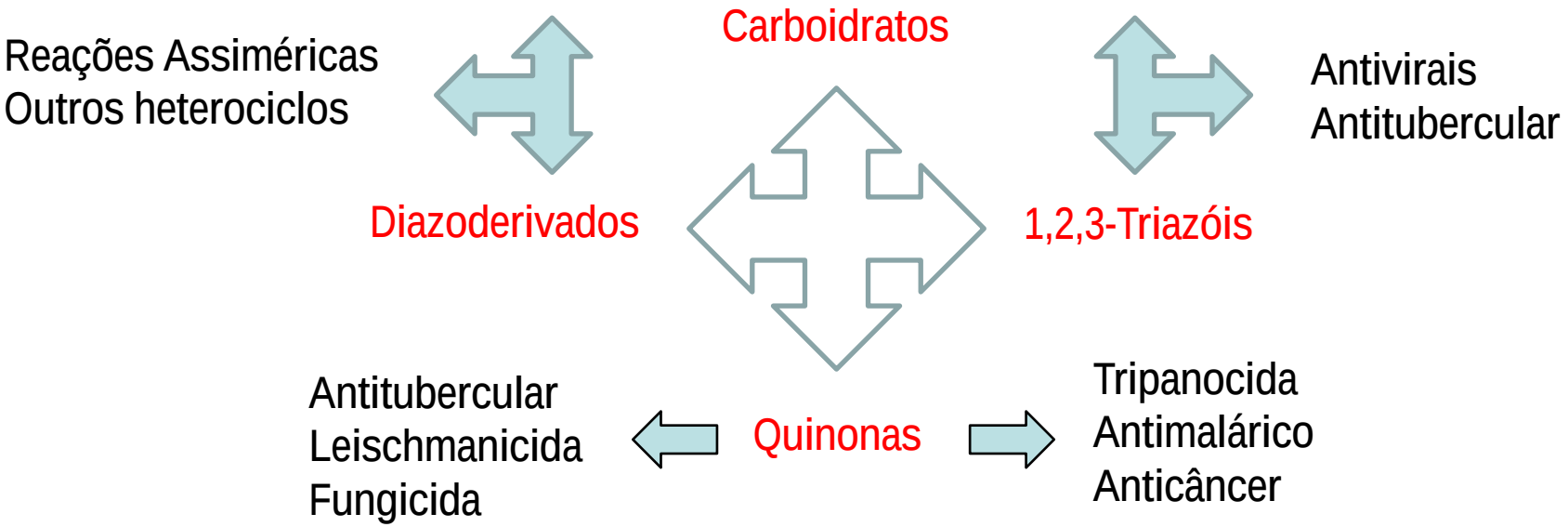
ACADEMIA BRASILEIRA DE CIÊNCIAS
MCMXVI

Avanços e Perspectivas da Ciência no Brasil, América Latina e Caribe
ACADEMIA BRASILEIRA DE CIÊNCIAS • 5 a 8 de novembro de 2012

Quem é o palestrante?...

- Graduação na Universidade Federal Fluminense 1997-2002
- Doutoramento na Universidade Federal Fluminense 2002-2007
- Estágio de pós-doutoramento na Universidade de Aveiro – 2007-2008
- Professor Adjunto 2 da Universidade Federal Fluminense desde 2009
- Editor Revista Virtual de Química e Journal of Organic Chemistry Research
- Secretário Regional do Rio de Janeiro da Sociedade Brasileira de Química
- Bolsista PQ 2 do CNPq

INTRODUÇÃO E GENERALIDADES: Áreas de interesse do nosso grupo de pesquisa



Fernando de C. da Silva, Alessandro K. Jordão, David R. da Rocha, Sabrina B. Ferreira, Anna C. Cunha, Vitor F. Ferreira; "Recent Advances on the Synthesis of Heterocycles from Diazo Compounds", *Current Organic Chemistry*, 2012, *16*, 224-251.

Vitor F. Ferreira, David R. da Rocha, Fernando de C. da Silva; "Potencialidades e oportunidades na química da sacarose e outros açúcares", *Química Nova*, 2009, *32*, 623-638.

Marcelo I. P. Reis, Fernando de C. da Silva, Gilberto A. Romeiro, Anderson A. Rocha, Vitor F. Ferreira; "Deposição Mineral em Superfícies: Problemas e Oportunidades na Indústria do petróleo", *Revista Virtual de Química*, 2011, *3*, 2-13.

Fernando de C. da Silva, Sabrina B. Ferreira, David R. da Rocha, Vitor F. Ferreira; "Chagas Disease: Challenges in Developing New Trypanocidal Lead Compounds", *Revista Virtual de Química*, 2012, *4*, 46-72.

Vitor F. Ferreira, Sabrina B. Ferreira, Fernando de C. da Silva; "Strategies for the synthesis of bioactive pyran naphthoquinones", *Organic & Biomolecular Chemistry*, 2010, *8*, 4793-4802.

