10340-84-8; H<sub>2</sub>C=CHCH(CH<sub>3</sub>)(CH<sub>2</sub>)<sub>2</sub>Br, 59822-10-5; C<sub>8</sub>H<sub>17</sub>CN, 2243-27-8;  $C_6H_{13}OCH_2Ph$ , 61103-84-2;  $C_{11}H_{24}$ , 1120-21-4;  $H_2C=CHCH(CH_3)(CH_2)_2Ph$ , 42524-30-1; 2-(3-chloropropyl)-2methyl-1,3-dioxolane, 5978-08-5; 5-(bromomethyl)bicyclo-[2.2.1]hept-2-ene, 17016-12-5; 5-(tosyloxymethyl)bicyclo[2.2.1]hept-2-ene, 50626-34-1; 5-(mesyloxymethyl)bicyclo[2.2.1]hept-2ene, 86646-41-5; (E)-[[(2-bromoethyl)-2-cyclohexen-1-ylidenemethyl]thio]benzene, 86646-42-6; (E)-[[(2-bromoethyl)-2-cyclohepten-1-ylidenemethyl]thio]benzene, 86646-43-7; 2-methyl-2-(4-penten-1-yl)-1,3-dioxolane, 86646-44-8; 5-pentylbicyclo-[2.2.1]hept-2-ene, 22094-82-2; bicyclo[2.2.1]hept-2-ene-5-methanol, 95-12-5; (R)-2-[4,8-dimethylnon-8-en-1-yl]pyridine, 86646-46-0; (E)-[[(2-cyclohexen-1-ylidene)hexylmethyl]thio]benzene, 86646-47-1; (Z)-[[(2-cyclohexen-1-ylidene)hexylmethyl]thio]benzene, 86646-48-2; (E)-[[(2-cyclohepten-1-ylidene)hexylmethyl]thio]benzene, 86646-49-3; (Z)-[[(2-cyclohepten-1-ylidene)hexylmethyl]thio]benzene, 86646-50-6; (Z)-[[(2-bromoethyl)-2-cyclohexen-1-ylidenemethyl]thio]benzene, 86646-51-7; (Z)-[[(2bromoethyl)-2-cyclohepten-1-ylidenemethyl]thio]benzene, 86646-52-8

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# Conversion of Acetals and Ketals to Carbonyl Compounds Promoted by Titanium Tetrachloride

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If many solutions have been proposed in the recent years for the conversion of thioketals into ketones under mild conditions,<sup>1,2</sup> only a few works were concerned with the deprotection of acetals and ketals and more particularly of dioxolanes, which remain the most usual protecting group for the ketone functionality. Generally, the carbonyl moiety is regenerated from acetals and ketals by aqueous acid hydrolysis or by strong-acid-catalyzed exchange with acetone.<sup>2</sup> However, such conditions are very often incompatible with the presence in the molecule of some other functional group like protected hydroxyl group.

Recently, more neutral reagents were described for the hydrolysis or exchange of acetals and ketals: acidified silica gel,<sup>3</sup> lithium tetrafluoroborate in wet acetonitrile,<sup>4</sup> acetone in the presence of pyridinium tosylate.<sup>5</sup> At least two nonaqueous methods have also been proposed for the deprotection of acetals and ketals with the exception of dioxolanes: the first one uses phosphorus triiodide and diphosphorus tetraiodide<sup>6</sup> while the second one is based on the electrophilicity of trimethylsilyl iodide.<sup>7</sup>

Scheme I  $1 \rightarrow \bigvee_{OR}^{+O_{R}} \rightarrow \bigcup_{OR}^{+O_{R}} + RO\overline{I}Cl_{4} \rightarrow DR + RO\overline{I}Cl_{4} \rightarrow RO\overline{I}Cl_$ 

We report now that the deprotection of acetals and ketals, including dioxolanes, can be effectively realized in mild conditions by titanium tetrachloride in diethyl ether at room temperature. The results obtained with eight acetals and ketals 1 are summarized in Table I.

