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Transition Metal Complexes-Catalyzed Synthesis of 2,4,7,9-Tetraoxadecane and Homologs

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Abstract : polyether molecules are readily available from cheap acetals with a catalyst system based on ruthenium and tin(II) chloride. As a model reaction 1,3-dioxolane 2 reacts with dimethoxymethane 3 to yield 78% of 2,4,7,9-tetraoxadecane 1. © 1998 Published by Elsevier Science Ltd. All rights reserved.

It is known that alkoxy derivatives of glycerol methyl ethers exhibit highly effective insecticidal properties.¹ Mamedov *et al.* have studied the biological activity of the alkoxy derivatives of the methyl ethers of ethylene glycol.² Moreover, methoxy-methyl ethers are commonly used for protection of OH-groups in natural product synthesis. In this context, polyoxygenated molecules such as 2,4,7,9-tetraoxadecane (TOD, 1) are interesting polyethers not only from a biological point of view, but also as a precursor in the synthesis of perfluorinated compounds,³ as a solvent, or as a cation-binding ligand.

However, among the molecules synthesized from 1,3-dioxolane and dialkoxymethanes, only TOD appears to have been reported. The most efficient syntheses found so far in the literature include either the reaction of α -chloromethylalkyl ethers with ethylene glycol in the presence of dimethylaniline⁴ or of the bis(chloromethyl)ether of glycol with the appropriate alkoxides⁵. The yields of TOD (calculated from ethylene glycol) remain however low (< 30%) and the synthetic interest of the method is strongly limited owing to the known carcinogenic properties of chloroalkylethers. Alternate procedures using alcohols and acetals with Brönsted or Lewis acids as catalysts have therefore been introduced for its preparation.⁶ 2,4,7,9-Tetraoxadecane was then obtained in 34 % yield from 2-methoxymethoxyethanol and dimethoxymethane (methylal, 3) in the presence of sulfuric acid.⁷

More recently, Gras proposed a more convenient synthetic route to TOD, directly from ethylene glycol and methylal with *p*-toluene sulfonic acid and lithium bromide as catalyst. The reaction, however, leads rapidly to a mixture of products including TOD, 2-methoxymethoxyethanol, and unreacted methylal.⁸ The synthesis of TOD directly from 1,3-dioxolane 2 and methylal was described in 1941 by Gresham but the yield Fax : 00-32-(0)4-366.34.97; E-mail : AF.Noels@ulg.ac.be was very poor (14%).⁹ The same reaction was also reported in a patent (50% yield) but neither the catalyst nor the reaction temperature were given.¹⁰ We now propose a new, ready and high yield catalytic synthesis of 1 from 2 and 3 and where methylal is used at the same time as reactant and solvent (Scheme 1).

Scheme 1



We have tested the catalytic activity of a variety of Lewis acids including *inter alia* group 3 metal triflates (Sc(OTf)₃, La(OTf)₃, Yb(OTf)₃, LaCl₃, ...) under our reaction conditions, *i.e.* in refluxing methylal. The results obtained were then quite similar to those reported in the literature, the yields rarely exceeding 30-40%. The observation that iron(III) chloride catalyzed the formation of TOD in more than 50% yield prompted us to test the catalytic efficiency of different transition metal chlorides. To the best of our knowledge, transition metal complexes have never been used as catalysts for the synthesis of polyethers or polyacetals. The efficiencies and specificities of the most active catalysts are summarized in table 1. RuCl₃ and RhCl₃ were show to be almost as

Catalyst	T(°C)	t (h)	Yield (%)		
			TOD	MME	HOPD
RuCl ₃ a	RT	48	41	2	12
,,	60	"	46	1	4
RuCl ₃ / SnCl ₂ ^b	RT	"	19	1	<1
"	60	"	78	7	2
RuCl ₃ / SnCl ₂ (toluene) ^c	"	"	15	3	3
RuCl ₃ / SnCl ₂ (CH ₂ Cl ₂) ^c	"	**	54	8	4
FeCl ₃ ^a	"	**	52	2	12
FeCl ₃ / SnCl ₂ ^b	"	7	32	<1	2
"	"	48	25	<1	2
RhCl ₃ a	,,,,,,,,,,,,,,,,,,,,,,,,,,,,,,,,,,,,,,,	"	46	2	10

Table 1. Transition metal complexes-catalyzed synthesis of 2,4,7,9-tetraoxadecane.

Reaction conditions : (a) 35 mL of methylal; 0.1 mol of dioxolane; 10^4 mol of catalyst; (b) 35 mL of methylal; 0.1 mol of dioxolane; 10^4 mol of catalyst; 2 10^4 mol of tin(II) chloride; (c) 0.1 mol of methylal; 0.1 mol of dioxolane; 10^4 mol of catalyst; 35 mL of solvent.

effective as $FeCl_3$ in catalyzing the formation of TOD. In addition to TOD, small amounts of 2methoxymethoxyethanol (MME, 4, yield < 8%) and of a new molecule, tentatively characterized as 2,4,7,9,12,14-hexaoxapentadecane (HOPD, max. yield 12%) were also formed. None of the other transition metal complexes tested (OsCl₃, CoCl₂, IrCl₃, TiCl₄, PdCl₂, ...) displayed a similar or higher efficiency. A most interesting synthetic aspect of the ruthenium-catalyzed reaction is the co-catalytic effect of tin(II) chloride. The yield of TOD was substantially improved (to 78%) after addition of 2 equiv. of SnCl₂. In this particular case, we observed a color change of the reaction medium after addition of SnCl₂, an indication that a redox reaction was probably taking place between Ru(III) and Sn(II) salts.¹¹ The promoting effect of tin(II) chloride was observed only with RuCl₃, SnCl₂ alone giving only a modest 5% yield of 1.