Doenças Negligenciadas, de Souza, W. (coord)., ABC, 2010, http://www.abc.org.br/article.php3?id_article=785

Triazóis

Reconhecida atividade farmacológica (bioconjugação)
Química de materiais – dendrímeros e polímeros, fases estacionárias modificadas, organogéis, etc.
Catalisadores

Freitas, L. B. O.; Ruela, F. A.; Pereira, G. R.; Alves, R. B.; Freitas, R. P. *Quim. Nova* 2011, *34*, 1791.
Melo, J. O. F.; Donnici, C. L.; Augusti, R.; Ferreira, V. F.; de Souza, M. C. B. V.; Ferreira, M. L. G.; Cunha, A. C. *Quim. Nova* 2006, *29*, 569-579.

Available online at www.sciencedirect.com
ScienceDirect
European Journal of Medicinal Chemistry 44 (2009) 373–383
EUROPEAN JOURNAL OF MEDICINAL CHEMISTRY
http://www.elsevier.com/locate/ejmech

Original article

Synthesis, HIV-RT inhibitory activity and SAR of 1-benzyl-1*H*-1,2,3-triazole derivatives of carbohydrates

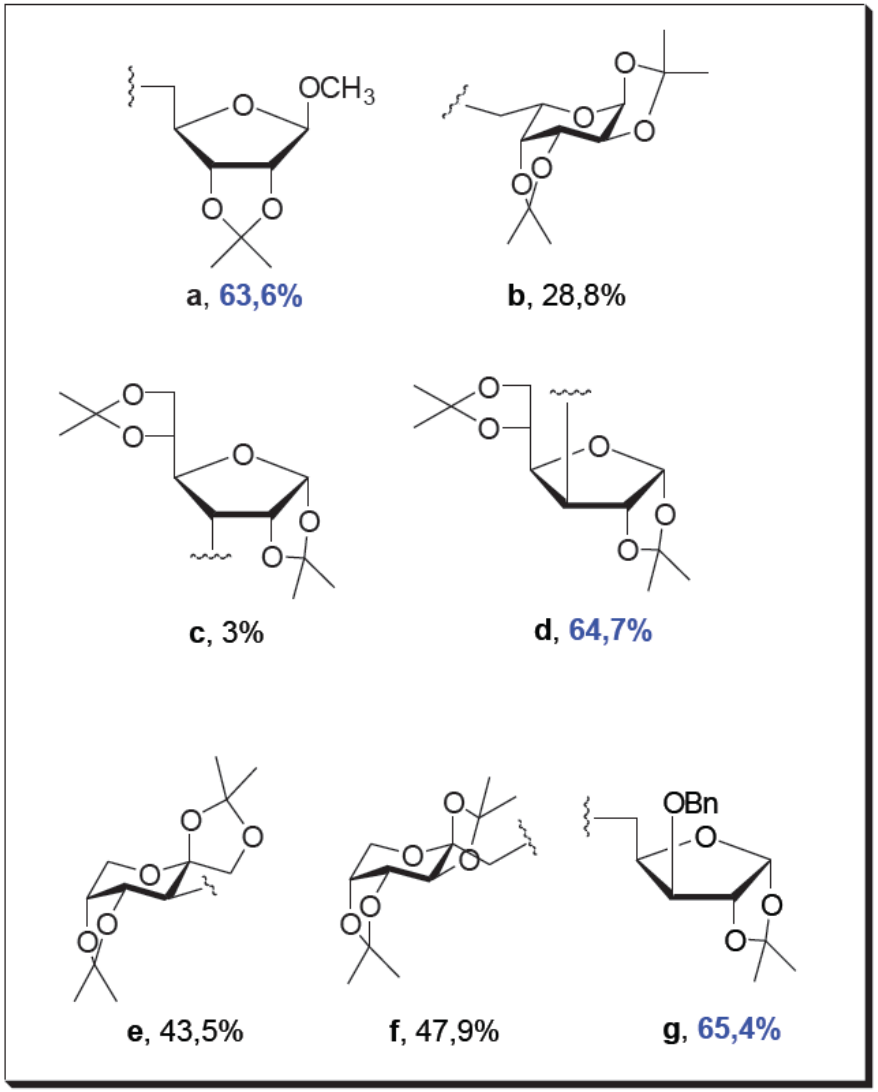
Fernando de C. da Silva [a], Maria Cecilia B.V. de Souza [a], Izabel I.P. Frugulhetti [b], Helena C. Castro [b], Silmara L. de O. Souza [b], Thiago Moreno L. de Souza [b], Diego Q. Rodrigues [b], Alessandra M.T. Souza [a], Paula A. Abreu [b], Fabiana Passamani [c], Carlos R. Rodrigues [c,*], Vitor F. Ferreira [a,**]

