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# Ring expansions of a spirocyclohexadienone system

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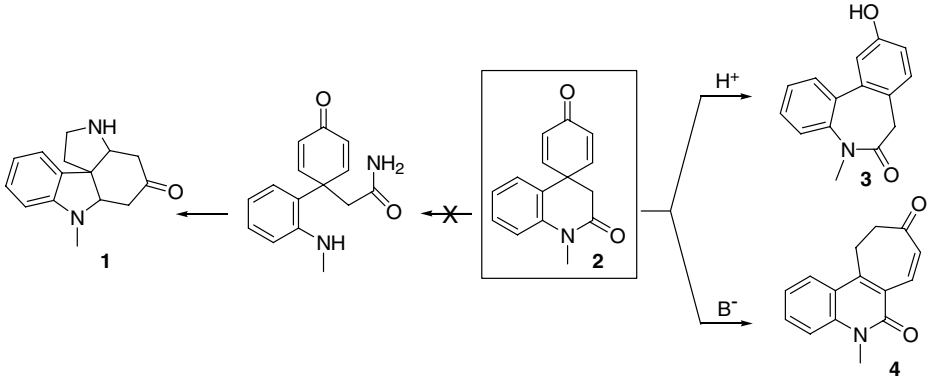
**Abstract**—The unexpected rearrangement of spirocyclohexadienone **2** under acidic or basic conditions is reported.


Aspidosperma alkaloids are one of the largest families of indole alkaloids with more than 200 compounds isolated to date.[1] Over the past decades, efforts led to the discovery of efficient synthetic pathways for their preparation.[2] These alkaloids share the same tetracyclic skeleton **1**[3] which was first synthesized in 1971 (Scheme 1). Also known as Buchi's ketone, this key intermediate has been exploited in the total or formal syntheses of numerous aspidosperma alkaloids among which is vindorosine.[4] In our general effort towards the synthesis of *Vinca* alkaloids,[5] we envisioned that Büchi's ketone could be obtained in a straightforward manner through the aminolysis of the lower ring of spirocyclohexadienone **2**, followed by a double conjugate addition on the dienone system. Unfortunately, attempts to open the lactam ring of **2** under either basic or acidic conditions led to unexpected compounds.

The purpose of the present letter is to report the divergent behaviour of spirocyclohexenone **2** when reacted under acidic or alkaline conditions. This resulted, in both cases, in the rearrangement of the polycyclic system by the ring expansion of the lower or upper carbocycle affording **3** and **4**, respectively.

The starting spirocyclohexa[2,5]diene-1,4′-quinolinedione system **2** was readily prepared starting from N-methyl aniline, which was coupled to 4-hydroxyphenylacetic acid in the presence of EDCI. The resulting amide **5** was treated with [(bis-trifluoroacetoxy) iodo] benzene (BTI) in trifluoroethanol. This led to the formation of the expected tricyclic compound **2**[6] in a 60% yield by aromatic electrophilic substitution of the phenol ring (Scheme 2).[7]

Direct aminolysis using condensed ammonia in MeOH was unsuccessful as **2** remained unaffected. However,




**Scheme 1.**

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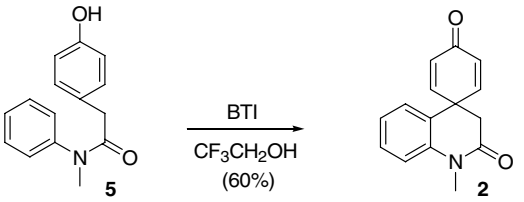
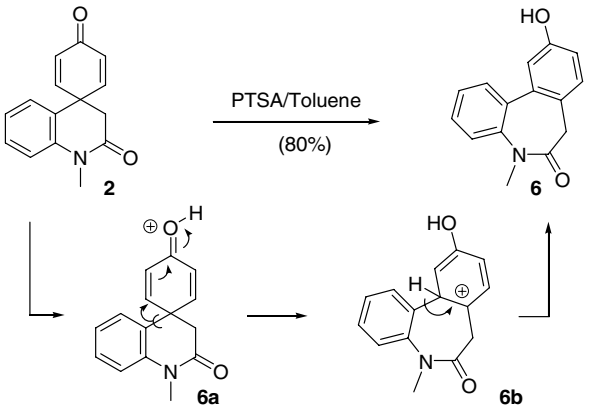
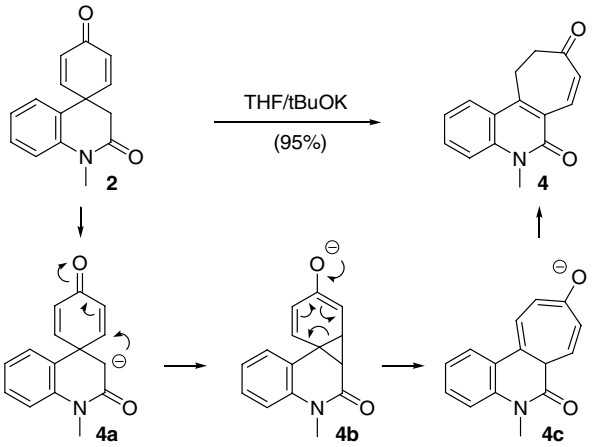



