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ORIGINAL PAPER

Synthesis of dioxolanes and oxazolidines by silica gel catalysis

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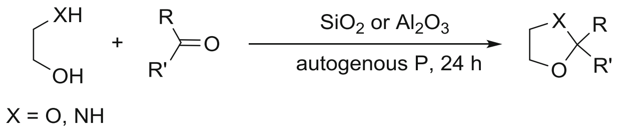
Abstract

Ethylene glycol condensed with carbonyl compounds in the presence of silica gel or alumina, without solvent and under pressure, affords 1,3-dioxolanes. 2-Amino-2-methylpropanol also condensed with carbonyl compounds in the presence of silica gel or an acid-activated clay, without solvent and under pressure, produces oxazolidines. To explain these results, we propose that the glycol and the aminopropanol react with Brønsted (H^+) and Lewis acid sites (Si and Al) located on the surface of the catalysts, leading to the products via various ionic intermediates.

Graphical abstract



Keywords 2-Amino-2-methylpropanol · Carbonyl compounds · Dioxolanes · Ethylene glycol · Oxazolidines

Introduction

Protic acids are well-known to suffer from a number of shortcomings, including their corrosive and noxious nature [1, 2]. The recent move towards green chemistry has seen silica gel, alumina, and clays gradually replacing mineral acids in the synthesis of organic compounds. Indeed, these non-polluting heterogeneous catalysts possess numerous advantages such as ready availability, efficient recycling, low cost, and ease of separation from crude reaction mixtures by simple filtration [3–5].

For example, the condensation of epoxystyrene with benzylmethylamine, the cyclization of enones, the vinylogous Michael double additions, the rearrangement of 1-amino-2-ketoesters and of 4-amino-3,4-dihydro-2*H*-1,4-thiazines have all been carried out in the presence of silica gel [6–8]. Alumina also catalyzes the oxidation of alcohols to ketones by trichloroacetic acid, the dehydration of alcohols to alkenes, the synthesis of isoxazolines and of 1,2-aminoalcohols [9–13]. Other studies have used natural aluminosilicates, such as clays, for the iodo-functionalization of alkenes by water and alcohols, the esterification of phenylacetic acid, the dehydration of glucose and the rearrangement of epoxy chalcones [14–17]. Ethylene glycol is frequently used in organic synthesis to protect aldehydes and ketones, enabling other functional groups in the molecule to undergo chemoselective transformations. These acetalization and ketalization reactions are typically carried out in ecologically harmful organic solvents, in the presence of noxious protic acids, at various temperatures and, typically, at atmospheric pressure [18–20] (Figs. 1, 2, 3).

To better understand the catalytic role played by these heterogeneous catalysts, we have decided to study their activity in the preparation of oxygen-containing five-

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István E. Markó prematurely passed away on July 31, 2017.

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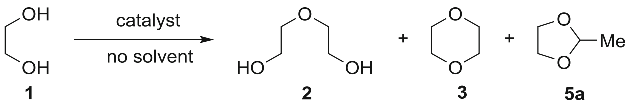


Fig. 1 Reaction of pure ethylene glycol (**1**) in the presence of sulfuric acid or silica gel under various experimental conditions

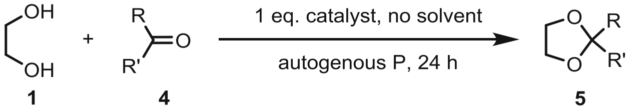


Fig. 2 Synthesis of dioxolanes **5b**–**5o** catalyzed by silica gel and alumina

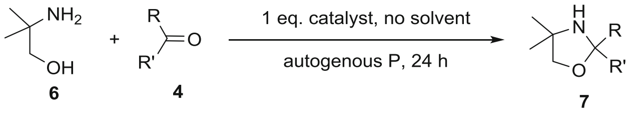


Fig. 3 Synthesis of oxazolidines **7g**–**7o** catalyzed by silica gel and activated clay

membered ring heterocycles, such as dioxolanes and oxazolidines, in the absence of solvent and under pressure, by the condensation of the corresponding carbonyl compounds with ethylene glycol and 2-amino-2-methylpropanol, respectively.

