

# Activation Reactions of 1,1-Dialkoxoalkanes and Unsaturated O-Donors by Titanium Tetrafluoride

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## Abstract

The reactivity of  $\text{TiF}_4$  with a variety of non cyclic 1,1-dialkoxoalkanes [ $\text{CH}_2(\text{OR})_2$ , R = Me, Et,  $\text{Me}_2\text{C}(\text{OMe})_2$ ,  $\text{MeCH}(\text{OEt})_2$ ,  $\text{ClCH}_2\text{CH}(\text{OEt})_2$ ,  $\text{CH}(\text{OMe})_3$ ,  $\text{PhC}\equiv\text{CCH}(\text{OEt})_2$ ], 1,3-dioxolane,  $\text{N}_2\text{CHCO}_2\text{Et}$  and 1,2-epoxybutane has been investigated. Activation, including fragmentation and/or rearrangement of the organic moiety, has been observed at room temperature in some cases; it generally occurs unselectively via C–O bond fission and the formation of new C–O, C–H and C–C bonds. Small differences in the structure of the organic substrate may determine significant differences in the reactivity with  $\text{TiF}_4$ .

*Keywords:* titanium / fluoride / activation / O-donor / coordination

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## 1. Introduction

The reactivity of titanium tetrafluoride has been much less developed with respect to that of the heavier congeners, especially the tetrachloride  $\text{TiCl}_4$  [1]. One of the reasons is probably related to the particular inertness of  $\text{TiF}_4$ , due to the polymeric structure in the solid state [2] and the strength of the Ti–F bond ( $D_0 = 584$  kJ/mol, to be compared with Ti–Cl,  $D_0 = 429.3$  kJ/mol, Ti–Br,  $D_0 = 366.9$  kJ/mol, and Ti–I,  $D_0 = 296.2$  kJ/mol) [3].

Titanium tetrafluoride and O-donors L generally form 1:2 adducts of formula  $\text{TiF}_4\text{L}_2$ , L = thf [4],  $\text{Ph}_3\text{PO}$  [5], disso [6], dimethylformamide [6c] dimethylacetamide [6c, 7], tetramethylurea [6c], substituted pyridine- and quinoline-*N*-oxide [8]. Complex  $\text{TiF}_4(\text{dme})$  is obtained by straightforward 1:1 reaction of  $\text{TiF}_4$  with 1,2-dimethoxyethane (dme) [9]. Polymeric fluorine-bridged complexes may be obtained with weak Lewis bases such as pyridine [7c] and benzonitrile [10]

Compounds of formula  $\text{TiF}_4\text{L}_2$  show generally the *cis*-configuration although *cis-trans* equilibria in solution have been observed when strongly donating, sterically hindered ligands are involved [8a, 11].

The strong Ti–F bond is not cleaved by alcohols, which react with TiF<sub>4</sub> affording TiF<sub>4</sub>(ROH)<sub>2</sub> adducts, R = Me [12], Et [6c, 12], Pr<sup>i</sup> [12]. It is remarkable that TiF<sub>4</sub> forms a stable coordination adduct upon reaction with water [13], in contrast with the behaviour normally exhibited by other early transition metal halides in high oxidation state, which rapidly hydrolyze to give oxide derivatives [14]. Moreover HF is not produced in the reaction of TiF<sub>4</sub> with salenH<sub>2</sub> in boiling thf, Scheme 1, which affords the 1:1 adduct TiF<sub>4</sub>(salenH<sub>2</sub>): cleavage of the Ti–F bond and formation of TiF<sub>2</sub>(salen) is achieved in the presence of the SiMe<sub>3</sub> fragment [15].

### **Scheme 1 about here**

Recently we reported on the reactions of MX<sub>5</sub> (M = Nb, Ta; X = F, Cl, Br, I), MoCl<sub>5</sub> and WCl<sub>6</sub> with *O*-donor species, showing that the formation of the strong M–O bond favours the C–O cleavage within the organic unit, possibly resulting in fragmentation and rearrangement reactions even at room temperature [16]. In particular the reactions involving diethers showed the formation of new C–C and C–O bonds, and higher reactivity was observed with 1,1-dialkoxyalkanes rather than 1,2-dialkoxyalkanes [17, 18]. These reactions are strongly influenced by the nature of the halide, the fluorides MF<sub>5</sub> (M = Nb, Ta) usually activating the diether at high temperatures only [16a].

At variance to niobium and tantalum derivatives, the group 4 tetrahalides MX<sub>4</sub> (M = Ti, Zr, X = Cl, Br, I) adducts with 1,2-dialkoxyalkanes are less prone to undergo activation of the coordinated organic fragments [9]. On the other hand, it was reported that TiCl<sub>4</sub> may show the “deprotecting” behaviour typical of Lewis acids with respect to 1,1-dialkoxyalkanes (acetal and ketals), thus determining the generation of the relevant carbonylic compounds [19]. Conversely, it was found that TiCl<sub>4</sub> was able to activate substituted dioxolanes to give chlorinated organic compounds [20].

In this context, we decided to explore the chemistry of the relatively inert  $\text{TiF}_4$  with 1,1-dialkoxoalkanes or unsaturated oxygen compounds. The results of this investigation are reported in the present paper.

## 2. Results and Discussion

Titanium tetrafluoride reacted slowly with  $\text{CH}_2(\text{OR})_2$ ,  $\text{R} = \text{Me, Et, Me}_2\text{C}(\text{OMe})_2, \text{MeCH}(\text{OEt})_2, \text{ClCH}_2\text{CH}(\text{OEt})_2$ , either at room temperature or at ca.  $80^\circ\text{C}$ , affording mixtures of products which prevented the identification of any coordination compound. However, it was possible to identify the products of the activation of the organic substrate after exhaustive hydrolysis of the reaction mixture, Table 1, runs 1-5.

### Table 1 about here

The data of Table 1 suggest that the reactions are not selective, similarly to what observed in the analogous reactivity of Group 5 metal pentahalides [17]. The reaction of  $\text{TiF}_4$  with  $\text{CH}_2(\text{OMe})_2$  (Table 1, run 1) produced methyl formate and dimethylether. These compounds were identified together with a significant amount of unreacted  $\text{CH}_2(\text{OMe})_2$ . In addition  $\text{MeOH}$  was found in the reaction mixture after hydrolysis. An increase of the reaction temperature and/or the  $\text{CH}_2(\text{OMe})_2/\text{Ti}$  molar ratio caused a substantial increase of dimethylether (Table 2, run 2). The presence of  $\text{HCO}_2\text{Me}$  and  $\text{Me}_2\text{O}$  suggests that the activation reaction proceeds with cleavage of  $\text{C-O}$  and  $\text{C-H}$  bonds followed by formation of new  $\text{C-O}$  and  $\text{C-H}$  bonds, see Scheme 2a,b. The presence of methanol might be the consequence of the formation of the  $[\text{Ti-OMe}]$  unit, see Scheme 2c.