The dimethyl acetal 1c is rapidly transformed to benzaldehyde (entry 3) at room temperature by treatment with 0.5 molar equiv of TiCl<sub>4</sub> (GC analysis reveals an almost quantitative yield). However, the same conditions are inoperant with acetal 1a derived from a saturated aldehyde after 48 h, only 10% deprotection is observed. The rate of this reaction is greatly improved by adding 1 molar equiv of lithium iodide, and the parent aldehyde is then obtained with good yield starting either from the methyl or the ethyl acetal (entries 1 and 2). The presence of this coreagent is not necessary in the case of the methyl ketal of cyclohexanone but it increases markedly the rate of the reaction (entries 4 and 5).

The other results show that the method is also effective for dioxolanes, mainly those of cyclohex-2-en-2-ones 1g and 1h, which are rapidly deprotected in the presence of a slight molecular excess of TiCl<sub>4</sub> (entries 9 and 10). It can be noticed that in the case of 1g, the same deprotectiondehydration process was previously done at room temperature by 2 N hydrochloric acid,<sup>8</sup> but the requisite time was then 10 h and the yield was lower. This example shows the efficiency of TiCl<sub>4</sub> for such a deprotection. Also, the case of 1h<sup>9</sup> is representative of the chemoselectivity of the reagent since the tetrahydropyranyloxy protective group was unaffected by conditions that remove completely the ethylene ketal group (entry 10).

If an aliphatic ketone is regenerated without any problem (entry 8), the case of the dioxolane of cyclohexanone was not completely solved. As shown by entry 6, the rate of the reaction is slow and cannot be increased: the use of a slight excess of TiCl<sub>4</sub> and the addition of lithium chloride or fluoride to the reaction mixture cause intense polymerization while lithium bromide and iodide are unefficient. In methylene chloride, a better solvent than ether for TiCl<sub>4</sub>, the acetal le has completely reacted after several hours at room temperature, but the reaction leads to a complicated mixture of unidentified products where cyclohexanone is absent. The best conditions for the conversion of le into cyclohexanone are those described in entry 6. The yield is good, but the starting material (20%) still remaining cannot be transformed by stretching out the reaction time to 48 h.

With regard to the mechanism of these transformations of acetals and ketals to carbonyl compounds, different processes (Scheme I) can be proposed depending on the

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<sup>(2)</sup> T. W. Greene, "Protective Group in Organic Synthesis", Wiley, New York, 1981, p 144.

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		Table I		
entry	starting material <sup>a</sup>	conditions <sup>e</sup>	product	yield, <sup>b</sup> %
1	$C_{7}H_{15}CH(OCH_{3})_{2}$ 1a	$\begin{array}{c} 0.5 \text{ TiCl}_4 + 1.1 \text{ LiI}, \\ \text{Et}_2 \text{O}, \text{rt}, 3 \text{ h} \end{array}$	octanal	85
2	$C_7H_{15}CH(OC_2H_5)_2$ 1b	$0.5 \text{ TiCl}_4 + 1.1 \text{ LiI}, \text{ Et}_2\text{O}, \text{ rt}, 6 \text{ h}$	octanal	85
3		0.5 TiCl <sub>4</sub> , Et <sub>2</sub> O, rt, 10 min	benzaldehyde	90
4		$\begin{array}{c} 0.5  \operatorname{TiCl}_4, \\ \mathrm{Et}_2 \mathrm{O},  \mathrm{rt},  6  \mathrm{h} \end{array}$	cyclohexanone	90
5	1d 1d	$0.5 \text{ TiCl}_4 + 1.1 \text{ LiI}, \text{ Et}_2\text{O}, \text{rt}, 3 \text{ h}$	cyclohexanone	88
6	(◯) 1e	0.8 TiCl <sub>4</sub> , Et <sub>2</sub> O, rt, 20 h	cyclohexanone	75°
7	1e	1.1 TiCl <sub>4</sub> , Et <sub>2</sub> O, rt, 20 h	cyclohexanone	20 <sup>d</sup>
8		2 TiCl <sub>4</sub> , Et <sub>2</sub> O, rt, 5 h	L CI	65
9	С°х ф 1g	1.2 TiCl <sub>4</sub> , Et <sub>2</sub> O, rt, 5 min		91
10		1.2 TiCl <sub>4</sub> , Et <sub>2</sub> O, rt, 5 min	О	65
	16			

