Identification and characterization of bisbenzimide compounds that inhibit human cytomegalovirus replication

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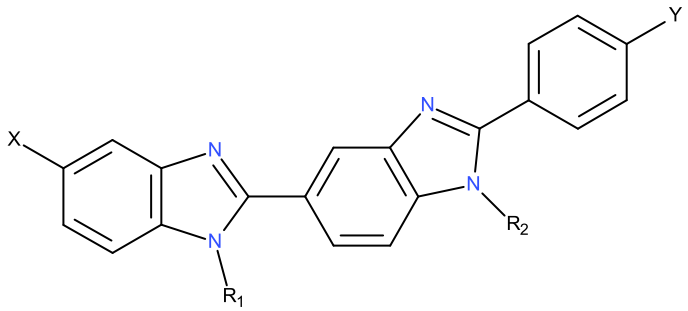
Supplementary Figure 1 Synthesis of MRT00210 compounds

In order to explore the importance of the various NH functionalities in RO-90-7510 a total of 5 compounds were designed and synthesised by LifeArc (see below).

Three these compounds explored the relative importance of the pendant NH2 groups of RO-90-7510; compound 423 had both amino groups replaced by hydrogens, compound 424 retained the amino group on the phenyl ring whilst the other NH_2 was replaced with H, and compound 425 retained the amino group on the terminal benzimidazole portion but had no NH_2 on the phenyl ring.

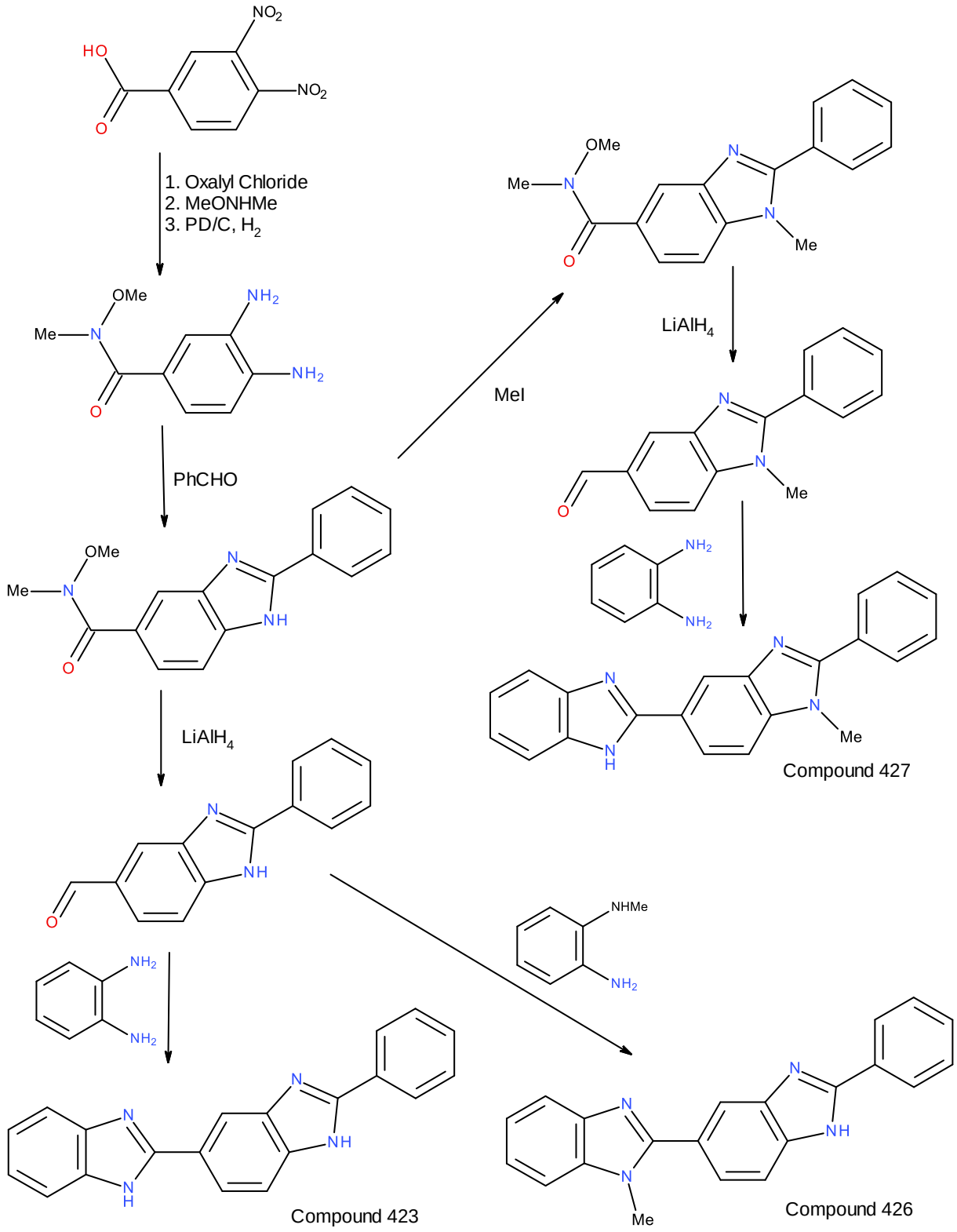
The other 2 compounds explored the importance of the benzimidazole NH. Based on the unsubstituted core compound 423, compound 426 had the terminal benzimidazole NH methylated whilst compound 427 had the central benzimidazole NH methylated.