### Table 2, Scheme 2 about here

According to the Me<sub>2</sub>O/MeOH molar ratio detected (16:1, Table 1, run 1), process **b** should occur more easily than process **c** (Scheme 2).

The reaction of TiF<sub>4</sub> with CH<sub>2</sub>(OEt)<sub>2</sub> proceeds similarly to what discussed for CH<sub>2</sub>(OMe)<sub>2</sub>. Thus HCO<sub>2</sub>Et and EtOH (ratio 1:3) have been identified after hydrolysis of the reaction mixture (Table 1, run 2). It is interesting to note that the analogous reaction involving MF<sub>5</sub> (M = Nb, Ta) gave the mixed ether OMeEt, as a consequence of the concerted activation of C–O and C–H bonds [17]. In the case of TiF<sub>4</sub> and CH<sub>2</sub>(OEt)<sub>2</sub>, ethers do not form thus suggesting that pathways **b** and **c** (Scheme 2) are almost non viable (see Scheme 3) and that a small variation in the structure of the substrate can determine strong difference in the nature of the reaction products.

### **Scheme 3 about here**

The hydrolysis of the mixture obtained by reaction of TiF<sub>4</sub> with MeCH(OEt)<sub>2</sub> gave only EtOH and Et<sub>2</sub>O as identifiable materials (Table 1, run 3). Although a similar process to that reported in Scheme 2 may be invoked, it has not been possible to identify the other products necessary for the full justification of the fragmentation scheme.

A substantially different reactivity was observed by formal substitution of a methyl hydrogen with chlorine. In fact the reaction between TiF<sub>4</sub> and ClCH<sub>2</sub>CH(OEt)<sub>2</sub> gave ClCH<sub>2</sub>CHO (Table 1, run 4): in this case, TiF<sub>4</sub> seems to behave as a traditional Lewis acid, “deprotecting” the carbonyl functionality (see Introduction) [19, 21]. Hydrolysis of the reaction mixture did not change the relative composition of the organic compounds. A similar result was obtained on increasing the reaction temperature or the substrate / Ti molar ratio (table 2, run 6).

The reaction of Me<sub>2</sub>C(OMe)<sub>2</sub> with TiF<sub>4</sub> was fast even at room temperature and gave, after hydrolysis, MeOH plus minor amounts of MeCO<sub>2</sub>Me, Me<sub>2</sub>O and Me<sub>2</sub>CO (Table 1, run 5). A possible scheme of formation is given (Scheme 4). It is interesting to note that the same reaction performed

with NbF<sub>5</sub> afforded mesityloxide [17], i.e. the product of acetone dehydration, thus confirming the higher affinity for water of NbF<sub>5</sub> with respect to TiF<sub>4</sub> [1, 14].

#### **Scheme 4 about here**

Trimethoxymethane reacted with TiF<sub>4</sub> at room temperature affording Me<sub>2</sub>O and HCO<sub>2</sub>Me in comparable amounts (molar ratio ca. 14:10; Table 1, run 6). Analogous activation process was observed previously in the case of NbF<sub>5</sub> [17]. The presence of dimethylether suggests that the coupling between different fragments, including the formation of a new C–O bond, is operative in the system, see Scheme 5. Methanol was observed in the reaction mixture after hydrolysis.

#### **Scheme 5 about here**

An interesting case of C–C bond formation was observed when a dichloromethane suspension of TiF<sub>4</sub> was treated with 1,3 dioxolane. After heating and hydrolysis steps, HCO<sub>2</sub>Me, 1,4-dioxane, MeO(CH<sub>2</sub>)<sub>2</sub>OMe, and Me<sub>2</sub>O were identified in 8:20:10:10 molar ratios (Table 1, run 7). With a conversion of ca. 20%, 1,4-dioxane represents the product formed in higher amount in this reaction. A tentative suggestion concerning the formation of 1,4-dioxane from 1,3 dioxolane is sketched in scheme 6 and implies the formation of a new C–C bond with intermolecular transfer of a [CH<sub>2</sub>] fragment.

#### **Scheme 6 about here**

In agreement with the relatively weak Ti–Cl bond (see Introduction), the reaction between  $\text{TiCl}_4$  and substituted dioxolanes proceeds with ring opening and chlorination of the organic fragment [20].

1,3-Dioxolane and  $\text{CH}_2(\text{OEt})_2$  were reacted with the acetonitrile adduct  $\text{TiF}_4(\text{CH}_3\text{CN})_2$ , which was considered more reactive than  $\text{TiF}_4$  in view of its mononuclear structure [10]. We observed that a low amount of acetonitrile (8 and 20%, respectively) was released after 20 days at room temperature or some hours at ca. 70 °C. No activation of the organic molecule was observed under the same experimental conditions used for the reactions with  $\text{TiF}_4$ .

In order to investigate in more detail the possibility of fluorine-transfer reactions, we allowed  $\text{TiF}_4$  to react with compounds containing unsaturated functionalities such as propargylic alcohol and the diethylacetal of phenylpropynal,  $\text{PhC}\equiv\text{CCH}(\text{OEt})_2$  (Table 1, run 8). No activation was observed in the first case while small amounts of EtOH were formed under drastic conditions in the latter reaction.

Even the three-membered ring of 1,2-epoxybutane was not activated by means of  $\text{TiF}_4$ , and the probable formation of a coordination adduct could not be demonstrated (Table 1, run 9). The treatment of the reaction mixture with water caused the presumable metal-assisted quantitative conversion to 1,2-diol [22]. It has to be remarked that epoxides easily undergo ring-opening reactions in the presence of metal halides of Group 5, affording either halo-alkoxo or ketone complexes depending on the halide [23].

Titanium tetrafluoride reacted with ethyldiazoacetate at room temperature affording  $\text{CH}_2\text{FCOOEt}$  as prevalent product, although in low yield (ca. 35 %) (Table 1, run 10, Scheme 7).

#### **Scheme 7 about here**

The formation of ethylfluoroacetate is the result of the formal addition of HF to the fragment obtained by dinitrogen loss. It is noteworthy that, under comparable experimental conditions, the

reaction of NbF<sub>5</sub> with N<sub>2</sub>CHCO<sub>2</sub>Et generated the stable coordination adduct NbF<sub>5</sub>[O=C(OEt)CHN<sub>2</sub>] [24].

### 3. Conclusions

Suspensions of TiF<sub>4</sub> in chlorinated solvents promote room temperature fragmentation and rearrangement of *O*-containing species, mainly 1,1-dialkoxyalkanes. The reactions are generally slow due to the polynuclear structure of TiF<sub>4</sub>. The organic compounds identified after hydrolysis of the reaction mixtures suggest that both cleavage and formation of C–O, C–H and C–C bonds may occur during the reactions. Interestingly, small structural differences within the organic compound may determine strong differences in the nature of the products. A summary of the reaction products is reported in Table 1.

The possible formation of Ti–OR species, evidenced on the basis of the nature of the products, may represent an exception to the general observation that the strong Ti–F bond is not cleaved by oxygen containing species, including protic reagents like water and alcohols.

