Tetrahedron Letters,Vol.27,No.42,pp 5135-5138,1986 0040-4039/86 $3.00 + .00
Printed in Great Britain Pergamon Journals Ltd.

SYNTHESIS WITH ORGANOBORANES. 2.[1]
SYNTHESIS OF α- AND γ-DAMASCONE[+]

Marek Zaidlewicz
Institute of Chemistry, Nicolas Copernicus University, 87-100 Torun, Poland

Abstract: Selective syntheses of α- and γ-damascone, using allylic organoboranes as the key intermediates, are described.

Damascones and closely related damascenones are important carotenoid aroma compounds. The isolation of β-damascenone from Bulgarian rose oil[2], stimulated a great interest in these compounds. Their occurrence and chemistry have been reviewed.[3-5] α-Damascone /6/[4-6] and γ-damascone /5/[4,5,7-13] have been prepared by various methods. Only recently, however, selective routes to 5 starting from readily available materials have been worked out.[10-13] In these preparations the exocyclic double bond formed via ylides and the side chain are introduced in separate steps.

The synthesis of 5 presented here is based on a new approach involving the addition of allylic organoborane 3 to crotonic aldehyde. The reaction proceeding with complete allylic rearrangement makes possible the formation of the exocyclic double bond and the side chain in one step. The key intermediate 3 is obtained via metalation of 1,3,3-trimethyl-1-cyclohexene /2/ following the general procedure described earlier.[1] This synthesis provides a short selective access to 5 in overall 18 % yield from 3-methyl-2-cyclohexenone /1/. None of its seven steps requires separation of mixtures. Acid catalyzed isomerization of 5 affords 6 in 87 % yield. Consequently, both 5 and 6 can be prepared starting from the same precursors. The approach also demonstrates the synthetic potential of dialkylallylicboranes as useful intermediates for the acylation of olefins.

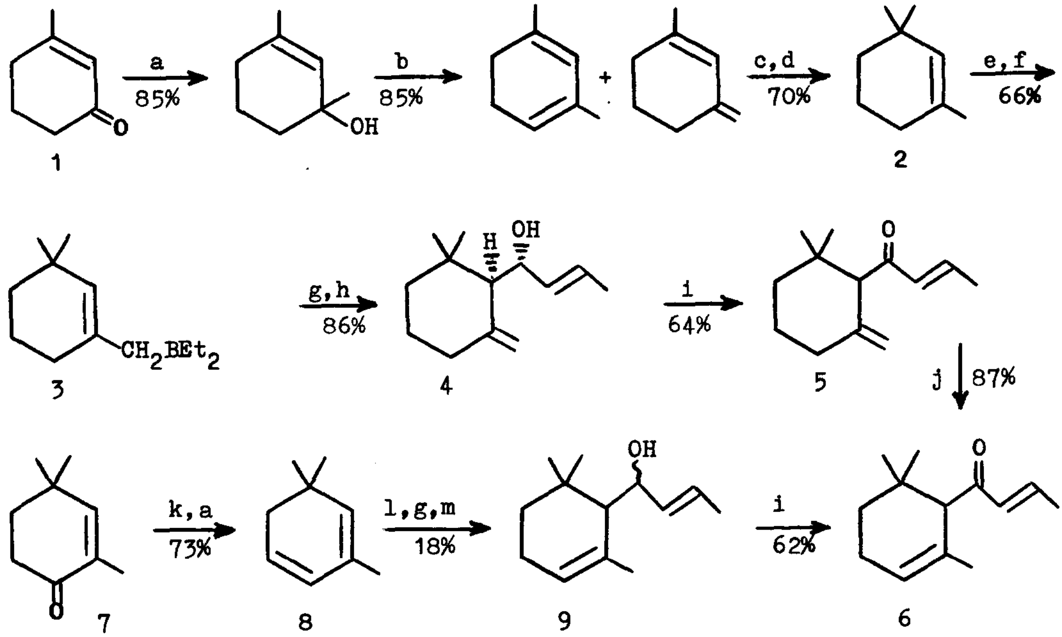
The starting ketone 1 was transformed into 2[14] according to the modified literature procedure[15]/Scheme/. The metalation of 2 with trimethylsilylmethylpotassium in cyclohexane using 100 % excess of the olefin proceeded in low yield. Fortunately, carring out the metalation reaction in neat 2, the organoborane 3 was obtained in 66 % yield. The unreacted olefin was recovered

---

[+] Dedicated to Professor George Zweifel on the occasion of his 60th birthday.

by pumping it off from the solid organopotassium compound. Consequently, no solvent is required for the metalation and the olefin can be readily recycled.

