C_3 symmetric Ti(IV) amine triphenolate complexes as sulfoxidation catalysts using aqueous hydrogen peroxide

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General Remarks: ^{1}H and ^{13}C NMR spectra were recorded at 301 K on a Bruker AC-300 and Bruker AC-250 instruments. ESI-MS experiments of complexes **2a-c** were performed in a ESI-TOF Mariner^{TM} Biospectrometry^{TM} Workstation of Applied Biosystems by flow injection analysis using methanol as mobile phase. GC analysis were performed using a Shimadzu GC-2010 gas chromatograph with a FID detector and a capillary column EQUITY^{TM}-5 using dodecane as external standard. All chemicals were used as provided without further purifications. Dry solvents were purchased from Fluka, Ti(IV) tetraisopropoxide, thioanisol, dibutylsulfide, benzyl phenyl sulfide, *n*-butyl *p*-tolyl sulfide, *p*-methoxy thioanisol, *p*-nitro thioanisol and 35 % aqueous hydrogen peroxide from Aldrich. Ligands **3a-c** were synthesized as previously reported.[1] Ti(IV) complexes were always handle and stored in glovebox, with exception of complex **2c** which could be handle in open air.

Synthesis of Ti(IV) complexes 2a-c.

Complexes **2a-c** were prepared in glovebox by mixing homogeneous solutions of the corresponding ligands **3a-c** (0.10 M) and Ti(O*i*-Pr)$_4$ (0.18 M) in $CHCl_3$ or $CDCl_3$ in a 1:1 ratio, using 1,2-dichloroethane as internal standard, to a final concentration 0.01 M of the complex obtaining a bright yellow solution which was use for kinetic experiments and reactions without further purifications and without removing the three equivalents

(1) Prins, L. J.; Mba, M.; Kolarović, A.; Licini, G. *Tetrahedron Lett.* **2006**, *47*, 2735-2738.

of *i*-PrOH released from the metal precursor. A quantitative conversion was observed in respect of the internal standard, DCE (3.78 ppm).

In all cases in the NMR spectra resonances relative to free *iso*-propanol released in the reaction were present: ^{1}H-NMR (300 MHz, $CDCl_3$): 4.04 (hept, 1H, J = 6.1 Hz, C*H*Me$_2$), 1.22 (6H, d, J = 6.1 Hz, CH(C*H*$_3$)$_2$). ^{13}C-NMR (50 MHz, $CDCl_3$): δ 64.5 (CH), 25.1 (CH_3).

Complex 2a. ^{1}H-NMR (300 MHz, $CDCl_3$): δ 7.16 (t, 3H, J = 7.8 Hz, ArH), 7.07 (d, 3H, J = 7.3 Hz, ArH), 6.82 (t, 3H, J = 7.3 Hz, ArH), 6.74 (d, 3H, J = 7.8 Hz, ArH), 5.14 (hept, 1H, J = 6.1 Hz, C*H*Me$_2$), 3.49 (bs, 6H, NC*H*$_2$), 1.55 (6H, d, J = 6.1 Hz, CH(C*H*$_3$)$_2$). ^{13}C-NMR (50 MHz, $CDCl_3$): δ 163.0 (C), 129.6 (CH), 129.3 (CH), 124.4 (C), 120.9 (CH), 116.2 (CH), 80.6 (CH, *i*-Pr), 58.7 (CH_2), 25.1 (CH_3, *i*-Pr). ESI-MS: 412.1608 (M+H$^+$), calc. 412.1208.