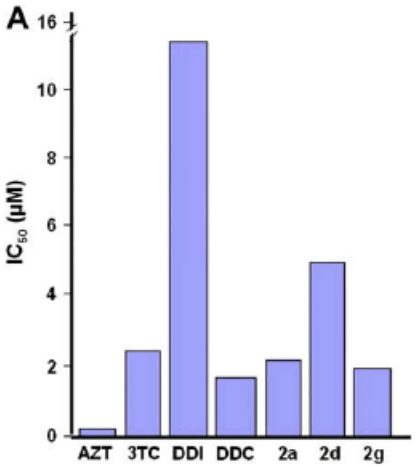
da Silva, F. C. ; Ferreira, V. F. ; Rianelli, R. S. ; Pereira, W. C. *Tetrahedron Lett.* 2002, *43*, 1165.
da Silva, F. C. ; de Souza, M. C. B. V. ; Ferreira, V. F. ; Sabino, S. J. ; Antunes, O. A. C. *Catal. Comm.* 2004, *5*, 151.
da Silva, F. C. ; Ferreira, V. F. ; de Souza, M. C. B. V. *Quim. Nova* 2006, *29*, 376.

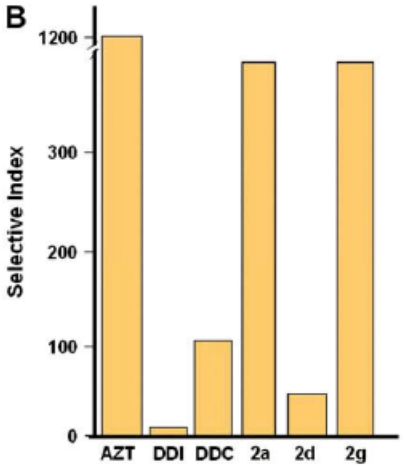
Teste de inibição da enzima transcriptase reversa do vírus HIV

PORCENTAGEM INIBITÓRIA DOS TRIAZÓIS (50 μM)

(testes realizados pela Profª Izabel Frugulhetti – IB/UFF)







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Bioorganic & Medicinal Chemistry 14 (2006) 8644–8653
Bioorganic & Medicinal Chemistry

Synthesis, tuberculosis inhibitory activity, and SAR study of N-substituted-phenyl-1,2,3-triazole derivatives

Marilia S. Costa,[a] Núbia Boechat,[a] Érica A. Rangel,[a] Fernando de C. da Silva,[b] Alessandra M. T. de Souza,[b] Carlos R. Rodrigues,[d] Helena C. Castro,[e] Ivan N. Junior,[c] Maria Cristina S. Lourenço,[c] Solange M. S. V. Wardell[a] and Vitor F. Ferreira[b,*]

Compound	R	MIC (µg/mL)	Inhibition (%)
3a	3,5–diCl	2.5	100
3b	3-CN	20.0	ND*
3c	4-CN	5.0	ND
3d	2-OCH_3	40.0	94
3e	4-OCH_3	10.0	100
3f	2,5-$(OCH_3)_2$	80.0	59
3g	3,4-$(OCH_3)_2$	80.0	0
3h	3-Cl	10.0	100
3i	4-Cl	5.0	ND
3j	4-Br	5.0	100
3k	4-CH_3	2.5	100
3l	4-NO_2	20.0	ND
4a	3,5-diCl	80.0	55
4b	3-CN	80.0	ND
4c	4-CN	20.0	ND
4d	2-OCH_3	40.0	86
4e	4-OCH_3	10.0	93
4f	2,5-$(OCH_3)_2$	80.0	74
4g	3,4-$(OCH_3)_2$	80.0	66
4h	3-Cl	80.0	54
4i	4-Cl	40.0	ND
4j	4-Br	20.0	75
4k	4-CH_3	40.0	87
4l	4-NO_2	40.0	ND
Rifampicina	-	1.0	ND
Etambutol	-	3.25	ND

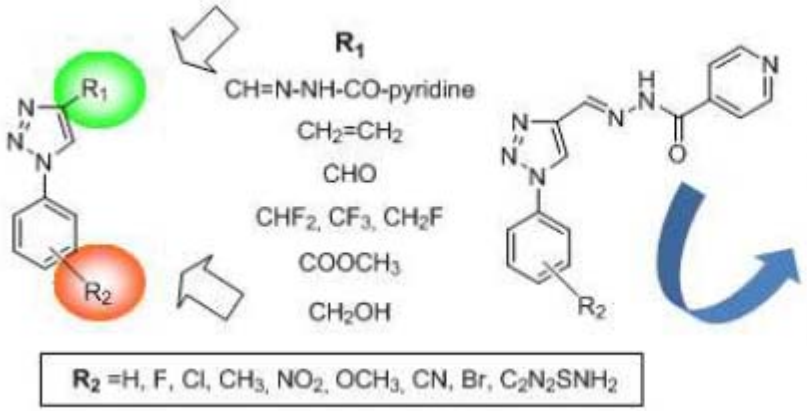
Journal of Medicinal Chemistry

ARTICLE

pubs.acs.org/jmc

Novel 1,2,3-Triazole Derivatives for Use against *Mycobacterium tuberculosis* H37Rv (ATCC 27294) Strain

