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SUPPORTING INFORMATION

Title: The (Schiff base)vanadium(V) Complex Catalyzed Oxidation of Bromide – A New Method for the in situ Generation of Bromine and Its Application in the Synthesis of Functionalized Cyclic Ethers
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Ref. No.: O040071

Contents

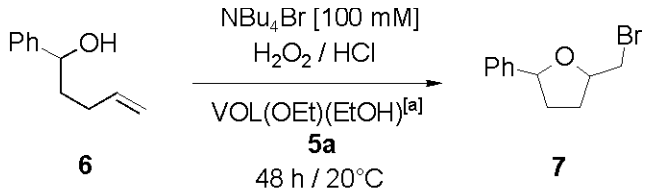
1. General Remarks

(i) The numbering of compounds is consistent with the associated publication, unless additional compounds are mentioned. (ii) The referencing is independent from the associated publication and refers only to this Supporting Information.

2. The Use of Aqueous H_2O_2 as Primary Oxidant in the (Schiff-base)vanadium(V)-catalyzed Oxidation of Bromide

In a typical experiment, defined volumes of stock solutions (9.5 mL) of 1-phenyl-4-penten-1-ol (**6**) (20 mM) and nBu$_4$NBr (0.1 M) in DMF were mixed with defined amounts of n-$C_{14}H_{30}$ (olefin free, internal GC-standard) and treated with VOL[1](OEt)(EtOH) (**5a**), H_2O_2 (30% aqueous solution) and HCl (18% aqueous solution). DMF was added until the total volume of the reaction mixture reached a value of 10 mL. This solution was stirred for 48 h at room temperature. The yields of 2-bromomethyl-5-phenyl tetrahydrofuran (**7**) were determined by GC. The ratios of the individual reagents and the associated yields of target compound **7** from likewise performed experiments are compiled in Table 1.

Table 2.1. Formation of 2-bromomethyl-5-phenyl tetrahydrofuran (**7**) from 1-phenyl-4-penten-1-ol (**6**)



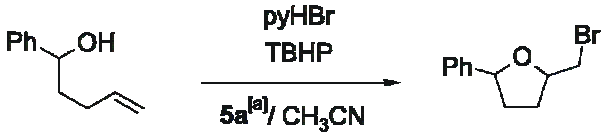
6 **7**

entry	[HCl][b]	[H_2O_2][c]	[**5a**][d]	yield **7**[%] [e]
1	0	4	1	–
2	5	4	1	–
3	5	4	0	6
4	20	22	1	27
5	0	22	1	–
6	0	22	20	–
7	20	22	0	28

[a] For general procedures see experimental part of the associated publication or refs.[1,2] For constitution of auxiliary L in catalyst **5a** refer to the associated publication. – [b] in mM, applied as 18 % aq. soln. (w/w). – [c] in mM, applied as 30 % aq. soln. (w/w). – [d] in mM. – [e] Yields of **7** were determined by GC analysis using n-$C_{14}H_{30}$ as internal standard (± 5 experimental uncertainty). Total yield of **7** as a mixture of *cis*/*trans*-isomers (the diastereomeric ratios of heterocycles **7** were not determined in these experiments).

3. (Schiff-base)vanadium(V)-catalyzed Oxidation of Bromide Using TBHP as Primary Oxidant – Optimization of Reaction Conditions

Table 3.1. Variation of the amount of catalyst VOL(EtO)(EtOH) (**5a**) in the oxidation of Br^- in the presence of TBHP.



6 **7**

entry	5a [mol %]	yield 7 [%][b]		
		24 h	48 h	72 h
1	0	17	29	36
2	1	57	72	74
3	5	69	73	73
4	10	67	73	73
5	50	44	45	45
6	100	43	44	45

[a] for catalyst **5a** refer to Table 2.1. – [b] refer to footnote [e] in Table 2.1.