The presence of one unsaturated group adjacent to the *O*-functionality does not substantially influence the nature of the products. Fluorine transfer has been clearly observed only in the case of the reaction of TiF<sub>4</sub> with ethyldiazoacetate, yielding CH<sub>2</sub>FCO<sub>2</sub>Et.

### 4. Experimental

All manipulations of air and/or moisture sensitive compounds were performed under an atmosphere of pre-purified argon using standard Schlenk techniques. The reaction vessels were oven dried at 150 °C prior to use, evacuated (10<sup>-2</sup> mmHg) and then filled with argon. TiF<sub>4</sub> was purchased from Sigma Aldrich, stored in sealed tubes under argon as received, and used without further purification. TiF<sub>4</sub>(CH<sub>3</sub>CN)<sub>2</sub> was prepared according to the literature [10].



$^1\text{H}$  NMR spectra were recorded on Bruker Avance DRX400 (BBFO probe) on  $\text{CDCl}_3$  solutions at 298 K. The chemical shifts were referenced to the non-deuterated aliquot of the solvent.

GC/MS analyses were performed on a HP6890 instrument, interfaced with a MSD-HP5973 detector and equipped with a Phenomenex Zebron column.

#### *4.1. Reactions between $\text{TiF}_4$ and $\text{TiF}_4(\text{CH}_3\text{CN})_2$ with O-donors: general procedure.*

Only the detailed procedure is described for  $\text{TiF}_4$ , that used with the acetonitrile adduct being substantially the same.  $\text{TiF}_4$ ,  $\text{CDCl}_3$  (0.5 mL),  $\text{CH}_2\text{Cl}_2$  ( $\text{CH}_2\text{Cl}_2/\text{Ti}$  molar ratio = 1) and the organic reagent were introduced into a NMR tube. The tube was sealed, stirred to obtain a homogeneous suspension and stored at room temperature. After variable periods of time (see Table 2), NMR spectra were recorded. Then the mixture was heated at temperature as high as 80 °C. Thus the tube was cooled to ca. -30 °C and opened: the mixture was treated with water (ca. 1 mL). After 1h stirring at room temperature, the resulting suspension was filtered and the solution was examined by NMR. Table 2 reports the experimental details of the reactions.

In the case of the reactions of  $\text{TiF}_4(\text{CH}_3\text{CN})_2$  with  $\text{CH}_2(\text{OEt})_2$  and 1,3-dioxolane, respectively 20% and 8% of acetonitrile was released into the solution after 20 days stirring at room temperature. In both cases, the organic reactant was the only product which could be detected after prolonged heating of the reaction mixture followed by hydrolysis.

### **Acknowledgements**

The authors wish to thank the Ministero dell'Istruzione, dell'Università e della Ricerca (MIUR, Roma), for financial support.

### **References**

- [1] (a) R. J. H. Clark, *The Chemistry of Titanium and Vanadium*, Elsevier, Amsterdam, 1968;  
(b) R. Colton, J. H. Canterford, *Halides of the Transition Elements: Halides of the First Row Transition Metals*, Wiley Interscience, London, 1969;  
(c) R. J. Clark, in *Comprehensive Inorganic Chemistry*, J. C. Bailar, Jr., H. J. Emeleus, R. S. Nyholm, A. F. Trotman-Dickenson (Eds.), Pergamon, Oxford 1973, 355.
- [2] H. Bialowons, M. Müller and B. G. Müller, *Z. Anorg. Allg. Chem.* 621 (1995) 1227.
- [3] J. E. Huheey, E. A. Keiter, R. L. Keiter, *Inorganic Chemistry: Principles of Structure and Reactivity*, 4<sup>th</sup> Edition, Harper and Collins, New York, 1993.
- [4] M. Jura, W. Levason, E. Petts, G. Reid, M. Webster, W. Zhang, *Dalton Trans.* 39 (2010) 10264.
- [5] E. G. Il'in, G. B. Nikiforov, G. G. Aleksandrov, *Dokl. Chem.* 396 (2004) 111.
- [6] (a) G. B. Nikiforov, S. G. Sakharov, E.G. Il'in, Yu.A. Buslaev, *Russ. J. Inorg. Chem.* 46 (2001) 1045;  
(b) E. G. Il'in, G. B. Nikiforov, G. G. Aleksandrov, V. S. Sergienko, Yu. A. Buslaev, *Dokl. Akad. Nauk* 367 (1999) 772;  
(c) E. L. Muetterties, *J. Am. Chem. Soc.* 84 (1960) 1082.
- [7] D. S. Dyer, R. O. Ragsdale, *Inorg. Chem.* 6 (1967) 8.
- [8] (a) F. E. Dickson, E. W. Gowling, F. F. Bentley, *Inorg. Chem.* 6 (1967) 1099;  
(b) D. S. Dyer, R. O. Ragsdale, *Inorg. Chem.* 6 (1967) 1116;  
(c) C. E. Michelson, D. S. Dyer, R. O. Ragsdale, *J. Chem. Soc. (A)* (1970) 2296.
- [9] F. Marchetti, G. Pampaloni, *Inorg. Chim. Acta* 363 (2010) 3670.
- [10] G. B. Nikiforov, C. Knapp, J. Passmore, A. Decken, *J. Fluorine Chem.* 127 (2006), 1398.
- [11] (a) E. Turin, R. M. Nielson, A. E. Merbach, *Inorg. Chim. Acta* 134 (1987) 67.
- [12] R. O. Ragsdale, B. B. Stewart, *Inorg. Chem.* 2 (1963) 1002.
- [13] (a) T. S. Cameron, A. Decken, E. G. Ilyin, G. B. Nikiforov, J. Passmore, *Eur. J. Inorg. Chem.* (2004) 3865;