The reaction can be generalized to other dialkoxymethanes such as ethylal, n-propanal and iso-propanal to give respectively 40, 35 and 28% of the corresponding 3,5,8,10-tetraoxadecane, 4,6,9,11-tetraoxatetraoxadecane and 2,11-dimethyl-4,6,9,11-tetraoxatetraoxadecane.

A plausible reaction mechanism is sketched in scheme 2. This catalytic cycle is closely related to that reported in the literature for the polymerization of 1,3-dioxolane catalyzed by Lewis acid.¹² Further studies are needed in order to assess more precisely the specific role of the transition metal and the fine tuning of the catalyst brought about by the addition of tin(II) chloride.



Scheme 2

2,4,7,9-tetraoxadecane and homologs are thus readily available from cheap starting materials. Further studies are under way to extend the reaction to other molecules.

Experimental section

The title molecules were prepared according to the procedure employed for TOD (1) : 5 10⁻⁴ mol of catalyst is added to a solution of 1,3-dioxolane 2 (7 mL, 0.1 mol) in 35 mL of dry methylal 3. The reaction mixture is then stirred for 48h at reflux temperature (60 °C) and the reaction monitored by GC. The yields were calculated by GC (FID with nitrogen as carrier gas) with *o*-xylene as internal standard, after calibration and introduction of substance-specific correction factors for the most important products. Products were identified by NMR and by comparison of their retention times with authentic samples (1 and 4) on at least two different GC fused silica capillary columns respectively a 30 m x 0.32 mm WCOT polydimethylsiloxane-CB column (RSL 150), and with a 30 m x 0.32 mm DB-FFAP WB.

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References

- 1. Mamedov, S.; Avanesyan, M.A.; Osipov, O.B.; Grishina, E.N. USSR Patent 136,981, 25 Mar 1961, Chem. Abstr. 1961, 55, 27758.
- 2. Mamedov, S.; Dzhalilov, T.N.; Osipov, O.B.; Seid-Rzaeva, Z.M. USSR patent 745,285, 1962; Byull. Izobr., 1962, N°20.
- Lagow, R.J. in Encyclopedia of Chemical Technology, vol. 11, Fluorine Compounds, Organic : direct Fluorination, J. Wiley and Sons Inc. (Eds.), 4th ed, 1994, p. 482-499.
- 4. Mamedov, S.; Avanesyan, M.A. Zh. Obshch. Khim., 1962, 32, 813.
- (a) Lichtenberger, J.L.; Martin, L. Bull. Soc. Chim., 1945, 12, 114; (b) Mamedov, S.; Dzhalilov, T.N. Zh. Obshch. Khim., 1963, 33, 846; (c) Ross, S.D.; Barry, J.E.; Finkelstein, M.; Rudd, E.J.J. Am. Chem. Soc., 1973, 95, 2193.
- Ivanov, V.V.; Sabirova, R.D.; Markevich, M.A.; Aleksanyan, Zh.G.; Enikolopyan, N.S. Dokl. Akad. Nauk. SSSR, 1968, 183, 371.
- 7. Sussman, S. US Patent 2,321,557, (08 Jun 1943), Chem. Abstr. 1943, 37, 6674.
- 8. Gras, J-L.; Kong Win Chang, Y.Y.; Guerin, A. Synthesis, 1985, 74.
- 9. Gresham, W.F. US patent 2,382,874, (14 Aug 1945), Chem. Abstr. 1946, 40, 592.
- 10. Bierschenk, T.R.; Juhlke, T.; Kawa, H.; Lagow, R.J. PCT. Int. Appl. WO 90 03,353 (05 Apr 1990), Chem. Abstr. 1991, 114, 31007w.
- 11. (a) Hamlin, J.E.; Maitlis, P.M. J. Mol. Catal., 1986, 11, 129; (b) Deshpande, V.M.; Patterson, W.R.; Narasimhan, C.S. J. Catal., 1990, 121, 165.
- (a) Höcker, H.; Keul, H. Adv. Mater., 21, 6, 1994 and references cited therein; (b) Curioni; A.; Sprik, M.; Andreoni, W.; Schiffer, H.; Hutter, J.; Parrinello, M. J. Am. Chem. Soc., 1997, 119, 7218-7229; (c)Sen, S.E.; Roach, S.L.; Boggs, J.K.; Ewing, G.J.; Magrath, J. J. Org. Chem., 1997, 62, 6684-6686.