4. Time-Dependent Formation of 2-Bromomethyl-5-phenyl Tetrahydrofuran (7)

In a typical run, a defined amount of catalyst (2.0 μmol, 1 mol%, rerferenced versus substrate **6**) was dissolved in a given solvent (1 mL). After addition of *tert*-butyl hydroperoxide (TBHP) (20 μl, 0.11 mmol, 1.1 equiv. 5.5 M in nonane, referenced versus **6**), the solution was heated for 2 min to reflux and was hereafter stirred for 5 min at 20 °C. This solution was added in a dropwise manner to a solution of 1-pheny-4-penten-1-ol (**6**) (16.2 mg, 0.10 mmol), pyHBr (24.1 mg, 0.15 mmol, 1.5 equiv.) and *n*-tetradecane (as internal GC-standard) in the selected solvent (1 mL). The mixture was stirred at 20 °C and the yields of **7** were determined by GC.

For constitution formulae of (Schiff-base)vanadium(V)-complexes **5a**–**g** refer to Figure 3 and Table 1 of the associated publication.

4.1 Application of (Schiff-base)vanadium(V)-Complexes 5a–g (1 mol%) in CH_3CN

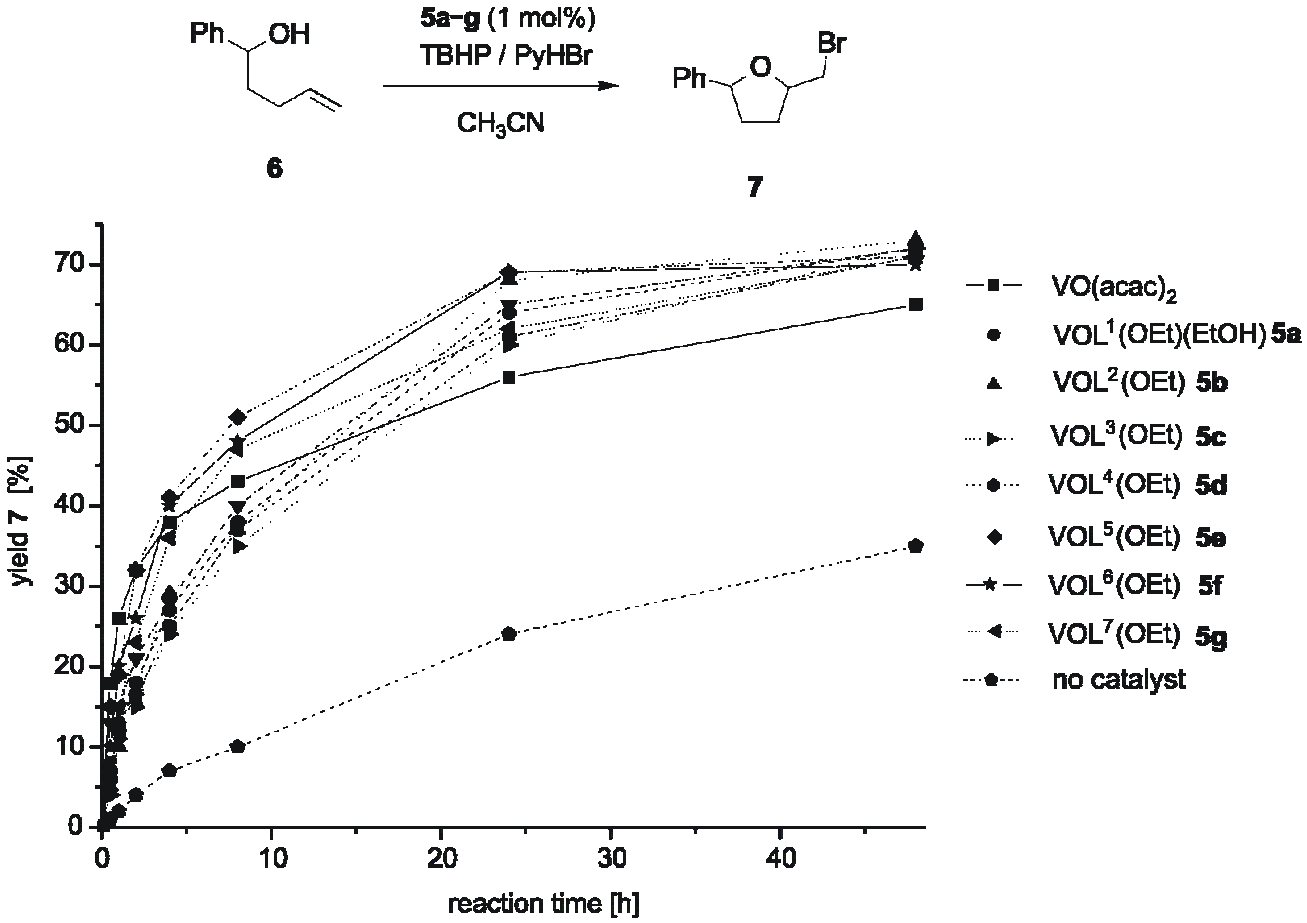


Figure 4.1. Yields of tetrahydrofuran **7** from the oxidation of Br^- in the presence of alkenol **6** and TBHP (GC).

Table 4.1. Formation of bromocyclization product **7** in dependence of added vanadium reagents

catalyst	Yield of **7** [%] (GC) after reaction periods of						
	0.5 h	1 h	2 h	4 h	8 h	24 h	48 h
none	1	2	4	7	10	25	35
$VO(acac)_2$	18	26	32	38	43	57	65
5a	7	12	18	27	38	57	72
5b	5	10	17	29	37	68	73
5c	4	11	15	24	35	61	72
5d	6	12	16	28	39	63	71
5e	10	20	26	40	48	76	70
5f	15	19	32	41	51	69	71
5g	8	15	23	36	47	62	71