Complex 2b. ^{1}H-NMR (300 MHz, $CDCl_3$): δ 7.08 (d, 3H, J = 7.3 Hz, ArH), 6.93 (d, 3H, J = 7.3 Hz, ArH), 6.75 (t, 3H, J = 7.3 Hz, ArH), 5.24 (hept, 1H, J = 6.1 Hz, C*H*Me$_2$), 3.49 (bs, 6H, NC*H*$_2$), 2.30 (9H, s, C*H*$_3$) 1.55 (6H, d, J = 6.1 Hz, CH(C*H*$_3$)$_2$). ^{13}C-NMR (50 MHz, $CDCl_3$): δ 161.7 (C), 130.4 (CH), 127.2 (CH), 124.9 (C), 124.0 (C), 120.5 (CH), 80.1 (CH, *i*-Pr), 58.7 (CH_2), 25.8 (CH_3, *i*-Pr), 16.5 (CH_3). ESI-MS: 454.1940 (M+H$^+$) calc. 454.1498.

Complex 2c: ^{1}H-NMR (300 MHz, $CDCl_3$): δ 7.19 (d, 3H, J = 7.8 Hz, ArH), 6.96 (d, 3H, J = 6.5 Hz, ArH), 6.77 (t, 3H, J = 7.5 Hz, ArH), 5.24 (hept, 1H, J = 6.1 Hz, C*H*Me$_2$), 3.94 (d, 3H, J = 13.0 Hz, NC*H*$_2$), 2.89 (d, 3H, J = 13.0 Hz, NC*H*$_2$), 1.51 (6H, d, J = 6.1 Hz, CH(C*H*$_3$)$_2$), 1.45 (s, 27H, *t*-Bu). ^{13}C-NMR (50 MHz, $CDCl_3$): δ 162.7 (C), 136.4 (C), 127.8 (CH), 126.4 (CH), 125.2 (C), 120.3 (CH), 80.2 (CH, *i*-Pr), 58.6 (CH_2), 35.1 (C), 29.7 (CH_3), 26.7 (CH_3, *i*-Pr). ESI-MS: 580.3605 (M+H$^+$), calc. 580.2906.

General procedure for monitoring the sulfoxidation reactions catalyzed by 2a-c using aqueous H_2O_2 as oxidant (Table 1).

A screw-cap NMR tube was charged with a solution of the corresponding *in situ* formed complex in $CDCl_3$ (0.003 mmol), solvent was removed under vacuum and then CD_3OD, the internal standard (1,2-dichloroethane, DCE), 35% aqueous H_2O_2 (0.3 mmol) and thioanisole (0.3 mmol) were added with a final volume of 0.6 ml. Concentrations of sulfide, sulfoxide and sulfone were determinated by integration of the methyl group

signals: Ph-S-*Me* (2.4 ppm), Ph-SO-*Me* (2.8 ppm) and Ph-SO_2-*Me* (3.1 ppm) in respect of the internal standard, DCE (3.78 ppm).

General procedure for monitoring the sulfoxidation reactions catalyzed by 2c using aqueous H_2O_2 as oxidant (Table 2).

A screw-cap NMR tube was charged with a solution of the *in situ* formed complex **2c** in $CDCl_3$, solvent was removed under vacuum and then CD_3OD followed by the internal standard (1,2-dichloroethane), 35% aqueous H_2O_2 and thioanisole (**4a**) were added with final concentrations as reported in Table 2 to a final volume of 0.6 ml. The monitoring of the concentration of sulfide, sulfoxide and sulfone was made by integration of the methyl group signals: Ph-S-*Me* (2.4 ppm), Ph-SO-*Me* (2.8 ppm) and Ph-SO_2-*Me* (3.1 ppm). Final yields were determined by quantitative GC analysis after complete H_2O_2 consumption (iodometric test) in respect of the internal standard 1,2-dichloroethane (3.78 ppm).

General procedure for sulfoxidation reactions catalyzed by 2c using aqueous H_2O_2 as oxidant (Table 3).