Results and discussion

Previous publications from various authors reported that the distillation of ethylene glycol (**1**) in the presence of sulfuric acid (4% by mass) leads to a mixture of four products [21–23]. According to these reports, 1,4-dioxane (**3**) is the major component of this reaction, while diethylene glycol (**2**), acetaldehyde, and 2-methyl-1,3-dioxolane (**5a**) are obtained in low yields.

Table 1 Reaction of pure ethylene glycol (**1**) in the presence of sulfuric acid or silica gel under different experimental conditions

Run	Catalyst	*T*/°C	*t*/h	**2**/%	**3**/%	**5a**/%
1	H_2SO_4 (4% wt)	196[a]	3	4	1	–
2	H_2SO_4 (4% wt)	150[b]	3	16	9	–
3	H_2SO_4 (4% wt)	150[b]	24	65	9	–
4	Silica gel	196	120	1	–	–
5	Silica gel	150	3	–	–	–
6	Silica gel	150	7	–	–	19

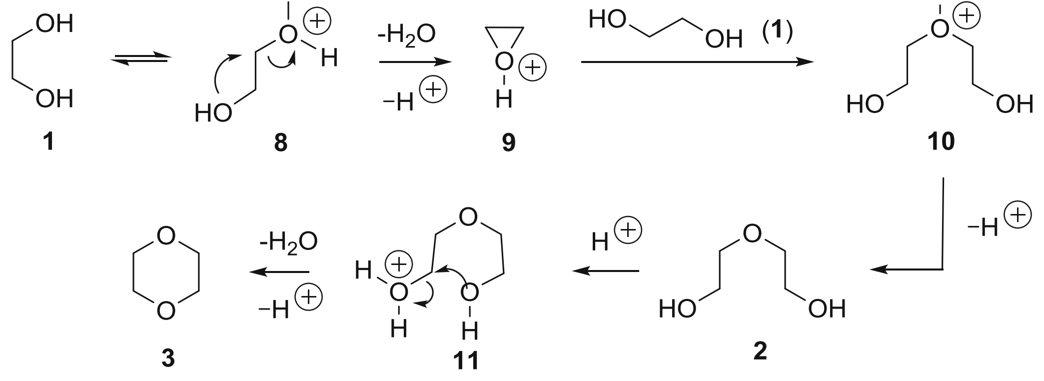
[a] P. atm: atmospheric pressure = 101 kPa. Reactor: 50 cm^3 flask

[b] P auto: autogenic pressure. P150° = 153 kPa

With the desire to convert this reaction into a more selective transformation, it was initially decided to reproduce this process under the previously described conditions. Hence, ethylene glycol was heated in the presence of H_2SO_4 (4% by mass) at 196 °C and under atmospheric pressure for 3 h. In contrast to the results reported in the literature [21–23], only diethylene glycol and 1,4-dioxane were obtained, in 4 and 1% yields (Table 1). It is interesting to note that the yield of compounds **2** and **3** increased after treatment of **1** with H_2SO_4 (4% by mass) in an autoclave, under pressure, at a temperature of 150 °C. Moreover, prolonged heating of this reaction mixture from 3 to 24 h considerably increased the amount of **2** (65%), while the quantity of **3** (9%) remained constant.