- (b) N. N. Greenwood, A. Earnshaw, 2nd Edition, Elsevier, Amsterdam, 1997;
- (c) Yu. A. Buslaev, D. S. Dyer, R. O. Ragsdale, *Inorg. Chem.* 6 (1967) 2208.
- [14] (a) F. Fairbrother, The Halides of Niobium and Tantalum, in *Halogen Chemistry*, V. Gutmann, Ed., 1967, Vol 3, p. 123.
- (b) A. D. Beveridge, H. C. Clark, Pentahalides of Transition Metals, in *Halogen Chemistry*, V. Gutmann, Ed., 1967, Vol 3, p. 179.
- [15] S. J. Coles, M. B. Hursthouse, D. G. Kelly, A. J. Toner, N. M. Walker, *J. Chem. Soc., Dalton Trans.* (1988) 3489.
- [16] (a) F. Marchetti, G. Pampaloni, *Chem. Commun.* (2012) 635;
- (b) S. Dolci, F. Marchetti, G. Pampaloni, S. Zacchini, *Dalton Trans.* (2010) 5367;
- (c) S. Dolci, F. Marchetti, G. Pampaloni, S. Zacchini, *Inorg. Chem.* 50 (2011) 3846.
- [17] F. Marchetti, G. Pampaloni, S. Zacchini, *Dalton Trans.* (2009) 8096.
- [18] F. Marchetti, G. Pampaloni, S. Zacchini, *Dalton Trans.* (2008) 7026.
- [19] G. Balme, J. Gorè, *J. Org. Chem.* 48 (1983) 3336.
- [20] P. Mastagli, M. de Nanteuil, *C. R. Acad. Sc. Paris* 268 (1969) 1970.
- [21] (a) T. W. Greene, P. G. M. Wuts, *Protecting Groups in Organic Synthesis*, J. Wiley, New York, 1999, 3<sup>rd</sup> Edition., ch. 4, p. 293; (b) R. C. Larock, *Comprehensive Organic Transformations*, Wiley-VCH, New York, 2<sup>nd</sup> Edition., 1999; (c) M. B. Smith, J. March, *March's Advanced Organic Chemistry*, J. Wiley, 5<sup>th</sup> Edition, New York, 2001.
- [22] (a) A. Gansäuer, A. Barchuk, F. Keller, M. Schmitt, S. Grimme, M. Gerenkamp, C. Mück-Lichtenfeld, K. Daasbjerg, H. Svith, *J. Am. Chem. Soc.* 129 (2007) 1359;
- (b) A. W. Eppley, N. I. Totah, *Tetrahedron* 53 (1997) 16545;
- (c) K. Fujiwara, T. Tokiwano, A. Murai, *Tetrahedron Lett.* 36 (1995) 8063;
- (d) M. Emziane, P. Lhoste, D. Sinou, *J. Mol. Cat.* 49 (1988) L23;
- (e) A. E. Vougioukas, H. B. Kagan, *Tetrahedron Lett.* 28 (1987) 6065.

[23] F. Marchetti, G. Pampaloni, S. Zacchini, *Polyhedron* 28 (2009) 1235.

[24] F. Marchetti, G. Pampaloni, S. Zacchini, *Dalton Trans.* (2008) 6759.

## Captions for Tables

Table 1. Summary of the organic compounds obtained from  $\text{TiF}_4$  and 1,1-dialkoxoalkanes,  $\text{CH}(\text{OMe})_3$ ,  $\text{PhC}\equiv\text{CCH}(\text{OEt})_2$ , 1,2-epoxybutane,  $\text{N}_2\text{CHCO}_2\text{Et}$ , after hydrolysis of the reaction mixtures.

Table 2. Experimental details of the reactions between  $\text{TiF}_4$  and *O*-donors.

**Table 1**

Run	Reagent (L)	Products (molar ratios) <sup>d</sup>
1	CH <sub>2</sub> (OMe) <sub>2</sub> <sup>a</sup>	HCO <sub>2</sub> Me + CH <sub>2</sub> (OMe) <sub>2</sub> + MeOH + Me <sub>2</sub> O (10 : 5 : 1 : 16)
2	CH <sub>2</sub> (OEt) <sub>2</sub> <sup>a</sup>	CH <sub>2</sub> Cl <sub>2</sub> + HCO <sub>2</sub> Et + CH <sub>2</sub> (OEt) <sub>2</sub> + EtOH (10 : 1 : 5 : 3)
3	MeCH(OEt) <sub>2</sub> <sup>a</sup>	CH <sub>2</sub> Cl <sub>2</sub> + MeCH(OEt) <sub>2</sub> + EtOH + Et <sub>2</sub> O (4 : 1 : 4 : 1)
4	ClCH <sub>2</sub> CH(OEt) <sub>2</sub> <sup>b,c</sup>	CH <sub>2</sub> Cl <sub>2</sub> + ClCH <sub>2</sub> CHO + ClCH <sub>2</sub> CH(OEt) <sub>2</sub> + ClCH <sub>2</sub> CO <sub>2</sub> Et (10 : 14 : 1 : 0.5)
5	Me <sub>2</sub> C(OMe) <sub>2</sub> <sup>a</sup>	CH <sub>2</sub> Cl <sub>2</sub> + MeCO <sub>2</sub> Me + MeOH + Me <sub>2</sub> O + Me <sub>2</sub> CO (10 : 0.4 : 4 : 0.3 : 0.4)
6	HC(OMe) <sub>3</sub> <sup>a</sup>	CH <sub>2</sub> Cl <sub>2</sub> + HCO <sub>2</sub> Me + MeOH + Me <sub>2</sub> O (10 : 7 : 1 : 5)
7	1,3-dioxolane <sup>a</sup>	CH <sub>2</sub> Cl <sub>2</sub> + HCO <sub>2</sub> Me + 1,3-dioxolane + 1,4-dioxane + MeO(CH <sub>2</sub> ) <sub>2</sub> OMe + Me <sub>2</sub> O (100 : 8 : 14 : 20 : 10 : 10)
8	PhC≡CCH(OEt) <sub>2</sub> <sup>a</sup>	CH <sub>2</sub> Cl <sub>2</sub> + PhCC≡CH(OEt) <sub>2</sub> + EtOH (5 : 3 : 3)
9	1,2-epoxybutane <sup>b</sup>	CH <sub>2</sub> Cl <sub>2</sub> + CH <sub>2</sub> (OH)CH(OH)Et (10 : 8)
10	N <sub>2</sub> CHCO <sub>2</sub> Et <sup>a</sup>	CH <sub>2</sub> Cl <sub>2</sub> + CH <sub>2</sub> FCO <sub>2</sub> Et (3 : 1)

<sup>a</sup> at 298 K. <sup>b</sup> After heating. <sup>c</sup> L/Ti molar ratio = 2. <sup>d</sup> CH<sub>2</sub>Cl<sub>2</sub> used as internal standard (CH<sub>2</sub>Cl<sub>2</sub> / Ti molar ratio = 1).

