# *Communications*

Unusual Oxidative Cleavage of Methyl Diphenyltartrate Promoted by Titanium Tetrachloride/Pyridine System

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This paper is concerned with an unusual oxidative cleavage of methyl diphenyltartrates **1a** (meso) and **1b** (*dl*) promoted by a titanium tetrachloride/pyridine system, at room temperature in THF solution (eq 1), in which the Ti(IV)–enolate **B** is assumed to be the reactive intermediate (Scheme I).
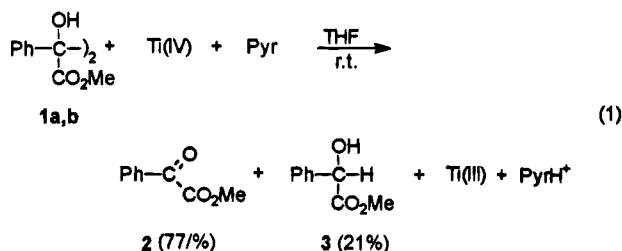
Compounds **1a,b** are to be considered peculiar 1,2-diols since the σ bond, cleaved under the reaction conditions used, links two capto-datively substituted carbon atoms.[1] Many literature reports[2] deal with meso/*dl* interconversion and/or disproportionation of catpo-datively substituted dimers that, owing to the low dissociation enthalpy, are activated toward homolysis. Both dimers, **1a** and **1b**, were found to be thermally stable in either THF or THF–Py solutions after prolonged refluxing (10 h).

However, when TiCl$_4$ (0.6 mmol of a 1.0 M CH$_2$Cl$_2$ solution) was added to a carefully degassed solution of **1a** or **1b** (0.3 mmol) in anhydrous THF (3 mL) and Pyr (0.8 mmol), kept under N$_2$ at 18 °C, with a syringe, in one portion, through a septum cap, an exothermic reaction took place with instantaneous formation of a yellow-green precipitate. When the reaction was quenched with water after 20 min, the precipitate dissolved and the blue color of Ti(III) appeared. Extraction with ethyl acetate, followed by usual workup of the organic layer, afforded methyl phenylglyoxalate (**2**) as the main product (Table 1, entry 1). Titration of the aqueous layer with a 0.1 N Ce(SO$_4$)$_2$ solution showed that 25% of titanium was in the Ti(III) state (0.15 mmol). Paragonable results were obtained with the *dl* isomer **1b** (Table 1, entry 3).

For the present, all our data may be accommodated by initial formation of a mono- or bidentate Ti(IV)–diol complex **A**, or **A′**, which then breaks down to **2** and Ti(IV)–enolate **B**,[3] *via* a two-electron process (Scheme 1). Most likely, the facile heterolytic cleavage will occur because of the special and favorable possibility of going directly from these complexes to the stabilized metal–

enolate **B**. Further oxidative dimerization of **B**, or **B′**, would account for both the Ti(III) formation and the high yield of **2**. In fact, dimerization of **C** and/or **C′**[3] regenerates **A** and/or **A′** which breaks down again, affording **2** in yield higher than 50%.[4]

Oxidative dimerization of stabilized carbanions[5] and enolate anions[6] by copper salts is a well-established reaction. Nevertheless, only a few scattered examples[7] are known for the Ti(IV)–promoted coupling of enolate anions. In the present case, the single electron transfer process (SET) leading to a stabilized radical may occur with unprecedented ease.[8]

Additional support to the mechanism of Scheme 1 comes from the following experimental findings: (a) Pyridine, which acts mainly as a base,[9] is essential to have quantitative fragmentation of the diols (entries 1 and 3); it drives the complexation equilibrium to the right and competes with the formation of **3**, thus favoring the oxidative process. (b) In the absence of pyridine (entries 2 and 4), diol cleavage is no longer quantitative: the dimerization process, not followed by quantitative breaking of the regenerate dimers, accounts for the meso/*dl* stereochemical equilibration observed. A dimer mixture meso/*dl* ratio of 77:23 was found starting from either pure **1a** or **1b**. (c) In the presence of an additional proton donor, such as *t*-BuOH instead of pyridine, both **1a** and **1b** were recovered unchanged, indicating that the metal–diol complexation is a condition *sine qua non* for the cleavage to occur. Competitive coordination of Ti(IV) with the alcohol would either increase the proton ion concentration (*nt*-BuOH + Ti(IV) → Ti(IV)(*t*-BuO)$_n$ + *n*H$^+$) or hamper further metal–diol complexation, as the environment around the metal ion is fairly bulky. (d) When the cleavage reaction of **1a** and **1b** was performed in the presence of *p*-tolylaldehyde or *p*-bromobenzaldehyde (0.6 mmol) and pyridine (0.8 mmol) *syn*-stereoselective addition[10] of **B** to the carbonyl carbon of the aldehyde occurred almost quantitatively, affording **2** and **4a** or **4b** (eq 2) in *ca.* 50% yield each (entries 5–7).