4.2 Application of (Schiff-base)vanadium(V)-Complexes 5a and 5c – CH_3CN and $CHCl_3$ as Solvents

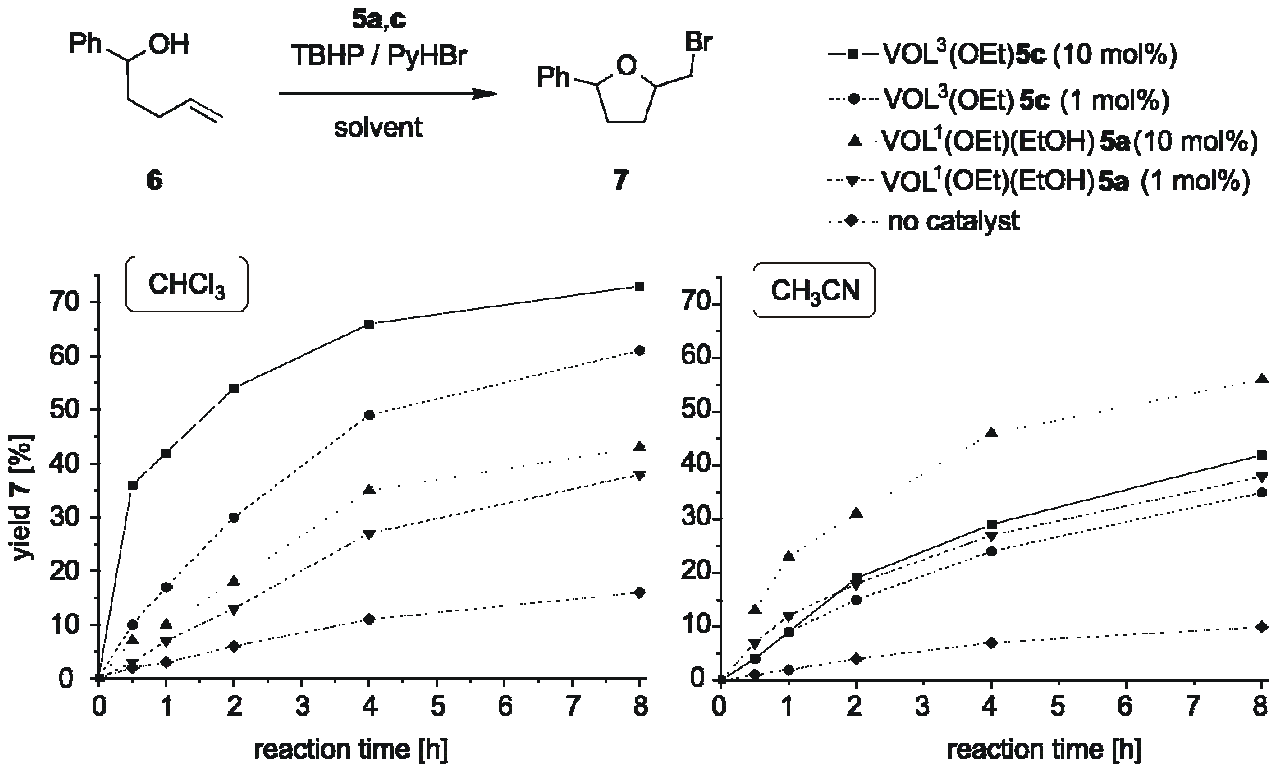


Figure 4.2. Formation of tetrahydrofuran **7** from alkenol **6**. Application of catalysts **5a** and **5c** in different solvents (GC).

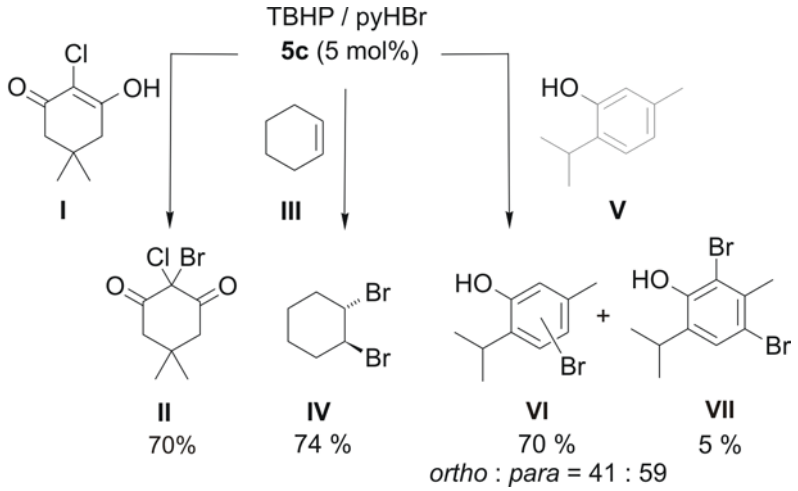
Table 4.2. Formation of bromocyclization product **7** in dependence of added vanadium reagents – reaction in CH_3CN

Catalyst	Yield of **7** [%] (GC) after a reaction period of				
	0.5 h	1 h	2 h	4 h	8 h
none	1	2	4	7	10
5a (1 mol%)	7	12	18	27	38
5a (10 mol%)	13	23	31	36	56
5c (1 mol%)	4	11	15	24	35
5c (10 mol%)	4	9	19	29	42

Table 4.3. Formation of bromocyclization product **7** in dependence of added vanadium reagents – reaction in $CHCl_3$

Catalyst	Yield of **7** [%] (GC) after a reaction period of				
	0.5 h	1 h	2 h	4 h	8 h
none	2	3	6	11	16
5a (1mol%)	3	7	13	27	38
5a (10 mol%)	7	10	18	35	45
5c (1 mol%)	10	17	30	49	61
5c (10 mol%)	36	42	54	66	73
5d (10 mol%)	13	23	35	53	70

