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THE PREPARATION OF ACYLACETYLENIC DERIVATIVES OF α-CYCLOCITRAL ON ROUTE TO PHYSIOLOGICALLY ACTIVE TERPENES

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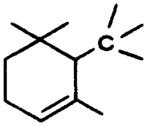
In connection with a program[1] directed toward the synthesis of physiologically active terpenes having a partial structure such as 1, we found ourselves in the need of an highly specific method for the preparation of acetylenic ketones such as 2a and 2b starting from the readily available α-cyclocitral[2] 3.



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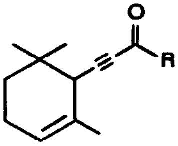
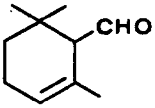


2a R = CH_3
2b R = OEt



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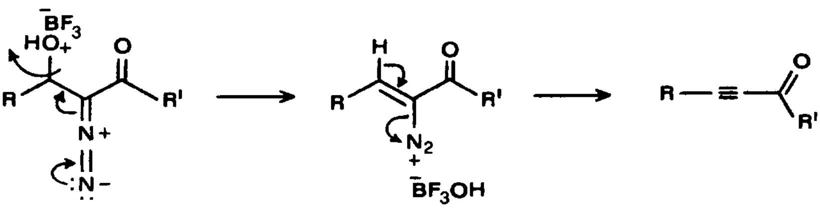
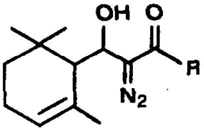
In this connection a new procedure for the preparation of acylacetylenes by treatment of α-diazo-β-hydroxycarbonyl compounds with $BF_3 \cdot Et_2O$ became of interest[3]. In this process[4] molecular nitrogen is evolved involving neighbouring group participation as illustrated in the following equation:

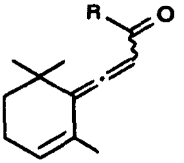


This procedure, which in spite of its high potential of applicability has not yet been exploited, was especially attractive for the solution of our synthetic goal.

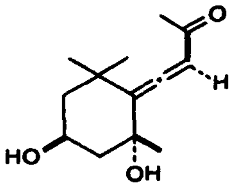
The starting α-diazo-β-hydroxycarbonyl derivatives 4a and 4b were prepared in high yields by the reaction of α-cyclocitral with diazo(lithio)acetone and ethyldiazo(lithio)acetate[5] respectively.



4a R = CH_3
4b R = OEt



5a R = CH_3
5b R = OEt



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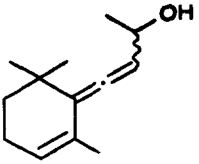
When 4a was treated with $BF_3 \cdot Et_2O$ in acetonitrile at -10°C for 20 min, 7,8-dehydro-α-ionone 2a [δ: 1.00, 1.05 (each s, Me), 1.78 (m, Me), 2.22 (s, $COCH_3$), 2.68 (m, C_1-H), 5.40 (m, olefinic H); ν_{max}: 2190, 1670][6] was obtained in quantitative yield. In an analogous manner ethyl-2,6,6-trimethylcyclohex-2-enyl propynoate 2b was obtained in 70% yield when 4b was treated with $BF_3 \cdot Et_2O$ in acetonitrile at 0°C for 16 hr [δ: 1.00, 1.06 (each s, Me), 1.27 (J = 7cps, t, $CH_2\underline{CH_3}$), 1.80 (m, Me), 2.65 (m, C_1-H), 4.10 (J = 7cps, q, $\underline{CH_2}CH_3$), 5.38 (m, olefinic H); ν_{max}: 2230, 1700].

Acetylenic ketones 2a and 2b are useful intermediates on route to a variety of natural compounds. Thus, when 2a was treated with sodium ethoxyde in ethanol at r.t. for 3 hr, 6,7-dehydro-α-ionone 5a, an interesting model on route to allenic natural products such as grasshoppher ketone 6[7], was obtained in 72%yield [δ: 1.12, 1.15 (each s, Me), 1.75 (m, Me), 2.11 (s, $COCH_3$), 5.65 (m, olefinic H), 5.90 (m, allenic H); ν_{max}: 1910, 1670].



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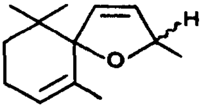

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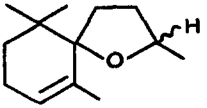

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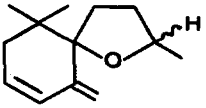

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The reduction of 5a with $LiAlH_4$ in Et_2O at 0°C for 30 min led quantitatively to 6,7-dehydro-α-ionol 7[9b].

Allenol 7 is easily transformed by acid treatment (e.g. PPA in petroleum ether for 2 hr) in 2,6,10,10-tetramethyl-1-oxaspiro[4.5]deca-3,5-diene 8[9b], a key intermediate in the synthesis of theaspiranes 9[8a-c], components of tea leaves, and of vetispiranes 10[9a,b], important aroma components of vanilla.

Finally, allenic ester 5b [δ: 1.07, 1.11 (each s, Me), 1.25 (J = 7.5 cps, t, $CH_2\underline{CH_3}$), 1.78 (m, Me), 4.10 (J = 7.5cps, q, $\underline{CH_2}CH_3$), 5.57 (m, olefinic H), 5.68 (m, allenic H); ν_{max}: 1290, 1710] was obtained quantitatively by fast elution with n-hexane of 2b through an Al_2O_3 packed chromatography column[10].

Further synthetic applications of the compounds above described will be reported in due course.

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5. 4a and 4b were obtained with the best yields (71 and 74% respectively) when lithium diisopropylamide was added to a mixture of α-cyclocitral 1

and diazo(lithio)acetone or ethyldiazo(lithio)acetate, respectively, in THF at -78°C. For the preparation of diazo(lithio)carbonyl compounds see: U.Schollkopf and H.Frasnelli, Angew. Chem., 82, 291 (1970); E.Wenkert and C.A.Mc Pherson, J. Amer. Chem. Soc., 94, 8084 (1972); R.Pellicciari and B.Natalini, J. Chem. Soc. Perkin I, 1977, 1822.

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