From 1,2-dialkoxyalkanes to 1,4-dioxanes. A transformation mediated by $NbCl_5$ *via* multiple C–O bond cleavage at room temperature†

Fabio Marchetti,‡[a] Guido Pampaloni*[a] and Stefano Zacchini[b]

Received (in Cambridge, UK) 14th March 2008, Accepted 28th April 2008
First published as an Advance Article on the web 9th June 2008
DOI: 10.1039/b804432e

The formation of 1,4-dioxanes and alkyl chlorides from the reactions of polyethers (dme, diglyme, 1,2-diethoxyethane, 1,2-dimethoxypropane) with $NbCl_5$ at room temperature is described; as far as dme is concerned, the reaction mainly occurs in two steps, consisting of (i) cleavage of one O–CH_3 bond, followed by (ii) cleavage of the second O–CH_3 bond and one of the two O–CH_2 linkages. The characterization of intermediate complexes and the isolation of $NbOCl_3$(dme) are reported.

The preparation of functionalized species starting from readily available materials *via* fast and selective reactions represents one of the most appealing goals for the synthetic chemist. The breaking of the C–O bond of ethers is a key step in several organic syntheses:[1] for instance, the acylative cleavage of ethers, mediated by Lewis acids or low-valent transition metal complexes, is an attractive reaction to obtain esters.[2]

On the other hand, the direct combination of ethers with oxophilic metal complexes (lanthanides, early transition elements) generally proceeds with formation of stable metal alkoxides.[3] In these cases, the starting ether does not transform into functionalized species, but breaks down into smaller fragments. For example, 1,2-dimethoxyethane, dme, that is widely used as a solvent in synthetic chemistry, can react with transition metal compounds[3f,g,4] undergoing degradation. This latter occurs with cleavage of one or two O–CH_2 bonds, and affords methoxy-derivatives[3f,g,4] and, in some cases, free[3f,4c,d] or coordinated ethylene.[4e] Otherwise, the cleavage of the dme O–CH_3 bonds is known to be performed by some aluminium derivatives under mild conditions.[5]

In the framework of our research on the activation of oxygenated species by Group 5 metal pentahalides, MX_5,[6] we were eager to investigate the reactivity of MX_5 (M = Nb, Ta, X = F, Cl, Br, I) with dme and similar molecules. Here, we report a study of the reaction of $NbCl_5$, **1**, with 1,2-dialkoxyalkanes, showing the formation, *inter alia*, of 1,4-dioxanes.

$NbCl_5$ rapidly dissolves in a large excess of dme at room temperature and, working under strictly anhydrous conditions, the crystalline compound $NbOCl_3$(dme), **2**, has been isolated and characterized by X-ray structural analysis,[7] see Fig. 1. The complex displays a distorted octahedral geometry, with the Nb(V) centre bound to three chlorides, one oxide and the oxygen atoms of one dme unit. The Nb(1)–O(1) interaction, at 1.6939(18) Å, is consistent with a niobium–oxygen double bond.[8] The oxygen atoms of dme respectively occupy *trans* and *cis* positions with regard to the oxide. A similar arrangement of the ligands has been found in other $NbOCl_3L_2$ complexes, such as $NbOCl_3(HMPA)_2$, HMPA = hexamethylphosphoramide,[9] and $NbOCl_3(CH_3CN)_2$.[10]

Noteworthy is the fact that the formation of compound **2** occurs under mild conditions (*i.e.* room temperature or below), in spite of the fact that all the known oxygen abstractions from ethers by metal complexes generally require high temperatures.[11–13]

The formation of **2**, accompanied by the production of methyl chloride and 1,4-dioxane (detected by GC/MS), can be represented by eqn (1):

$$NbCl_5 + 2C_4H_{10}O_2 \rightarrow \underset{\mathbf{2}}{NbOCl_3(C_4H_{10}O_2)} + 2CH_3Cl + \tfrac{1}{2}C_4H_8O_2 \qquad (1)$$

Compound **2** has been prepared in optimal yield by reacting $NbCl_5$ with two equivalents of dme, coherently with the

