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A mild and efficient synthesis of spiroquinolinones *via* an unexpected rearrangement

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ABSTRACT

A mild and efficient synthesis of spiroquinolinones **6** *via* condensation of chlorooxoindolines **5** and benzene-1,2-diamines **3** is reported. Instead of expected spirooxindole product **4'**, spiroquinolinones **6** were isolated in up to 95% yield. A plausible mechanism involving an interesting ring rearrangement to form spiroquinolinones is proposed.

The spirooxindole motif is a unique architecture found in many natural products and synthetic drugs.[1] After the discovery of NITD609 as a new chemotype with a novel mechanism of action for the treatment of malaria (Figure 1),[2] we recently identified another spirooxindole **1** with promising anti-dengue activity.[3] These interesting findings further enhanced our confidence and interest in the design and synthesis of further novel spirooxindole scaffolds as potential drug lead candidates.[4]

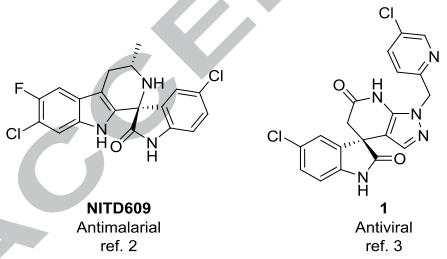
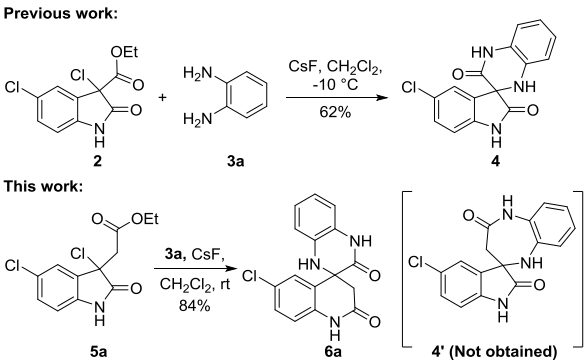


Figure 1. Spriooxindoles identified as possessing antimalarial and antiviral activity.

Previously, we reported a new approach for the synthesis of spriooxindole **4** by condensation of chloroxoindoline **2** with benzene-1,2-diamines **3a** under mild conditions (Scheme 1).[4b] Following a similar approach, we attempted to use compound **5a** with an extended methylene as the substrate for this reaction. However, to our surprise under similar reaction conditions, spiroquinolinone **6a** was formed with excellent yield (84%) instead of the expected spirooxindole **4'** (Scheme 1). The structure of compound **6a** was unambiguously confirmed by single crystal X-ray analysis (Figure 1).[5]



Scheme 1. Synthesis of unexpected spiroquinolinone **6a**.

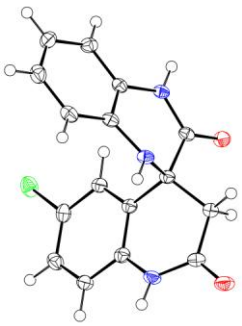


Figure 1. The X-ray crystal structure of compound **6a**.

Following this interesting observation, herein, we report the synthesis of a series of novel spiroquinolinones. We initially

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