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REDUCTIVE COUPLING OF α,β UNSATURATED KETONES III[+]
(+)-PULEGONE : AN EXAMPLE OF UMPOLUNG

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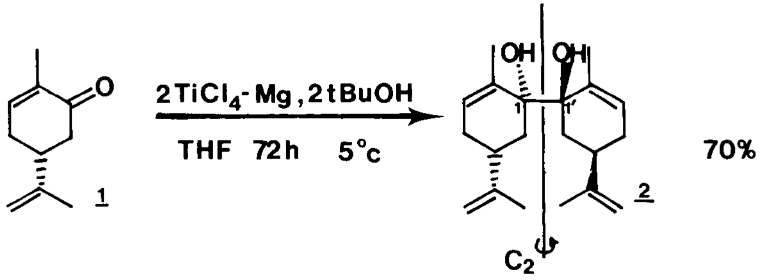
Summary :

Treatment of (+)-pulegone with $TiCl_4$-Mg/THF complex unexpectedly yields a) menthone (when the reaction is carried out with t-butyl alcohol),b) allylmenthadienes (when it is carried out with allylic halides), c) ketol dimers (when no additive electrophilic species is used); a bielectronic transfer mechanism, leading to an umpolung on (+)-pulegone is proposed as an explanation for the formation and the structure of the products.

For about 15 years the chemistry of low-valent Ti complexes has received great attention (1) and now many of the reactions involving them are commonly used in synthesis (2). Our current work has been focused on the reductive duplication of α- β unsaturated ketones by the low-valent Ti(II) complex we prepare by reduction of 1 equivalent of $TiCl_4$ by 1 equivalent of Mg in THF. We have been able to show that enones, with reduction potential minor to -1.90 V _vs_ sce (3), lead to symmetric dimers (trienes and/or allylic diols) (4) ; the formation of which involving the well-known coupling of two identical radical anions (5). For example (-)-carvone _1_ leads after 72 h. at 5°C. (6) to the diol _2_ with a yield of 70 % (7).



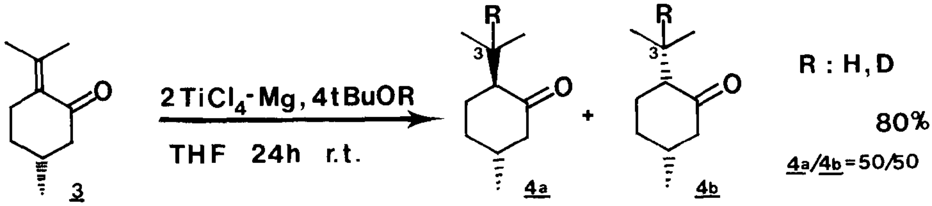
The formation of _2_ is interesting in that it has a C_2 symmetry axis (8) and therefore may be used for asymmetric induction (9).

But (+)-pulegone _3_ reacts in quite a different way (although it should have a similar reduction potential, about -2.30 V _vs_ sce according to House and al. (3), to the previously studied enones). As a matter of fact both a 1,4 reduction and an alkylation reaction take place ; even the dimers do not result from the usual coupling (C_1-C'_1) of two identical radical anions.

[+] for part II see : Ref : 14.

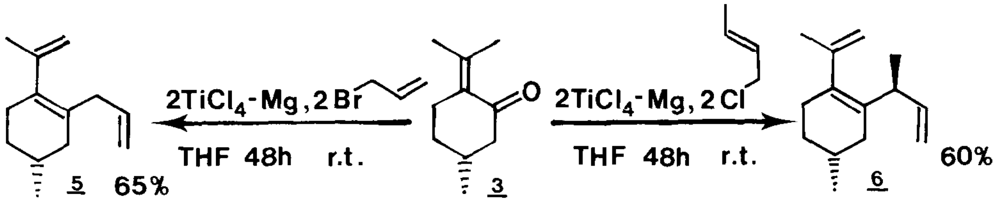
Results :

When the reaction is carried out for 48 h. with t-butyl alcohol at r.t. (+)-pulegone leads to a mixture of (R, S) and (R, R)-menthone 4a and 4b with a yield of 80 %.



