

Cyclodimerisation of α,β -unsaturated ketones promoted by the TiCl_4/Sm system

Daqing Shi^{a,b}, Liangce Rong^a, Juxian Wang^a, Qiya Zhuang^a,
Xiangshan Wang^a, Shujiang Tu^a and Hongwen Hu^b

^aDepartment of Chemistry, Xuzhou Normal University Xuzhou 221009, P.R.China

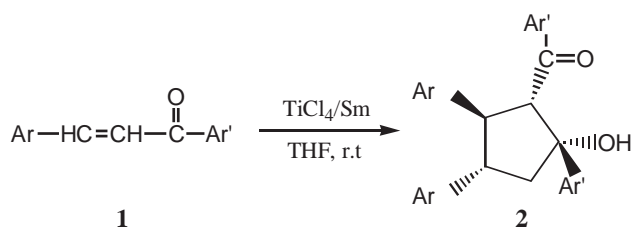
^bDepartment of Chemistry, Nanjing University, Nanjing 210093, P.R.China

The cyclodimerisation of α,β -unsaturated ketones induced by the TiCl_4/Sm system was studied, cyclopentanol derivatives are prepared in good yields under neutral and mild conditions.

Keywords: cyclopentanol, α,β -unsaturated ketone, low-valent titanium

Carbon-carbon bond formation is the essence of organic synthesis and the reductive coupling of carbonyl derivatives is one of the most valuable methods for establishing carbon-carbon bonds. Low-valent titanium reagents have an exceedingly high ability to promote reductive coupling of carbonyl compounds and are attracting increasing interest in organic synthesis.¹ Many other functional groups can also be coupled.²⁻⁵ Recently, we have reported the cyclodimerisation of α,β -unsaturated nitrile compounds using the $\text{TiCl}_4/\text{Sm}/\text{THF}$ system.⁶ Here, we wish to describe a new synthetic method for reducing α,β -unsaturated ketones by the $\text{TiCl}_4/\text{Sm}/\text{THF}$ system to give cyclopentanol derivatives.

When α,β -unsaturated ketones (**1**) were treated with low-valent titanium, which was prepared from titanium tetrachloride and samarium powder in anhydrous THF, the cyclodimerisation products (**2**) were obtained (Scheme 1).



Scheme 1

Table 1 Reaction of α,β -unsaturated ketones promoted by TiCl_4/Sm system

Entry	Ar	Ar'	Isolated yield/%
2a	C_6H_5	C_6H_5	82
2b	4- ClC_6H_4	C_6H_5	78
2c	4- $\text{CH}_3\text{C}_6\text{H}_4$	C_6H_5	80
2d	4- $\text{CH}_3\text{OC}_6\text{H}_4$	C_6H_5	77
2e	3,4- $\text{OCH}_2\text{OC}_6\text{H}_3$	C_6H_5	71
2f	3,4- $(\text{CH}_3\text{O})_2\text{C}_6\text{H}_3$	C_6H_5	81
2g	C_6H_5	4- ClC_6H_4	73
2h	C_6H_5	4- BrC_6H_4	75
2i	4- $\text{CH}_3\text{OC}_6\text{H}_4$	4- ClC_6H_4	70

Table 1 summarises the results on the reaction of a number of substrates. In the reactions, the chloro, bromo, alkoxy groups of the substrates are not reduced. The reaction was completed within about 2h and afforded the corresponding substituted cyclopentanol in good yield. There are several

reports on the cyclodimerisation of the of α,β -unsaturated ketones induced by metal systems, such as Yb^7 , tributyltin hydride⁸, NdCl_3 -lithium naphthalide⁹ and TiCl_4 - Zn^{10} . However, our results have advantages over these in the literature in yield and selectivity.