Replacing sulfuric acid by silica gel led to almost no dimerization of glycol **1** to diethylene glycol (1%), and no products **3** and **5a** were obtained even after refluxing for 5 days (Table 1, run 4). However, heating compound **1** at 150 °C, under pressure, resulted in a mixture of diethylene glycol and 2-methyl-1,3-dioxolane in yields depending upon the reaction time (Table 1, runs 5 and 6). In all cases, compound **2** remained a minor component of this mixture (1–3%), while the yield of dioxolane **5a** reached a value of

Scheme 1



22% after 24 h of heating. It then decreased slowly with time. It is interesting to note that diethylene glycol is stable on silica gel even after heating at 150 °C for 24 h, without solvent, and under pressure. This result demonstrates that the acidity of the catalyst plays an important role in the various pathways leading to the different products obtained in this transformation. Indeed, the linear dimer **2** is dehydrated to the cyclic dimer **3** in the presence of strong Brønsted acids such as sulfuric acid, while it is inert with respect to the Lewis acidic sites present in the silica gel.

Next, we tested the stability of the dioxolane **5a** by heating it in the presence of wet silica gel at 150 °C for 24 h. The recovery of a small amount of ethylene glycol (10%) from 2-methyl-1,3-dioxolane (**5a**) confirmed our assumption that **5a** is hydrolysed under these conditions, affording compounds **1** and absence of acetaldehyde. The absence of acetaldehyde can be explained by its release, either during the heating process or during the treatment of the crude reaction mixture at ambient temperature (bp 24 °C). It is noteworthy that other studies have also shown that 1,3-dioxolanes are unstable in the presence of protic acids (AcOH, TsOH, and HCl) and Lewis acid (BF_3) [4, 24–27].

At this stage, we can conclude that the selectivity of the reaction pathways when ethylene glycol is treated with various acids depends upon the nature of the catalyst used and the pressure exerted on the system. Brønsted acids activate the dimerization reaction of glycol **1**, delivering a mixture of diethylene glycol and 1,4-dioxane, whilst Lewis acids mainly convert compound **1** into 2-methyl-1,3-dioxolane via acetaldehyde.

Following these promising results, we decided to generalize this heterogeneous ketalization reaction to a variety of carbonyl compounds **4b–4o** by treating them with ethylene glycol, in the presence of catalytic amounts of silica gel, under solventless conditions, and at various temperatures. All these experiments were conducted in an autogenous pressure autoclave; the correlation between the temperature and the inner pressure is given in Table 2.

The results collected in Table 3 reveal that the aliphatic aldehydes **4b** and **4c** are almost inert under these conditions. However, unsaturated and aromatic aldehydes **4d–4g**, bearing inductive and mesomeric donor groups react with glycol **1** to afford the corresponding dioxolanes **5d–5g** with yields ranging from 9 to 24%. On the other hand, the presence of the strongly electron-withdrawing *para*-nitro substituent activates the carbonyl group of the aldehyde **4h** and dramatically increases the yield of dioxolane **5h** (86%).

In addition, we have studied the reaction of ethylene glycol with ketones **4i–4o** in the presence of silica gel. We noticed that ketones **4i–4l** are transformed into dioxolanes **5i–5l** in modest yields (5–8%). On the other hand, the presence of a phenyl substituent alpha to the carbonyl group of **4m** and **4n** greatly raised the yield of dioxolane **5m** and **5n** (24–26%). Even more advantageous is the use of chloroacetone (**4o**), which is more reactive than other ketones by virtue of the electron-withdrawing inductive effect of the chlorine atom, providing dioxolane **5o** in excellent yield (78%).

Furthermore, the results in Table 4 show that the ketalization of benzaldehyde (**4g**) and of phenylacetone (**4m**) by ethylene glycol, in the presence of a large amount

Table 2 Variation of the autogenous pressure as a function of temperature

T/°C	40	70	90	110	140	150
Auto. P./kPa	108	119	122	132	146	153

Table 3 Synthesis of dioxolanes **5b**–**5o** catalyzed by silica gel and alumina