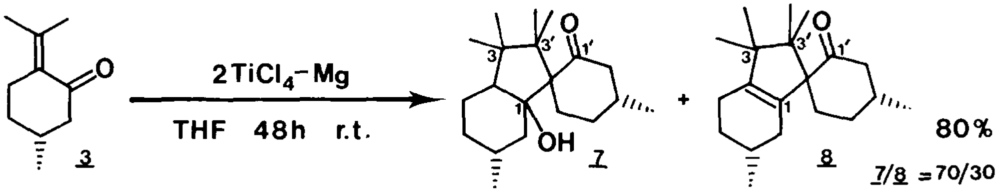
Working with tBuOD instead of tBuOH we have been able to establish the introduction of the deuterium on the C_3 position.

- Moreover, if the electrophilic species is now an allylic halide, such as allyl bromide or crotyl chloride, the main product of the reaction becomes a 3-allyl-p-mentha-3,8-diene without changing any of the other reaction conditions.



Two things are worth noting : First, when we use crotyl chloride the reaction yields only the 3-(1'-buten-3'-yl) p-mentha-3,8 diene 6 (10) and secondly, the allylic halides are not reduced by the Ti(II) complex under the reaction conditions (11).

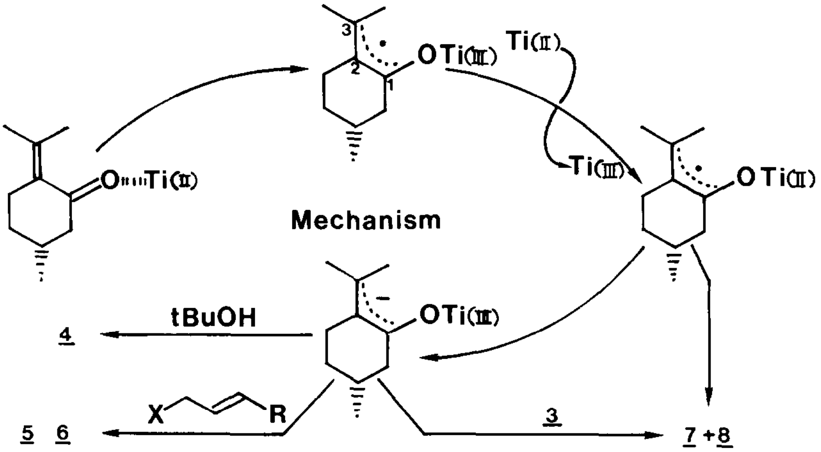
- Lastly, if (+)-pulegone is allowed to react with the Ti(II) complex only, it leads to the dimers 7 and 8 ; all of them have a C_3-C'_3 bond and not a C_1-C'_1 one.



Pascual and al. had previously obtained the ketols 7 by reduction of (+)-pulegone by Al(Na) in Et_2O (12).

Discussion - Mechanism

Because (+)-pulegone leads to menthone and reacts with allylic halides giving allylic menthadienes and, not having detected any dimers resulting from the usual C_1-C'_1 coupling, we think that the following mechanism leading to an umpolung (13) on pulegone is most likely the right one ; As far as we know this is the first time such a reactivity inversion is reported about (+)-pulegone.



We have already postulated a bielectronic transfer in the case of fluorenone (14), but it could be explained by the reduction potential values of that ketone : -1.29 V vs sce for the formation of the radical anion and -1.95 V vs sce for the formation of the dianion (3). In the present case, the s-cis configuration of (+)-pulegone seems to be the more acceptable explanation for the occurence of an anionic mechanism (15) ; as a matter of fact the transfer of a second electron to pulegone gives the dianion intermediate a pseudo aromatic character and therefore stabilizes it (this is of course not true of an s-trans enone like (-)-carvone for instance).

Experiments are currently being carried out to know whether the reactivity we have brought to light with (+)-pulegone is extendable to other s-cis enones.

REFERENCES AND NOTES

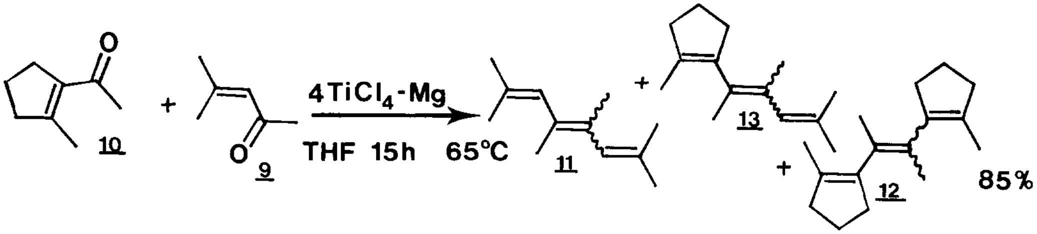
1 - a) S. TYRLIK and WOLOCHOWICZ, Bull. Soc. Chim. Fr., 1973, 2147.
  b) T. MUKAIYAMA, M. HAYASHI and K. NARASAKA, Chem. Lett., 1973, 291.
  c) A. CLERICI and O. PORTA, La Chim. et L'Industr., 1985, 67, 187 ; for reviews, see :
  d) J.E. Mc MURRY, Acc. Chem. Res., 1983, 16, 405.
  e) T. MUKAIYAMA, Org. React., 1982, 28, 203.