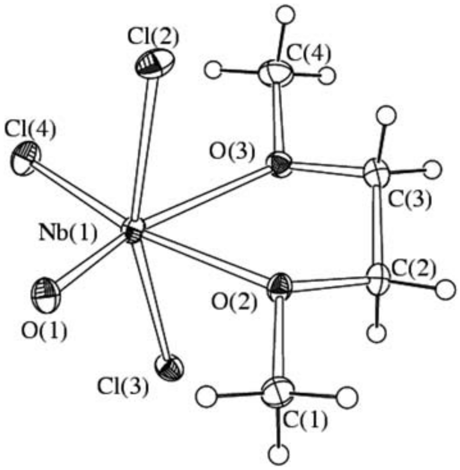


Fig. 1 ORTEP drawing of $NbOCl_3$(dme), **2**. Displacement ellipsoids are at the 30% probability level. Selected bond lengths (Å) and angles (°): Nb(1)–O(1) 1.6939(18), Nb(1)–Cl(2) 2.3721(6), Nb(1)–Cl(3) 2.3777(6), Nb(1)–Cl(4) 2.3334(7), Nb(1)–O(2) 2.1879(17), Nb(1)–O(3) 2.3801(18); O(1)–Nb(1)–O(2) 92.57(8), O(1)–Nb(1)–Cl(4) 103.22(7), O(1)–Nb(1)–Cl(2) 97.73(6), O(1)–Nb(1)–Cl(3) 97.48(6).

---

[a] Dipartimento di Chimica e Chimica Industriale, University of Pisa, Via Risorgimento 35, I-56126 Pisa, Italy. E-mail: pampa@dcci.unipi.it; Fax: +050-2219-246; Tel: +050-2219-219
[b] Dipartimento di Chimica Fisica e Inorganica, University of Bologna, Viale Risorgimento 4, I-40136 Bologna, Italy

† Electronic supplementary information (ESI) available: Analytical data and experimental details of the X-ray crystal structure of compound **2**. CCDC 679568. For ESI and crystallographic data in CIF or other electronic format see DOI: 10.1039/b804432e

‡ Born in Bologna, Italy, in 1974.

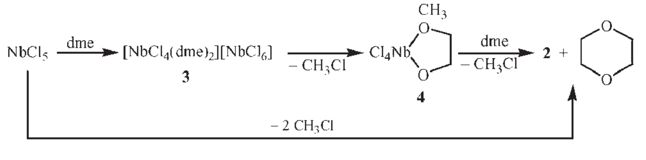
equation above.[14] However, in these conditions, minor amounts of the known complex $NbCl_5$(1,4-dioxane)[6b] have been detected by NMR,[15] this compound resulting from the coordination of 1,4-dioxane to the still unreacted $NbCl_5$. Moreover, small quantities of 1,2-dichloroethane and of the chloromethoxy derivative $[NbCl_3(OCH_3)_2]_2$[16] have been found (NMR, GC/MS), suggesting that diverse fragmentation pathways of dme are operating during the reaction with $NbCl_5$. A quantification of the relative amounts of the products has been possible by ^1H NMR spectroscopy, by using CH_2Cl_2 as reference.[15]

In order to discover possible intermediates, we carried out the reaction of **1** with one equivalent of dme, in $CDCl_3$ at −30 °C. ^1H NMR spectroscopy indicated the fast and complete disappearance of the resonances due to free dme and the growth of two resonances at 4.01 and 3.70 ppm, attributed to coordinated dme within the ionic species $[NbCl_4(dme)_2][NbCl_6]$, **3** (*vide infra*), containing a presumably octa-coordinated niobium centre. Octa-coordinated niobium adducts have been reported in the literature,[17] the most pertinent example being the ionic hexachloroniobate $[NbCl_4(S_2R_2)_2][NbCl_6]$, R = Me, Pr^i.[18] The resonances shown by **3** rapidly disappeared on warming at room temperature, due to conversion into the neutral $NbCl_4[O(CH_3)CH_2CH_2O]$, **4**, with concomitant formation of one equivalent of methyl chloride. Compound **4** has been identified by comparison of its NMR data with those collected for the product prepared by reaction of $NbCl_5$ with one equivalent of 2-methoxyethanol.[19]

Compound **3** was not isolated due to its thermal instability, but evidence of its ionic character was obtained by monitoring the conductivity during the reaction carried out in dichloromethane. The conductivity of the starting solution, $NbCl_5$ in CH_2Cl_2 at −30 °C, corresponded to 10 μSi immediately after the addition of dme, but was raised to 155 μSi after a few minutes due to the formation of the ionic species **3**. When the solution was allowed to warm up to room temperature (20 min), the conductivity decreased to 11 μSi, in agreement with the formation of neutral **4**, which is stable in the absence of uncoordinated dme. The successive formation of compound **2**, CH_3Cl and 1,4-dioxane (detected by ^1H NMR) takes place upon addition of further dme, see Scheme 1.