The relative stereochemistry of products was assigned by a 2D NMR study as shown in Fig.1. The NOESY experiment of compound **2a**, which was performed on a Bruker 500 instrument, gave us clear evidence of the *cis*-positions of C_5 - H_b with C_4 - H and of C_5 - H_a with the hydrogen atom of the OH group. We observed NOE effects between C_2 - H and C_4 - H and of C_3 - H with the hydrogen atom of the OH group. These observations lead us to establish the relative stereochemistry of compound **2a**, which is the *1RS,2SR,3RS,4SR* structure. The stereochemistry of compound **2a** is in agreement with that of the same compound by Takaki⁷ using Yb-HMPA-THF and Zhou¹⁰ using the TiCl_4 - Zn system.

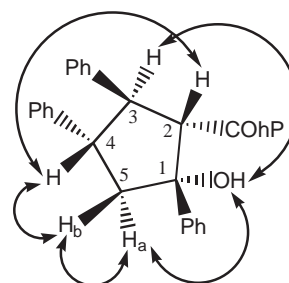


Fig.1 Observed NOEs of **2a**.

Experimental

Tetrahydrofuran(THF) was distilled from sodium-benzophenone immediately prior to use. All reactions were performed under a nitrogen atmosphere.

Melting points were uncorrected. ¹H NMR spectra were obtained for solutions in CDCl_3 with Me_4Si as internal standard using an Inova-400 spectrometer, Microanalyses were carried out using a Perkin-Elmer 2400 II analyzer. IR spectra were recorded on an FTIR-8101 spectrometer in KBr.

General procedure for the TiCl_4/Sm promoted cyclodimerisation of α,β -unsaturated ketone: TiCl_4 (1.1ml,10mmol) was added dropwise using a syringe to a stirred suspension of Sm powder (1.5g, 10mmol) in freshly distilled dry THF(15ml) at room temperature under N_2 . After the completion of the addition, the mixture was refluxed for 2h. The suspension of the low-valence titanium reagent formed was cooled to room temperature and a solution of α,β -unsaturated ketone (**1**) (3mmol) in anhydrous THF (5ml) was added. The mixture was stirred for 2h at room temperature under N_2 (the reaction was monitored by TLC). The reaction mixture was quenched with 5% HCl (100ml) and extracted with CHCl_3 (3 \times 50ml). The combined extracts were washed with water (3 \times 50ml) and dried over anhydrous Na_2SO_4 . After evaporation of the solvent under reduced pressure, the crude products **2a-i**

* To receive any correspondence. E-mail: dqshi@xzn.edu.cn

† This is a Short Paper, there is therefore no corresponding material in *J. Chem. Research (M)*.

were purified by silica gel column chromatography (200–300 mesh, ethyl acetate – benzene – cyclohexane (1:4:8) as eluent).

1RS,2SR,3RS,4SR-2-benzoyl-1,3,4-triphenyl cyclopentanol 2a: m.p. 188–190°C (lit.,¹¹ 192–194°C). ν/cm^{-1} 3437, 1648, 1597, 1493, 1447, 1387, 1246, 1051, 910, 753. δ_{H} 2.58(1H, dd, $J_1=14.4\text{Hz}$, $J_2=6.0\text{Hz}$, $\text{C}_5\text{-H}$), 3.01(1H, dd, $J_1=14.4\text{Hz}$, $J_2=10.7\text{Hz}$, $\text{C}_5\text{-H}$), 3.77(1H, ddd, $J_1=10.7\text{Hz}$, $J_2=10.0\text{Hz}$, $J_3=6.0\text{Hz}$, $\text{C}_4\text{-H}$), 4.10(1H, dd, $J_1=11.7\text{Hz}$, $J_2=10.0\text{Hz}$, $\text{C}_3\text{-H}$), 4.55(1H, d, $J=11.7\text{Hz}$, $\text{C}_2\text{-H}$), 5.25(1H, s, OH), 7.10–7.65(20H, m, ArH).

