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A NOVEL C_{10} TERPENE SYNTHON : 2-METHYL-6-METHYLENE-1,3E,7-OCTATRIENE

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Summary :

The reaction of a hydroxylated base with 3-chloro-2-methyl-6-methylene 1,7-octadiene in the presence of a palladium complex and a quaternary ammonium salt gives a novel tetraene : 2-methyl-6-methylene-1,3E,7-octatriene, which is a new C_{10} terpene synthon. A novel access to pseudo-ionone is also described.

Polyisoprene chains are found in many natural products, such as Vitamins E, A and carotenoids [1]. Acyclic C_{10} components have proved to be very valuable building blocks for the construction of polyisoprene chains. For example 3,7-dimethyl-1,3E,5E,7-octatetraene [2] and 3,7-dimethyl-2,6 octadienyl-1-phenyl sulfone [3] in the sulfone series, or (3,7-dimethyl-2,6-octadienyl) triphenyl phosphonium bromide [4] and methyl-4,8-dimethyl-3,7-nonadieneoate [5].

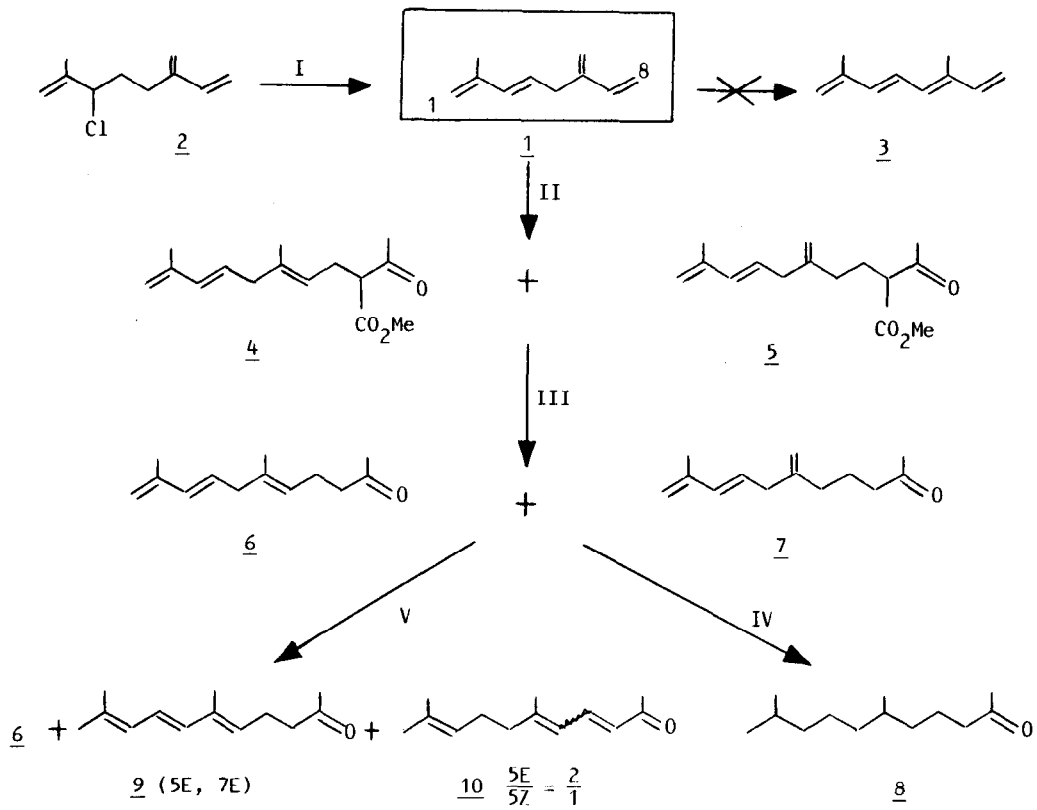
In this paper we describe the synthesis and the use of a novel C_{10} terpene synthon : 2-methyl-6-methylene-1,3E,7-octatriene 1 [6]. The tetraene 1 is prepared by dehydrochlorination of 3-chloro-2-methyl-6-methylene-1,7-octadiene 2 [7].

