Transition Metal-Catalyzed Oxidations. 12 [1]

α-Chlorination of Silylenol Ethers with *tert*-Butyl Hydroperoxide and $TiCl_2(OiPr)_2$

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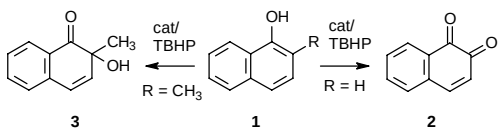
Dedicated to Prof. H. Marsmann on the Occasion of his 60th Anniversary

Abstract. Enolsilyl ethers (**4**, **6**, **8**, **10**, **12**, **14**) are chlorinated to the α-monochloro ketones (**5**, **7**, **9**, **11**, **13**, **15**) with *tert*-butyl hydroperoxide in the presence of dichlorotitanium diisopropoxide in 69 – 92% yield.

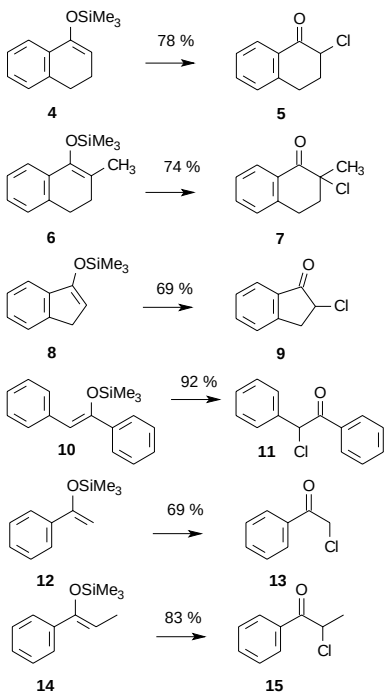
In preceding communications we described the oxygenation of the **vinylic** position of phenols such as naphthol (**1**) to form selectively the *ortho*-quinones **2** (R = H, Scheme 1) [2, 3] or the transformation to unsaturated α-hydroxy ketones **3** (R = methyl) [4]. *tert*-Butyl hydroperoxide (TBHP) was used as the oxidant and transition metal alkoxides served as the catalysts. These results suggested to try the α-hydroxylation of enolates with this system to test if the methods of Vedejs [5] using the Mimoun molybdenumoxodiperoxo complex or that of Davies [6] employing *N*-sulfonyloxaziridines could be improved using less expensive and environmentally safe reagents.



Scheme 1

Preliminary experiments with titanium or zirconium alkoxides and TBHP in the reaction of titanium enolates lead to reprotonation of the enolates. The problem was recently overcome by Schulz *et al*. [7] by using lithium *tert*-butyl hydroperoxide as the oxidant. However, in connection with the halogenation of phenols [1] we wondered if titanium enolates could be converted to the α-chlorinated ketones by the $TiCl_m(OiPr)_n$/TBHP system. α-Chloroketones are required in a number of transformations for instance in the Favorskii-reaction [8, 9], the preparation of oxazoles [10] or thiocarboxylic acids [11]. In fact, the anticipated chlorination reaction turned out to be feasible, and we now report on the convenient and effective α-chlorination of enolsilyl ethers with $TiCl_2(OiPr)_2$/TBHP to yield α-chloroketones.

Three cyclic ketones of different steric hindrance and ring size and three open chain ketones were selected to test the chlorination reaction. The corresponding titanium enolates were prepared *via* the corresponding silylenol ethers **4**, **6**, **8**, **10**, **12**, and **14** obtained in 93 – 98% yield in the usual manner by deprotonation of the corresponding ketones with LDA and quenching with trimethylsilyl chloride. The reaction with the dichlorotitanium complex $TiCl_2(OiPr)_2$ proved to be superior as compared with the monochloro compound $TiCl(OiPr)_3$ employed in the chlorination of phenols [1]. Furthermore, the addition of small amounts of pyridine with THF as the solvent was advantageous to prevent premature acid-catalyzed cleavage of the silylenol ethers.



Scheme 2

The isolated yields of 69 – 92% of the α-**mono**chloro ketones **5**, **7**, **9**, **11**, **13**, and **15** (Scheme 2) compare favorably with

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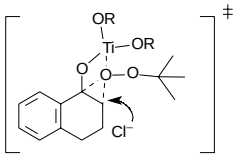
known methods of chlorination of silylenol ethers [12–21]. **Poly**chlorinations can usually not be excluded in the reaction of ketones with elementary chlorine [15] or polyhalogenated organic compounds [16, 17]. Most other methods require more expensive (*e.g.* MCPBA [13]) or toxic reagents such as lead salts [14], and the method presented here offers clear advantages in terms of operational simplicity, yields, and environmental safety. However, attempts for enantioselective chlorination of the enolsilyl ethers with chirally modified titanium catalysts were not yet successful (maximum ca. 30% *e.e.*).



