Tetrahedron Letters, Vol.22, No.40, pp 3965 - 3968, 1981
Printed in Great Britain

0040-4039/81/403965-04$02.00/0

REDUCTIVE COUPLING OF α,β-ENONES I : REDUCTION OF METHYL-VINYL KETONE AND MESITYL OXIDE.

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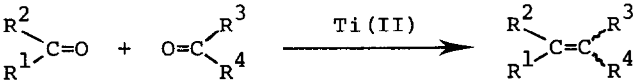
Summary : Reductive coupling of methyl-vinyl ketone with $TiCl_4$*-Mg gives pinacol* 1 *(25 %). According to the reducing agents, mesityl oxide yields 2,4,5,7-tetramethyl-octa-2,4,6-triene* 3 *(with* $4TiCl_3$*-*$LiAlH_4$ *), triene* 3 *or 2,4,5,7-tetramethyl-octa-2,6-dien-4,5-diol* 5 *(with* $TiCl_4$*-Mg), pinacol* 5 *(with* VCl_3*-Mg), and 2-acetyl-1,3,3,4,4-pentamethyl-cyclopentene* 7 *(with* $CrCl_3$*-Mg or* $FeCl_3$*-Mg or* $ZrCl_4$*-Mg) as major products.*

Recently, Ti(II) species formed by reaction of $TiCl_3$ and $LiAlH_4$ (McMurry's Reagent) have been shown to be useful in organic synthesis (1). Such Ti(II) complexes efficiently induce reductive coupling of carbonyls (intermolecular (1c, 2-6) or intramolecular (1c,3,7) reductive coupling) :

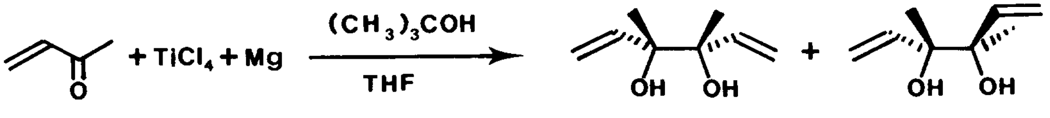


$$R^1R^2C{=}O + O{=}CR^3R^4 \xrightarrow{Ti(II)} R^1R^2C{=}CR^3R^4$$

Other titanium reagents prepared by reduction of $TiCl_4$ with Mg(Hg) elicit only pinacol dimerization without deoxygenation (1c,8,9). Although several results are reported on saturated aldehydes or ketones, only few studies concerning unsaturated aldehydes have been published (1c, 10). We now describe our preliminary results on the reduction of α,β-enones.

A - Methyl-vinyl ketone :

In a typical example, the action of $TiCl_4$-Mg on methyl-vinyl ketone in the presence of t-butyl alcohol (molar proportions 1:1:1:1) produces as major product pinacol 1 (overall yield 25 %; meso/d,l : 30/70)(11); (higher-boiling oils were obtained).



1m 1dl

B - Mesityl oxide :

Mesityl oxide 2 reduction with low-valent species of Ti, V, Cr, Fe and Zr leads to products 3-8 (12). Following scheme illustrates our results:

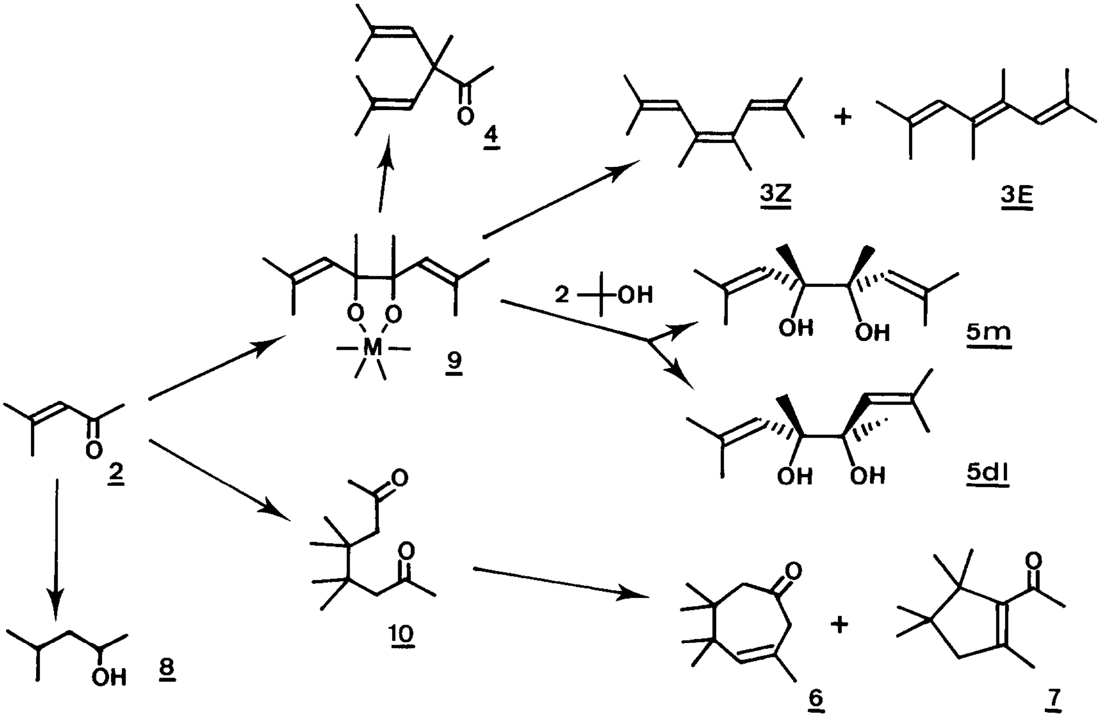


Table : Comparison of methods for reductive coupling of mesityl oxide 2 :

Entry	Reactants	2 %	3Z† %	3E† %	4† %	5dl† %	5m† %	6† %	7† %	8† %
a	2/4TiCl$_3$-LiAlH$_4$ (1:1)	-	30	65	-	-	-	-	-	-
b	2/TiCl$_4$/Mg (1:4:4)	-	25	60	-	-	-	-	-	-
c	2/TiCl$_4$/Mg/ (CH$_3$)$_3$COH (1:2:2:1)	-	18	27	-	35	20	-	-	-
d	2/TiCl$_4$/Mg/ (CH$_3$)$_3$COH (1:1:1:1)	-	5.5	10	37	14.5	8.5	20	5	-
e	2/TiCl$_4$/Mg/ (CH$_3$)$_3$COH (2:1:1:1)	50	3		80	4		12	1	-
f	2/VCl$_3$/Mg/ (CH$_3$)$_3$COH (1:1:1.5:1)	-	-	-	-	49	26	-	-	25
g	2/CrCl$_3$/Mg/ (CH$_3$)$_3$COH (1:4:4:4)	10	-	-	13	-	-	-	62	-
h	2/FeCl$_3$/Mg/ (CH$_3$)$_3$COH (1:4:4:4)	5	-	-	16	-	-	-	39	-
i	2/ZrCl$_4$/Mg/ (CH$_3$)$_3$COH (1:2:2:2)	25	-	-	29	-	-	-	37	-

†yields are calculated on the fraction of mesityl oxide reduced.

Entry a : to 150 ml of distilled THF under N_2 was added cautiously 4TiCl$_3$-LiAlH$_4$ (McMurry' Reagent, ALFA Products) (16.4 g, 25 mmol) and mesityl oxide (2.45 g, 25 mmol). The suspension was stirred at reflux for 10 h. Ether, water were added. After usual work-up, the combined organic layer dried over MgSO$_4$, filtered and concentrated are distilled.

Entry b : to magnesium turnings (FLUKA AG)(2.43 g, 100 mmol) in 100 ml of distilled THF under N_2 cooled to -30 ° was added dropwise $TiCl_4$ (19 g, 100 mmol). The yellow suspension was stirred and the temperature was raised to r.t. in 2 h. To the resulting black solution, mesityl oxide (2.45 g, 25 mmol) was added and the reaction mixture was stirred at reflux for 10 h. Ether, water were added. Usual work-up was carried out as entry a.

