A TOTAL SYNTHESIS OF *a*-DAMASCONES

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Since β -damascenone (<u>1</u>) was first isolated from Bulgarian rose oil¹, extensive attention¹⁻¹⁰ has been drawn to the preparation of this odoriferous enone as well as to that of its related compounds which are of equal industrial interest. The existing syntheses of <u>trans</u>- (<u>2</u>) and <u>cis</u>- α -damascone (<u>3</u>) involve modifications of α -cyclocitral¹ or α -ionone^{2,6-8}. We wish to report an efficient total synthesis of α -damascones without relay.



The starting keto ester $\underline{4}$ was prepared by boron trifluoride catalyzed condensation of ethyl acetoacetate with acetone according to the procedure of Rubinstein¹¹. This reaction gave, in our hands, a mixture of $\underline{4}$ and its positional isomer $\underline{5}^{12}$ in a ratio of <u>ca</u>. 2:1. The two isomers could be separated by extensive column chromatography and $\underline{4}$, upon treatment with 1,2-ethanedithiol and boron trifluoride etherate, gave thicketal ester <u>6</u> in near quantitative yield. In a more convenient procedure, the mixture of $\underline{4}$ and $\underline{5}$ was subjected directly to the thicketalization without the laborous separation. At 0° for 7 hr., $\underline{4}$ reacted with 1,2-ethanedithiol exclusively and completely to give <u>6</u> whereas <u>5</u> remained totally unreacted.

4129

In order to install the ketonic sidechains of the α -damascones, the ester grouping of <u>6</u> was first converted to an aldehyde. Lithium aluminum hydride reduction of <u>6</u> afforded, in 80% yield, crystalline alcohol <u>7</u>, m.p. 46-47°. Moffatt oxidation of <u>7</u> using dicyclohexylcarbodiimide, dimethyl sulfoxide, trifluoroacetic acid and pyridine¹³ produced, in addition to the desired aldehyde <u>8</u>, a substantial quantity of the dehydration product. The oxidation proceeded smoothly however when phosphoric acid was substituted¹⁴ for trifluoroacetic acid and pyridine and an 80% yield of <u>8</u>, m.p. 62-63°, was obtained.

Subsequent treatment of 8 with propenyl magnesium bromide prepared $^{\perp}$ from a mixture of cis- and trans-l-bromopropene (Aldrich) gave two isomeric alcohols 9 and 10 (m.p. 93-94°) in approximately equal amounts with a total yield of 93%. Separation of these two alcohols was readily achieved by preparative thin-layer chromatography on silica gel. Oxidation of 9 with a thirty-fold excess of activated manganese dioxide¹⁵ in methylene chloride at room temperature for 10 hr. afforded an 85% yield of trans-enone <u>ll</u>: ir (film) 1685, 1665, and 1625 cm⁻¹; nmr (CCl₄) δ 0.86, 1.07 (both s, 3H each), 1.60 (d, 3H, J = 2 Hz), 1.90 (dd; 3H, J = 6.5, J' = 1.5 Hz, 3.29 (s, 4H), 5.69 (br. s, 1H), 6.21 (qd, 1H, J = 15, J' = 151.5 Hz), and 6.80 (qd, 1H, J = 15, J' = 6.5 Hz). Upon oxidation under the same conditions, the cis-isomer 10 gave a 45% yield of the expected cis-enone 12 [ir (film) 1680, 1655, and 1610 cm⁻¹; nmr (CCl_A) δ 0.99, 1.07 (both s, 3H each), 1.63 (d, 3H, J = 2 Hz), 2.07 (m, 3H), 3.26 (s, 4H) 5.67 (br. s, 1H), and 6.16 (m, 2H)and in addition, trans-enone $\underline{11}^{16}$ in 31% yield. Interestingly, when the reaction was carried out using a lesser quantity of manganese dioxide (twelve-fold excess), 10 was oxidized cleanly without isomerization to give 12 in 91% yield. Thus, under slightly different conditions, cis-alcohol 10 can be used either to provide additional amount of trans-enone 11 or to form exclusively the corresponding ketone 12.

The thicketal groups of <u>11</u> and <u>12</u> were removed by treatment with W-2 Raney nickel (deactivated in refluxing acetone for 8 min.) in 98% ethanol. Under these conditions, <u>11</u> gave exclusively <u>trans- α -damascone</u> (<u>2</u>) in 56% yield whereas <u>12</u> afforded equal amounts of <u>2</u> and <u>3¹⁷</u> in a total yield of 64%. The ir, nmr, and mass spectra of the two α -damascones thus obtained were shown to be identical with those reported in the literature¹.





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References and Footnotes

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- 16. The isomerization most likely occurred prior to the oxidation since further treatment of $\underline{12}$ with manganese dioxide under the same conditions did not produce any detectable amount of $\underline{11}$.
- 17. At present we are unable to effect the desulfurization without partial isomerization of the double bond.