Nubia Boechat,*,† Vitor F. Ferreira,‡ Sabrina B. Ferreira,‡ Maria de Lourdes G. Ferreira,† Fernando de C. da Silva,‡ Monica M. Bastos,† Marilia dos S. Costa,† Maria Cristina S. Lourenço,‡ Angelo C. Pinto,∥ Antoniana U. Krettli,⊥ Anna Caroline Aguiar,⊥ Brunno M. Teixeira,‡ Nathalia V. da Silva,‡ Priscila R. C. Martins,‡ Flavio Augusto F. M. Bezerra,§ Ane Louise S. Camilo,† Gerson P. da Silva,†,∥ and Carolina C. P. Costa†

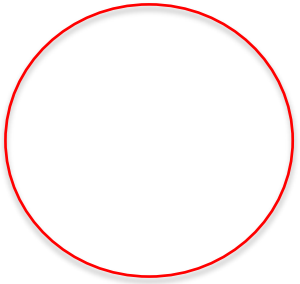


Entry	MIC	IS
Isoniazid	0.06 (0.437)	-----
Rifampicin	1.0 (1.21)	-----
4-Cl	0.62 (1.8)	>1612
3-CH_3	0.62 (2.0)	>422
2-OCH_3	0.62 (1.9)	>1612

J. Med. Chem. 2011, *54*, 5988.

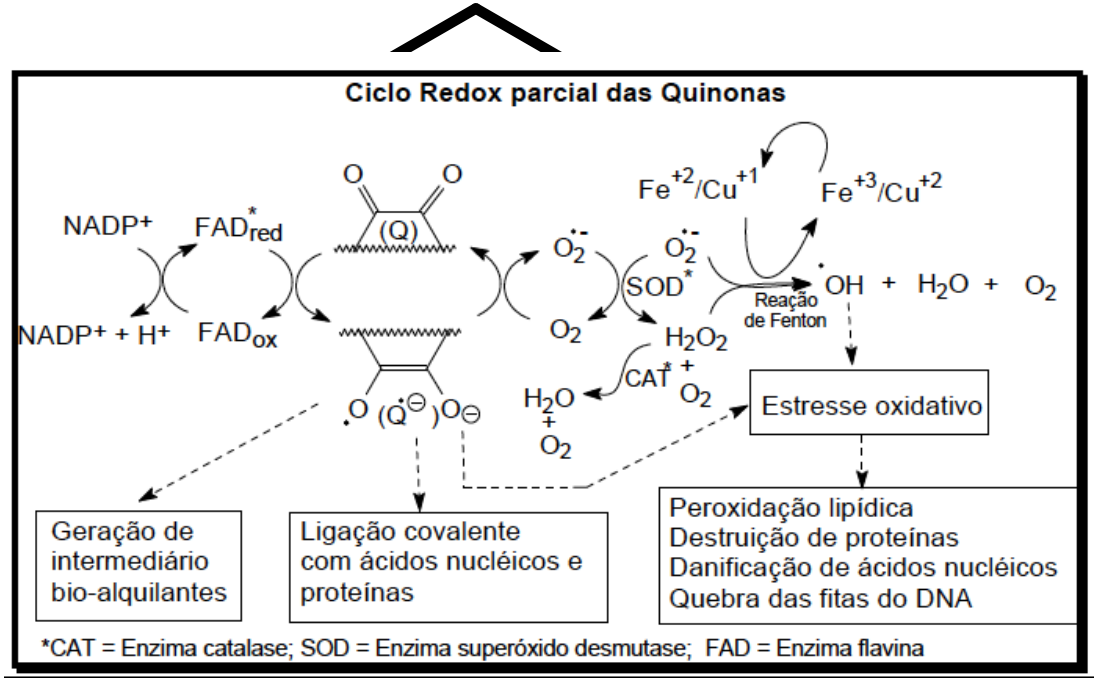
Quinonas (Lapachonas)

Antitumoral, moluscicida, parasiticida, leishmanicida, anti-inflamatória, fungicida, antimicrobiana e tripanocida.



Fase clinica II,
Cod. ARQ501
Câncer de pâncreas

Ferreira, V. F. ; Ferreira, S. B. ; da Silva, F. C. *Org. Biomol. Chem.* 2010, *8*, 4793



J. Braz. Chem. Soc., Vol. 20, No. 8, 1478-1482, 2009.
Printed in Brazil - ©2009 Sociedade Brasileira de Química
0103 - 5053 $6.00+0.00

Article

Synthesis of α- and β-Lapachone Derivatives from Hetero Diels-Alder Trapping of Alkyl and Aryl *o*-Quinone Methides

Fernando de C. da Silva,[a,b] Sabrina B. Ferreira,[a,b] Carlos R. Kaiser,[b] Angelo C. Pinto[b] and Vitor F. Ferreira[*,a]*

[a]*Departamento de Química Orgânica, Instituto de Química CEG, Universidade Federal Fluminense, Campus do Valonguinho, 24020-150 Niterói-RJ, Brazil*

[b]*Instituto de Química, Universidade Federal do Rio de Janeiro, Centro de Tecnologia, Bloco A, Cidade Universitária, 21949-900 Rio de Janeiro-RJ, Brazil*

Arch. Pharm. Chem. Life Sci. 2010, *343*, 81–90

Full Paper

Synthesis of α- and β-Pyran Naphthoquinones as a New Class of Antitubercular Agents

Sabrina B. Ferreira[1,2], Fernando de Carvalho da Silva[1,2], Flávio A. F. M. Bezerra[3], Maria C. S. Lourenço[3], Carlos R. Kaiser[1], Angelo C. Pinto[1], and Vitor F. Ferreira[2]

Table 3. The *in-vitro* activity of compounds **14a–j** in μg/mL (μmol/L) against *M. tuberculosis* H37Rv strain (ATCC 27294) and clogP.