1RS,2SR,3RS,4SR-2-benzoyl-1-phenyl-3,4-di(4-chlorophenyl)cyclopentanol 2b: m.p. 190–191°C (lit.,¹¹ 192–194°C). ν/cm^{-1} 3433, 1635, 1595, 1491, 1446, 1374, 1246, 1092, 1014, 822, 782, 755, 700. δ_{H} 2.49(1H, dd, $J_1=14.4\text{Hz}$, $J_2=6.0\text{Hz}$, $\text{C}_5\text{-H}$), 2.96(1H, dd, $J_1=14.4\text{Hz}$, $J_2=10.6\text{Hz}$, $\text{C}_5\text{-H}$), 3.63(1H, ddd, $J_1=10.6\text{Hz}$, $J_2=10.0\text{Hz}$, $J_3=6.0\text{Hz}$, $\text{C}_4\text{-H}$), 4.00(1H, dd, $J_1=11.7\text{Hz}$, $J_2=10.0\text{Hz}$, $\text{C}_3\text{-H}$), 4.52(1H, d, $J=11.7\text{Hz}$, $\text{C}_2\text{-H}$), 5.01(1H, s, OH), 6.92–7.76(18H, m, ArH).

1RS,2SR,3RS,4SR-2-benzoyl-1-phenyl-3,4-di(4-methylphenyl)cyclopentanol 2c: m.p. 186–187°C (lit.,¹¹ 188–190°C). ν/cm^{-1} 3441, 1639, 1595, 1513, 1447, 1377, 1244, 1055, 814, 760, 698. δ_{H} 2.15(3H, s, CH_3), 2.28(3H, s, CH_3), 2.52(1H, dd, $J_1=14.4\text{Hz}$, $J_2=6.6\text{Hz}$, $\text{C}_5\text{-H}$), 2.98(1H, dd, $J_1=14.4\text{Hz}$, $J_2=10.6\text{Hz}$, $\text{C}_5\text{-H}$), 3.67(1H, ddd, $J_1=10.6\text{Hz}$, $J_2=10.2\text{Hz}$, $J_3=6.6\text{Hz}$, $\text{C}_4\text{-H}$), 4.13(1H, dd, $J_1=11.8\text{Hz}$, $J_2=10.2\text{Hz}$, $\text{C}_3\text{-H}$), 4.48(1H, d, $J=11.8\text{Hz}$, $\text{C}_2\text{-H}$), 5.24(1H, s, OH), 6.78–7.56(18H, m, ArH).

1RS,2SR,3RS,4SR-2-benzoyl-1-phenyl-3,4-di(4-methoxyphenyl)cyclopentanol 2d: m.p. 146–148°C. ν/cm^{-1} 3425, 1744, 1638, 1514, 1447, 1251, 1178, 1037, 815, 759, 698. δ_{H} 2.51(1H, dd, $J_1=14.4\text{Hz}$, $J_2=6.0\text{Hz}$, $\text{C}_5\text{-H}$), 2.97(1H, dd, $J_1=14.4\text{Hz}$, $J_2=10.6\text{Hz}$, $\text{C}_5\text{-H}$), 3.61–3.70(4H, m, OCH_3 , $\text{C}_4\text{-H}$), 3.76(3H, s, OCH_3), 4.00(1H, dd, $J_1=11.6\text{Hz}$, $J_2=10.8\text{Hz}$, $\text{C}_3\text{-H}$), 4.47(1H, d, $J=11.6\text{Hz}$, $\text{C}_2\text{-H}$), 5.26(1H, s, OH), 6.63–6.75(18H, m, ArH). Anal. Calc. for $\text{C}_{32}\text{H}_{30}\text{O}_4$: C, 80.31, H, 6.32; Found: C, 80.57, H, 6.08%.

