

Supplementary Materials

Chemicals and biochemicals : [α S] 2-oxo-clopidogrel (SR121883), 3'-methoxyphenacyl-*cis*-thiol (SAR206251) and 4'-bromophenacyl-*endo*-thiol (SAR195539) were gifts of Sanofi-Aventis. All other products including enzymes were from Sigma-Aldrich (St Quentin Fallavier, France).

Microsomal Incubations: Human microsomes (pool, 10 mg protein/mL) were obtained from BD-Gentest (Le Pont de Claix, France). Typical incubations were performed in potassium phosphate buffer (0.1M, pH 7.4) containing 2 mM CaCl_2 , 100 mM KF, microsomes (1 mg protein/mL), 2-oxo-clopidogrel (100 μM) and a reducing agent (20 mM ascorbic acid, or 0.5 mM dithiothreitol, or 5 mM glutathione (GSH)) with or without NADPH generating system (1 mM NADP, 15 mM glucose-6-phosphate, 2 u/mL of glucose-6-phosphate dehydrogenase) at 37°C for 30 min. Reactions were stopped by adding one half volume of CH_3CN : CH_3COOH (9:1) and proteins were removed by centrifugation at 13000g.

HPLC-MS studies were performed on a Surveyor HPLC instrument coupled to an LCQ Advantage ion trap mass spectrometer (Thermo, Les Ulis, France), using a Gemini C18 column (100 x 2 mm, 3 μm ; Phenomenex), and a gradient starting at 40% B for 1 min then increasing linearly to 100% B in 15 min (A= ammonium acetate buffer (10 mM, pH 4.6) and B= CH_3CN : CH_3OH : H_2O (7:2:1)) at 200 $\mu\text{L}/\text{min}$. Mass spectra were obtained by electrospray ionization (ESI) in positive ionization mode detection under the following conditions : source parameters: sheath gas 20, auxiliary gas 5, spray voltage 4.5 kV, capillary temperature 200°C, capillary voltage 15V, m/z range for MS recorded generally between 300 and 700 (except for exploratory experiments with a wider range 300-800). MS^2 energy were tested between 20 and 40 eV and were generally 35 eV.

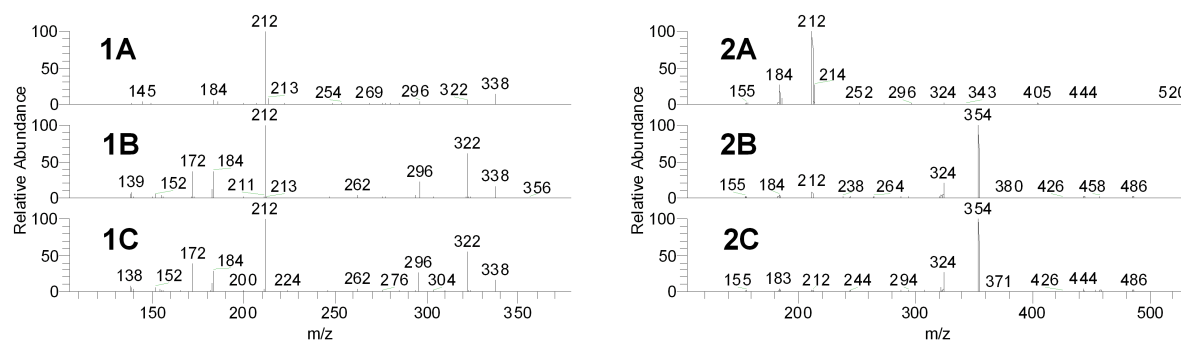


Figure S1 : MS^2 spectra of *endo* and *cis* thiols

Panel 1 shows the MS^2 spectra of the thiols at $m/z = 356$ (1A *endo*, 1B and 1C *cis* thiols). Panel 2 shows the MS^2 spectra of the 3'-methoxyphenacyl derivatized thiols at $m/z = 504$: (2A *endo* and 2B and 2C *cis* thiols).