Compound	MIC[c], μg/mL (μmol/L)	cLogP
14a	>100.0 (>344.46)[a]	3.42
14b	>100.0 (>328.58)[a]	3.74
14c	>100.0 (>314.09)[a]	4.05
14d	>100.0 (>307.91)[a]	4.03
14e	>100.0 (>324.36)[a]	3.48
14f	>100.0 (>270.84)[a]	4.12
14g	>100.0 (>312.17)[a]	3.32
14h (*syn*)	>100.0 (>235.06)[a]	5.15
14h (*anti*)	>100.0 (>235.06)[a]	5.15
14i	Nd[b]	5.24
14j (*syn*)	>100.0 (>258.75)[a]	5.08
14j (*anti*)	>100.0 (>258.75)[a]	5.08

Table 4. The *in-vitro* activity of compounds **15a–j** in μg/mL (μmol/L) against *M. tuberculosis* H37Rv strain (ATCC 27294) and clogP measurements.

Compound	MIC μg/mL (μmol/L)	cLogP
15a	2.5 (8.6)	3.36
15b	1.25 (4.10)	3.68
15c	3.12 (9.80)	4.00
15d	2.5 (7.69)	3.98
15e	2.5 (8.10)	3.42
15f	3.12 (8.45)	4.06
15g	6.25 (19.51)	3.26
15h	2.5 (5.87)	4.36
15i	3.12 (8.20)	5.18
15j	6.25 (16.17)	5.03

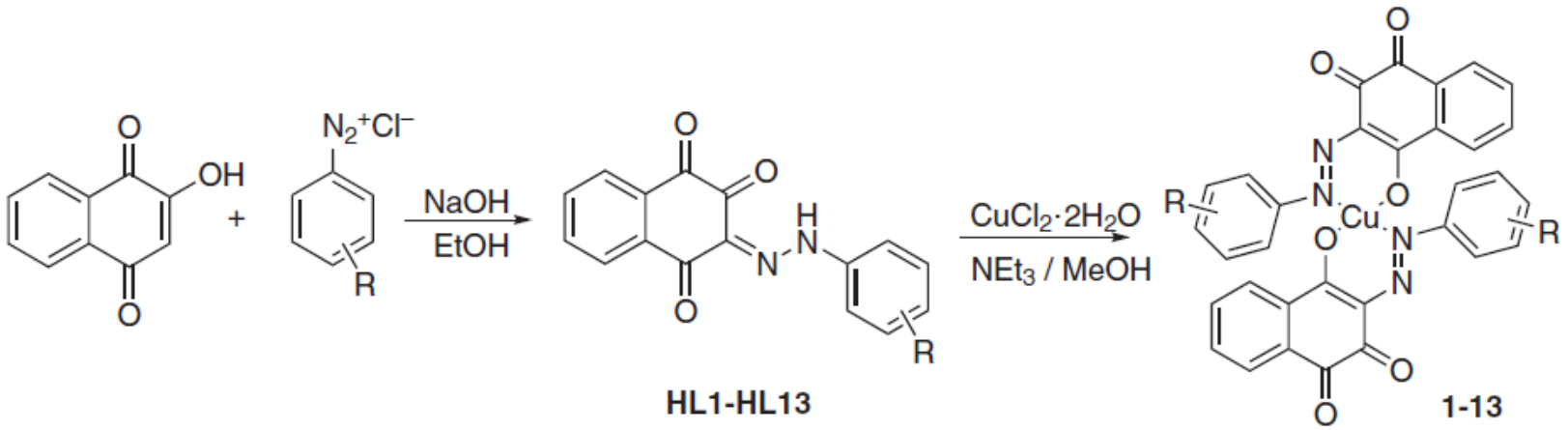
1,25 μg/mL
4,10 μM

J. Braz. Chem. Soc., Vol. 21, No. 7, 1293-1302, 2010.
Printed in Brazil - ©2010 Sociedade Brasileira de Química
0103 - 5053 $6.00+0.00

Article

Theoretical Studies of the Tautomerism in 3-(2-R-Phenylhydrazono)-naphthalene-1,2,4-triones: Synthesis of Copper(II) Complexes and Studies of Antibacterial and Antitumor Activities

Acácio I. Francisco,[a] Maria D. Vargas,,[a] Thaís P. Fragoso,[a] J. Walkimar de M. Carneiro,[a] Annelise Casellato,[b] Fernando de C. da Silva,[a] Vitor F. Ferreira,[a] Jussara P. Barbosa,[c] Claudia Pessoa,[d] Letícia V. Costa-Lotufo,[d] José D. B. Marinho Filho,[d] Manoel O. de Moraes[d] and Antonio S. Mangrich[e]*



Scheme 1. Synthesis of hydrazono compounds **HL1-HL13** and of their respective complexes **1-13**; R = 4-OMe, 4-N=NC_6H_5, 4-Cl, 4-I, 3-I, 2-I, 4-COOH, 3-COOH, 4-CN, 3-CN, 4-NO_2, 3-NO_2 and 2-NO_2.