Entry c : This reaction was carried out as entry b with magnesium (1.215 g, 50 mmol), $TiCl_4$ (9.5 g, 50 mmol) and t-butyl alcohol (1.85 g, 25 mmol) was added with mesityl oxide (2.45 g, 25 mmol). The reaction mixture was stirred at r.t. for 36 h.

Entry d : This reaction was carried out as entry c with magnesium (1.215 g, 50 mmol), $TiCl_4$ (9.5 g, 50 mmol), t-butyl alcohol (3.7 g, 50 mmol), and mesityl oxide (4.9 g, 50 mmol).

Entry e : This reaction was carried out as entry d with mesityl oxide (9.8 g, 100 mmol).

Entry f : to magnesium turnings (0.73 g, 30 mmol) in 30 ml of distilled THF under N_2 at r.t. was added VCl_3 (3.15 g, 20 mmol). The suspension was stirred for 4 h at r.t. To the black solution, mesityl oxide (1.96 g, 20 mmol) and t-butyl alcohol (1.48 g, 20 mmol) were added and the reaction mixture was stirred at r.t. for 72 h.

Entry g : to magnesium turnings (1.25 g, 50 mmol) in 100 ml of distilled THF under N_2 at r.t. was added $CrCl_3$ (7.9 g, 50 mmol). The pink suspension was stirred at reflux for 3 h. To the green solution, mesityl oxide (1,23 g, 12.5 mmol) and t-butyl alcohol (3.70 g, 50 mmol) were added and the reaction mixture was stirred at reflux for 10 h.

Entry h : this reaction was carried out as entry g with $FeCl_3$ (8.1 g, 50 mmol).

Entry i : to magnesium turnings (1.25 g, 50 mmol) in 100 ml of distilled THF under N_2 at r.t. was added $ZrCl_4$ (11.7 g, 50 mmol). The suspension was stirred at reflux for 5h. To the grey solution, mesityl oxide (2.45 g, 25 mmol) and t-butyl alcohol (3.7 g, 50 mmol) were added and the reaction mixture was stirred at reflux for 10 h.

Discussion :

* Ketone 4 results of the pinacol rearrangement of diol 5 (13).

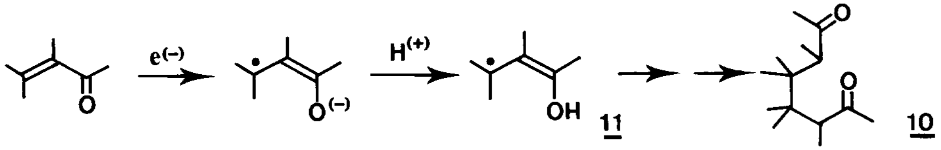
* Ketones 6 and 7 can occur from the intramolecular condensation, in the reaction mixture, of the diketone 10 (not isolated). 7 is one product of the electrolytic reduction of mesityl oxide (14,15,16).

* Ti(IV) species formed in the reaction mixture are LEWIS acids and their presence can explain the isomerization of 5 and the cyclization of 10.

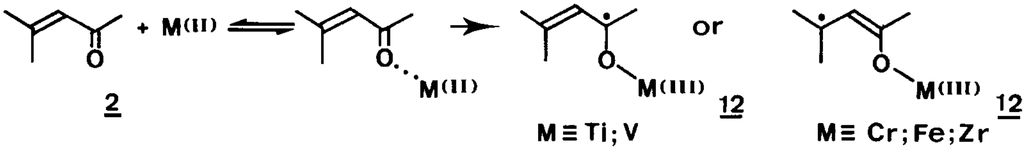
* The presence of t-butyl alcohol increases the yield of diol 5 without alteration of reducing power of the reagent.This is certainly due to a transesterification of ester 9.

