



2-Methylcyclopentane-1,3-Dione: An Efficient Synthon for the Synthesis of (±)- α -Cuparenone.

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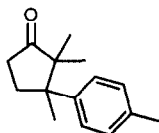
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Abstract: A very short and efficient synthesis of (±)- α -cuparenone was achieved in 4 steps from 2-methylcyclopentane-1,3-dione. © 1997 Elsevier Science Ltd.

(±)- α -Cuparenone and congeners isolated from the essential oils of *Mayur pankhi*¹ tree and liverwort *Mannia fragrans*² have been a synthetic challenge owing to the presence of two contiguous quaternary centers in the cyclopentane ring.

The reported syntheses of α -cuparenone, whether racemic or chiral, employ diverse methodologies.³ Nevertheless, there are to date relatively few efficient approaches to this simple molecule.



(±)- α -cuparenone

The recent synthesis of (±)- α -cuparenone described by Kulkarni and others⁴ urges us to report our brief high-yield synthesis of (±)- α -cuparenone starting from the commercially available 2-methylcyclopentane-1,3-dione.

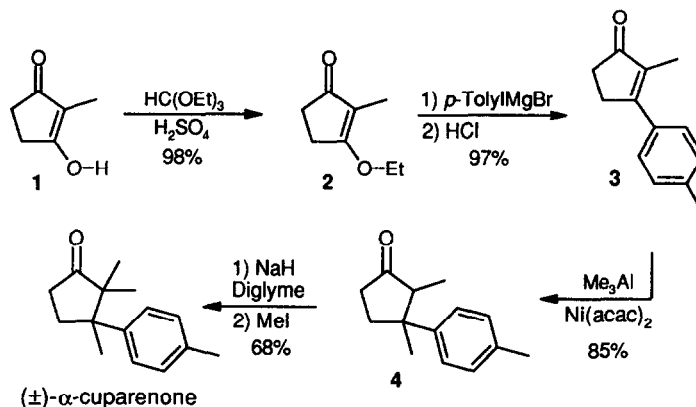
2-Methylcyclopentane-1,3-dione **1** was converted to (±)- α -cuparenone in four steps. The first step was the transformation of 2-methylcyclopentane-1,3-dione into the corresponding ethyl enol ether **2** (0.5 M ethanolic solution), by using ethyl orthoformate (4 eq) in the presence of H₂SO₄ (1 eq) (yield = 98 %). The ethyl enol ether **2** was then converted into the substituted cyclopentenone **3** by addition of *p*-tolylmagnesium bromide in THF (1 eq), followed by aqueous acidic work up (HCl, 5N). After flash chromatography on silica gel (EtOAc/petroleum ether = 1/4), the enone **3** was isolated (yield = 97%).

The introduction of the methyl group on C-3 was achieved by using Me₃Al (1.05 eq) in the presence of a catalytic amount of Ni(acac)₂.⁵ We have to point out that the addition of Me₂CuLi on enone **3** did not lead to the expected cyclopentanone **4**.

The trisubstituted cyclopentanone **4** was isolated (yield = 85%) and converted to (±)- α -cuparenone⁶ by quenching the thermodynamic enolate (NaH, diglyme, R.T.)⁷ by methyl iodide (3 eq) (yield = 68%).

(±)- α -Cuparenone was thus obtained, in a very efficient way, from the commercially available 2-methylcyclopentane-1,3-dione in 4 steps with an overall yield of 55 % (Scheme).

Scheme: Synthesis of (\pm)- α -cuparenone from 2-methylcyclopentane-1,3-dione.



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6. (\pm)- α -Cuparenone:

IR (film): 2960; 1735; 1510; 1460; 815 cm^{-1} . **$^1\text{H NMR}$** (CDCl_3 , 300 MHz) δ (ppm): 0.63 (s, 3H); 1.18 (s, 3H); 1.39 (s, 3H); 1.92 (m, 1H); 2.35 (s, 3H); 2.50 (m, 2H); 2.68 (m, 1H); 7.22 (m, 4H). **$^{13}\text{C RMN}$** (CDCl_3 , 75 MHz) δ (ppm): 18.3 (q); 20.7 (q); 22.0 (q); 25.2 (q); 29.6 (t); 33.6 (t); 48.2 (s); 53.1 (s); 126.3 (d); 128.8 (d); 135.7 (s); 141.8 (s); 22.4 (s). **MS** (70 eV): 216 (M^+ , 99); 201 (23); 145 (100); 132 (52); 91 (43).
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