Run	4	*R*	*R′*	*T*/°C	5	SiO_2	Al_2O_3	References
1	**4b**	H	CH_3CH_2	40	**5b**	Traces	Traces	[31, 32]
2	**4c**	H	$(CH_3)_2CH$	40	**5c**	Traces	Traces	[32, 33]
3	**4d**	H	4-$MeOC_6H_4$	140	**5d**	9	8	[34, 35]
4	**4e**	H	PhCH = CH	140	**5e**	14	18	[36]
5	**4f**	H	4-MeC_6H_4	140	**5f**	23	23	[37, 38]
6	**4g**	H	C_6H_5	150	**5g**	24	22	[39, 40]
7	**4h**	H	4-$O_2NC_6H_4$	140	**5h**	86	76	[41, 42]
8	**4i**	CH_3CH_2	CH_3CH_2	90	**5i**	5	4	[43, 44]
9	**4j**	CH_3	C_6H_5	140	**5j**	7	8	[45, 46]
10	**4k**	CH_3	CH_3	40	**5k**	8	9	[30–47]
11	**4l**	CH_3	CH_3CH_2	70	**5l**	6	8	[48, 49]
12	**4m**	CH_3	$PhCH_2$	140	**5m**	24	20	[50, 51]
13	**4n**	$PhCH_2$	$PhCH_2$	140	**5n**	26	23	[45–52]
14	**4o**	CH_3	$ClCH_2$	110	**5o**	78	56	[53, 54]

Table 4 Synthesis of dioxolanes **5g** and **5m** catalyzed by silica gel (10 eq)

Carbonyl compound	Run	*T*/°C	*t*/h	Dioxolanes **5**/%
4g	1	40	7	3
R = H; *R′* = C_6H_5	2	150	7	15
	3	150	24	29
4m	4	150	48	24
R = CH_3; *R′* = $PhCH_2$	5	140	7	13
	6	140	24	29

of silica gel (10 eq), depends upon the temperature and the duration of the reaction. It is also noteworthy that lowering the amount of silica gel (1 eq) slightly decreases the yield of dioxolanes **5g** and **5m** (compare Tables 3, 4).

The results obtained thus far, using silica gel, prompted us to test another solid catalyst known for its Lewis acidity, i.e., alumina [9–13]. The experimental results reported in Table 3 clearly show that alumina catalyzes the synthesis of dioxolanes substituted with electron-donating groups in yields close to those obtained with silica gel. However, condensation of ethylene glycol with *para*-nitrobenzaldehyde (**4h**) and chloroacetone (**4o**), in the presence of alumina, results in dioxolanes **5h** and **5o** in yields much lower than those obtained using silica gel.

It appears that the reaction of the carbonyl compounds **4h** and **4o**, carrying electron-withdrawing groups is easier with the catalyst possessing the largest specific surface area (SBET: silica gel 415 m^2/g, alumina 20 m^2/g). Curiously, in all these ketalization reactions, we did not obtain a mixture of 2-methyl-1,3-dioxolane and either monosubstituted or disubstituted dioxolanes **5b** after treatment of reagent **1** with **4b–4o** in the presence of silica gel or alumina (Tables 4, 5). The absence of **5a** indicates that the ketalisation reaction of **4b–4o** is much faster than the competitive dehydration of **1** into acetaldehyde.

This observation suggests that the sp^2 oxygen of the carbonyl compounds **4** could react more readily with the Lewis sites of the silica gel and the alumina than the hydroxyl groups of the excess ethylene glycol, leading to a single dioxolane **5**. It is also possible that hydrogen bonding between the remaining ethylene glycol and ketal **5** could prevent its subsequent rearrangement into dioxolane **5a**. It should be noted that silica gel and alumina (Lewis acids) catalyze the preparation of dioxolanes with yields close to those reported in the literature. Indeed, the microwave irradiation of a mixture of ethylene glycol and *para*-nitrobenzaldehyde (**4h**) or acetophenone (**4j**), in the presence of the *para*-toluene sulfonic acid (Brønsted acid) and under solventless conditions, leads to the dioxolanes **5h** and **5j** in 93 and 13% yields, respectively [28].

