A Novel Approach to Bicyclo[3.3.0]octane-2,8-dione

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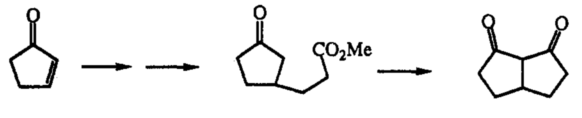
Bicyclo[3.3.0]octane-2,8-dione (1) has been prepared in several different ways.[1] However, with one exception (a nine-step preparation beginning with 5-(hydroxymethyl)-norbornene)[1b], all these syntheses start with cyclopentenone, a sensitive compound which either has to be bought at a relatively expensive price or made independently; and with no exceptions, they end with a Dieckmann condensation of keto ester 2, a reaction which, at least in our hands, has been somewhat tricky. We report here a new approach to 1 which avoids both of these problems.



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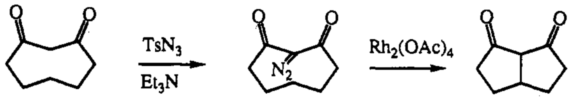
In the course of our work on strained molecules, we have been using the rhodium(II) acetate catalyzed decomposition of α-diazo diketones to produce novel structures by a transannular addition reaction.[2] It occurred to us that a transannular insertion reaction might work just as well to produce the title compound. We are pleased to report that this approach has been successful.

Cyclooctane-1,3-dione can be prepared from diethyl pimelate in about 65% yield by the method of Pirrung and Webster.[3] Diazo transfer followed by rhodium acetate-catalyzed decomposition of the diazo compound 3 provides 1 in high yield, as shown below. Working out conditions for this reaction were not trivial. Both 3 and 1 decomposed somewhat on attempted chromatography, so removal of the excess tosyl azide and the byproduct tosyl amide became a problem. Normally this is solved by use of mesyl azide as the transfer agent[4] and following the reaction with base extraction; however, in our case, treatment of the reaction mixture with base caused complete loss of the diazo compound 3. Others have observed the same problem on occasion.[5] We discovered that tosyl amide could be removed easily by precipitation with a nonpolar solvent such as carbon tetrachloride or petroleum ether, but excess tosyl azide was nearly impossible to remove without chromatography. Our only recourse was to ensure that there was no excess tosyl azide by using exactly stoichiometric amounts. This requires that the cyclooctanedione be quite pure (*solid!*).[6] Under these conditions, the conversion proceeds in 85% yield or better. In a significant break from all previous syntheses of this versatile intermediate, the product, which is acknowledged to be a sensitive compound,[1b] requires no manipulation other than a filtration and a distillation.



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We are confident that other bicyclic diketones can be made by a similar sequence of reactions, and we are pursuing the question of how far the intramolecular insertion can be pushed.

Experimental Section

Bicyclo[3.3.0]octane-2,8-dione. To an open Erlenmeyer flask containing 0.400 g (2.86 mmol) of cyclooctane-1,3-dione[3] and 0.544 g (2.76 mmol) of tosyl azide in 4 mL of acetonitrile was added 0.5 mL of triethylamine. The solution was stirred for 1 h at room temperature and then diluted with 70 mL of carbon tetrachloride. The resulting white precipitate was filtered and the filtrate was concentrated on a rotary evaporator. When approximately 10 mL remained, another 30 mL of carbon tetrachloride was added, the mixture was again filtered, and the filtrate was concentrated to provide 3 as a yellow oil: NMR ($CDCl_3$) δ 2.94 (4H, t, J = 7.5 Hz), 1.91 (4H, distorted pentet), 1.71 (2H, m). This material was taken up in chloroform, and a tiny amount of rhodium acetate dimer was added. The mixture gave off bubbles for about 1 h and then the mixture was filtered into a small round-bottomed flask, concentrated, and kugelrohr-distilled at 95 °C under vacuum to give 330 mg (87% based on tosyl azide, 84% based on dione) of 1 as a colorless solid. Crystallization from carbon tetrachloride/petroleum ether gave crystals, mp 58.5–60 °C (lit.[1b] 61-61.5 °C).

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