Analogous reaction with the less electrophilic cyclobu-

(3) **B** and **B′**, as well as **C** and **C′**, are limit cases; the extent of bond breaking between the metal ion, Ti(III) or Ti(IV), and the developing anion or radical anion is strongly dependent on the ion-solvating power and dielectric constant of the solvent, while the equilibrium concentrations of **C** and **C′**, and of **B** and **B′**, are mainly related to the proton ion concentration. Moreover, owing to steric control in the dimerization step, the ratio meso/*dl* of dimers formed will depend upon the nature of the species that are going to recombine.

(4) The heterolytic cleavage, not followed by oxidative dimerization of the reactive intermediate, as well as the disproportionation of the radical formed, by a possible homolytic cleavage, would afford **2** and **3** in equal quantities.

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(9) The coordinative valences of Ti(IV) may well be saturated by THF and pyr molecules.

(10) An X-ray diffraction analysis of the prevailing isomer **4a** shows that the structure corresponds to a *syn*-diastereoselectivity. Malpezzi, L. To be published.

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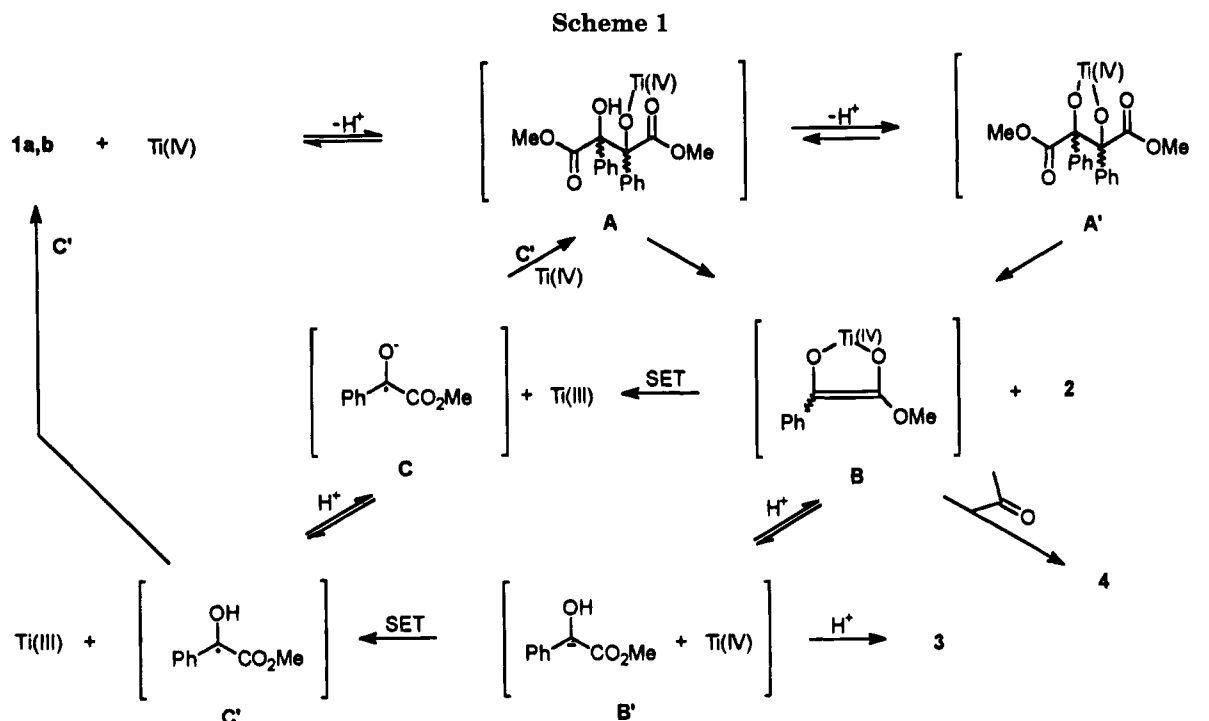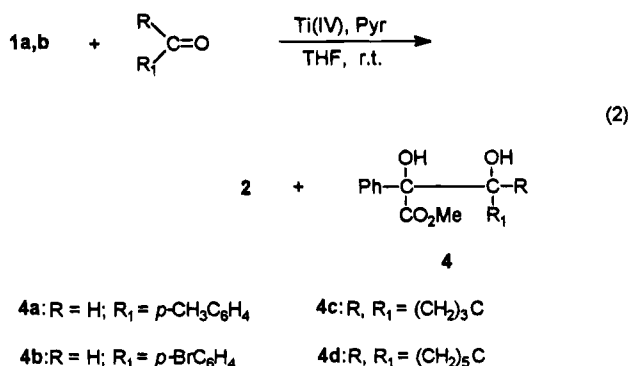
Scheme 1