Células Leucêmicas (HL-60)

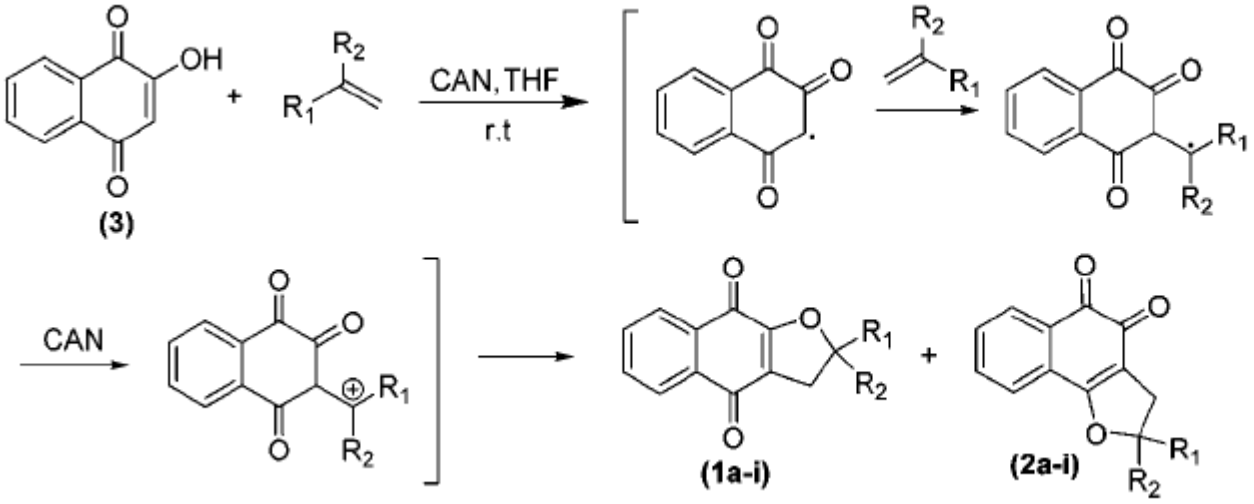
R = NO_2

4.56 μM

Synthesis and biological evaluation of substituted α- and β-2,3-dihydrofuran naphthoquinones as potent anticandidal agents†

Cristina Pessoa Veloso Freire,[a] Sabrina Baptista Ferreira,[b] Nivea Suely Melo de Oliveira,[a] Ani Beatriz Jackisch Matsuura,[c] Ivson Lelis Gama,[b] Fernando de C. da Silva,[b] Maria Cecília B. V. de Souza,[b] Emerson Silva Lima[a] and Vitor Francisco Ferreira*[b]

Received 7th June 2010, Accepted 8th July 2010
DOI: 10.1039/c0md00074d



a, R_1 = H, = R_2 = C_6H_5
b, R_1 = H, R_2 = *p*-CH_3-C_6H_5
c, R_1 = H, R_2 = *p*-Cl-C_6H_5
d, R_1 = H, R_2 = *p*-F-C_6H_5
e, R_1 = H, R_2 = *p*-Br-C_6H_5
f, R_1 = CH_3, R_2 = C_6H_5
g, R_1 = H, R_2 = 2,4-diCH_3-C_6H_5
h, R_1 = R_2 = CH_3
i, R_1 = R_2 = cyclopentene

(MIC, μM)

Compound	*C. albicans*	*C. tropicalis*	*C. kefyr*	*C. parapsilosis*	*C. krusei*	*C. dubliniensis*	ATCC 90028
1h	0.54	3.42	27.38	109.53	13.41	13.69	54.76
1i	2.09	3.27	52.46	13.11	12.85	3.27	13.11
Itraconazole	4.42	0.17	0.08	0.02	0.70	0.02	0.17
Fluconazole	1.63	313.44	1.63	1.63	104.48	1.63	1.63

European Journal of Medicinal Chemistry 46 (2011) 3071–3077

Contents lists available at ScienceDirect

European Journal of Medicinal Chemistry

journal homepage: http://www.elsevier.com/locate/ejmech

Short communication

Synthesis and anti-*Trypanosoma cruzi* activity of β-lapachone analogues

Sabrina Baptista Ferreira [a], Kelly Salomão [b], Fernando de Carvalho da Silva [c], Antônio Ventura Pinto [d], Carlos Roland Kaiser [a], Angelo C. Pinto [a], Vitor Francisco Ferreira [c], Solange L. de Castro [b,*]

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Table 1
Activity of the compounds against bloodstream trypomastigote forms of *T. cruzi*.