In conclusion, the reaction of $NbCl_5$ with dme (⩾2 equivalents) proceeds in two main steps: in the first step one O–CH_3 bond breaks giving methyl chloride and the methoxyniobium species **4**, whereas the second step consists of the cleavage of two C–O bonds (the remaining O–CH_3 bond and one of the two O–CH_2 bonds), with consequent formation of the oxo-derivative **2**, 1,4-dioxane and further methyl chloride.

The sequence of reactions reported in Scheme 1 is unprecedented, since it takes place through cleavage of three of the four dme C–O linkages at room temperature. These C–O bond breakages are partially counterbalanced by the establishment of one new C–O bond, inside the dioxane unit, thus the driving force of the overall process is presumably the formation of the strong niobium–oxygen double bond.[20] Actually the formation of strong Group 5 metal–oxygen bonds may be also related to the efficiency of MX_5 (M = Nb, Ta) as catalysts for the acylative cleavage of ethers.[2]



Scheme 1

The synthesis of the oxychloride species **2**, by combination of **1** with dme at room temperature, deserves further comment. In fact, examples of redox processes involving early transition metal halides and taking place in dme solutions have been reported; significantly, the reduction of $NbCl_5$ to Nb(III) is carried out by $SnBu_3H$ in dme.[21] According to the results discussed in the present communication, those processes might proceed *via* the formation of intermediates generated by preliminary reaction of the metal complex with dme itself.

The multiple C–O bond activation process described above occurs also when other 1,2-dialkoxyalkanes, different from dme, are involved. Thus, preliminary results indicate that the reactions of $NbCl_5$ with $CH_3O(CH_2)_2O(CH_2)_2OCH_3$ (diglyme), or with $C_2H_5O(CH_2)_2OC_2H_5$ give 1,4-dioxane/CH_3Cl or 1,4-dioxane/C_2H_5Cl, respectively, in quantities comparable to those observed for the reaction of **1** with dme. More interestingly, the reaction of $NbCl_5$ with two equivalents of 1,2-dimethoxypropane has led to the formation of 2,5-dimethyl-1,4-dioxane (GC/MS), indicating a new potential route for the synthesis of substituted 1,4-dioxanes.

This work was supported by the Consiglio Nazionale delle Ricerche (CNR, Roma), and the Ministero dell'Università e della Ricerca Scientifica (MIUR, Roma).

Notes and references

1 (*a*) R. L. Burwell, Jr, *Chem. Rev.*, 1954, **54**, 615; (*b*) M. V. Bhatt and S. U. Kulkarni, *Synthesis*, 1983, 249; (*c*) R. C. Larock, *Ether Cleavage in Comprehensive Organic Transformations*, Wiley-VCH, Weinheim, 2nd edn, 1999, p. 1013.

2 Q. Guo, T. Miyaji, R. Hara, B. Shen and T. Takahashi, *Tetrahedron*, 2002, **58**, 7327, and references therein.

3 (*a*) W. J. Evans, T. A. Ulibarri and J. W. Ziller, *Organometallics*, 1991, **10**, 134; (*b*) C. Eaborn, P. B. Hitchcock, K. Izod and J. D. Smith, *J. Am. Chem. Soc.*, 1994, **116**, 12071; (*c*) B.-J. Deelman, M. Booij, A. Meetsma, J. H. Teuben, H. Kooijman and A. L. Spek, *Organometallics*, 1995, **14**, 2306; (*d*) F. Preuss, G. Hornung, W. Frank, G. Reiss and S. Müller-Becker, *Z. Anorg. Allg. Chem.*, 1995, **621**, 1663; (*e*) K. Takaki, M. Maruo and T. Kamata, *J. Org. Chem.*, 1996, **61**, 8332; (*f*) D. J. Duncalf, P. B. Hitchcock and G. A. Lawless, *Chem. Commun.*, 1996, 269; (*g*) M. C. Cassani, M. F. Lappert and F. Laschi, *Chem. Commun.*, 1997, 1563; (*h*) C. A. Bradley, L. F. Veiros, D. Pun, E. Lobkovsky, I. Keresztes and P. J. Chirik, *J. Am. Chem. Soc.*, 2006, **128**, 16600.

