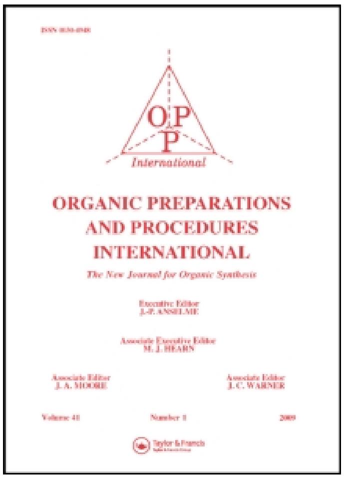

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A FACILE SYNTHESIS OF β-DAMASCONE

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A FACILE SYNTHESIS OF β-DAMASCONE

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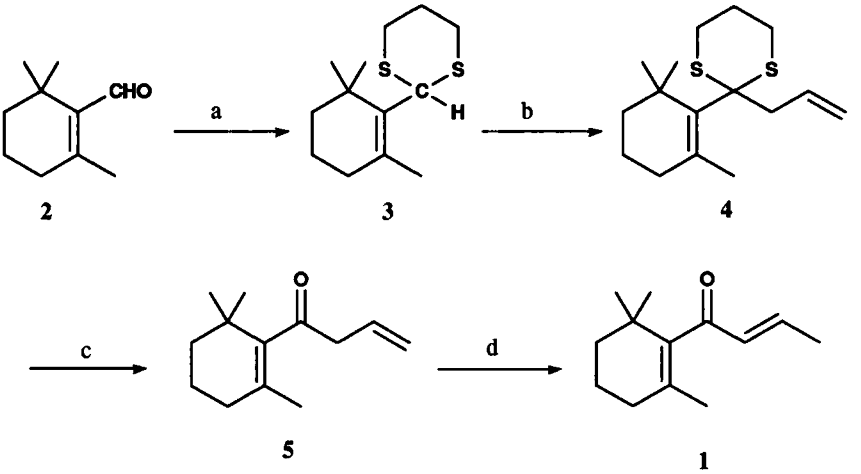
β-Damascone (1), an important naturally occurring carotenoid aroma compound detected as a neutral constituent of tobacco, tea and rose oils,[1,2] is now well known for its valuable fragrance and flavor properties. Much effort has been devoted on the synthesis of this compound and several syntheses have been reported.[3-10] Several of these routes used ketone 5 as a key intermediate,[3,5,9,10] which may be obtained from β-cyclocitral (2)[11] or a suitable derivative thereof with an organometallic reagent prepared from allyl bromide. We now describe a convenient preparation of 5 and a facile synthesis of β-damascone (1) using β-cyclocitral (2) as the starting material.

β-Cyclocitral (2) was converted to thioacetal 3 by reaction with 1,3-propanedithiol and BF_3•Et_2O in $CHCl_3$[12] in order to achieve *umpolung*[13] of the carbonyl group. Allylation of 3 with allyl bromide followed by deprotection of the resulting thioacetal 4 using $AgNO_3$[14] furnished the ketone 5 which was easily converted to β-damascone (1) by *p*-TsOH catalyzed rearrangement of the terminal double bond.



a) $HS(CH_2)_3SH$, BF_3•Et_2O b) *n*-BuLi, CH_2=$CHCH_2Br$
c) $AgNO_3$ d) *p*-TsOH, C_6H_6

EXPERIMENTAL SECTION

GC Analyses were performed on a Hewlett-Packard 5730A-3390A instrument. NMR ($CDCl_3$) spectra were obtained on a Hitachi R-600 or Bruker-WH-360 instrument. IR spectra were run on a Shimadzu-8101 FT-IR Spectrometer and MS were obtained using a Varian MAT 113 instrument.

"Usual workup" denotes extraction with ether, washing of the organic phase with saturated aq. NaCl solution, drying over anhydrous $MgSO_4$ and removal of solvent by distillation *in vacuo* using a rotary evaporator.