A summary schema of the 5 compounds is shown below:



	X	Y	R_1	R_2
423	H	H	H	H
424	H	NH2	H	H
425	NH2	H	H	H
426	H	H	Me	H
427	H	H	H	Me

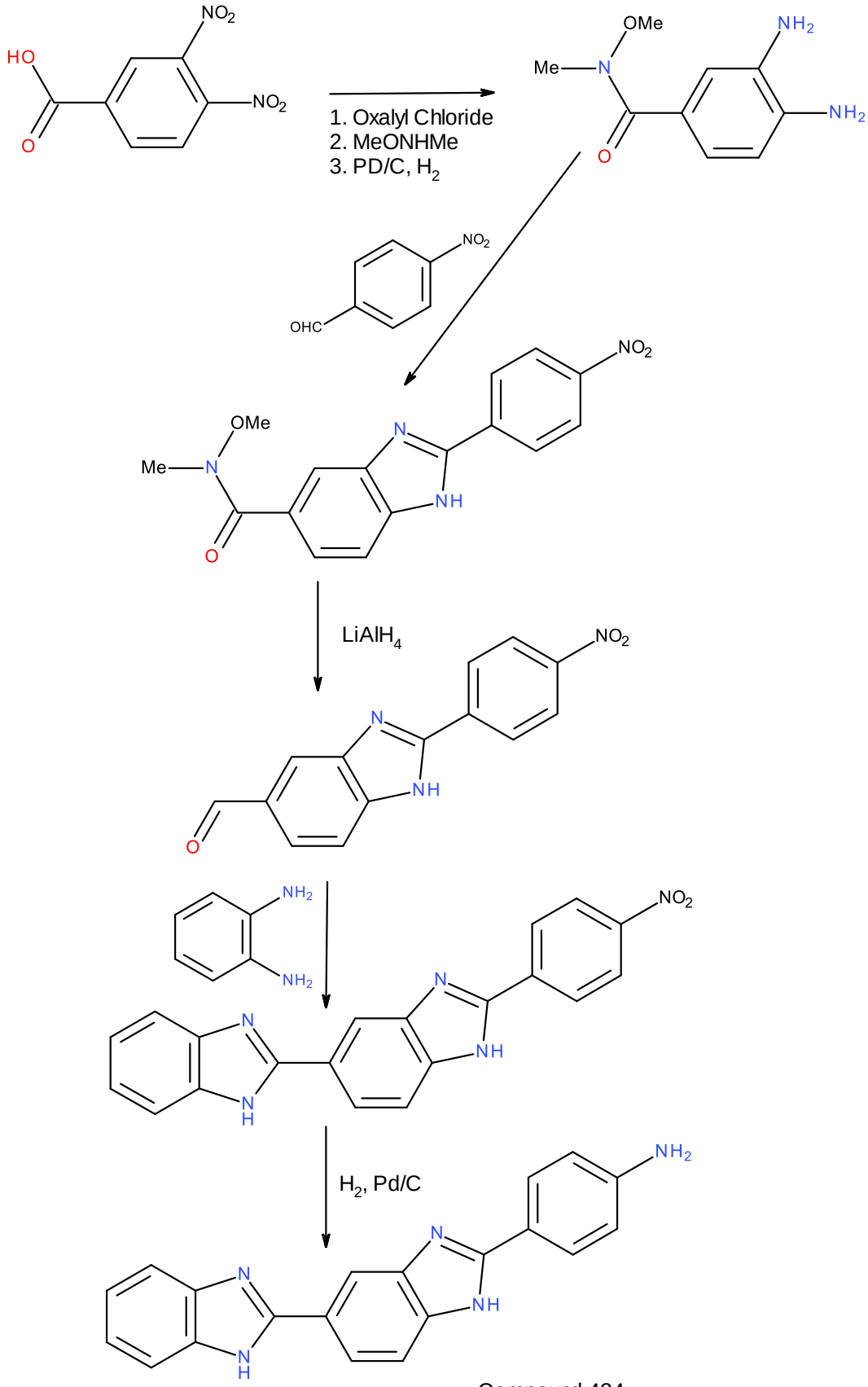
21 Syntheses of compounds 423, 426 and 427:



22

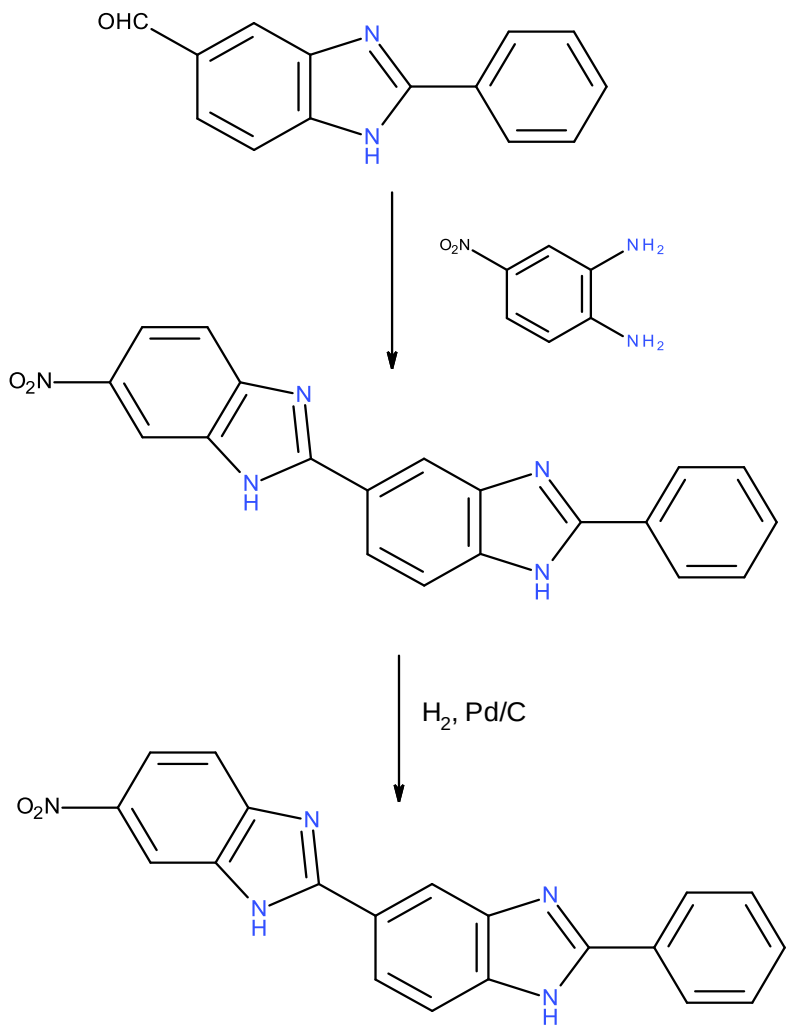
23

24 Synthesis of compound 424:



25 Compound 424

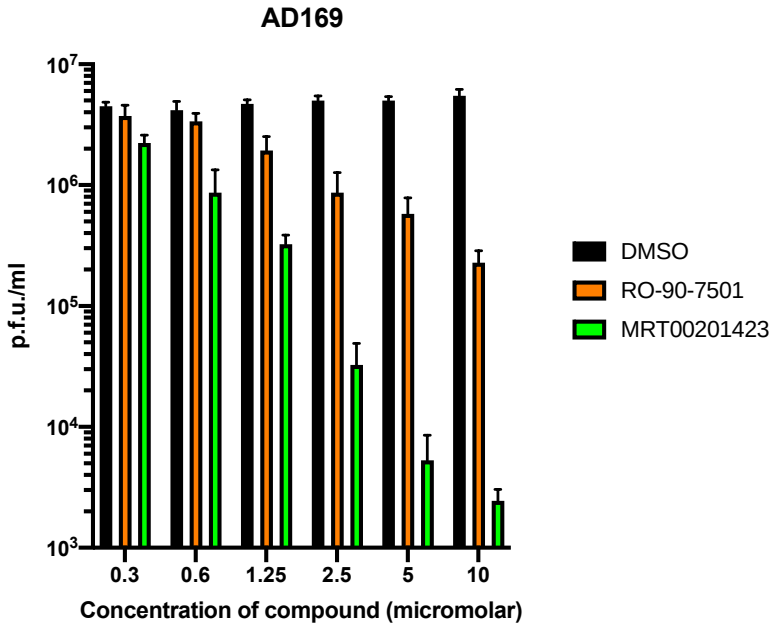
Synthesis of compound 425:



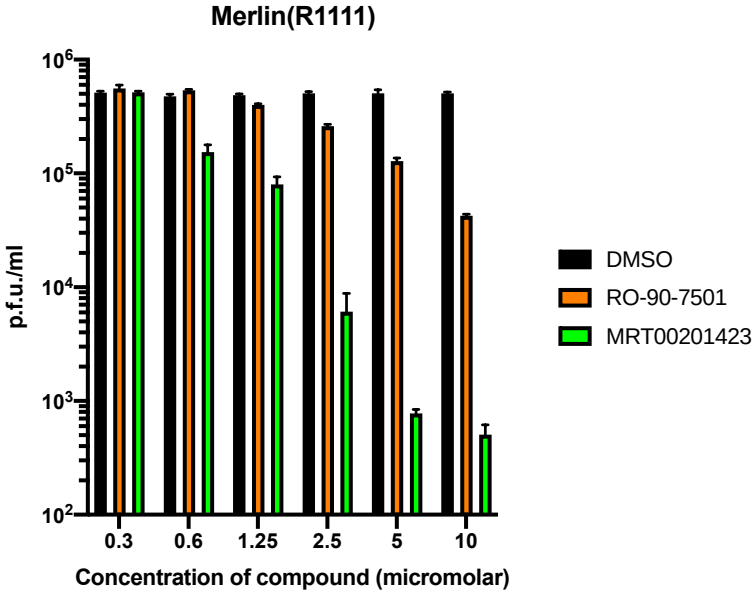
Compound 425

Supplementary Figure 2 Titre of virus replication in the presence of bisbenzimide compounds. The titre of (A) AD169 and (B) Merlin(R1111) viruses from which the drug susceptibility data in Figures 4A and 4B, respectively, was derived.

A



B



Supplementary Figure 3 Investigation of MRT00210423 analogues association with DNA. A molecular weight DNA marker was introduced into agarose gels containing either (A) MRT00210423, (C) MRT00210426 or (E) MRT00210427 using electrophoresis, which were then exposed to UV light and photographed. Gels were then washed in SYBR, exposed to UV light and photographed (panels (B), (D) and (F)).