4 (*a*) Y. K. Gun'ko, P. B. Hitchcock and M. F. Lappert, *J. Organomet. Chem.*, 1995, **499**, 213; (*b*) M. C. Cassani, Y. K. Gun'ko, P. B. Hitchcock, A. G. Hulkes, A. V. Khvostov, M. F. Lappert and A. V. Protchenko, *J. Organomet. Chem.*, 2002, **647**, 71; (*c*) S. Le Caër, M. Heninger, J. Lemaire, P. Boissel, P. Maître and H. Mestdagh, *Chem. Phys. Lett.*, 2004, **385**, 273; (*d*) S. La Caër, M. Heninger, P. Pernot and H. Mestdagh, *J. Phys. Chem. A*, 2006, **110**, 9654; (*e*) C. A. Bradley, L. F. Veiros and P. J. Chirik, *Organometallics*, 2007, **26**, 3191.

5 (*a*) A. Ecker, R. Köppe, C. Üffing and H. Schnöckel, *Z. Anorg. Allg. Chem.*, 1998, **624**, 817; (*b*) W. Uhl, A. Vester, D. Fenske and G. Baum, *J. Organomet. Chem.*, 1994, **464**, 23; (*c*) W. Uhl, R. Gerdin and A. Vester, *J. Organomet. Chem.*, 1996, **513**, 163; (*d*) W. Uhl, *Coord. Chem. Rev.*, 1997, **163**, 11; M. Westerhausen, C. Birg, H. Nöth, J. Knizek and T. Seifert, *Eur. J. Inorg. Chem.*, 1999, 2209.

6 (*a*) F. Marchetti, G. Pampaloni and S. Zacchini, *Dalton Trans.*, 2007, 4343; (*b*) F. Marchetti, G. Pampaloni and S. Zacchini, *Inorg. Chem.*, 2008, **47**, 365; (*c*) F. Marchetti, G. Pampaloni and T. Repo, *Eur. J. Inorg. Chem.*, 2008, 2107; (*d*) F. Marchetti, G. Pampaloni and S. Zacchini, *Polyhedron*, 2008, **27**, 1969.

7 *Crystal data* for **2**: $C_4H_{10}Cl_3O_3Nb$: M = 305.38, T = 100(2) K, orthorhombic, space group *Pbca*, a = 7.3270(7), b = 11.9741(11), c = 23.187(2) Å, V = 2034.2(3) $Å^3$, Z = 8, D_c = 1.994 g cm^{-3}, μ = 1.932 mm^{-1}, graphite-monochromatized Mo-Kα radiation (λ = 0.71073 Å). Final R indices were R_1 = 0.0239 and wR_2 = 0.0562 for 2150 independent reflections having $I > 2\sigma(I)$ ($R_{\rm int}$ = 0.0323). The diffraction experiments were carried out on a Bruker APEX II diffractometer equipped with a CCD detector and using Mo-Kα radiation. Data were corrected for Lorentz polarization and absorption effects [empirical absorption correction SADABS (G. M. Sheldrick, SADABS, *Program for empirical absorption correction*, University of Göttingen, Göttingen, Germany, 1997)]. Structures were solved by direct methods and refined by full-matrix least-squares based on all data using F^2 [G. M. Sheldrick, *SHELX97*, *Program for crystal structure determination*, University of Göttingen, Göttingen, Germany, 1997]. H-atoms were placed in calculated positions and treated isotropically using 1.2 × $U_{\rm iso}$ value of the parent atom except methyl protons, which were assigned 1.5 × $U_{\rm iso}$ value of the parent C-atom. All non-hydrogen atoms were refined with anisotropic displacement parameters.