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<sup>*a*</sup> Acetals and ketals were prepared by conventional methods.<sup>12</sup> <sup>*b*</sup> Yields of products isolated by column chromatography. The reaction were run on a  $10^{-3}$ -mol scale. <sup>*c*</sup> Presence of 20% of starting material 1e. <sup>*d*</sup> Presence of polymers. <sup>*e*</sup> rt = room temperature.

structure of the starting material 1. The first process  $(A)^{10}$ would be operative with an acetal such as 1c or a ketal such as 1d where an intermediate carbocationic species is stabilized while the second one (B) concerns the aliphatic acetals 1a and 1b, which need lithium iodide to be converted to the parent ketone (the comparison of entries 1 and 2 and of entries 4 and 5 argues for this hypothesis). However, these two processes are not supported by experimental data in the case of dioxolanes 1e-h. On one hand, the rate of transformation of 1e into cyclohexanone is not increased by the presence of lithium iodide but is markedly increased by the addition of 1 molar equiv of pyridine (under the conditions of entry 6, it takes about 1 h to consume 80% of 1e, the yield of cyclohexanone being lower). On the other hand, it was not possible to detect the presence of 2-chloroethanol in the reaction mixture. Consequently, process C is proposed in the case of ethylene ketals.

In conclusion, it appears that titanium tetrachloride in ether can be a mild reagent for the conversion of acetals and ketals to carbonyl compounds. The success of the association  $TiCl_4$ -LiI in the case of methyl acetal 1a suggests that this reagent could convert methyl ethers to the parent alcohols. Consequently, a solution of 1-methoxyheptane in dichloromethane was treated overnight at room temperature with 1.1 molar equiv of  $TiCl_4$  and 1.5 molar equiv of LiI: heptanol was then obtained in quantitative yield.

This useful reaction<sup>11</sup> is under study as well as the eventual conversion of thicketals into thiones by the same reagent.

### **Experimental Section**

The procedure used in the case of acetal 1b is given as an example. Freshly distilled titanium tetrachloride (0.054 mL, 0.5  $\times$  10<sup>-3</sup> mol) is dropped with a syringe into a stirred solution of 1a (10<sup>-3</sup> mol) in dry ether (5 mL). Lithium iodide (1.1  $\times$  10<sup>-3</sup> mol) is then added to the resulting solution, and the brown reaction mixture is stirred for 3 h before the addition of water at room temperature (3 mL). The reaction mixture is diluted with ether, and the organic phase is successively washed with a 10% solution of sodium thiosulfate, a saturated aqueous sodium carbonate solution, and water and then dried over magnesium sulfate. The extract is then concentrated under reduced pressure and the residue chromatographed on silica gel (eluent: ether-petroleum ether, 1:1) to give 85% pure octanal.

<sup>(10)</sup> Such a process has been previously proposed for other reactions of acetals initiated by titanium tetrachloride or trimethylsilyl iodide. See for examples, (a) H. Sakurai, H. Sasaki, and A. Hosomi, *Tetrahedron Lett.*, **22**, 745 (1981); (b) H. Nishiyama and K. Itoh, *J. Org. Chem.*, **47**, 2496 (1982).

<sup>(11)</sup> The transformation of methyl ethers into alcohols by trimethylsilyliodide is a well-documented process. (a) T. L. Ho and G. A. Olah, Angev. Chem., Int. Ed. Engl., 15, 774 (1976); (b) M. E. Jung and M. A. Lyster, J. Am. Chem. Soc., 99, 968 (1977); (c) G. A. Olah, A. Husain, B. G. Balaram Gupta, and S. C. Narang, Angew. Chem. Int. Ed. Engl., 204, 690 (1981) and references there in.