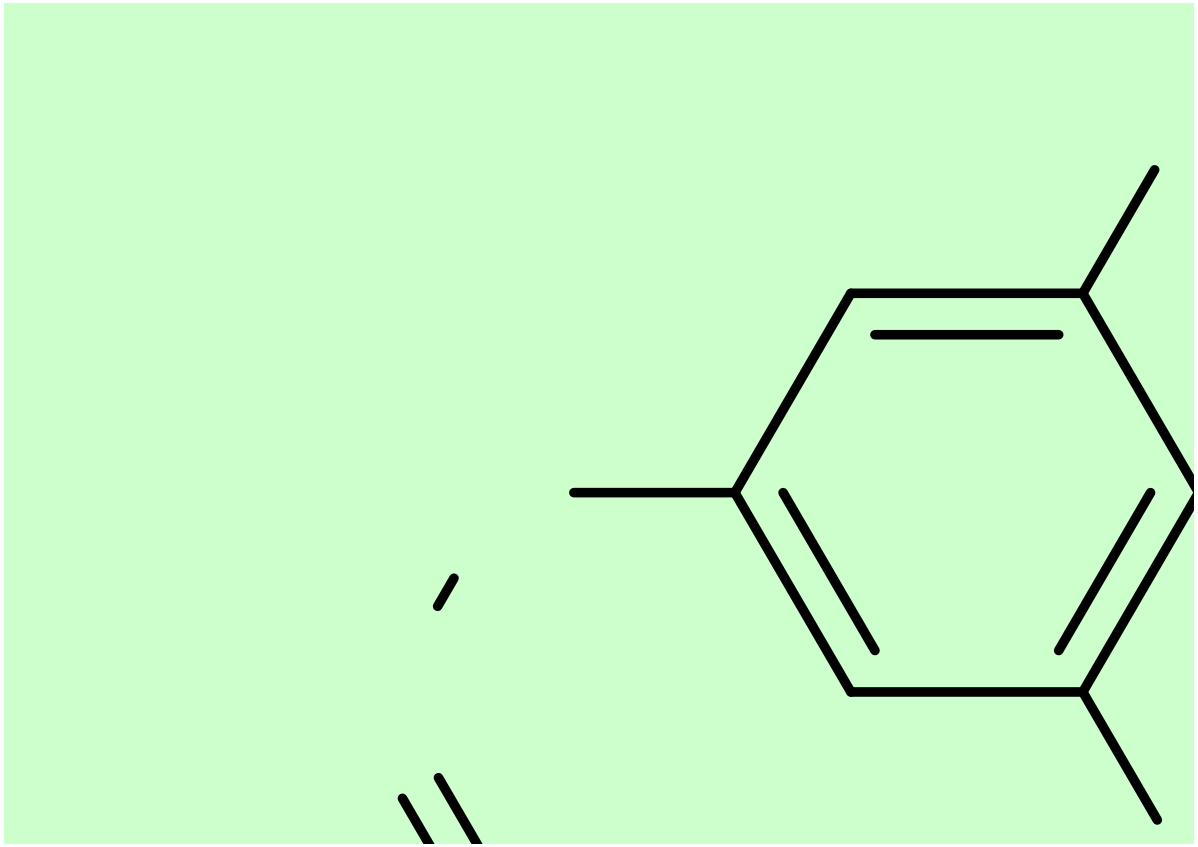
Compound	IC_{50}/24 h[a] (μM)
1	56.0 ± 5.3
2	20.2 ± 4.0
3	51.4 ± 14.9
4	121.4 ± 24.7
5	97.6 ± 11.8
6	132.2 ± 19.2
7	122.9 ± 25.3
8	687.5 ± 71.3
9	>4000
10	849.2 ± 79.8
11	1859.4 ± 201.3
12	62.6 ± 5.5
13	161.1 ± 19.6
14	35.4 ± 12.2
15	330.9 ± 45.3
16	880.3 ± 71.9
Benznidazole	103.6 ± 0.6
β-Lapachone	391.5 ± 16.5

[a] Mean ± standard deviation of at least three independent experiments.