8 E. M. Shustorovich, M. A. Porai-Koshits and Yu. A. Buslaev, *Coord. Chem. Rev.*, 1975, **17**, 1.

9 L. G. Hubert-Pfalzgraf and A. A. Pinkerton, *Inorg. Chem.*, 1977, **16**, 1895.

10 C. Chavant, J.-C. Daran, Y. Jeannin, G. Constant and R. Marancho, *Acta Crystallogr., Sect. B.*, 1975, **31**, 1828.

11 (*a*) W. Menzel and M. Fröhlich, *Ber. Dtsch. Chem. Ges.*, 1942, **75**, 1055; (*b*) F. Fairbrother, A. H. Cowley and N. Scott, *J. Less-Common Met.*, 1959, **1**, 206; (*c*) K. Dehnicke, *Naturwissenschaften*, 1965, 58.

12 The room-temperature generation of oxychlorides from the reaction of MCl_5 (M = Nb, Ta) with compounds containing E=O functionalities (E = C, P, As, S) under mild conditions (see ref. 13) is probably due to the presence of adventitious water rather than to a genuine E=O bond activation of the organic substrate (F. Marchetti, G. Pampaloni and S, Zacchini, *Eur. J. Inorg. Chem.*, 2008, 453).

13 R. A. Walton, *Prog. Inorg. Chem.*, 1972, **16**, 1.

14 A suspension of $NbCl_5$, **1** (0.220 g, 0.814 mmol), in CH_2Cl_2 (20 mL), was treated with dme (0.18 mL, 1.73 mmol), and the resulting mixture was stirred at room temperature for 5 h, during which progressive dissolution of the solid was noted. The volatile materials were removed *in vacuo* and recrystallization of the residue from CH_2Cl_2–pentane at room temperature gave pale yellow crystals of **2**. Yield: 0.174 g (70%).

15 CH_2Cl_2 (0.0289 mL, 0.451 mmol) and dme (0.0465 mL, 0.447 mmol) were introduced into a NMR tube containing a suspension of compound **1** (0.0600 g, 0.222 mmol) in $CDCl_3$ (0.80 mL). The tube was sealed, and a dark solution formed in 3 h. Subsequent ^1H and ^{13}C NMR analyses (recorded at 243 and at 298 K) revealed the presence of CH_2Cl_2, compound **2**, CH_3Cl [^1H NMR: 3.00 ppm (C. J. Pouchert and J. Behnke, *The Aldrich Library of ^{13}C and ^1H FT NMR Spectra*, Aldrich Chemical Company Inc., Milwaukee, USA, 1st edn, 1993)], 1,4-dioxane, 1,2-dichloroethane and the known complexes $NbCl_5$(1,4-dioxane) (see ref. 6*b*) and $[NbCl_3(OCH_3)_2]_2$ (*see* ref. 16), in *ca.* 20 : 9 : 17 : 2 : 1 : 2 : 1 ratio. GC/MS analysis of the solution, filtered on alumina to remove the inorganic materials, indicated the presence of dme, CH_3Cl, 1,4-dioxane and 1,2-dichloroethane.

16 A. Antiñolo, A. Otero, F. Urbanos, S. Garcia-Blanco, S. Martinez-Carrera and J. Sanz-Aparicio, *J. Organomet. Chem.*, 1988, **350**, 25.

17 T. Waters, A. G. Wedd, M. Ziolek and I. Nowak, Niobium and Tantalum, , in *Comprehensive Coordination Chemistry II*, ed. J. A. McCleverty, T. J. Meyer and A. G. Wedd, Elsevier, Pergamon, 2004, p. 260 and ff, vol. 4.

18 P. J. McKarns, M. J. Heeg and C. H. Winter, *Inorg. Chem.*, 1998, **37**, 4743.

19 A. J. Jones and J. D. Wilkins, *J. Inorg. Nucl. Chem.*, 1976, **38**, 95.

20 M. W. M. Hisham and S. W. Benson, *J. Phys. Chem.*, 1986, **90**, 885.

21 S. F. Pedersen, J. B. Hartung, Jr, E. J. Roskamp and P. S. Dragovich, *Inorg. Synth.*, 1992, **29**, 119.