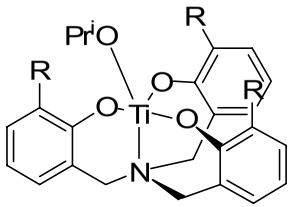
To a 1 ml solution of the corresponding thioethers **4a-f** (0.5 mmol) and catalyst **2c** (0.005 mmol) in MeOH, was added 35% aqueous H_2O_2 (0.5 mmol). The mixture was stirred at rt until all the oxidant has been consumed (iodometric test), and $CHCl_3$ was added. The mixture was washed with 5% sodium metabisulfite aqueous solution, the layers were separated and the aqueous one extracted twice with chloroform. The organic layers were washed with brine, dried over $MgSO_4$ and the solvent was removed under reduce pressure. Ratios sulfoxide:sulfone were determinated by quantitative GC analysis and by ^{1}H NMR ($CDCl_3$, 300 MHz). Yields were determinated by quantitative GC analysis. The sulfoxides **5a-f** and sulfones **6a-f** ^{1}H NMR spectra match those already reported in the literarture.[2]

Oxidation of thioanisole on gram-scale.

(2) a) Brunel, J. M.; Diter, P.; Duetsch, M.; Kagan, H. B. *J. Org. Chem.* **1995**, *60*, 8086. b) Rebiere, F.; Samuel, O.; Ricard, L.; Kagan, H. B. *J. Org. Chem.* **1991**, *56*, 5991. c) Pitchen, P.; Dunach, E.; Dshmukh, M. N.; Kagan H. B. *J. Am. Chem. Soc.* **1984***, 106,* 8188.

To a solution of thioanisole (**4a**) (859 mg, 6.9 mmol) and catalyst **2c** (42 mg, 0.069 mmol) in MeOH (13.8 ml), was added 35% aqueous H_2O_2 (0.63 ml, 6.9 mmol). The mixture was stirred at rt for 9h, then concentrated to half volume and chloroform was added. The mixture was washed with 5% sodium metabisulfite aqueous solution, the layers were separated and the aqueous one extracted with chloroform. The organic layers were washed with brine, dried over $MgSO_4$ and the solvent was removed under reduce pressure. A conversion of 97% with sulfoxide:sulfone ratio 98:2 was obtained (quantitative GC analysis and ^{1}H NMR ($CDCl_3$, 300 MHz). The crude was purified by column chromatography on silica gel (petroleum ether/ ethyl acetate 1:2) obtaining 897mg (93%) of methyl phenyl sulfoxide (**5a**) and 31 mg (3%) of methyl phenyl sulfone (**6a**) corresponding to a ratio sulfoxide:sulfone 97:3 and 96% conversion. The sulfoxide and sulfone ^{1}H NMR spectra match those already reported in the literarture. [2]

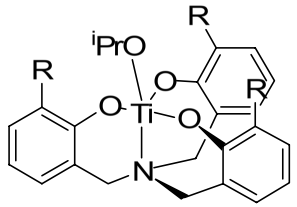
Complex **2c**
$CDCl_3$,300 MHz



2c R=tert-Bu

Complex 2c
CDCl3, 62.9 MHz
2c R=tert-Bu
R
O
Ti
N
PiO
162.7356
136.3951
127.7791
126.3676
125.1767
120.2488
80.2368
58.6012
35.0469
29.7097
(ppm)

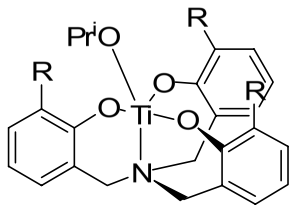
300 MHz, $CDCl_3$



2b R = Me

Complex 2b
CDCl3, 62.9 MHz
161.7305
130.4049
127.2363
124.9940
124.0015
120.4874
80.1486
58.6817
25.8122
16.5196
2b R=Me
R
O
Ti
N
PiO
(ppm)