To extend the scope of this method to other five-membered ring oxygen-containing heterocycles, 2-amino-2-methylpropanol (**6**) was selected and used instead of ethylene glycol. As expected, silica gel promoted the formation of oxazolidines **7** in yields usually higher than for their dioxolane counterparts (Table 5). Under these conditions, oxazolidines **7g** and **7o** are obtained in a satisfactory yield of 42%.

However, the ketones **4j–4o** with a methyl group are converted into oxazolidines **7j–7o** in yields ranging from 15 to 28%. Moreover, we have also studied the condensation between reagents **4** and **6** in the presence of a third, natural catalyst based upon silica and alumina. For that purpose, we employed H_2-activated clay possessing

Table 5 Synthesis of oxazolidines **7** catalyzed by silica gel and activated clay

Run	Catalyst	**4**	*R*	*R′*	*T*/°C	**7**/%	References
1	Silica gel	**4g**	H	C_6H_5	150	42	[55]
2	Activated clay	**4g**	H	C_6H_5	140	47	
3	Silica gel	**4j**	CH_3	C_6H_5	90	11	[56]
4	Silica gel	**4j**	CH_3	C_6H_5	140	14	
5	Activated clay	**4j**	CH_3	C_6H_5	140	15	
6	Silica gel	**4k**	CH_3	CH_3	40	22	[57]
7	Activated clay	**4k**	CH_3	CH_3	40	23	
8	Silica gel	**4l**	CH_3	CH_3CH_2	70	17	[58]
9	Activated clay	**4l**	CH_3	CH_3CH_2	70	22	
10	Silica gel	**4m**	CH_3	$PhCH_2$	90	25	[59]
11	Silica gel	**4m**	CH_3	$PhCH_2$	140	21	
12	Activated clay	**4m**	CH_3	$PhCH_2$	140	24	
13	Silica gel	**4n**	$PhCH_2$	$PhCH_2$	140	21	[59]
14	Activated clay	**4n**	$PhCH_2$	$PhCH_2$	140	28	
15	Silica gel	**4o**	CH_3	$ClCH_2$	140	16	[59]
16	Activated clay	**4o**	CH_3	$ClCH_2$	140	42	

Brønsted and Lewis sites on its active surface [21–23]. From the results collected in Table 4, we can conclude that this natural heterogeneous catalyst is much more efficient than silica gel in the synthesis of oxazolidines **7**. Chloroacetone (**4o**) and 2-amino-2-methylpropanol (**6**) condense even better in the presence of H_2-activated clay than with silica gel (SBET: silica gel 415 m^2/g; clay 169 m^2/g). These results reveal that the specific surface area of the catalyst is not the only criterion, but that the number of Brønsted and Lewis sites located on the active surface of the H_2-clay is also important in the formation of oxazolidine **7o**.

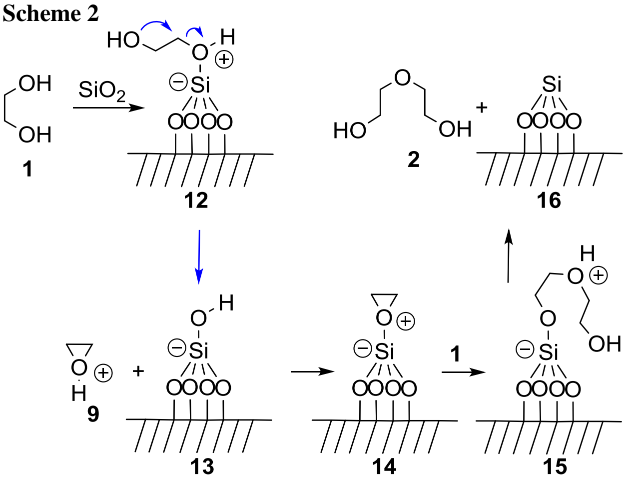
From these observations, we can conclude that the yield of oxazolidine **7** depends upon the temperature of the reaction and the autogenous pressure exerted on the system. It is also interesting to note that, whatever the catalyst used, we have not isolated ketal by addition of 2-aminoalcohol **6**.