1,3,3-Trimethyl-2-(1',3'-dithiacyclohexyl)-cyclohex-2-ene (3).- The aldehyde **2** (3.80 g, 0.025 mol) in $CHCl_3$ (250 mL) was stirred with 1,3-propanedithiol (2.70 g, 0.025 mol) and $BF_3{\bullet}Et_2O$ at 0°. The reaction was followed by TLC until completion. The mixture was washed with KOH solution (7%, 50 mL) and with H_2O (50 mL). The usual workup and purification by column chromatography (silica gel, hexane) gave **3** as a pale yellow liquid (5.88 g, 97%, bp. 106-115°/0.5 Torr). IR(neat): 1665, 1385, 1365, 810 cm^{-1}, ^1H NMR: δ 1.20 (2s, 6H), 1.60 (s, 3H), 1.3-2.2 (br m, 8H), 2.75 (m, 4H), 4.7 (s, 1H), MS: 242 [M^+], 119.

Anal. Calcd for $C_{13}H_{22}S_2$: C,64.39; H, 9.14. Found: C, 64.21; H, 9.16

2-(2-Propenyl)-2-(2',2',6'-trimethylcyclohexenyl)-1,3-dithiane (4).- To a solution of the thioacetal **3** (2.90 g, 0.012 mol) in anhydrous THF (35 mL) under N_2 at -78°, *n*-BuLi (7.8 mL, 0.0125 mol, 1.6 N in hexane) was added, warmed to 5°, stirred for 1 hr and cooled to -78°. Allyl bromide (1.38 g, 0.0114 mol) was added and the mixture was stirred for 20 min at this temperature. The reaction was quenched by adding a saturated NH_4Cl solution (25 mL). The usual workup and a short path distillation of the residue at reduced pressure (bp. 120-134°/0.2 Torr) gave the thioacetal **4** (2.44 g, 72%). IR (neat): 3130, 1640, 990, 920 cm^{-1}, ^1H NMR: δ 1.15 (s, 6H), 1.56 (s, 3H), 1.3-2.2 (br m, 8H), 1.9 (d, 2H), 2.80 (m, 4H), 5.10 (br d, J = 18, 1H), 5.18 (br d, J = 11, 1H), 6.03 (m, 1H), MS: 282 [M^+], 158, 132, 123, 119, 41.

Anal. Calcd for $C_{16}H_{26}S_2$: C, 68.02; H, 9.27. Found: C, 67.85; H, 9.25

1-(2',2',6'-Trimethyl-1'-cyclohexenyl)-buten-1-one (5).- To a stirred solution of **4** (1.69 g, 0.0059 mol) in ether (750 mL) at -5°, a solution of $AgNO_3$ (2.04 g, 0.0120 mol) in H_2O (5 mL) was added. The reaction was stirred for 2 hrs at -5° and then was washed with aq. NH_4Cl. The usual workup and chromatography (silica gel, EtOAc:hexane, 1:39) gave the ketone **5** (1.11 g, 97%). ^1H NMR: 1.07 (s, 6H), 1.57 (s, 3H), 5.11 (br. d, J = 18, 1H), 5.18 (br. d, J = 11, 1H), 6.01 (m, 1H); MS: 192[M^+], 177, 151, 120, 81.

(E)-1-(2',2',6'-Trimethyl-1'-cyclohexenyl)-2-buten-1-one (β-Damascone) (1).- A mixture of the ketone **4** (0.90 g, 0.00468 mol) and *p*-toluenesulfonic acid (0.050 g) in dry benzene (15 mL) was refluxed for 3 hrs. Solvent was removed under reduced pressure and the residue was purified by column chromatography (silica gel, EtOAc:hexane, 1:39) to afford (E)-β-damascone (**1**) (0.81 g, 90%). UV (95%, EtOH): λ_{max} 227 (129000), 272 (2030) nm; IR (neat): 1670, 1640, 1620, 1440, 1370, 1360, 1280, 1230, 1160, 970, 930 cm^{-1}. ^1H NMR: δ 1.02 (s, 6H), 1.46 (m, 2H), 1.51 (s, 3H), 1.69 (m, 2H), 1.92 (dd, J = 7, 1.5, 3H), 1.99 (dd, J = 6, 6, 2H), 6.16 (br. d, J = 15, 1H), 6.73 (dq, J = 15, 7, 1H); MS: 192[M^+], 177, 135, 123, 107, 81, 69.

Anal. Calcd for $C_{13}H_{20}O$: C, 81.19; H, 10.48. Found: C, 81.22; H, 10.65

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