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Novel iminocoumarine derived imidazo[4,5-*b*]pyridnes as potential antioxidants

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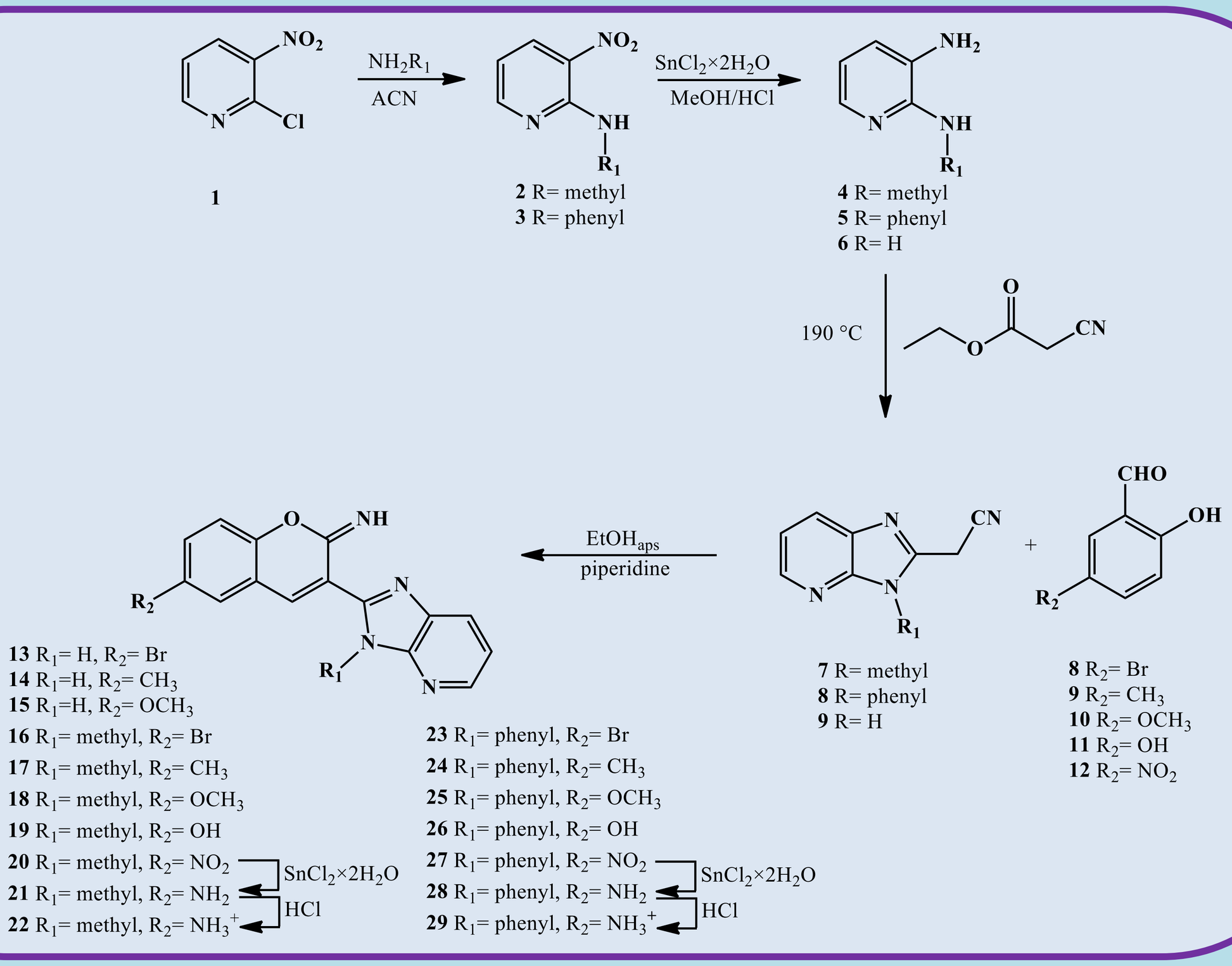
Antioxidants are small organic molecules which have important role of maintaining healthy balance between reactive oxygen species and antioxidants by scavenging free radicals. It is well known that overproduction of ROS is linked to oxidative stress which is important factor in the development of many diseases and disorders. Many of naturally occurring and synthetic coumarines were vastly studied for their biological activities including antioxidant capacity. [1,2]



Scheme 1. Synthesis of targeted compounds

Targeted iminocounarins were prepared in condensation reaction with 5-substituted salicylaldehydes with 2-cyanomethlyimidazo[4,5-*b*]pyridines. Additionally, amino-substituted derivatives were prepared by the reduction with $SnCl_2 \times 2H_2O$ which were further protonated to obtain their hydrochloride salts.

The structures of newly prepared compounds were confirmed by means of ^1H and ^{13}C NMR spectroscopy as well as MS spectrometry.

Newly prepared compounds were tested for their antioxidative activity *in vitro* by using several spectroscopic methods such as ABTS, DPPH and FRAP. Some of the tested compounds showed moderate antioxidative activity.

Figure 1. ^1H NMR spectrum of 19

Table 1. Antioxidative activity of tested compounds

Compound	DPPH (%)	FRAP/ mmolFe^{2+}/mol$_c$
13	18.98±0.19	10.58±1.07
14	19.40±0.3	34.74±0.45
15	12.99±0.942	54.90±8.57
16	19.40±0.3	12.96±0.76
17	10.32±0.314	46.23±3.07
18	18.98±0.19	52.08±1.3
20	20.04±1.19	18.77±2.18
21	12.43±0.785	9.89±0.22
23	16.95±0.42	59.99±1.03
24	15.87±4.081	78.89±1.60
25	7.21±0.628	48.59±0.95
27	20.68±1.01	47.66±0.27
BHT		2089.34±55.98

Table 2. Antioxidative activity of tested compounds

Compound	DPPH (IC_{50} / mM)	ABTS (IC_{50} / mM)	FRAP/ mmolFe^{2+}/mol$_c$
19	11.58±0.81	1.922±0.15	61.34±0.38
21		13.78±0.40	9.89±0.22
22	0.9519±0.03	9.038±0.01	18.94±0.08
26	12.22±1.53	1.8575±0.26	67.54±0.25
28	126.8±9.12	1.407±0.01	54.59±0.50
29	1.728±0.01	1.0415±0.02	91.27±0.50
BHT	0.025±4.2	-	2089.34±55.98

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[1] Perin N, Cindrić M, Vervaeke P, Liekens S, Mašek T, Starčević K, Hranjec M (2021) Medicinal Chemistry 17:8.
[2] Boček I, Starčević K, Novak Jovanović I, Vianello R, Hranjec M (2021) Journal of Molecular Liquids 342:117527-117540.