5. Synthesis and Spectral Data of Selected Organobromine Compounds



5.1 Preparation of 2-Bromo-2-chlorodimedone II[3]

$VOL^3(OEt)$ (**5c**) (1.83 mg, 5.0 μmol, 5 mol %) was dissolved in $CDCl_3$ (0.4 mL). TBHP (20 μl of a 5.5 M solution in nonane, 0.11 mmol, 1.1 equiv.) was added. This solution was heated to reflux for 1 min. Afterwards, it was stirred for 5 min at 20 °C and was subsequently added in a dropwise manner to a solution of 2-chlorodimedone **I** (17.5 mg, 0.10 mmol) and pyridinium hydrobromide (24.1 mg, 0.15 mmol, 1.5 equiv.) in $CDCl_3$ (1 mL). The reaction mixture was stirred for 24 h at 20 °C to furnish 70 % of 2-bromo-2-chlorodimedone **II**. The yield of product **II** was determined by ^1H NMR using pyridine as internal standard. ^1H NMR ($CDCl_3$, 250 MHz): δ = 0.81 (s, 3 H, CH_3), 1.17 (s, 3 H, CH_3), 2.62 (dq, *J* = 14.5, 1.5 Hz, 2 H, CH_2), 3.36 (dq, *J* = 14.3, 0.9 Hz, 2 H, CH_2).

5.2 Formation of *trans*-1,2-Dibromocyclohexane (IV)[4]

Cyclohexene (82.2 mg, 1.0 mmol) (**III**) was treated with **5c**, TBHP and pyHBr in CH_2Cl_2 as outlined for the bromination of 2-chlorodimedone **I** to provide 179 mg (74 %) of *trans*-1,2-dibromocyclohexane (**IV**) after filtration of the crude product through a short pad of Al_2O_3 [petroleum ether/Et_2O = 1:1 (v/v)], concentration of the eluate in vacuo, and drying of the residue. ^{1}H NMR ($CDCl_3$, 250 MHz): δ = 1.55 (m_c, 2 H, CH_2), 1.85 (m_c, 4 H, CH_2), 2.47 (m_c, CH_2), 4.45 (m_c, 2 H, CH). ^{13}C NMR ($CDCl_3$, 63 MHz): δ = 22.4, 31.9, 55.2.

5.3 Bromination of Thymol V[5]

Thymol **V** (150 mg, 1.0 mmol) was treated with TBHP, pyHBr, and (Schiff-base)vanadium(V)-complex **5c** in CH_2Cl_2 as outlined in section 5.1 to provide a total yield of 166 mg of mono- and dibrominated thymols **VI** (70 %) and **VII** (5 %) after column chromatography [SiO_2, petroleum ether/Et_2O = 6:1 (v/v)]. **4-Bromothymol *para*-VI**: ^{1}H NMR ($CDCl_3$, 250 MHz): δ = 1.23 (d, *J* = 6.7 Hz, 6 H, CH_3), 2.30 (s, 3 H, CH_3), 3.17 (sept, *J* = 6.7 Hz, 1 H, CH), 4.62 (s, 1 H, OH), 6.64 (d, *J* = 0.6 Hz, 1 H, Ar-H), 7.30 (s,1 H, Ar-H). ^{13}C NMR ($CDCl_3$, 63 MHz): δ = 22.4, 22.5, 26.8, 115.6, 117.6, 130.0, 134.0, 135.9, 151.8. **6-Bromothymol *ortho*-VI**: ^{1}H NMR ($CDCl_3$, 250 MHz): δ = 1.24 (d, *J* = 7.0, 6 H, CH_3), 2.38 (s, 3 H, CH_3), 3.30 (sept, *J* = 7.0 Hz, 1 H, CH), 5.70 (s, 1 H, OH), 6.79 (d, *J* = 7.9 Hz, 1 H, Ar-H), 7.05 (d, *J* = 7.9 Hz, 1 H, Ar-H). ^{13}C NMR ($CDCl_3$, 63 MHz): δ = 22.4, 22.9, 27.9, 113.6, 122.0, 124.9, 133.1, 135.3, 149.3. **4,6-Dibromothymol VII**: ^{1}H NMR ($CDCl_3$, 250 MHz): δ = 1.23 (d, *J* = 7.0 Hz, 6 H, CH_3), 2.53 (s, 3 H, CH_3), 3.27 (sept, *J* = 7.0 Hz, 1 H, CH), 5.69 (s, 1 H, OH), 7.33 (s, 1 H, Ar-H). ^{13}C NMR ($CDCl_3$, 63 MHz): δ = 22.3, 23.8, 28.0, 113.9, 114.9, 129.2, 134.2, 134.8, 148.9.

6. References

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