Total Synthesis and Revised Structure of BIYOUYANAGIN A (Part II)

With diene 3 in hand, Hyperolactone C (4) remained to be synthesised before the final [2+2] cycloaddition, which would render Biyouyanagin A.

1) Hyperolactone C (4) was synthesised from L-malic acid (8). Suggest reagents and provide reasonable mechanisms for the conversion of L-malic acid (8) to hydroxylactone 9.

2) What is the structure of 10? Let’s image you happen to be one of the new post-Docs in his lab. He comes around and tells you that he will not buy any Dess-Martin Periodane (DMP) under any circumstances as it is too expensive. How would you make it from cheaper sources (remember: you don’t want to get K.C. irritated in your first days at Scripps, you gotta think fast!)?

3) Suggest reagents for c) and account for the moderate diastereoselective ratio of 11?
4) Lactone 11 undergoes a palladium–catalyzed carbonylative insertion cascade, which leads to spyrolactone 12. Given most of intermediates, suggest a reaction mechanism for the overall process accounting for any stereochemical issues.

5) Spyrolactone 12 was then converted to Hyperolactone C (4) in a 3 step process shown below. Provide a reaction mechanism for the sequence and suggest an alternative protocol for the same conversion.

With the required fragments in hand, the stage was now set to investigate the key [2+2] photoinduced cycloaddition.

6) What is the structure of 2′-acetone-naphtone? Based on the structure, explain what role can it be performing in the reaction?

7) Why do you think the diene is used in reasonably large excess in the reaction?

In conclusion, a 12-step total synthesis of biyoutanagin A has been accomplished and led to the stereochemical reassignment of the natural product from 1a or 1b to 2b.