To explain the dimerization of ethylene glycol by sulfuric acid to a mixture of diethylene glycol and 1,4-dioxane, we suggest that protonation of one of the hydroxyl functions of glycol **1** by the Brønsted acid leads either to a primary carbocation (high energy pathway, disfavored) or to the protonated epoxide **9** by direct intramolecular cyclization of **8** (favored pathway). The addition of a second molecule of ethylene glycol to the epoxonium ion **9** generates diethylene glycol via hydronium cation **10**. Protonation of dimer **2** provides cation **11** that cyclizes to dioxane **3**.

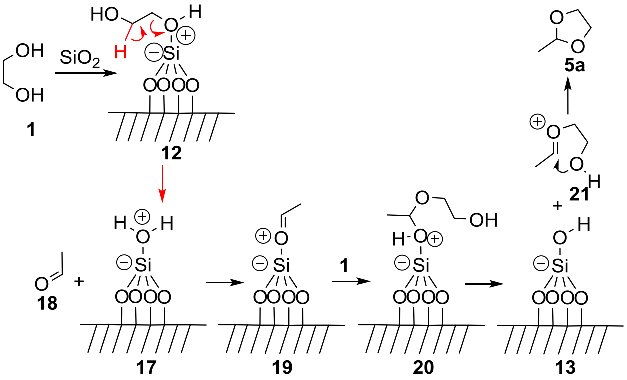
Studies have shown that the silicon atom in heterogeneous catalysts possesses vacant electron-accepting orbitals, akin to those of aluminum and boron and capable of acting as Lewis acids. Indeed, Sakuri [28] reported that lithium 2,2′-biphenolate reacts with alkenyltrichlorosilanes to form β-allylic alcohols via lithium silicate intermediates (Scheme 1).

To explain the formation of 1,3-dioxolane **5a** from ethylene glycol and silica gel, we suggest the mechanistic pathways depicted in Schemes 2 and 3. It is well-known that the active surface of the silica gel has siloxy (SiO) groups and silanol (SiOH) functions [29]. These Lewis sites form coordinating bonds with electron donors, namely the hydroxyl groups of ethylene glycol. The heterolytic cleavage of the C–O bond of the oxonium silicate **12** leads to the ionic intermediates **13** and **9**. The epoxonium cation **9** can lose a proton and react with silica gel to form the epoxonium silicate **14**, which immediately condenses with excess ethylene glycol to yield coordinated diethylene glycol **15**. Proton exchange and release of silica liberates the dimer **2** (Scheme 2). It is important to note that dioxane **3** was not isolated, probably owing to the stability of diethylene glycol again this Lewis acid.

Scheme 2



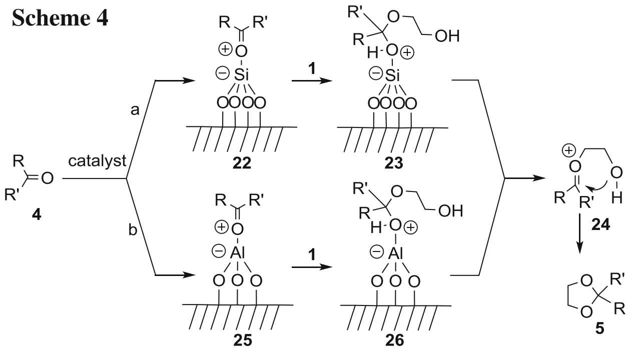
Scheme 3



On the other hand, loss of proton from **12** can afford directly acetaldehyde (**18**) and wet silica **17**. The oxygen of the carbonyl group of acetaldehyde can then be attached to the silicon atom located on the active surface of the catalyst to give oxonium silicate **19**. The addition of ethylene glycol to **19** forms hydronium silicate **20**. Cyclization of **20** to 2-methyl-1,3-dioxolane most probably proceeds via the oxonium cation **21**, ultimately releasing water and regenerating the silica catalyst (Scheme 3).