Único Fármaco desde 1970

Resultados não publicados e perspectivas

1,2,3-Triazóis

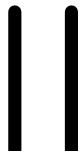


Lapachonas triazólicas

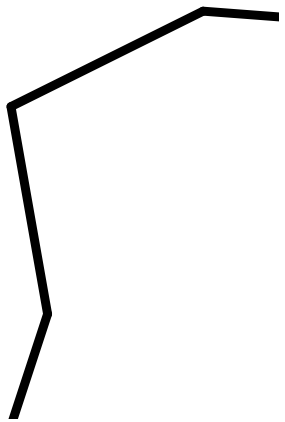
Atividade antitumoral

11-99% (5 µg/mL)
Melanoma, Intestino, Mama

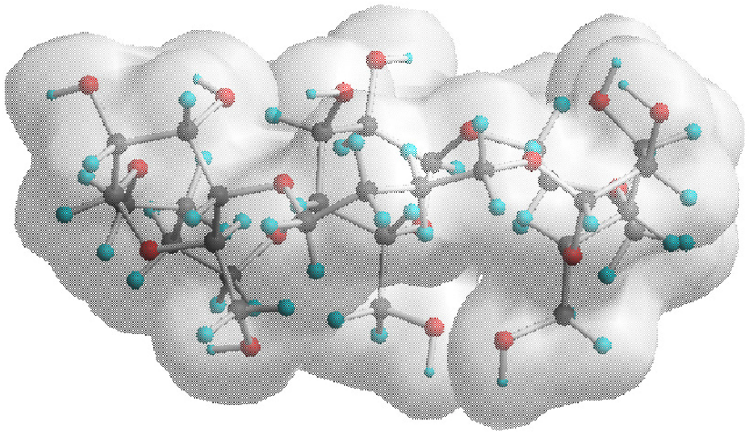
97-100% (5 µg/mL)
Melanoma, Intestino, Mama

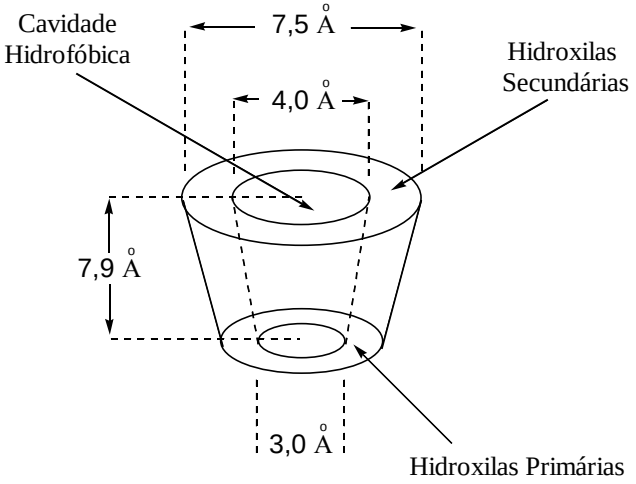


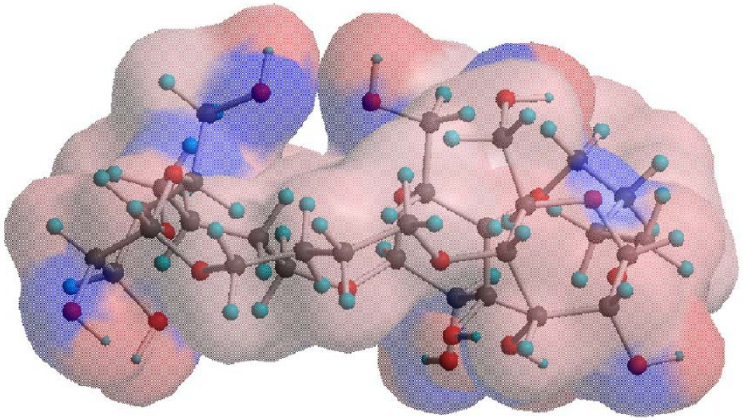
Glicoderivados de Inclusão

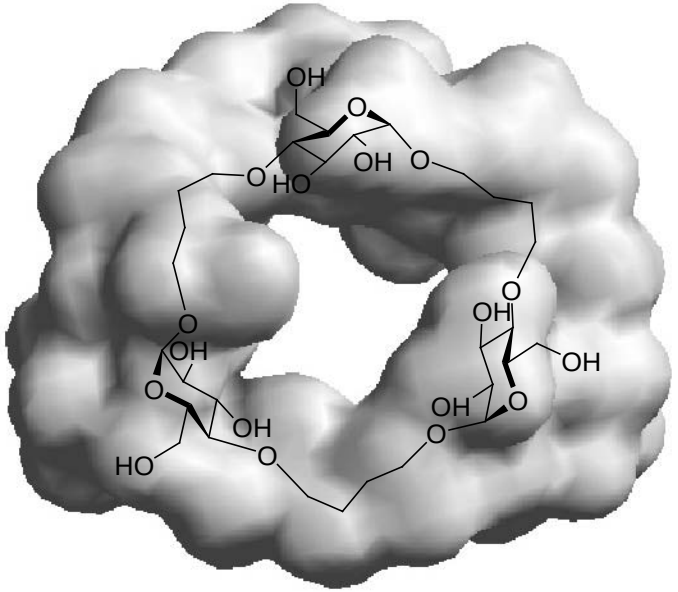


Oligossacarídeo Cíclico de 3 membros









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- ✓ Prof. Vitor Francisco Ferreira (IQ-UFF)
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- ✓ Mauricio Lanznaster (IQ-UFF)
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UFF, UA, UFRJ, CAPES, FAPERJ, CNPq

✓ Alunos

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