2 - a) J.E. Mc MURRY, G.K. BOSCH and P. KOCOVSKY, Tetrahedron Letters, 1985, 26, 2167.
  b) L.A. PAQUETTE, G.J. WELLS and G.J. WICKHAM, J. Org. Chem., 1984, 49, 3618.
  c) O. TAKAZAWA, K. KOGAMI and K. HAYASHI, Bull. Chem. Soc. Jpn., 1985, 58, 389.

3 - H.O. HOUSE, L.E. HUBER and M.J. UMEN, J. Amer. Chem. Soc., 1972, 94, 8471.

4 - J-M PONS, J-P ZAHRA and M. SANTELLI, Tetrahedron Letters, 1981, 22, 3965.

Moreover, if two enones, with similar values of reduction potential such as mesityl oxide 9 (-2.20 V vs sce) and acetyl methyl cyclopentene 10 (-2.30 V vs sce)(2) are allowed to react at the same time with the Ti(II) complex, under conditions leading to trienes, the repartition between the crossed and the symmetrical products is a statistical one : 11 (E/Z = 70/30) 21 % ; 12 (E/Z = 80/20) 29 % ; 13 (E/Z = 50/50) 50 %. The overall yield of the reaction being 90 %.



5 - a) R. DAMS, M. MALINOWSKI, I. WESTDORP and H.Y. GEISE, J. Org. Chem., 1982, 47, 248.
b) J.E. Mc MURRY, M.P. FLEMING, K.L. KEES and L.R. KREPSKI, J. Org. Chem., 1978, 43, 3255.

6 - The typical experimental procedure is the following :
To magnesium turnings (1.43 g, 100 mmol.) in 100 ml of distilled THF cooled to -70°C, is added dropwise $TiCl_4$ (18.97 g, 100 mmol.) under Ar. The yellow suspension is stirred and the temperature left to rise to r.t.. To the resulting black solution, both the enone (50 mmol.) and the electrophilic species (t-BuOH or an allylic halide) (100 mmol.), if there is one, are added gently. The reaction mixture is then stirred (time and temperature are mentioned on the schemes). After hydrolysis, usual work-up is carried out.

7 - Mass Spectrometric, Nuclear Magnetic Resonance (proton and carbon 13) and Infra-Red data are consistent with the indicated structure of all the new compounds.

8 - Only ten signals appear on the carbon 13 NMR spectrum ($CDCl_3$) : 20.83 ; 20.95 ; 30.67 ; 37.78 ; 37.94 ; 77.42 ; 108.82 ; 128.05 ; 136.01 ; 149.01 ppm. M.p. 162-163 °C.

9 - R. NOYORI, Pure appl. Chem., 1981, 53, 2315.

10 - M. EL IDRISSI, Thèse d'Etat, Marseille 1985, (to be published).

11 - G.A. OLAH and G.K. SURYA PRAKASH, Synthesis, 1976, 607.

12 - a) J. BARTUAL, F. CAMPS, J. PARES and J. PASCUAL, Anal. Fis. Quim., 1968, 64, 157.
b) J. BARTUAL, J.M. FONT, E. FORNE, J. PASCUAL and J. ROQUE, Anal. Quim., 1972, 68, 483.
c) J.M. FONT-CISTERO and J. PASCUAL, Anal. Quim., 1974, 70, 90.

13 - For a review on the umpolung see : D. SEEBACH, Ang. Chem. Int. Ed. Engl., 1979, 18, 239.

14 - J-M PONS and M. SANTELLI, Tetrahedron Letters, 1982, 23, 4937.

15 - That explanation is in agreement with results, Von Rague Schleyer and coworkers published recently, on the relative stability of different configurations of the 1,4-dilithio-2-butene :
A.J. KOS, P. STEIN, P. Von RAGUE SCHLEYER, J. Organomet. Chem., 1985, 280, C1.

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