Scheme



Reagents: /a/ MeLi, Et_2O; /b/ $KHSO_4$; /c/ HCl, 0°C; /d/ MeMgBr, Et_2O; /e/ KCH_2SiMe_3; /f/ $ClBEt_2$, Et_2O; /g/ $OHCCH{=}CHCH_3$, Et_2O; /h/ aq. NaOH; /i/ PDC, DMF; /j/ TsOH, C_6H_6; /k/ $TsNHNH_2$, EtOH; /l/ 9-BBN, THF; /m/ $HOCH_2CH_2NH_2$, Et_2O.

The addition of 2 to crotonic aldehyde was highly stereoselective giving exclusively one diastereomer as indicated by ^{13}C NMR. Diastereomeric γ-damascols show chemical shift differences of all carbon atoms and can be readily differentiated. The addition product was identified by ^1H NMR as 4. The spectrum showed a doublet, $\delta=1.65$ ppm, J=6.0 Hz, characteristic of this diastereomer.[7] The alcohol 4 was oxidized with pyridinium dichromate to give 5 which was isomerized to 6 by refluxing its solution in benzene containing a catalytic amount of p-toluenesulfonic acid for 5h. The physical constants, IR, MS, and ^1H NMR spectra of 5 and 6 were in agreement with the reported data for γ-damascone[7] and α-damascone,[16] respectively.

The latter ketone was also prepared starting from 2,4,4-trimethyl-2-cyclohexenone /7/[17] which was transformed into 3,5,5-trimethyl-1,3-cyclohexadiene /8/[18,19] by the reaction of its tosylhydrazone /mp. 114-115°C; Anal. calc. for $C_{16}H_{22}N_2O_2S$ /306.43/: C 62.72, H 7.24, N 9.14, S 10.46; found: C 62.50, H 7.38, N 9.25, S 10.36/ with methyllithium. Hydroboration of 8 with one equivalent of 9-BBN in THF was sluggish at room temperature and after 24h unreacted 9-BBN was still present in the mixture. The reaction was completed by refluxing the solution for 1h. The hydroboration product was used without isolation for the reaction with crotonic aldehyde. The alcohol 9 obtained in 18 % yield /diastereomeric composition not established/ was oxidized with pyridinium dichromate in DMF to give 6.

Following is the procedure for the synthesis of 5. Bis/trimethylsilylmethyl/mercury[20] /37.5 g, 0.1 mole/ was added to a mixture of 2 /248.5 g, 2.0 moles/ and potassium sand /8.2 g, 0.21 mole/ at 20 - 30°C under argon atmosphere. The mixture was stirred at room temperature for 48h. The olefin and TMS were pumped off at room temperature and the solid organopotassium compound was added to a solution of diethylchloroborane[21] /20.8 g, 0.2 mole/ in diethyl ether /200 ml/ at -78°C. After stirring for 3h at room temperature, the solids were filtered off and washed with ether. The organoborane 3 was isolated by distillation, 25.3 g, 66 %, bp. 46-47°C/0.01 mm Hg, n_D^{20}= 1.4570, ^{1}H NMR /80 MHz/, neat, δ , 0.91 /s, 6H, CH_3/, 0.91 /t, J= 6 Hz, CH_3/, 1.06 - 1.66 /m, 8H, CH_2/, 1.71 /m, 2H, $CH_2C=C$/, 1.95 /s, 2H, $BCH_2C=C$/, 4.94 /bs, 1H, CH=C/; Anal. calc. for $C_{13}H_{25}B$ /192.15/: B 5.63; found: B 5.56.

A solution of 3 /19.2 g, 0.1 mole/ in diethyl ether /20 ml/ was added to a solution of crotonic aldehyde /7.0 g, 0.1 mole/ in diethyl ether /80 ml/ at 0°C and the mixture was left for 2h at room temperature. Aqueous 3M sodium hydroxide /37 ml, 0.11 mole/ was added at 0°C. After 1h stirring at room temperature, the organic layer was separated and the aqueous layer was extracted with ether. The etheral solution was washed with water and dried over magnesium sulfate. Distillation gave 4, 16.7 g, 86 %, bp. 60-61°C/0.1 mm Hg, n_D^{20}= 1.4906, ^{13}C NMR /25.156 MHz/, $CDCl_3$, δ , 148.11 /s/, 135.47 /d/, 126.84 /d/, 112.80 /t/, 71.48 /d/, 59.72 /d/, 36.02 /t/, 34.50 /s/, 33.15 /t/, 29.15 /q/, 29.04 /q/, 23.14 /t/, 17.69 /q/.