1RS,2SR,3RS,4SR-2-benzoyl-1-phenyl-3,4-di(3,4-methylene-dioxyphenyl)cyclopentanol 2e: m.p. 185–186 °C (lit.,¹¹ 183–184°C). ν/cm^{-1} 3453, 1640, 1486, 1446, 1246, 1041, 933, 815, 760, 699. δ_{H} 2.51(1H, dd, $J_1=14.4\text{Hz}$, $J_2=6.1\text{Hz}$, $\text{C}_5\text{-H}$), 2.98(1H, dd, $J_1=14.4\text{Hz}$, $J_2=10.5\text{Hz}$, $\text{C}_5\text{-H}$), 3.68(1H, ddd, $J_1=10.5\text{Hz}$, $J_2=10.0\text{Hz}$, $J_3=6.1\text{Hz}$, $\text{C}_4\text{-H}$), 4.03(1H, dd, $J_1=11.8\text{Hz}$, $J_2=10.0\text{Hz}$, $\text{C}_3\text{-H}$), 4.41(1H, d, $J=11.8\text{Hz}$, $\text{C}_2\text{-H}$), 5.20(1H, s, OH), 5.80(2H, s, OCH_2O), 5.88(2H, s, OCH_2O), 6.54–7.56(16H, m, ArH).

1RS,2SR,3RS,4SR-2-benzoyl-1-phenyl-3,4-di(3,4-dimethoxyphenyl)cyclopentanol 2f: m.p. 146–147°C. ν/cm^{-1} 3458, 1642, 1591, 1518, 1448, 1239, 1026, 875, 849, 814, 764, 696, 649. δ_{H} 2.56(1H, dd, $J_1=14.4\text{Hz}$, $J_2=6.0\text{Hz}$, $\text{C}_5\text{-H}$), 2.98(1H, dd, $J_1=14.4\text{Hz}$, $J_2=11.0\text{Hz}$, $\text{C}_5\text{-H}$), 3.59–3.63(4H, m, OCH_3 , $\text{C}_4\text{-H}$), 3.75(3H, s, OCH_3), 3.84(3H, s, OCH_3), 3.89(3H, s, OCH_3), 4.01(1H, dd, $J_1=11.6\text{Hz}$, $J_2=10.0\text{Hz}$, $\text{C}_3\text{-H}$), 4.49(1H, d, $J=11.6\text{Hz}$, $\text{C}_2\text{-H}$), 5.22(1H, s, OH), 6.51–7.58(16H, m, ArH). Anal. Calc. for $\text{C}_{34}\text{H}_{34}\text{O}_6$: C, 75.81, H, 6.36; Found: C, 75.84, H, 6.27%.

1RS,2SR,3RS,4SR-2-(4-chlorobenzoyl)-1-(4-chlorobenzoyl)-3,4-diphenylcyclopentanol 2g: m.p. 174–176 °C. ν/cm^{-1} 3447, 1638, 1590, 1490, 1454, 1403, 1245, 1214, 1178, 1094, 1056, 1011, 876,

846, 825, 798, 765, 735, 701. δ_{H} 2.56(1H, dd, $J_1=14.4\text{Hz}$, $J_2=6.0\text{Hz}$, $\text{C}_5\text{-H}$), 2.92(1H, dd, $J_1=14.4\text{Hz}$, $J_2=10.8\text{Hz}$, $\text{C}_5\text{-H}$), 3.79(1H, ddd, $J_1=10.8\text{Hz}$, $J_2=10.2\text{Hz}$, $J_3=6.0\text{Hz}$, $\text{C}_4\text{-H}$), 4.06(1H, dd, $J_1=11.6\text{Hz}$, $J_2=10.2\text{Hz}$, $\text{C}_3\text{-H}$), 4.40(1H, d, $J_1=11.6\text{Hz}$, $\text{C}_2\text{-H}$), 5.30(1H, s, OH), 7.06–7.57(18H, m, ArH). Anal. Calc. for $\text{C}_{30}\text{H}_{24}\text{Cl}_2\text{O}_2$: C, 73.92, H, 4.96; Found: C, 74.13, H, 4.78%.