Table 1. Products Cleavage of *meso-* and *dl*-Methyl Diphenyltartrates (1a and 1b) by TiCl₄ in the Presence of Different Additives

			products (¹H NMR yield, %)[a]						
entry	dimer	additive	2	3	1a	1b	1a:1b	4	*syn/anti*
1	1a	pyr	76	22	traces	traces			
2	1a	none	31	22	36	11	76:24		
3	1b	pyr	77	21	traces	traces			
4	1b	none	41	33	20	6	77:23		
5	1a	pyr + p-CH₃C₆H₄CHO	52					48 (4a)	88:12
6	1a	pyr + p-BrC₆H₄CHO	50					50 (4b)	91:9
7	1b	pyr + p-BrC₆H₄CHO	51					49 (4b)	87:13
8	1a	p-BrC₆H₄CHO	40	19	17	6	74:26	18 (4b)	60:40
9	1a	pyr + (CH₂)₃CO	54	8				38 (4c)	
10	1a	pyr + (CH₂)₅CO	52	8				40 (4d)	

[a] Calculated from the peaks area of the COOMe proton singlets. Me proton shifts (δ ppm): 1a, 3.85; 1b, 3.80; 2, 2.98; 3, 3.75; 4a(*syn*) 3.90; 4a(*anti*), 3.62; 4b(*syn*), 3.85; 4b(*anti*), 3.67; 4c, 3.83; 4d, 3.83.

$$\textbf{1a,b} \ + \ \underset{R'}{\overset{R}{>}}C=O \ \xrightarrow[\text{THF, r.t.}]{\text{Ti(IV), Pyr}}$$

$$\textbf{2} \ + \ Ph\overset{OH}{\underset{CO_2Me}{\overset{|}{C}}}\text{————}\overset{OH}{\underset{R_1}{\overset{|}{C}}}\text{-}R \tag{2}$$

4

4a: R = H; R₁ = p-CH₃C₆H₄   4c: R, R₁ = (CH₂)₃C

4b: R = H; R₁ = p-BrC₆H₄   4d: R, R₁ = (CH₂)₅C

tanone or cyclohexanone produces, in addition to **4c** or **4d**, a small amount of **3** also, due to competitive protonation of the reactive intermediate (entries 9 and 10). However, in the absence of pyridine, formation of **3** competes also with the nucleophilic addition to the aldehyde (entry 8) and the diol cleavage becomes no longer quantitative, leading to meso/*dl* equilibration. (e) Lastly, the observation that, in a competitive experiment,[11] **1b** is cleaved five times faster than **1a** strongly supports the intermediacy of a bidentate **A'** rather than a monodentate complex **A**. The rate difference for the

cleavage may well result from a difference in transition state energies, due to the increased steric interaction between the *cis* phenyl groups of the meso-transition state, as compared with the *trans* phenyl groups of the *dl*-transition state.[12] The meso/*dl* equilibrium found in entries 2, 3, and 8 may well be a result of the different rate of cleavage of the regenerates **1a** and **1b**, in addition to stereochemical control in the dimerization step.[3]

Further work on related systems is underway.

(11) The experiment was carried out by reacting equimolar quantities of **1a** and **1b** (0.15 mmol each) in the presence of p-bromobenzaldehyde (0.6 mmol) and pyr (0.8 mmol) in THF solution (3 mL) with an amount of TiCl₄ (0.05 mmol) such as a maximum of 33% of either substrates would be consumed. Since the aldehyde quantitatively traps the intermediate anion (entries 6 and 7) the meso/*dl* ratio, found at the end of the reaction, would reflect the different rates of cleavage of the two diols.

(12) This criterion has been adopted for determining the mechanism of glycol oxidation by LTA and other oxidants. March, J. *Advanced Organic Chemistry*, 3rd ed., J. Wiley and Sons: New York, 1985; p 1063.