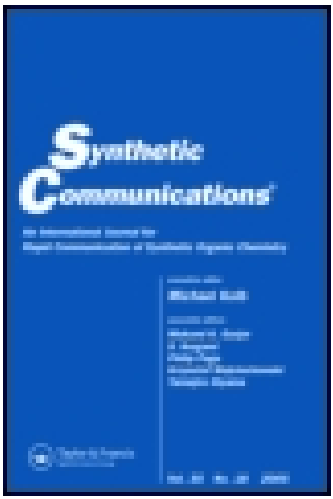

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A New Access to "Iso"-beta-ionone from Delta-Pyronene

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A NEW ACCESS TO "ISO"-BETA-IONONE FROM DELTA-PYRONENE

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Abstract : New uses of delta-pyronene as an intermediate to terpenic synthesis have been studied. In particular, we proposed a new way to "iso"-beta-ionone from delta-pyronene.

We recently reported[1] that delta-pyronene **3** could easily be obtained from myrcene **2**, an available raw material from beta-pinene **1**, which is itself a constituent of turpentine (Scheme 1).

Preliminary work[2] concerning the reactivity of delta-pyronene **3** showed that, via its mono-epoxide **4**, this compound is an interesting intermediate in the synthesis of beta-cyclocitral **5** and beta-ionone **6** (Scheme 2).

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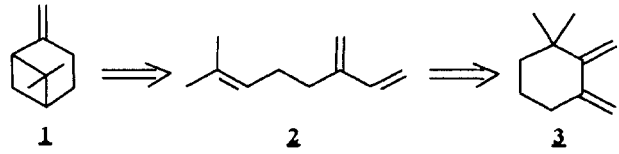
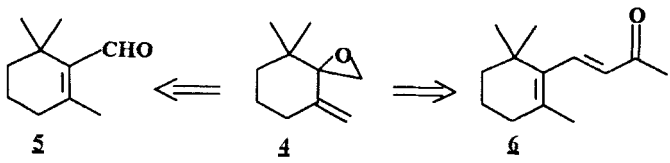


Scheme 1



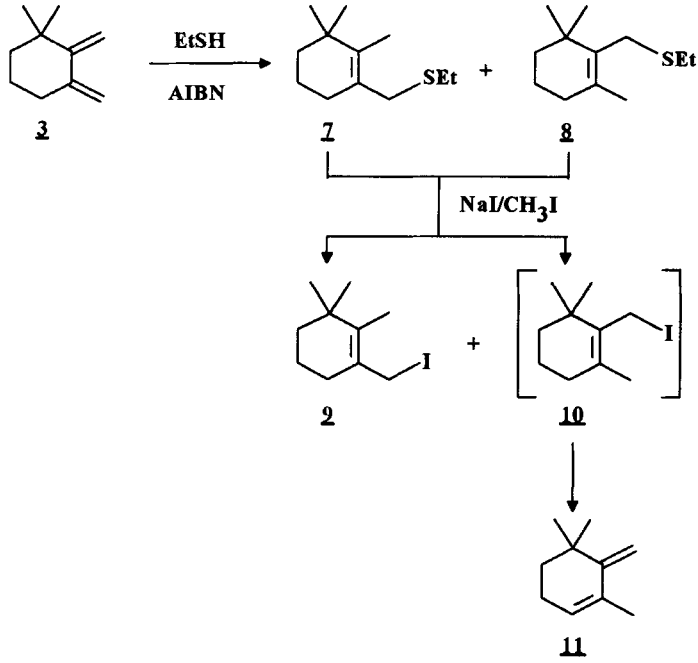
Scheme 2

The latter two are key compounds of industrial interest for the manufacture of perfumes, vitamin A and other retinoids[3-6].