1RS,2SR,3RS,4SR-2-(4-bromobenzoyl)-1-(4-bromobenzoyl)-3,4-diphenylcyclopentanol 2h: m.p. 176–178 °C. ν/cm^{-1} 3451, 1639, 1584, 1515, 1485, 1452, 1398, 1244, 1073, 1008, 821, 764, 730, 701. δ_{H} 2.55(1H, dd, $J_1=14.4\text{Hz}$, $J_2=5.6\text{Hz}$, $\text{C}_5\text{-H}$), 2.90(1H, dd, $J_1=14.4\text{Hz}$, $J_2=10.6\text{Hz}$, $\text{C}_5\text{-H}$), 3.79(1H, ddd, $J_1=10.6\text{Hz}$, $J_2=10.4\text{Hz}$, $J_3=5.6\text{Hz}$, $\text{C}_4\text{-H}$), 4.06(1H, dd, $J_1=11.6\text{Hz}$, $J_2=10.4\text{Hz}$, $\text{C}_3\text{-H}$), 4.38(1H, d, $J_1=11.6\text{Hz}$, $\text{C}_2\text{-H}$), 5.29(1H, s, OH), 6.95–7.52(18H, m, ArH). Anal. Calc. for $\text{C}_{30}\text{H}_{24}\text{Br}_2\text{O}_2$: C, 62.52, H, 4.20; Found: C, 62.79, H, 4.03%.

1RS,2SR,3RS,4SR-2-(4-chlorobenzoyl)-1-(4-chlorobenzoyl)-3,4-di(4-methoxyphenyl)cyclopentanol 2i: m.p. 187–189°C. ν/cm^{-1} 3446, 1639, 1586, 1513, 1380, 1246, 1176, 1094, 1030, 1834. δ_{H} 2.49(1H, dd, $J_1=14.6\text{Hz}$, $J_2=6.0\text{Hz}$, $\text{C}_5\text{-H}$), 2.87(1H, dd, $J_1=14.6\text{Hz}$, $J_2=11.6\text{Hz}$, $\text{C}_5\text{-H}$), 3.63–3.70(4H, m, OCH_3 , $\text{C}_4\text{-H}$), 3.74(3H, s, OCH_3), 3.96(1H, dd, $J_1=12.0\text{Hz}$, $J_2=10.8\text{Hz}$, $\text{C}_3\text{-H}$), 4.34(1H, d, $J_1=12.0\text{Hz}$, $\text{C}_2\text{-H}$), 5.25(1H, s, OH), 6.65–7.58(16H, m, ArH). Anal. Calc. for $\text{C}_{32}\text{H}_{28}\text{Cl}_2\text{O}_4$: C, 70.20, H, 5.15; Found: C, 70.36, H, 4.97%.

We thank the “Surpassing Project” of Jiangsu Province, the Natural Science Foundation of the Education Committee of Jiangsu Province (00KJB150008) and the Key Laboratory of Organic Synthesis, Suzhou University for financial support.

Received 7 October 2002; accepted 20 January 2003
Paper 02/1573

References

- J.E. McMurry, *Chem.Rev.*, 1989, **89**, 1513.
- D. Lenoir, *Synthesis*, 1989, 883.
- D.Q. Shi, J.X. Chen, W.Y. Chai, W.X. Chen and T.Y. Kao, *Tetrahedron Lett.*, 1993, **34**, 2963
- D.Q. Shi, L.L. Mu, Z.S. Lu, and G.Y. Dai, *Synth.Commun.*, 1997, **27**, 4121.
- D.Q. Shi, Z.S. Lu, L.L. Mu, and G.Y. Dai, *Synth.Commun.*, 1998, **28**, 1073.
- D.Q. Shi, H. Zhao, X.S. Wang and S.J. Tu, *J. Chem. Cryst.* 2002, 385
- K.Takaki, F. Beppu, S. Tanaka, Y. Tsubaki, T. Jintoku and Y. Fujiwara, *J. Chem. Soc., Chem. Commun.*, 1990, 516.
- E.J. Enholm and K.S. Kinter, *J. Org. Chem.* 1995, **60**, 4850.
- J. Bao, M. Bei, J. Lu, J. Zhang and Q. Song, *Chin. Chem. Lett.*, 1993, **4**, 593.
- L.H. Zhou, D.Q. Shi, G.Y. Dai and W.X. Chen, *Tetrahedron Lett.*, 1997, **38**, 2729.
- L.H. Zhou and Y.M. Zhang, *Synth.Commun.*, 2000, **30**, 597.