We can also propose a similar ionic mechanism, passing through oxonium silicates **22** or oxonium aluminates **25**, to explain the formation of dioxolanes **5b**–**5o** from ethylene glycol and carbonyl compounds **4b**–**4o** in the presence of silica gel or alumina. Thus, the Lewis (Si and Al) sites located on the active surface of these two catalysts form coordination complexes with the *sp*^{2} oxygen of the carbonyl compound **4** (Scheme 4). The nucleophilic attack of ethylene glycol on the tetra coordinated aluminates **25** (route b) and the pentacoordinated silicates **22** (route a) leads to zwitterions **26** and **23**. Finally, cyclization of these intermediates, probably through oxonium cation **24**, gives

Scheme 4



dioxolanes **5**, releases water and regenerates the corresponding catalysts.

The formation of oxazolidines **7** from 2-amino-2-methylpropanol and carbonyl compounds **4** can also be rationalized by similar ionic mechanisms (Scheme 5). Under acidic conditions, such as acid-activated clay, protonation of ketones **4** generates oxonium species **27** that reacts with **6** to form the protonated hemiaminal **28**. Proton shift, followed by loss of water, leads to iminium ion **30** that cyclizes to O,N-acetal **7** (Scheme 5).

In the catalytic process using silica or alumina, adsorption of the carbonyl compound **4** onto the active surface of the catalysts takes place, leading to the oxonium silicate **22** and the oxonium aluminate **25**. Subsequent nucleophilic attack of the nitrogen of aminoalcohol **6** on the zwiterions **22** and **25** generates the ammonium aluminate **32** and ammonium silicate **31** that cyclize to oxazolidine **7**, via iminium ion **30**, release water and regenerate the clay (Scheme 6, routes a and b).

Conclusions

We have developed a novel method for the synthesis of dioxolanes and oxazolidines in the presence of catalysts based on silica and alumina. The reactions proceed under pressure, without solvent, and generate the desired adducts in satisfactory yields. The extension of these reactions to the synthesis of other heterocycles, in the presence of these solid catalysts and under optimum experimental conditions responding to the demands of green chemistry, is currently being pursued in our laboratory.

Experimental

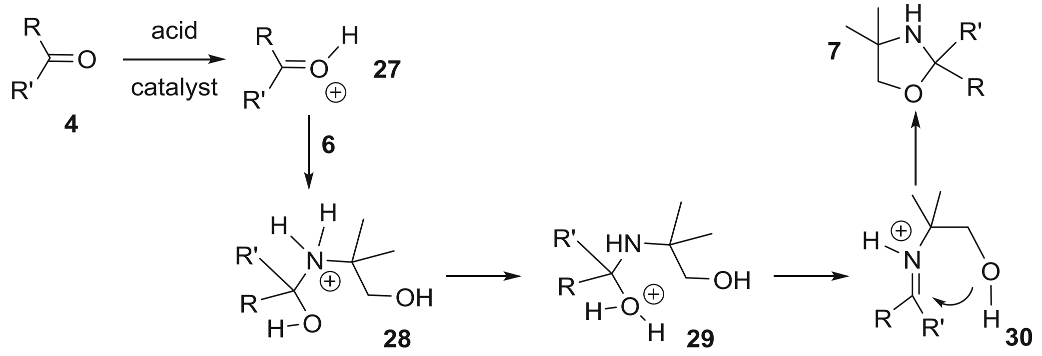
NMR spectra were recorded on a Bruker AC spectrometer (300 MHz ^{1}H and 75 MHz ^{13}C) in $CDCl_3$ solution. The chemical shift (δ) of the signals described is expressed in ppm relative to TMS taken as internal reference. The following abbreviations are used: s: singlet, d: doublet, t: triplet, m: multiplet, l: large. The coupling constants (*J*) are expressed in Hz. The reagents are from Aldrich. The silica gel is commercial type Merck 60 (70–230 mesh) and alumina is an Aldrich commercial product. The clay H_2 is prepared by acid activation, for 2 h, from the original Hb-clay from Morocco.