The use of classical elimination reagents was unsuccessful. However, the use of complexes of palladium [8] or molybdenum [9] in the presence of a base resulted in the required reaction. This dehydrochlorination was readily accomplished by the action of a hydroxylated base on 2 in the presence of a palladium complex ($[^3\mu C_3H_5PdCl]_2$, $Pd(TPP)_4$ or $Pd(dba)_2$) and a quaternary ammonium salt (Et_3NHCl, $n\text{-}Bu_4NCl$) in a solvent such as THF at 20°C. Isomerisation to cosmene 3 was not observed under these operating conditions.[13]

The interesting compound 1 can be selectively condensed with methyl acetylacetate, catalyzed by the water-soluble rhodium / tris-(sodium-3-sulfophenyl) phosphine (TPPTS) [10]. A mixture of compounds 4 and 5 (ratio 45/55) was isolated in 90 % yield. Since the catalyst is water-soluble, it is easily separated from the organic layer and can be recycled without any loss of activity. Saponification of 4 and 5 gives compounds 6 and 7 in quantitative yield [11] [12].

The action of methylacetylacetate on 1 is highly regioselective : exclusive attack at position 8 is observed. This regioselectivity was confirmed by ^{13}C N.M.R. analysis of the products of hydrogenation of 6 and 7 (H_2 - Pd / C - MeOH). Ketone 8 was the sole product [12].

Isomerisation of the mixture of 6 and 7 with catalytic quantities of rhodium complexes [$RhCl(TPP)_3$, $RhH(CO)(TPP)_3$] gives a mixture of 6, 9 and 10 in wich the major product is pseudo ionone 10 [12].



I $[^{3}\mu C_3H_5PdCl]_2$-$P\emptyset_3$-NaOH-$(nBu)_4NCl$-THF-20 h-20°C - TT=95 % - RT=81 %

II $CH_3COCH_2CO_2Me$-$[RhCl(COD)]_2$-TPPTS-H_2O-MeOH-100°C- RT=90 % - 4 / 5 = 45 / 55

III NaOH - H_2O - 50°C - 2 h - RT ~ 85 %

IV H_2 - Pd / C - MeOH

V $RhH(CO)(TPP)_3$: 4 % W / W - $\emptyset CH_3$ - 24 h - 110°C [6-9-10 : 11,6 % - 20,5 % - 57,3 %]

SCHEME 1

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Preparation of tetraene 1 :

In a 250 ml round-bottomed flask was placed 11.98 g (200.5 mmol) of finely ground sodium hydroxide, 3.95 g (15.1 mmol) of triphenylphosphine, 2.76 g (9.9 mmol) of tetrabutylammonium chloride and 1.09 g (3 mmol) of $[3\mu C_3H_5PdCl]_2$. Air was replaced by argon, 100 ml THF and 53.26 g (312 mmol) of 3-chloro-2-methyl-6-methylene-1,7-octadiene were added and the reaction mixture stirred at 20°C for 20 h. 100 ml of water was added and the mixture was extracted three times with pentane. The organic layers were dried over magnesium sulphate. After filtration and evaporation of the solvent, 51.94 g of a yellow oil was obtained.

A g.c. analysis with internal standard showed :

- conversion of 2 : 94.6 %
- yield of 1 / 2 : 81.4 %

Distillation of the latter under reduced pressure gave 27.2 g of a clear oil containing 93.3 % of 2-methyl-6-methylene-1,3,7-octatriene. b.p. = 54°C / 9 mmHg (60 % yield).

References and Notes :

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[4] J.D. SURMATIS and A. OFNER, J. Org. Chem., 28, 2735, 1963.

[5] G. MIGNANI and D. MOREL, Rhône-Poulenc - EP 145,555 (19.06.85).