* A very clean reaction occurs with V(II) species although overreduction to saturated alcohol 8 is observed.

These results can be compared with other reductive couplings of α,β-enones. The reduction by the addition of electrons from a suspension of alkali metal, from a solution of an alkali metal, or from a mercury cathode in an electrolysis cell involves the successive addition of an electron (or a metal atom) and a proton to form the allylic radical 11, yielding monomeric and dimeric products (17) :



Reduction of mesityl oxide with low-valent forms of Ti and V leads to pinacol 5 (or triene 3) as major product. This suggest that highest spin density for the radical anion complex 12 is in position 2 (19). In contrast with low-valent forms of Cr, Fe and Zr, ketone 7 is the major product, showing that the highest spin density for 12 is in position 4 :



References and Notes :

1a J.E. McMURRY, *Acc. Chem. Res.*, 7, 281, (1974).

b T. MUKAIYAMA, *Angew. Chem. Int. Ed. Engl.*, 16, 817, (1977).

c T.L. HO, *Synthesis*, 1979, 1.

2 D. LENOIR and H. BURGHARD, *J. Chem. Research* (*S*) 1980, 396, (*M*) 1980, 4715 and references cited therein.

3 J.E. McMURRY, M.P. FLEMING, K.L. KEES and L.R. KREPSKI, *J. Org. Chem.*, 43, 3255, (1978).

4 S. NISHIDA and F. KATAOKA, *ibid.*, 43, 1612, (1978).

5 D. LENOIR, *Chem. Ber.*, 111, 411, (1978).

6 D. FERINGA and H. WYNBERG, *Rec. Trav. Chim.*, 97, 249, (1978)

7 A.L. BAUMSTARK, C.J. McCLOSKEY and K.E. WITT, *J. Org. Chem.*, 43, 3609, (1978).

8 S. TYRLIK and I. WOLOCHOWICZ, *Bull. Soc. Chim. Fr.*, 1973, 2147.

9 E.J. COREY, R.L. DANHEISER and S. CHANDRASEKARAN, *J. Org. Chem.*, 41, 260, (1976).

10 J.B. CONANT and H.B. CUTTER, *J. Amer. Chem. Soc.*, 48, 1016, (1926).

11 J. WIEMANN, M.R. MONOT and J. GARDAN, *C.R. Acad. Sci. France*, 245, 172, (1957)

12 All compounds gave satisfactory spectral data (IR, mass, ^{13}C and ^{1}H NMR). For triene 3, Z configuration was attributed to the isomer in the mass spectrum of which the M^{+} − 15 peak is the most important.

13 In an aqueous acid solution (pH 1) of 5, a methyl group migration occurs leading to 2,5,5,7-tetramethyl-octa-2,6-dien-4-one (14).

14 J. SIMONET, *C.R. Acad. Sci. France*, 267, 1548, (1968).

15 M. HAUSER, *Chem. Rev.*, 63, 311, (1963).

16 J. WIEMANN and M.L. BOUGUERRA, *Ann. Chim.* (*Paris*), 2, 35, (1967).

17 K.W. BOWERS, R.W. GIESE, J. GRIMSHAW, H.O. HOUSE, N.H. KOLODNY, K. KRONBERGER and D.K. ROE, *J. Amer. Chem. Soc.*, 92, 2783 and 2800, (1970).

18 I.H. ELSON, T.J. KEMP and T.J. STONE, *ibid.*, 93, 7091, (1971).

19 The first stage of the reaction corresponds to a rapid equilibrium between Ti(II) or V(II) species and ketone; the electron transfer occurs in the rate determining step (20-22).

20 D.D. DAVIS and W.B. BIGELOW, *J. Amer. Chem. Soc.*, 92, 5127, (1970).

21 J. KONSTANTATOS, E. VRACHNOU-ASTRA, N. KATSAROS and D. KATAKIS, *ibid.*, 102, 3035, (1980).

22 C. WALLING, *ibid.*, 102, 6854, (1980).

(Received in France 26 April 1981)