<sup>(12)</sup> F. A. J. Meskens, Synthesis, 501 (1981).

The conditions for the other reactions are given in Table I. During the deprotection of dioxolanes, one can note the formation of a white precipitate, which is solubilized in water at the hydrolysis.

Registry No. 1a, 10022-28-3; 1b, 54889-48-4; 1c, 1125-88-8; 1d, 2658-60-8; 1e, 177-10-6; 1f, 1124-92-1; 1g, 32622-01-8; 1h, 86690-13-3; TiCl<sub>4</sub>, 7550-45-0; LiI, 10377-51-2; octanal, 124-13-0; benzaldehyde, 100-52-7; cyclohexanone, 108-94-1; 5-chloro-3methyl-2-pentanone, 1187-81-1; 3,5-dimethyl-4-methylene-2cyclohexen-1-one, 59159-01-2; 3,5-dimethyl-4-[4-[(tetrahydro-2H-pyran-2-yl)oxy]-2-butynylidene]-2-cyclohexen-1-one, 86695-79-6.

## A New Transformation of Amines to Carbonyl Compounds<sup>1</sup>

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Facile transformation of amines and their derivatives to carbonyl compounds (eq 1) is often an important process



in organic synthesis, while hitherto known methods using oxidizing agents  $(Ag^{2+}, t-BuOCl, photochemical, etc.)$ and nonoxidative methods,<sup>6,7</sup> are not always satisfactory in yields and/or versatility.

In the present paper, we report an application of our continuing study on the anodic oxidation of carbamates<sup>8-12</sup> to the conversion of amines to the corresponding aldehydes or ketones.

## **Results and Discussion**

As shown in Scheme I, the anodic methoxylation<sup>8</sup> of carbamates 2 prepared from primary amines 1 bearing a primary alkyl group gave  $\alpha$ -methoxycarbamates 3 in good

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yields. The transformation of 3 to dimethyl acetals 4, was successfully accomplished by the treatment of 4 with 5%  $H_2SO_4$  in methanol.<sup>13</sup>

As shown in Table I, this method is useful for the synthesis of dialdehyde from the corresponding dicarbamate and  $\omega$ -formyl carboxylic acids<sup>15</sup> from  $\omega$ -amino acids in high yields.

Interestingly, the electrochemical oxidation of carbamates 5 bearing a secondary alkyl group in methanol containing tetraethylammonium p-toluenesulfonate (TEATS) as a supporting electrolyte gave directly dimethyl ketals 6 in good yields (Scheme II).

Although there is no concrete evidence to support the intervention of  $\alpha$ -methoxylated carbamates 7, the dimethyl ketals 6 were probably formed by methanolysis of the  $\alpha$ -methoxy carbamates 7 catalyzed by acid generated in situ. Typical results are given in Table II.

In addition, the electrochemical method can also be applied to the synthesis of alicyclic ketones that are not necessarily synthesizable easily by the common chemical methods.<sup>17</sup> As exemplified in Scheme III, the anodic oxidation of carbamate 9 synthesized from norbornanecarboxamide (8) gave norcamphor dimethyl ketal (10) in 85% yield (Scheme III).

In view of its simplicity and versatility, this electrochemical method is undoubtedly one of the promising methods for the transformation of amines to carbonyl compounds.

## **Experimental Section**

Synthesis of Carbamates 2 and 5. Carbamates were prepared from the corresponding amines according to the known methods.<sup>20</sup>

(13) Mitzlaff has reported<sup>14</sup> that the treatment of  $\alpha$ -methoxy-Nacylazacycloalkanes with methanol gave a small amount of the corresponding dimethyl acetals or ketals.

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(15) Some  $\omega$ -formyl carboxylic acid derivatives have been prepared by the anodic oxidation<sup>16</sup> of the corresponding lactams. (16) Warning, K.; Mitzlaff, M. Tetrahedron Lett. 1979, 1563.

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