**Table 2**

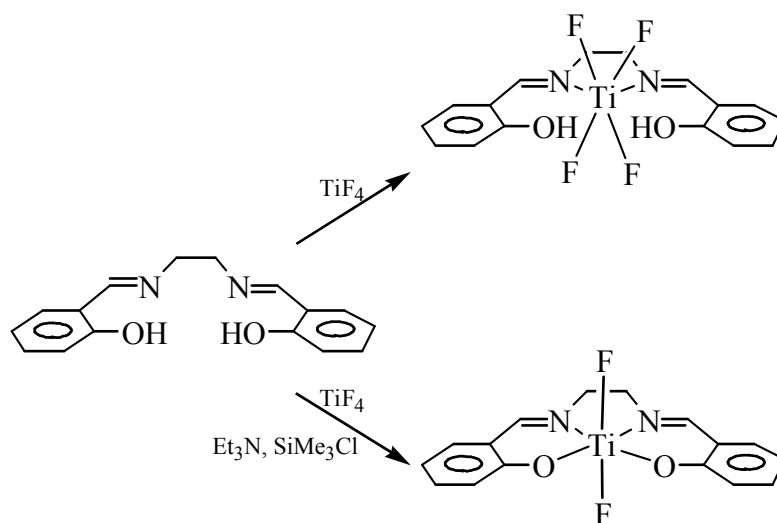
Run	TiF <sub>4</sub> (mmol)	L	L/M molar ratio	Reaction time (h)	NMR spectra
1	0.44	CH <sub>2</sub> (OMe) <sub>2</sub>	1	48	<sup>1</sup> H NMR: HCO <sub>2</sub> Me [8.11 (s, CH), 3.79 ppm (s, Me)]; CH <sub>2</sub> (OMe) <sub>2</sub> [4.61 (s, CH <sub>2</sub> ), 3.39 ppm (s, Me)]; 3.48 ppm (br), Me <sub>2</sub> O [3.39 ppm (s, Me)]; HCO <sub>2</sub> Me: CH <sub>2</sub> (OMe) <sub>2</sub> : Me <sub>2</sub> O = 10:6:3. After hydrolysis (12 h): <sup>1</sup> H NMR: HCO <sub>2</sub> Me [8.08 (s, CH), 3.76 ppm (s, Me)]; CH <sub>2</sub> (OMe) <sub>2</sub> [4.58 (s, CH <sub>2</sub> ), 3.37 ppm (s, Me)]; MeOH [3.48 ppm (s, Me)]; Me <sub>2</sub> O [3.33 ppm (s, Me)]; HCO <sub>2</sub> Me: CH <sub>2</sub> (OMe) <sub>2</sub> : MeOH: Me <sub>2</sub> O = 10:5:1:16. <sup>13</sup> C NMR: CH <sub>2</sub> (OMe) <sub>2</sub> [97.4 (CH <sub>2</sub> ), 55.0 ppm (CH <sub>3</sub> )]; HCO <sub>2</sub> Me [161.9 ppm (CH), 50.8 ppm (Me)]; Me <sub>2</sub> O [60.4 ppm].
2	0.45	CH <sub>2</sub> (OMe) <sub>2</sub>	2	48	After heating, no hydrolysis: <sup>1</sup> H NMR: HCO <sub>2</sub> Me [8.05 (s, CH), 3.73 ppm (s, Me)]; CH <sub>2</sub> (OMe) <sub>2</sub> [4.56 (s, CH <sub>2</sub> ), 3.34 ppm (s, Me)]; Me <sub>2</sub> O [3.36 ppm (s, Me)]; HCO <sub>2</sub> Me : CH <sub>2</sub> (OMe) <sub>2</sub> : Me <sub>2</sub> O = 4:1:7. <sup>1</sup> H NMR: CH <sub>2</sub> Cl <sub>2</sub> [5.31 ppm]; HCO <sub>2</sub> Et [8.06 (s, CH), 4.24 (q, CH <sub>2</sub> ), 1.31 ppm (t, CH <sub>3</sub> )]; CH <sub>2</sub> (OEt) <sub>2</sub> [4.69 (s, CH <sub>2</sub> (OEt) <sub>2</sub> ), 3.61 ppm (q, CH <sub>2</sub> (OC <sub>2</sub> H <sub>5</sub> CH <sub>3</sub> )) 1.22 ppm (t, CH <sub>3</sub> )]; 3.38 ppm (s), 1.38 ppm (t), CH <sub>2</sub> Cl <sub>2</sub> : HCO <sub>2</sub> Et : CH <sub>2</sub> (OEt) <sub>2</sub> = 10:1:5. After hydrolysis: <sup>1</sup> H NMR: CH <sub>2</sub> Cl <sub>2</sub> [5.30 ppm]; HCO <sub>2</sub> Et [8.05 (s, CH), 4.23 (m, CH <sub>2</sub> ), 1.31 ppm (t, CH <sub>3</sub> )]; CH <sub>2</sub> (OEt) <sub>2</sub> [4.67 (s, CH <sub>2</sub> (OEt) <sub>2</sub> ), 3.61 (m, CH <sub>2</sub> (OC <sub>2</sub> H <sub>5</sub> CH <sub>3</sub> )), 1.22 ppm (m, CH <sub>3</sub> )]; EtOH [3.70 (quint, CH <sub>2</sub> ), 2.02 (br, OH), 1.22 (m, CH <sub>3</sub> )]; 3.37 ppm, CH <sub>2</sub> Cl <sub>2</sub> : HCO <sub>2</sub> Et : CH <sub>2</sub> (OEt) <sub>2</sub> : EtOH = 10:1:5:3. After hydrolysis: <sup>1</sup> H NMR: CH <sub>2</sub> Cl <sub>2</sub> [5.29 ppm]; MeCH(OEt) <sub>2</sub> [4.67 ppm (q, CH), 3.57 ppm (m, CH <sub>2</sub> ), 1.29 ppm (d, CH <sub>3</sub> CH), 1.21 (t, OCH <sub>2</sub> CH <sub>3</sub> )]; EtOH [3.66 (q, CH <sub>2</sub> ), 2.66 (s, OH), 1.20 ppm (t, Me)]; Et <sub>2</sub> O [3.47 (q, CH <sub>2</sub> ), 1.18 ppm (t, Me)]; CH <sub>2</sub> Cl <sub>2</sub> : MeCH(OEt) <sub>2</sub> : EtOH: Et <sub>2</sub> O = 4:1:4:1. <sup>13</sup> C NMR: CH <sub>2</sub> Cl <sub>2</sub> [53.4 ppm]; Et <sub>2</sub> O [67.5 (CH <sub>2</sub> ), 15.2 ppm (Me)]; EtOH [58.0 (CH <sub>2</sub> ), 18.1 ppm (Me)].
3	0.69	CH <sub>2</sub> (OEt) <sub>2</sub>	1	96	At 298 K: <sup>1</sup> H NMR: ClCH <sub>2</sub> CHO [9.62 (s, CH), 4.07 ppm (s, CH <sub>2</sub> )]; ClCH <sub>2</sub> CH(OEt) <sub>2</sub> [4.64 (t, CH), 3.61 ppm (m, OCH <sub>2</sub> ), 3.52 (d, ClCH <sub>2</sub> ), 1.24 ppm (t, Me)]. ClCH <sub>2</sub> CHO: ClCH <sub>2</sub> CH(OEt) <sub>2</sub> = 1:5. <sup>13</sup> C NMR: ClCH <sub>2</sub> CH(OEt) <sub>2</sub> [101.6 (CH), 62.5 ppm (OCH <sub>2</sub> ), 43.8 (ClCH <sub>2</sub> ), 15.1 ppm (CH <sub>3</sub> )]. After heating (18 h): <sup>1</sup> H NMR: ClCH <sub>2</sub> CHO [9.62 (s, CH), 4.07 ppm (s, CH <sub>2</sub> )]; ClCH <sub>2</sub> CH(OEt) <sub>2</sub> [4.64 ppm (t, CH), 3.51 ppm (d, ClCH <sub>2</sub> ), 3.66 (m, OCH <sub>2</sub> ), 1.24 (t, Me)]. ClCH <sub>2</sub> CHO: ClCH <sub>2</sub> CH(OEt) <sub>2</sub> = 1:5. <sup>1</sup> H NMR: CH <sub>2</sub> Cl <sub>2</sub> [5.29 ppm]; ClCH <sub>2</sub> CHO [9.41 ppm (s, CH), 4.01 ppm (s, br, CH <sub>2</sub> )]; ClCH <sub>2</sub> CH(OEt) <sub>2</sub> [4.60 (t, CH), 3.48 (d, ClCH <sub>2</sub> ), 3.63 (m, OCH <sub>2</sub> ), 1.21 ppm (m, Me)]. CH <sub>2</sub> Cl <sub>2</sub> : ClCH <sub>2</sub> CHO: ClCH <sub>2</sub> CH(OEt) <sub>2</sub> = 10:2:10. <sup>13</sup> C NMR: CH <sub>2</sub> Cl <sub>2</sub> [53.4 ppm]; ClCH <sub>2</sub> CH(OEt) <sub>2</sub> [101.6 (CH), 62.5 (OCH <sub>2</sub> ), 43.8 (ClCH <sub>2</sub> ), 15.1 ppm (Me)]. After heating (18 h): <sup>1</sup> H NMR δ(ppm): CH <sub>2</sub> Cl <sub>2</sub> [5.29 ppm]; ClCH <sub>2</sub> CHO [9.40 ppm (s, CH), 4.04 ppm (s, CH <sub>2</sub> )]; 5.90 ppm; ClCH <sub>2</sub> CH(OEt) <sub>2</sub> [4.60 (m, CH), 3.62 (m, OCH <sub>2</sub> ), 3.47 (m, ClCH <sub>2</sub> ), 1.20 (m, Me)]. CH <sub>2</sub> Cl <sub>2</sub> : ClCH <sub>2</sub> CHO: ClCH <sub>2</sub> CH(OEt) <sub>2</sub> = 10:1:15.
4	0.71	MeCH(OEt) <sub>2</sub>	1	96	After heating (18 h) and hydrolysis: <sup>1</sup> H NMR: CH <sub>2</sub> Cl <sub>2</sub> [5.27 ppm]; ClCH <sub>2</sub> CHO [9.39 (s, CH), 4.02 ppm (s, CH <sub>2</sub> )]; ClCH <sub>2</sub> CH(OEt) <sub>2</sub> [4.58 (t, CH), 3.61 (m, OCH <sub>2</sub> ), 3.46 (d, ClCH <sub>2</sub> ), 1.18 ppm (t, Me)]; ClCH <sub>2</sub> CO <sub>2</sub> Et [4.20 (q, OCH <sub>2</sub> ), 4.02 (s, ClCH <sub>2</sub> ), 1.29 ppm (br, Me)]. CH <sub>2</sub> Cl <sub>2</sub> : ClCH <sub>2</sub> CHO: ClCH <sub>2</sub> CH(OEt) <sub>2</sub> : ClCH <sub>2</sub> CO <sub>2</sub> Et = 10:14:1:0.5.
5	0.48	ClCH <sub>2</sub> CH(OEt) <sub>2</sub>	1	96	<sup>1</sup> H NMR: CH <sub>2</sub> Cl <sub>2</sub> [5.31 ppm]; 3.72 (br) ppm. After hydrolysis: <sup>1</sup> H NMR: CH <sub>2</sub> Cl <sub>2</sub> [5.31 ppm]; MeCO <sub>2</sub> Me [3.67 (s, CO <sub>2</sub> Me), 2.06 ppm (s, MeCO <sub>2</sub> )]; MeOH [3.48 (s, Me), 1.85 ppm (br, OH)]; Me <sub>2</sub> O [3.32 ppm (s, Me)]; Me <sub>2</sub> CO [2.17 ppm (s, Me)]. CH <sub>2</sub> Cl <sub>2</sub> : MeCO <sub>2</sub> Me: MeOH: Me <sub>2</sub> O: Me <sub>2</sub> CO = 10:0.4:0.3:0.4. <sup>13</sup> C NMR: CH <sub>2</sub> Cl <sub>2</sub> [53.4 ppm]; MeOH [50.6 ppm].
6	0.70	ClCH <sub>2</sub> CH(OEt) <sub>2</sub>	2	96	<sup>1</sup> H NMR: CH <sub>2</sub> Cl <sub>2</sub> [5.30 ppm]; HCO <sub>2</sub> Me [8.06 (s, CH), 3.74 ppm (s, Me)]; Me <sub>2</sub> O [3.31 (s, Me)]. CH <sub>2</sub> Cl <sub>2</sub> : HCO <sub>2</sub> Me: Me <sub>2</sub> O = 10:7:5. <sup>13</sup> C NMR: CH <sub>2</sub> Cl <sub>2</sub> [53.4 ppm]; HCO <sub>2</sub> Me [161.3 (CH), 50.8 ppm (Me)]; Me <sub>2</sub> O [60.5 ppm (Me)]. After hydrolysis: <sup>1</sup> H NMR: CH <sub>2</sub> Cl <sub>2</sub> [5.30 ppm]; HCO <sub>2</sub> Me [8.05 (s, CH), 3.74 (s, Me)]; MeOH [3.45 (s, Me)]; Me <sub>2</sub> O [3.30 (s, Me)]; CH <sub>2</sub> Cl <sub>2</sub> : HCO <sub>2</sub> Me: MeOH: Me <sub>2</sub> O = 10:7:1:5. <sup>13</sup> C NMR: CH <sub>2</sub> Cl <sub>2</sub> [53.4 ppm]; HCO <sub>2</sub> Me [161.9 (CH), 50.8 (Me)]; Me <sub>2</sub> O [60.3 ppm]; MeOH [50.8 ppm].
7	0.75	Me <sub>2</sub> C(OMe) <sub>2</sub>	1	96	<sup>1</sup> H NMR: CH <sub>2</sub> Cl <sub>2</sub> [5.31 ppm]; 3.72 (br) ppm. After hydrolysis: <sup>1</sup> H NMR: CH <sub>2</sub> Cl <sub>2</sub> [5.31 ppm]; MeCO <sub>2</sub> Me [3.67 (s, CO <sub>2</sub> Me), 2.06 ppm (s, MeCO <sub>2</sub> )]; MeOH [3.48 (s, Me), 1.85 ppm (br, OH)]; Me <sub>2</sub> O [3.32 ppm (s, Me)]; Me <sub>2</sub> CO [2.17 ppm (s, Me)]. CH <sub>2</sub> Cl <sub>2</sub> : MeCO <sub>2</sub> Me: MeOH: Me <sub>2</sub> O: Me <sub>2</sub> CO = 10:0.4:0.3:0.4. <sup>13</sup> C NMR: CH <sub>2</sub> Cl <sub>2</sub> [53.4 ppm]; MeOH [50.6 ppm].
8	0.65	HC(OMe) <sub>3</sub>	1	96	<sup>1</sup> H NMR: CH <sub>2</sub> Cl <sub>2</sub> [5.30 ppm]; HCO <sub>2</sub> Me [8.06 (s, CH), 3.74 ppm (s, Me)]; Me <sub>2</sub> O [3.31 (s, Me)]. CH <sub>2</sub> Cl <sub>2</sub> : HCO <sub>2</sub> Me: Me <sub>2</sub> O = 10:7:5. <sup>13</sup> C NMR: CH <sub>2</sub> Cl <sub>2</sub> [53.4 ppm]; HCO <sub>2</sub> Me [161.3 (CH), 50.8 ppm (Me)]; Me <sub>2</sub> O [60.5 ppm (Me)]. After hydrolysis: <sup>1</sup> H NMR: CH <sub>2</sub> Cl <sub>2</sub> [5.30 ppm]; HCO <sub>2</sub> Me [8.05 (s, CH), 3.74 (s, Me)]; MeOH [3.45 (s, Me)]; Me <sub>2</sub> O [3.30 (s, Me)]; CH <sub>2</sub> Cl <sub>2</sub> : HCO <sub>2</sub> Me: MeOH: Me <sub>2</sub> O = 10:7:1:5. <sup>13</sup> C NMR: CH <sub>2</sub> Cl <sub>2</sub> [53.4 ppm]; HCO <sub>2</sub> Me [161.9 (CH), 50.8 (Me)]; Me <sub>2</sub> O [60.3 ppm]; MeOH [50.8 ppm].