PDC /14.1 g, 0.0375 mole/ was added to a solution of 4 /4.9 g, 0.025 mole/ in DMF /25 ml/ at 20-25°C and the mixture was stirred for 5h. Water /200 ml/ was added and the product was extracted with n-pentane. The extracts were washed with water and dried over magnesium sulfate. Distillation gave 5, 3.1 g, 64 %, bp. 58-60°C/0.1 mm Hg, n_D^{20}= 1.4940.

Acknowledgement. Financial support of this work by the Polish Academy of Sciences under the project MR.I.12 is acknowledged.

References and Notes

1. M.Zaidlewicz, J.Organometal.Chem., 293, 139 /1985/.
2. E.Demole, P.Enggist, U.Sauberli, M.Stoll and E.sz.Kovats, Helv.Chim.Acta, 53, 541 /1970/.
3. G.Ohloff in "Progress in the Chemistry of Organic Natural Products", Ed., W.Herz, H.Grisenbach and G.W.Kirby, Vol.35, Springer, Wien, 1978, p.431.
4. W.Hoffmann, Seifen, Öle, Fette, Wachse, 104, 127 /1978/.
5. S.Torii, K.Uneyama and T.Inokuchi, Koryo, 125, 47 /1979/; Chem.Abstr., 93, 8292n /1980/.
6. Recent reports: T.Mandai, K.Mizobuchi, M.Kawada and J.Otera, J.Org.Chem., 49, 3403 /1984/; R.L.Snowden, B.L.Muller and K.H.Schulte-Elte, Tetrahedron Lett., 335 /1982/; H.J.Liu, H.K.Hung, G.L.Mhehe and M.L.D.Weinberg, Can.J. Chem., 56, 1368 /1978/; M.Kasano and Y.Matsubara, Kinki Daigaku Rikogakubu Kenkyu Hokohu, 13, 37 /1978/; Chem.Abstr., 89, 163794p /1978/; Y.Arai, T.Miyakoshi, H.Ohmichi and S.Saito, Koen Yashishu-Koryo, Terupen oyobi Seiyu Kagaku ni kansuru Toronkai 23rd, 153 /1979/; Chem.Abstr., 93, 26571g /1980/.
7. K.H.Schulte-Elte, V.Rautenstrauch and G.Ohloff, Helv.Chim.Acta, 54, 1805 /1971/.
8. K.H.Schulte-Elte, B.L.Muller and G.Ohloff, Helv.Chim.Acta, 56, 310 /1973/.
9. F.Näf and A.Decorzant, Helv.Chim.Acta, 57, 1317 /1974/.
10. O.Takazawa, K.Saigo, K.Narasaka and T.Mukayama, Chem.Lett., 757 /1977/.
11. T.Mukayama, K.Saigo and O.Takazawa, Jpn.Patent, 34751 /1978/.
12. S.Saito and N.Ito, Jpn.Patent, 40633 /1981/.
13. N.Ito, T.Miyakoshi, H.Ohmichi and S.Saito, Koen Yoshishu-Koryo, Terupen oyobi Seiyu Kagaku ni kansuru Toronkai 23rd, 150 /1979/; Chem.Abstr., 93, 132631m /1980/.
14. Bp.137-138°C, n_D^{20}=1.4500 /lit.[15] bp.137°C, n_D^{20}=1.4580/; ^{1}H NMR /80 MHz/, CDCl$_3$, δ, 0.91 /s, 6H, CH$_3$/, 1.59 /m, 3H, CH$_3$/, 1.25-1.87 /m, 6H, CH$_2$/, 5.11 /m, 1H, C=CH/; ^{13}C NMR /25.156 MHz/, CDCl$_3$, δ, 132.18 /d/, 131.39 /s/, 37.33 /t/, 31.69 /s/, 30.20 /t/, 30.20 /q/, 23.85 /q/, 20.16 /t/.
15. R.Ya.Levina, V.K.Daukshas and T.P.Surikova, Zhur.Obshch.Khim., 30, 2145 /1960/.
16. G.Ohloff and G.Uhde, Helv.Chim.Acta, 55, 531 /1970/.
17. H.A.Smith, B.J.L.Huff, W.J.Powers III and D.Caine, J.Org.Chem., 32, 2851 /1967/.
18. Bp.132-133°C, n_D^{20}=1.4592 /lit.[19] bp.133.3-133.4°C/750 mm Hg, n_D^{20}=1.4608/, ^{1}H NMR and MS spectra in agreement with the reported data.[22]
19. H.Pines and R.H.Kozlowski, J.Am.Chem.Soc., 78, 3776 /1956/.
20. D.Seyferth and W.Freyer, J.Org.Chem., 26, 2604 /1961/.
21. R.Köster, Inorg.Synth., 15, 149 /1974/.
22. C.Arnoud and J.Huet, Bull.Soc.Chim.Fr., 4170 /1972/.

(Received in UK 14 August 1986)