

SUPPORTING INFORMATION FOR:

N-O-Isopropyl Sulfonamido-Based Hydroxamates: Design, Synthesis and Biological Evaluation of Selective Matrix Metalloproteinase 13 Inhibitors as Potential Therapeutic Agents for Osteoarthritis

*Elisa Nuti,¹ Francesca Casalini,¹ Stanislava I. Avramova,¹ Salvatore Santamaria,¹
Giovanni Cercignani,² Luciana Marinelli,³ Valeria La Pietra,³ Ettore Novellino,³
Elisabetta Orlandini,¹ Susanna Nencetti,¹ Tiziano Tuccinardi,¹ Adriano Martinelli,¹
Ngee Han Lim,⁴ Robert Visse,⁴ Hideaki Nagase⁴ and Armando Rossello^{*1}*

¹ Dipartimento di Scienze Farmaceutiche, Università di Pisa, via Bonanno 6, 56126 Pisa, Italy

² Dipartimento di Biologia, Unità di Biochimica, Università di Pisa, Via San Zeno 51, 56127 Pisa,
Italy

³ Dipartimento di Chimica Farmaceutica e Tossicologica, Università di Napoli "Federico II", Via
Domenico Montesano, 49, 80131 Napoli, Italy;

⁴ Department of Matrix Biology, The Kennedy Institute of Rheumatology Division, Imperial
College, London, W6 8LH, United Kingdom

CONTENT:	Page
HPLC analysis data	S2
Combustion analysis data	S3

* Corresponding author. Email: aros@farm.unipi.it . Telephone: +39 050 2219562. Fax: +39 050 2219605.

HPLC purity analysis for final compounds (4a-l, 5).

The purity of final compounds was determined by HPLC on a Merck Hitachi D-7000 liquid chromatograph. HPLC purity was determined to be >95% for all final products using a Discovery C18 column (250 mm × 4.6 mm, 5 µm, Supelco), with a gradient of 20% water/80% methanol at a flow rate of 1.4 mL/min over a total run of 15 min at room temperature, with UV monitoring at the fixed wavelength of 256 nm. (See Data in the Table below).

Compound	RT (min)	HPLC Purity (%)
4a	2.49	96.07
4b	2.28	98.82
4c	2.78	97.77
4d	2.88	97.15
4e	3.13	>99
4f	2.29	95.99
4g	10.03	98.37
4h	2.33	98.91
4i	2.60	97.91
4l	2.91	96.49
5	3.37	>99

Combustion analysis data of final compounds (4a-l, 5)

Compound	Formula	calculated			found		
		%C	%H	%N	%C	%H	%N
4a	C ₁₈ H ₂₂ N ₂ O ₅ S ₂	52.66	5.40	6.82	52.75	5.46	6.78
4b	C ₁₈ H ₂₂ N ₂ O ₆ S	54.81	5.62	7.10	55.03	5.91	6.92
4c	C ₂₁ H ₂₈ N ₂ O ₆ S	57.78	6.47	6.42	58.04	6.59	6.70
4d	C ₂₄ H ₂₅ ClN ₂ O ₆ S	57.08	4.99	5.55	57.22	5.15	5.24
4e	C ₂₅ H ₂₆ N ₂ O ₅ S	64.36	5.62	6.00	64.51	5.89	6.25
4f	C ₁₇ H ₂₀ N ₂ O ₆ S	53.67	5.30	7.36	53.90	5.49	7.20
4g	C ₂₁ H ₂₆ N ₂ O ₅ S ₂	55.98	5.82	6.22	56.26	6.07	6.02
4h	C ₁₅ H ₁₇ FN ₂ O ₅ S ₂	46.38	4.41	7.21	46.61	4.73	7.49
4i	C ₁₇ H ₂₂ N ₂ O ₅ S ₂	51.24	5.56	7.03	51.35	5.65	7.26
4l	C ₁₆ H ₂₀ N ₂ O ₆ S ₂	47.99	5.03	7.00	48.20	5.15	7.18
5	C ₂₇ H ₃₁ ClN ₂ O ₆ S	59.28	5.71	5.12	59.50	5.95	5.01