**Table 2, continued**

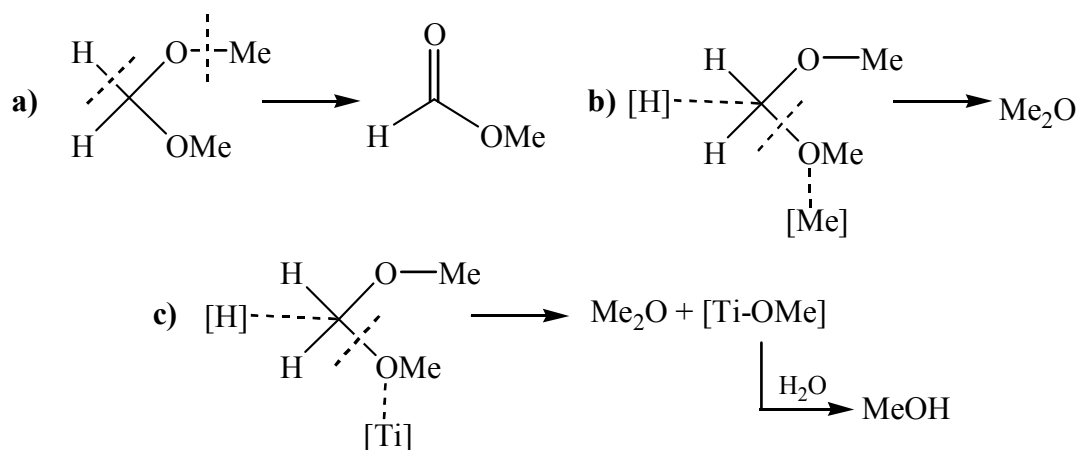
Run	TiF <sub>4</sub> (mmol)	L	L/M molar ratio	Reaction time (h)	NMR spectra
9	0.84	1,3-dioxolane	1	96	<sup>1</sup> H NMR δ(ppm): CH <sub>2</sub> Cl <sub>2</sub> [5.31 ppm]; HCO <sub>2</sub> Me [8.09 (s, CH), 3.74 ppm (s, Me)]; 1,3-dioxolane [4.92 (s, OCH <sub>2</sub> O), 3.89 ppm (s, OCH <sub>2</sub> CH <sub>2</sub> )], CH <sub>2</sub> Cl <sub>2</sub> ; HCO <sub>2</sub> Me: 1,3-dioxolane = 5:1:2. After heating (12 h): <sup>1</sup> H NMR: CH <sub>2</sub> Cl <sub>2</sub> [5.31 ppm]; HCO <sub>2</sub> Me [8.08 (s, CH), 3.76 ppm (s, Me)]; 1,3-dioxolane [4.91 (s, OCH <sub>2</sub> O), 3.89 ppm (s, OCH <sub>2</sub> CH <sub>2</sub> )], CH <sub>2</sub> Cl <sub>2</sub> ; HCO <sub>2</sub> Me: 1,3-dioxolane = 100:13:8. After heating (18 h) and hydrolysis: <sup>1</sup> H NMR: CH <sub>2</sub> Cl <sub>2</sub> [5.30 ppm]; HCO <sub>2</sub> Me [8.07 (s, CH), 3.74 ppm (s, Me)]; 1,3-dioxolane [4.89 ppm (s, OCH <sub>2</sub> O), 3.87 ppm (s, OCH <sub>2</sub> CH <sub>2</sub> )], 1,4-dioxane [3.69 (s, CH <sub>2</sub> ); MeO(CH <sub>2</sub> ) <sub>2</sub> OMe [3.53 (s, CH <sub>2</sub> ), 3.37 ppm (s, CH <sub>3</sub> )]; Me <sub>2</sub> O [3.30 ppm (s, Me)]; CH <sub>2</sub> Cl <sub>2</sub> ; HCO <sub>2</sub> Me: 1,3-dioxolane: 1,4-dioxane: MeO(CH <sub>2</sub> ) <sub>2</sub> OMe: Me <sub>2</sub> O = 100:8:14:20:10:10. After hydrolysis: <sup>1</sup> H NMR: CH <sub>2</sub> Cl <sub>2</sub> [5.30 ppm]; 9.44 ppm; PhCC≡CH(OEt) <sub>2</sub> [7.50, 7.34 (m, Ph), 5.51 (s, CH), 3.85, 3.71 (m, CH <sub>2</sub> ), 1.30 ppm (t, Me)]; EtOH [3.68 (q, CH <sub>2</sub> ), 1.25 ppm (t, CH <sub>3</sub> )]; CH <sub>2</sub> Cl <sub>2</sub> ; PhCC≡CH(OEt) <sub>2</sub> : EtOH = 5:3:3. <sup>13</sup> C NMR: CH <sub>2</sub> Cl <sub>2</sub> [53.4 ppm]; PhC≡CCH(OEt) <sub>2</sub> [133.3, 131.9, 128.8, 128.2 (CH), 121.9 (m, Ph), 91.8, 85.2 (C≡C), 60.9 (CH <sub>2</sub> ), 15.1 ppm (CH <sub>3</sub> )]; EtOH [58.3 (CH <sub>2</sub> ), 18.3 ppm (CH <sub>3</sub> )].
10	0.43	PhC≡CCH(OEt)	1	72	<sup>1</sup> H NMR: CH <sub>2</sub> Cl <sub>2</sub> [5.32 (br), 1.57 (br), 0.96 ppm (m)]. After hydrolysis: <sup>1</sup> H NMR: CH <sub>2</sub> Cl <sub>2</sub> [5.31 ppm]; CH <sub>2</sub> (OH)CH(OH)Et [3.53 (m), 1.47 (m), 0.97 ppm (m)]. CH <sub>2</sub> Cl <sub>2</sub> ; CH <sub>2</sub> (OH)CH(OH)Et = 1:1. After heating (5h) and hydrolysis: <sup>1</sup> H NMR: CH <sub>2</sub> Cl <sub>2</sub> [5.31 ppm]; CH <sub>2</sub> (OH)CH(OH)Et [3.52 (br), 1.57 (br), 0.96 ppm (m)]. CH <sub>2</sub> Cl <sub>2</sub> ; CH <sub>2</sub> (OH)CH(OH)Et = 10:8
11	0.75	1,2-epoxybutane	1	96	<sup>1</sup> H NMR: CH <sub>2</sub> Cl <sub>2</sub> [5.33 ppm]; CH <sub>2</sub> FCO <sub>2</sub> Et [4.85 (d, J <sub>HF</sub> = 47 Hz, CH <sub>2</sub> F), 4.30 (q, CH <sub>2</sub> O), 1.33 ppm (t, CH <sub>3</sub> )]; CH <sub>2</sub> Cl <sub>2</sub> ; CH <sub>2</sub> FCO <sub>2</sub> Et = 2:1. <sup>13</sup> C NMR: CH <sub>2</sub> Cl <sub>2</sub> [53.4 ppm]; CH <sub>2</sub> FCO <sub>2</sub> Et [168.1 (d, CO <sub>2</sub> ), 77.8 (d, CH <sub>2</sub> F), 61.5 (CH <sub>2</sub> O), 14.2 ppm (CH <sub>3</sub> )]. After hydrolysis: <sup>1</sup> H NMR: CH <sub>2</sub> Cl <sub>2</sub> [5.33 ppm]; CH <sub>2</sub> FCO <sub>2</sub> Et [4.85 (d, J <sub>HF</sub> = 47 Hz, CH <sub>2</sub> F), 4.30 (q, CH <sub>2</sub> O), 1.33 ppm (t, CH <sub>3</sub> )]; CH <sub>2</sub> Cl <sub>2</sub> ; CH <sub>2</sub> FCO <sub>2</sub> Et = 3:1.
12	0.73	N <sub>2</sub> CHCO <sub>2</sub> Et	1	96	<sup>1</sup> H NMR: CH <sub>2</sub> Cl <sub>2</sub> [5.33 ppm]; CH <sub>2</sub> FCO <sub>2</sub> Et [4.85 (d, J <sub>HF</sub> = 47 Hz, CH <sub>2</sub> F), 4.30 (q, CH <sub>2</sub> O), 1.33 ppm (t, CH <sub>3</sub> )]; CH <sub>2</sub> Cl <sub>2</sub> ; CH <sub>2</sub> FCO <sub>2</sub> Et = 3:1.