A

Under mechanistic aspects, two pathways can be considered. On the one hand, the $TiCl_2(OiPr)_2$/TBHP system can oxidize the chloride to an electrophilic chlorine species such as hypochlorite that can attack the double bond of the enol ether. On the other hand, a transition state such as **A** (Chart 1), similar to that assumed for the naphthol oxidation (Scheme 1), cannot be excluded [4]. It is known that titanium enolates are generated from the enolsilyl ethers and titanium tetrachloride [22]. The titanium enolate can exchange one ligand by attack of *tert*-butyl hydroperoxide and formation of transition state **A**. The α-chloroketones are then formed by attack of chloride.

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Experimental

For general methods and instrumentation see [23]. The assignment in signals marked with * is interchangeable.

Preparation of Silylenol Ethers 4, 6, 8, 10, 12, 14

The silylenol ethers **4**, **6**, **8**, **10**, **12**, and **14** were prepared in the usual manner by treatment of the corresponding ketones (10 mmol) with LDA (13 mmol) in dry THF (–60 °C to 0 °C). The products were purified by bulb to bulb distillation (yields 90 – 96%) and characterized by ^{1}H NMR (200 MHz, $CDCl_3$). – ^{1}H NMR data for **4**: δ/ppm = 0.34 (s, 9H, $Si(CH_3)_3$), 2.40 (m, 2H, 3-H), 2.84 (t, $J_{4,3}$ = 7.9 Hz, 2H, 3-H), 5.27 (t, $J_{2,3}$ = 4.6 Hz, 1H, 2-H), 7.1–7.3(m, 3H, Ar-H), 7.49 (d, $J_{8,7}$ = 6.5 Hz, 1H, 8-H). **6**: δ/ppm = 0.34 (s, 9H, $Si(CH_3)_3$), 1.96 (s, 3H, CH_3), 2.37 (t, $J_{3,4}$ = 7.91 Hz, 2H, 3-H), 2.87(t, $J_{4,3}$ = 7.87 Hz, 2H, 4-H), 7.1–7.5(m, 4H, Ar-H). **8**: δ/ppm = 0.37 (s, 9H, $Si(CH_3)_3$), 3.35 (d, $J_{3,2}$ = 2.34 Hz, 2H, 3-H), 5.52 (t, $J_{2,3}$ = 2.34 Hz, 1H, 2-H), 7.3–7.5 (m, 4H, Ar-H). **10**: δ/ppm = 0.14 (s, 9H, $Si(CH_3)_3$), 6.22 (s, 1H, 2-H), 7.1–7.8 (m, 10H, Ar-H). **12**: δ/ppm = 0.34 (s, 9H, $Si(\underline{CH_3})_3$), 4.49 (d, $J_{2,2'}$ = 1.06 Hz, 1H, 2-H), 4.98 (d, $J_{2',2}$ = 1.05 Hz, 1H, 2-H′), 7.3–7.7 (m, 5H, Ar-H). **14**: δ/ppm = 0.24 (s, 9H, $Si(\underline{CH_3})_3$), 1.83 (d, $J_{3,2}$ = 6.86 Hz, 3H, 3-H), 5.42 (q, $J_{2,3}$ = 6.86 Hz, 1H, 2-H), 7.3–7.6 (m, 5H, Ar-H).

α-Chlorination of Silylenol Ethers with $Cl_2Ti(OiPr)_2$ (General Procedure)

A solution of the silylenol ether (1 mmol) in dry THF (10 ml) was treated with pyridine (0.32 ml, 4 mmol) and powdered molecular sieve (3 Å, 50 mg). After 15 min of stirring $TiCl_2(OiPr)_2$ (2.1 ml, 1.05 mmol, 0.5 mol/l in CH_2Cl_2, prepared by reaction of equivalent amounts of $TiCl_4$ and $Ti(OiPr)_4$) was added. The suspension was stirred for 45 min at room temperature and TBHP (1.0 ml, 3 mmol, 3 mol/l in CH_2Cl_2) was added at –50 °C. The cooling bath was removed after 1 h, and stirring was continued for 12 h at room temperature. The mixture was quenched by addition of water (10 ml), the suspension was filtered, and the phases were separated. The aqueous phase was extracted with CH_2Cl_2 (15 ml), the combined organic phases were washed with 10% HCl (5 ml), dried ($MgSO_4$), the solvent was evaporated at reduced pressure, and the residue purified by chromatography on silica gel (CH_2Cl_2); yields see Scheme 2.