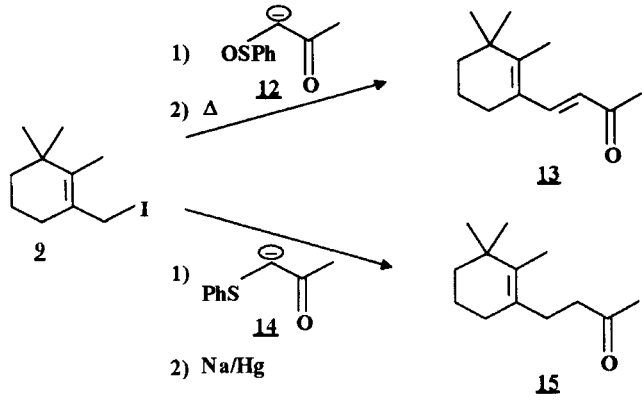
In this paper, we propose other potential applications for delta-pyronene in order to obtain new terpenic compounds with a cyclogeranyl skeleton.

The reaction of delta-pyronene **3** with ethanethiol[7] in the presence of AIBN thus produces a 60/40 mixture of allylic sulfides **7** and **8**, resulting from 1,4-addition reactions on the dienic system. The yield of this reaction is 95% (Scheme 3).

Treatment of the major allylic sulfide **7** with NaI/CH_3I in an acetonitrile solution[8] quantitatively gives the iodide derivative **9** with 80% yield of isolated product after silica gel chromatography This iodide derivative **9** may be used in alkylation reactions with C_3 units in order to obtain new cyclogeranyl derivatives with a C_{13} skeleton (Scheme 4).



Scheme 3



Scheme 4

Homologation with the anion of keto-sulfoxide **12** followed by a 50°C elevation of the temperature led to the α,β-unsaturated ketone **13**, isomer of the beta-ionone **6** with a 72% yield. The major interest of this synthetic route is the possible direct obtention of "iso"-beta-ionone **13** from delta-pyronene (with an overall yield of 35%) without isolating either the allylic sulfide **7** or the iodide derivative **9**. We have noticed indeed that the other iodide isomer **10**, expected from substitution of allylic sulfide **8**, underwent an elimination reaction leading to gamma-pyronene **11**. This hydrocarbon compound was easily extracted from the crude reaction mixture by evaporation under reduced pressure.

In a similar alkylation reaction, we realised the homologation of iodide derivative **9** with the anion of keto-sulfide **14**, followed by a desulfurization of the intermediate adduct with an Na/Hg amalgam. We obtained the "iso"-dihydrobeta-ionone **15**, isomer of the dihydrobeta-ionone with an overall yield of 32%.

Regarding the reactivities of delta-pyronene derivatives for the preparation of new terpenic compounds with a cyclogeranyl skeleton further work is in progress.

Experimental section

The keto-sulfide **14** is prepared from chloracetone by the method described by S. Warren[9]. Its oxidation with sodium metaperiodate in $MeOH/H_2O$ solution yields quantitatively the keto-sulfoxide **12**.

Addition of ethanethiol to δ-pyronene. A mixture of 4.08 g (30 mmoles) of δ-pyronene, 500 mg of AIBN, and 4.4 ml (60 mmoles) of ethanethiol was heated, under N_2, at 50°C for 5 h. After cooling, the mixture was diluted

with ether, washed with 1 N NaOH solution and water and dried over $MgSO_4$. Removal of solvent gave 5.645 g (95%) of a 60/40 mixture of sulfides 7 and 8.

7 : ^{1}H NMR ($CDCl_3$, 250 MHz) δ 1.00 (s,6H), 1.25 (t,3H), 1.65 (s,3H), 2.47 (q,2H), 3.14 (s,2H); ^{13}C NMR ($CDCl_3$, 62.5 MHz) δ 13.4 (q), 15.0 (q), 19.4 (t), 25.6 (t), 28.0 (2q), 29.7 (t), 34.9 (s), 35.1 (t), 39.5 (t), 126.3 (s), 137.2 (s).