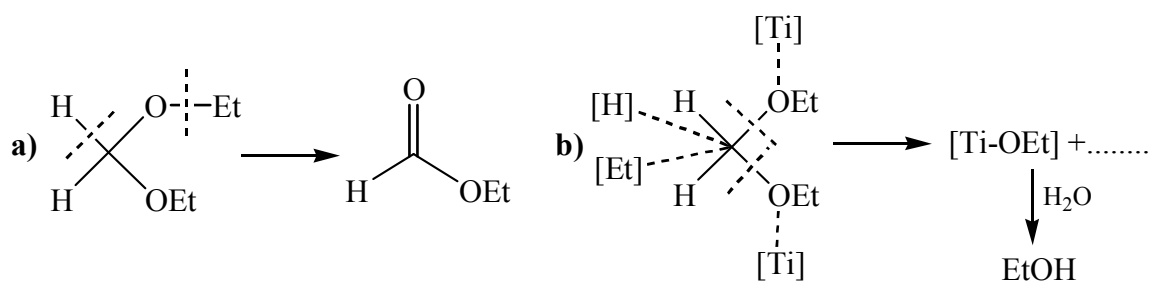
## Scheme 1



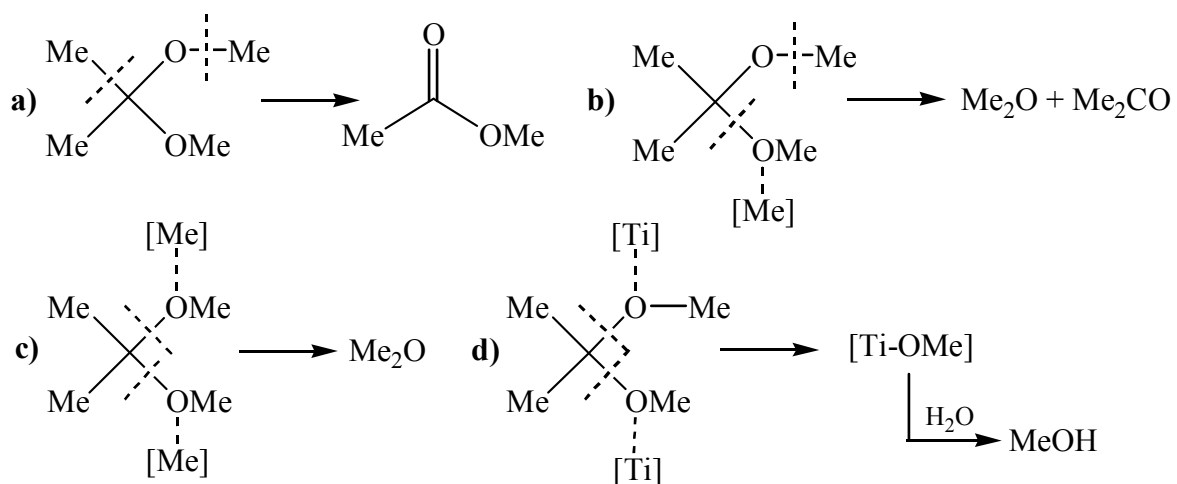
## Scheme 2



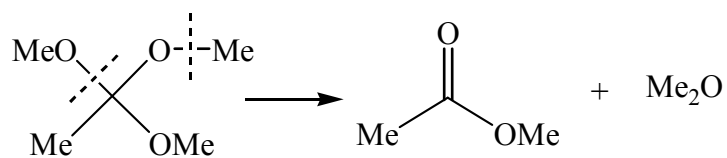
## Scheme 3



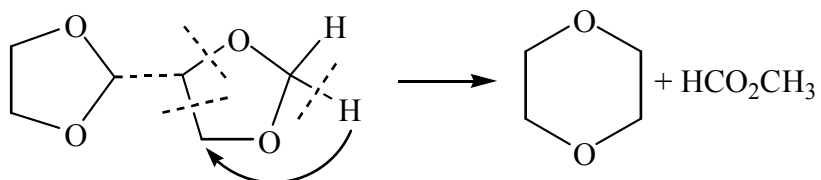
### Scheme 4



### Scheme 5



### Scheme 6



### Scheme 7