2-Chloro-1-tetralone (**5**) [14]

^{1}H NMR (200 MHz, $CDCl_3$): δ/ppm = 2.41–2.71 (m 2H, 4-H), 2.96–3.10 (m, 1H, 3-H), 3.26–3.41 (m, 1H, 3-H′), 4.67 (dd, *J* = 7.54 Hz, *J* = 4,03 Hz, 1H, 2-H), 7.29–7.42 (m, 2H, 5-H, 7-H), 7.56 (m, 1H, 6-H), 8.12 (dd, $J_{8,7}$ = 7.81 Hz, $J_{8,6}$ = 1.18 Hz, 1H, 8-H). – ^{13}C NMR (50 MHz , $CDCl_3$): δ/ppm = 26.7 (t, C-4), 32.8 (t, C-3), 60.4 (d C-2), 127.5 (d, C-7)*, 129.0 (d, C-5)*, 129.1 (d, C-6), 130.9 (s, C-9), 134.6 (d, C-8), 143.7 (s, C-10), 191.3 (s, C-1).

2-Chloro-2-methyl-1-tetralone (**7**) [24]

^{1}H NMR (200 MHz, $CDCl_3$): δ/ppm = 1.86 (s, 3H, CH_3), 2.3–2.5 (m, 2H, 4-H), 2.7–3.0 (m, 1H, 3-H), 3.3–3.4 (m, 1H, 3-H'), 7.2–7.6 (m, 3H, Ar-H), 8.1 (d, $J_{8,7}$ = 6,6 Hz, 1H, 8-H). – ^{13}C NMR (50 MHz , $CDCl_3$): δ/ppm = 26.4 (q, CH_3), 27.0 (t, C-4), 38.8 (t, C-3), 68.1 (s, C-2), 127.4 (d, C-7)*, 129.1 (d, C-5)*, 129.2 (d, C-6)*, 130.1 (s, C-9), 134.2 (d, C-8), 143.5 (s, C-10), 191.7 (s, C-1).

2-Chloroindanone (**9**)

^{1}H NMR (200 MHz, $CDCl_3$): δ/ppm = 3.34 (dd, $J_{3,3'}$ = 17.60 Hz, $J_{3,2}$ = 3.92 Hz, 1H, 3-H), 4.16 (dd, $J_{3'3}$ = 17.61 Hz, $J_{3'2}$ = 7.74 Hz, 1H, 3-H′), 4.59 (dd, $J_{2,3}$ = 7.75 Hz, $J_{2,3'}$ = 4.02 Hz, 1H, 2-H), 7.2–7.8 (m, 4H, Ar-H). – ^{13}C NMR (50 MHz , $CDCl_3$): δ/ppm = 37.9 (t, C-3), 56.3 (d, C-2), 125.4 (d, C-4)*, 126.9 (d, C-6)*, 128.8 (d, C-5)*, 129.9 (s, C-8), 136.5 (d, C-7), 151.2 (s, C-9), 199.7(s, C-1).

2-Chloro-2-phenylacetophenone (Desylchlorid) (**11**)

m.p. 62 °C (Lit. [25]: 62–63 °C). – ^{1}H NMR (200 MHz, $CDCl_3$): δ/ppm = 6.42 (s, 1H, 2-H), 7.3–8.1 (m, 10 H, Ar-H).

2-Chloroacetophenone (**13**)

m.p. 53 °C (Lit. [26] 53.5–54.2 °C). – ^{1}H -NMR (200 MHz, $CDCl_3$): 4.76 (s, 2H, 2-H), 7.5–7.7 (m, 3H, 3′-H, 4′-H), 7.98 (dd, $J_{2'3'}$ = 7.05 Hz, *J* = 1.48 Hz, 2H, 2′-H). – ^{13}C NMR (50 MHz, $CDCl_3$): 46.6 (t, C-2), 128.9 (d, C-3′), 129.3 (d, C-4′), 134.5 (d, C-2′), 134.6 (s, C-1′), 191.5 (s, C-1).

2-Chloro-1-phenyl-1-propanone (**15**) [27]

^{1}H NMR (200 MHz, $CDCl_3$): δ/ppm = 1.77 (d, $J_{3,2}$ = 6.67 Hz, 3H, 3-H), 5.29 (q, $J_{2,3}$ = 6.66 Hz, 1H, 2-H), 7.5–7.7 (m, 3H, 3′-H, 4′-H), 8.04 (dd, $J_{2'3'}$ = 6.97 Hz, *J* = 1.61 Hz, 2H, 2′-H).

– ^{13}C NMR (50 MHz, $CDCl_3$): δ/ppm = 20.4 (q, C-3), 53.2 (d, C-2), 129.2 (d, C-3ς)*, 129.4 (d, C-4′)*, 134.2 (d, C-2′), 134.5 (s, C-1′), 194.0 (s, C-1).

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