8 : ^{1}H NMR ($CDCl_3$, 250 MHz) δ 1.06 (s,6H), 1.28 (t,3H), 1.73 (s,3H), 2.55 (q,2H), 3.20 (s,2H); ^{13}C NMR ($CDCl_3$, 62.5 MHz) δ 14.8 (q), 19.3 (t), 20.2 (q), 27.7 (t), 28.7 (2q), 30.6 (t), 32.8 (t), 34.6 (s), 39.5 (t), 131.9 (s), 133.3 (s).

Conversion of sulfide 7 to iodide derivative 9. 523 mg (2.6 mmoles) of sulfide 7 was stirred with 4 ml of methyl iodide and 530 mg of sodium iodide in 3 ml of acetonitrile for 3 h. After removal of solvent, the mixture was filtered and washed with CCl_4. The solvent was evaporated and the residu was chromatographed on silica gel with petroleum ether to give 550 mg (80%) of iodide derivative 9.

9 : ^{1}H NMR ($CDCl_3$, 250 MHz) δ 1.06 (s,6H), 1.75 (s,3H), 2.31 (t, 2H), 3.50 (s, 2H); ^{13}C NMR ($CDCl_3$, 62.5 MHz) δ 15.2 (q), 19.6 (t), 28.1 (2q), 32.5 (t), 35.5 (s), 39.5 (t), 58.7 (t), 124.6 (s), 142.7 (s).

Synthesis of "iso"-beta-ionone 13. 1.346 g (7.4 mmoles) of keto-sulfoxide 12 in 8 ml dry THF was added dropwise to 150 mg (6 mmoles) sodium hydride suspended in 23 ml THF by vigorous stirring at room temperature, under N_2. There was a rapid evolution of hydrogen to give the yellow anion. 1.573 g (6 mmoles) of iodide derivative 9 was syringed in and stirring

continued for 4 h, ammonium chloride solution added and the aqueous layer extracted with chloroform. The organic fractions were dried ($MgSO_4$) and evaporated. The crude product was then dissolved in 25 ml CCl_4 and heated to reflux for 4 h. The reaction mixture was concentrated in vacuo and chromatographed on Al_2O_3 (6% H_2O) to yield 830 mg (72%) of "iso"beta-ionone **13**.

13 : IR ν (cm^{-1}) 1660 (C=O); ^1H NMR ($CDCl_3$, 250 MHz) δ 1.00 (s, 6H), 1.84 (s, 3H), 2.22 (s, 3H), 6.03 (m, 1H), 7.63 (m, 1H); ^{13}C NMR ($CDCl_3$, 62.5 MHz) δ 14.2 (q), 18.7 (t), 26.2 (t), 27.5 (q), 27.7 (2q), 36.3 (s), 38.7 (t), 125.0 (d), 127.2 (s), 142.4(d), 151.3(s), 199.1(s).

Synthesis of "iso"-dihydrobeta-ionone 15. In a similar manner we realised the alkylation of keto-sulfide **14** (800 mg; 4.31 mmoles) with the iodide derivative **9** (1.016g; 4.81 mmoles) to afford 850 mg (73%) of alkylated product. This compound was then added, under N_2, to a mixture of 4.5 g pulverized 6% sodium amalgam and 2.976 g anhydrous disodium hydrogen phosphate in 60 ml dry methanol at O°C. The solution was stirred for 1 h, poured into an ammonium chloride solution and extracted with chloroform. After usual work-up the crude product was chromatographed on Al_2O_3 (6% H_2O) to give 437 mg (80%) of pure "iso"-dihydrobeta-ionone **15**.

15 : IR ν (cm^{-1}) 1713 (C=O); ^1H NMR ($CDCl_3$, 250 MHz) δ 0.87 (s, 6H), 1.56 (s, 3H), 2.13 (s, 3H); ^{13}C NMR ($CDCl_3$, 62.5 MHz) δ 13.0 (q), 19.5 (t), 28.0 (2q), 28.3 (t), 29.9 (q), 30.4 (t), 34.4 (s), 39.5 (t), 42.2 (t), 128.3 (s), 134.3 (s), 209.1 (s).

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