[6] a) For experimental details see G. MIGNANI and D. MOREL, Rhône-Poulenc EP 152,324 (21.08.85).
b) 1 : ^{1}H-NMR (360 MHz, $CDCl_3$, Sppm) :
1.78 (S) ; 2.96 (d-J=7 Hz) ; 4.83 [S - H(1)] ; 4.96 and 5.00 [m-CH_2=(6)] ; 5.02 [d-J=10 Hz - H(8)] ; 5.19 [d-J=17,5 Hz - H(8)] ; 5.65 [dt-J=15 Hz and J=7 Hz - H(4)] ; 6.13 [d-H(3)] ; 6.35 [dd - H(7)]
I.R. (neat, cm^{-1}) : 3080, 2920, 1680, 1600, 990, 970, 895.
M.S. [m/z (%)] : 134(23), 119(44), 105(27), 93(31), 92(37), 91(67), 79(100), 78(18), 77(28), 53(14), 41(23), 39(15).
U.V. (EtOH) : λ_{max} = 224 nm ($\log \varepsilon$ = 4.56)

[7] RHONE-POULENC - EP 145,554 (19.06.85) for synthesis of 2.

[8] a) J. TSUJI, T. TAMAKAWA, M. KAITO and T. MANDAI, Tetrahedron Letters, 19(24), 2075 (1978).

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[9] B. TROST, M. LAUTENS and B. PETERSON, Tetrahedron Letters, 24, 4525 (1983).

[10] For other reactions of this type see : RHONE-POULENC - EP 44,711 (11.05.81).

[11] O.P. VIG. B. RAM, U. RANI and J. KAUR, Indian. J. Chem., 12 68 (1974).

[12] The stereochemistry will be discussed in the full paper. All new compounds have given a satisfactory analytical and spectrochemical (^{1}H, ^{13}C NMR, I.R., Mass) data wich will be described with the experimental details in the full paper.

6 : ^{1}H-NMR (360 MHz, $DCCl_3$, ppm, TMS)

1.54 (S) ; 1.77 (S) ; 2.07 (S) ; 2.21 (dt-J = 7 Hz) ;
2.41 [t-J = 7 Hz] ; 2.68 [d-J = 7 Hz] ; 4.82 and 4.83 (S) ;
5.05 [t-J = 7 Hz] ; 5.53 [dt-J = 15 Hz and J = 7 Hz] ;
6.06 [d-J = 15 Hz].

IR (Neat, cm^{-1}) : 3080, 2930, 1715, 1640, 1610, 970, 895.

7 : ^{1}H-NMR (360 MHz, $CDCl_3$, ppm)

1.66 (m) ; 1.78 (S) ; 1.96 [t-J = 7 Hz] ; 2.07 (S) ;
2.37 [t-J = 7 Hz] ; 2.73 [d-t = 7 Hz] ; 4.70 and 4.72 (S) ;
4.82 and 4.83 (S) ; 5.57 [dt-J = 15 Hz and J = 7 Hz] ;
6.09 [d-J = 15 Hz].

I.R. (neat, cm^{-1}) 3080, 2930, 1715, 1640, 1610, 970, 895.

8 : ^{13}C-NMR (90 MHz, $CDCl_3$, ppm)

19.4 (q) ; 21.4 (t) ; 22.4 (q) ; 22.5 (q) ; 24.6 (t) ;
27.9 (d) ; 29.5 (q) ; 32.6 (d) ; 36.5 (t) ; 37.1 (t) ;
39.3 (t) ; 44.0 (t) ; 208.3 (S)

9 : ^{1}H-NMR (360 MhZ, $CDCl_3$, ppm)

1.72 (S) ; 1.73 (S) ; 2.08 (S) ; 2.34 [dt-J = 7 Hz] ;
2.45 [t-J = 7 Hz] ; 5.31 [t-J = 7 Hz] ; 5.79 [d-J = 10.5 Hz] ;
6.03 [d-t = 15 Hz] ; 6.27 [d-J = 10.5 Hz and J = 15 Hz].

[13] No absorption in U.V. at 317nm. corresponding to 3. See J. APSIMON " The Total Synthesis of Natural Product " Vol 2, p. 14. J. WILEY Intersciences 1973.

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