Scheme 2.




Scheme 3.




Scheme 4.

upon acidic treatment (e.g., catalytic PTSA in refluxing toluene), **2** underwent a facile rearrangement leading to the dibenzoazepinone derivative **6**[8] in an 80% yield (Scheme 3). This transformation probably involves the protonation of ketone (**6a**) followed by the 1,2-shift of the spiro carbon–carbon bond. The resulting carbocation **6b** is then trapped by the aromatization of the upper ring. The same type of dienone to phenol rearrangement has already been observed and commented on by others when working with related systems.[9]

Interestingly, under basic conditions (e.g., 1 equiv of *t*-BuOK in THF at room temperature) a completely different behaviour was observed as, this time, the upper ring underwent rearrangement (Scheme 4). Upon addition of potassium *tert*-butanolate, the colour of the reaction mixture immediately turned to yellow as a result of the formation of the highly conjugated system **4**. This transformation can be rationalized through the formation of a cyclopropane intermediate **4b** resulting from the conjugate addition of anion **4a** on the dienone system. Cyclopropane **4b** then undergoes fragmentation to give the rearranged product **4c**. The latter spontaneously evolves to cycloheptaquinolinedione derivative **4** by conjugation of the double bond with the enone system. Compound **4**[10] is obtained in a 95% yield. To the best of our knowledge, this base mediated 2,5-dienone rearrangement has never been observed.

In summary, we report here the rearrangement of a spirocyclohexa[2,5]diene-1,4′-quinolinedione under either basic or acidic conditions. While acidic treatment of our key product leads to the ring expansion of the lower ring, the use of a base (e.g., potassium *tert*-butoxide) induces the rearrangement of the upper carbocycle. The latter process involves the formation of a cyclopropane intermediate, which readily undergoes fragmentation. The reactions described herein should be of a synthetic utility in the construction of complex carbocycles.

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6. $^1$H NMR of **2** ($CDCl_3$, 300 MHz): $\delta$ 2.77 (s, 2H), 3.44 (s, 3H), 6.34 (d, $J = 10.5$ Hz, 2H), 6.94 (d, $J = 10.5$ Hz, 2H), 7.04–7.11 (m, 3H), 7.32 (m, 1H).
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8. $^1$H NMR of **6** ($CDCl_3$, 300 MHz): $\delta$ 3.27 (s, 3H), 3.34 (d, $J = 12.9$ Hz, 1H), 3.86 (d, $J = 12.9$ Hz, 1H), 6.92 (d, $J = 8.5$ Hz, 1H), 7.13 (m, 1H), 7.23–7.33 (m, 3H), 7.40 (dd, $J = 8.5$ Hz, $J = 1.9$ Hz, 1H), 7.53 (d, $J = 7.3$ Hz, 1H).
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10. $^1$H NMR of **4** ($CDCl_3$, 300 MHz): $\delta$ 2.76 (m, 2H), 3.25 (m, 2H), 3.75 (s, 3H), 6.33 (d, $J = 12.8$ Hz, 1H), 7.28 (dd, $J = 8.5$ Hz, $J = 7.3$ Hz, 1H), 7.39 (d, $J = 8.5$ Hz, 1H), 7.61 (d, $J = 8.5$ Hz, 1H), 7.80 (d, $J = 12.8$ Hz, 1H), 7.92 (d, $J = 8.5$ Hz, 1H).