A New Synthesis of (-)-Furodysin

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Abstract. A synthesis of furodysin from trans-limonene oxide involves transformation into the phenylcarbamate of 2,8-menthadien-1-ol, allylic displacement with lithium di-(β-furylmethyl)cuprate, and cyclization.

A number of furanosesquiterpenes occur in marine invertebrates.1 Interestingly, furodysin and furodysinin have been elaborated in both enantiomeric forms, e.g., the (+)-isomers by an Australian variety of sponges Dysidea herbacea2 and the (-)-isomers by those collected in Fiji3 and by the Mediterranean species D. tupha.4 These metabolites show significant antiparasitic activities.

The synthesis of (-)-furodysin 1 and (-)-furodysinin 2 has been accomplished starting from (+)-9-bromocamphor,5 and also their racemates obtained from a longer route.6 Here we wish to report a convenient approach to furodysin from trans-limonene oxide 3.

Reaction of 3 with dimethylamine (40% aqueous solution) in a sealed vessel at 150°C gave the amino alcohol 47 which was converted into the N-oxide with 30% hydrogen peroxide and then pyrolyzed to afford trans-p-2,8-menthadien-1-ol 58 in an overall 44% yield. We planned to effect an SN2' displacement of the allylic alcohol with a furfurylmethyl substituent on the same side as the oxygen functionality which is cis to the isopropenyl group at C-4. Previous experience9 indicated that allylic carbamates undergo syn-selective SN2' reactions with cuprate reagents therefore the N-phenylcarbamate 6 was prepared (77% yield) by a DMAP-catalyzed reaction of 5 with phenyl isocyanate with the intention of using it in such a reaction. Toward this
end, the reaction of 6 with lithium di-(β-furylmethyl)cuprate furnished compound 7 (91% yield) whose spectral data is in total agreement with those reported. The final cyclization to culminate in a furodysin synthesis was effected following the established protocol of mercuration, trapping, and reduction.

**Some Physical data:**

5: \[\alpha\]_D +63.9° (c=0.325 CHCl₃). δ_H (300 MHz, CDCl₃) 1.29 (3H, s), 1.4-1.65 (4H, m), 1.73 (3H, s), 1.8-1.85 (4H, m), 2.65 (1H, m), 4.73 (1H, s), 4.77 (1H, s), 5.66 (1H, d, J 11 Hz), 5.68 (1H, d, J 11 Hz). δ_C (75 MHz, CDCl₃) 20.83, 24.85, 29.37, 36.68, 43.41, 67.45, 110.57, 132.13, 133.88, 148.13.

6: mp 57-59°C. \[\alpha\]_D -55° (c=0.369 CHCl₃). M+ 271.1577. ν 3375, 1685 cm⁻¹. δ_H 1.5-1.8 (3H, m), 1.62 (3H, s), 1.70 (3H, s), 2.18 (1H, m), 2.20 (1H, m), 2.68 (1H, m), 4.74 (2H, s), 5.72 (1H, dd, J 9, 2 Hz), 6.16 (1H, d, J 9 Hz). 6.43 (1H, br.), 6.98 (1H, m). 7.2-7.35 (4H, m). δ_C 20.56, 24.20, 26.13, 35.22, 43.38, 77.73, 110.74, 118.43, 122.92, 128.83, 130.61, 133.55, 138.22, 147.83, 152.70.

7: \[\alpha\]_D +300° (c=0.092 CHCl₃). δ_H 1.62 (3H, s), 1.70 (3H, s), 4.70 (1H, s), 4.87 (1H, s), 5.38 (1H, m), 6.23 (1H, d, J 1.5 Hz). 7.16 (1H,d, J 0.9 Hz). 7.33 (1H, dd, J 1.5, 0.9 Hz). δ_C 22.46, 22.81, 23.54, 25.93, 30.76, 36.79, 43.79, 110.13, 111.50, 123.83, 124.93, 133.88, 139.41, 142.47, 147.66.

2: \[\alpha\]_D -40° (c=0.116 CHCl₃). δ_H 1.25 (3H, s), 1.27 (3H, s), 1.66 (3H, s), 2.19 (1H, m), 2.56 (2H, m), 5.60 (1H, m), 6.10 (1H, d, J 2 Hz), 7.23 (1H, d, J 2 Hz). δ_C 19.51, 23.21, 23.77, 27.29, 30.73, 31.58, 31.72, 34.51, 45.59, 109.78, 112.95, 126.39, 133.11, 140.40, 156.77.

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**References**


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