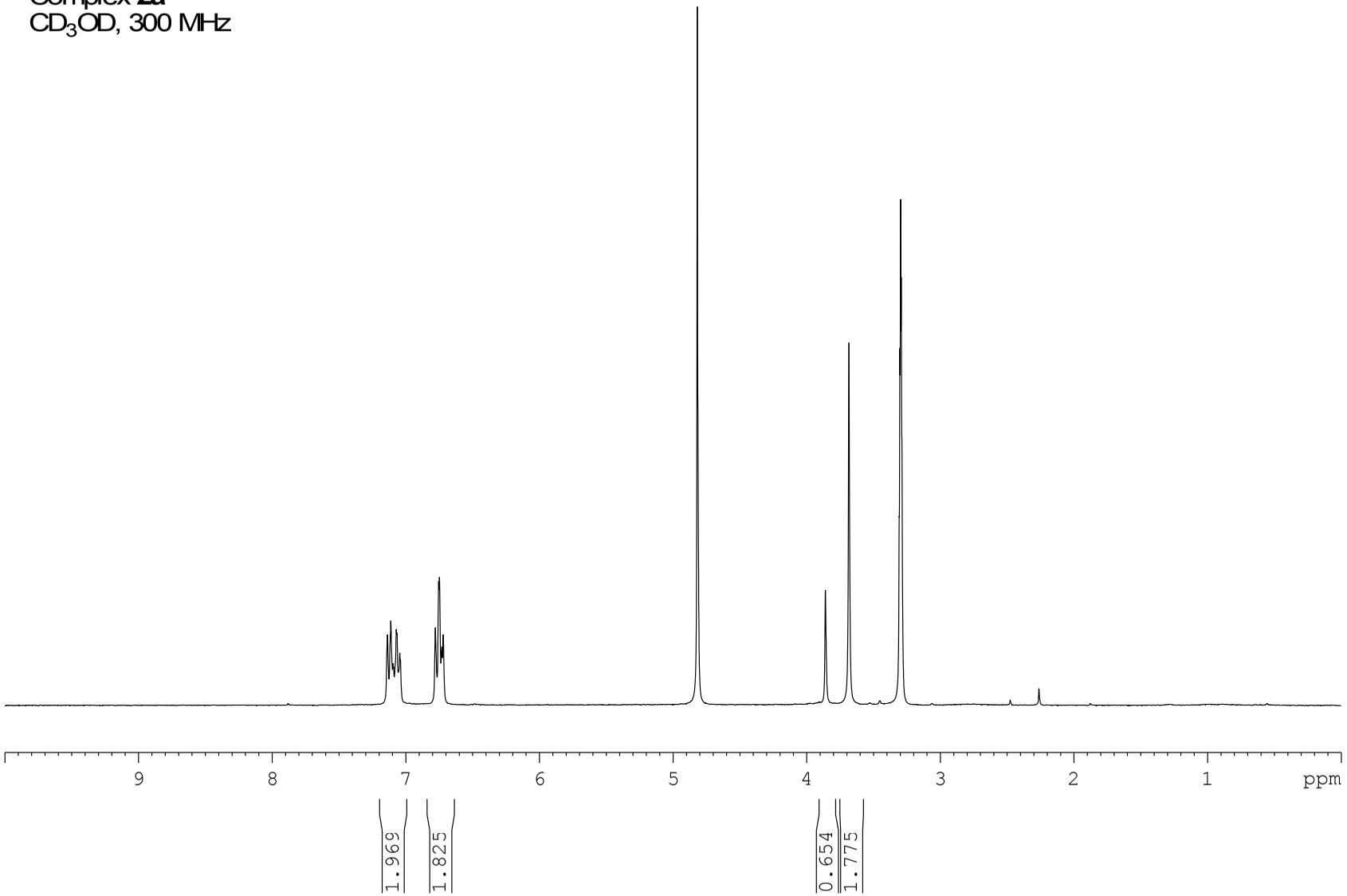
Complex **2a**
$CDCl_3$, 300 MHz

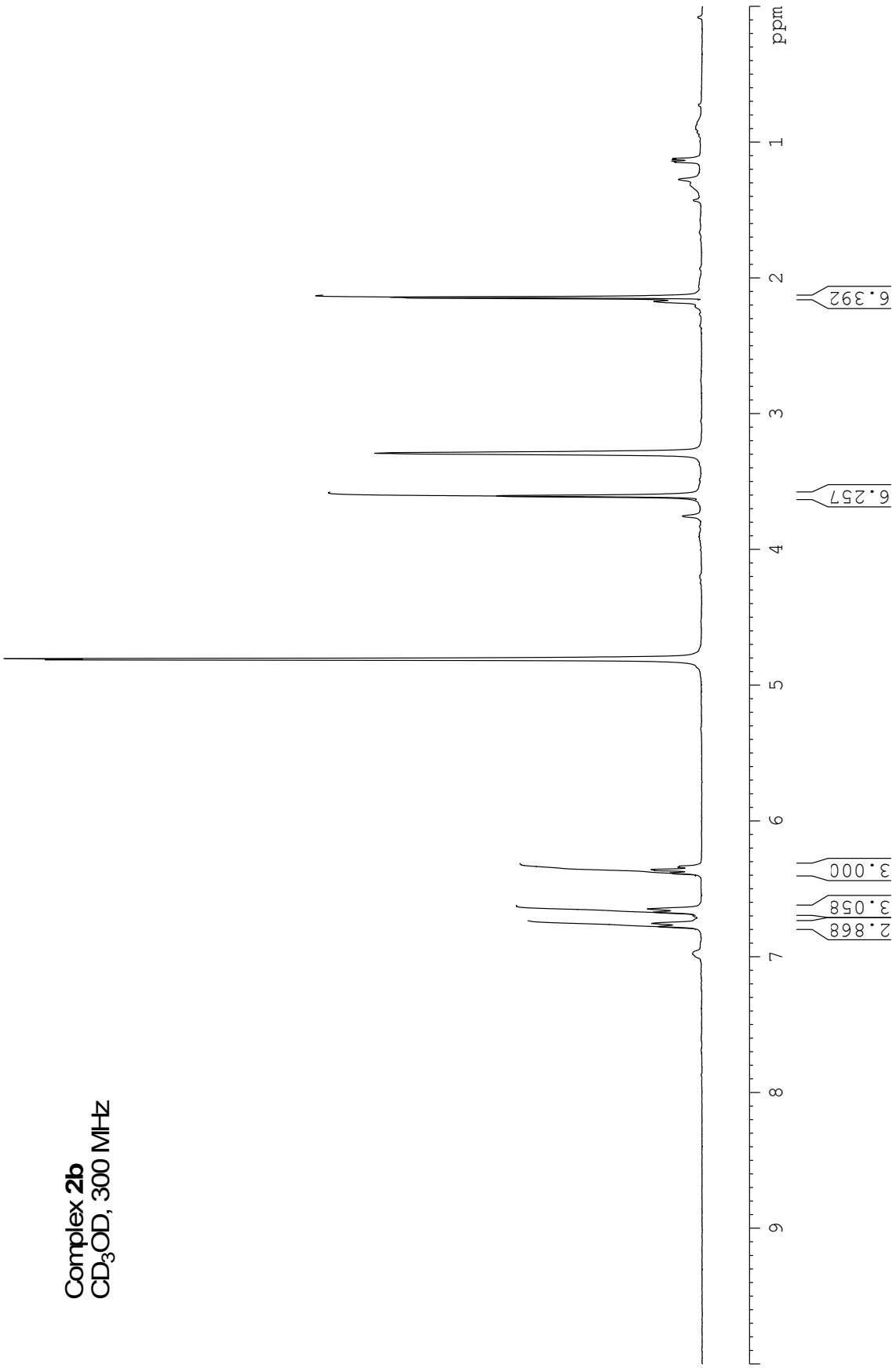


2a R=H

Complex 2a
CDCl3, 62.9 MHz
2a R=H
163.8244
129.6109
129.2580
124.4926
120.9212
116.1793
80.5603
58.6964
25.0697

Complex **2a**
CD_3OD, 300 MHz




Complex 2b
CD3OD, 300 MHz
ppm
9
8
7
6
5
4
3
2
1
6.392
6.257
3.000
3.058
2.868

Complex **2c**
MeOD, 250 MHz