In all the experiments, ethylene glycol (**1**) or 2-amino-2-methylpropanol (**6**) present in the crude reaction product is removed by adding water to the crude reaction mixture. After treatment, a mixture of carbonyl compounds **4** and dioxolane **5** or oxazolidine **7** is recovered. The yields of products **5** and **7** are estimated from the ^{1}H NMR and ^{13}C NMR spectra of the crude reaction mixtures to avoid their decomposition during chromatographic purifications, as reported in other work [15]. Compounds **2**, **3**, **5a**, **5k**, and **5l** are identified by comparing their ^{1}H and ^{13}C NMR spectra with authentic samples marketed by Aldrich.

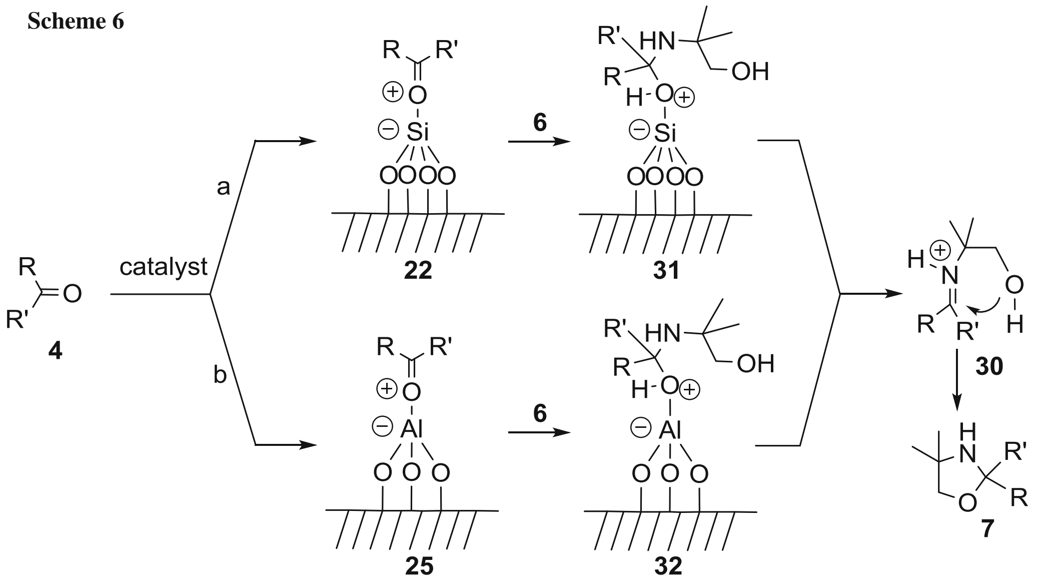
Synthesis of 1,3-dioxolanes

Synthesis of 2-methyl-1,3-dioxolane (5a) using sulfuric acid Procedure at atmospheric pressure: 7.67 g of ethylene glycol (**1**, 124 mmol) and H_2SO_4 (4% by mass) are placed in a flask (50 cm^3) equipped with a reflux condenser

Scheme 5



Scheme 6



and then heated at 196 °C for 3 h. After cooling, 20 cm^3 of water is added to the crude mixture to remove residual ethylene glycol. The aqueous solution is extracted with ether (3 × 50 cm^3). The organic phases are combined and then dried over $MgSO_4$. After filtration and evaporation of the ether in vacuo, a mixture of **2** and **3** is recovered. The yields of products **2** and **3** are displayed in Table 1.

Procedure under pressure: 7.67 g of ethylene glycol (**1**, 124 mmol) and H_2SO_4 (4% by mass) are placed in an autoclave (100 cm^3). The sealed reactor is heated at 150 °C for 3 h or for 24 h. After cooling, the residue is treated in the same manner as described above. The yields of products **2** and **3** are listed in Table 1.

Synthesis of 2-methyl-1,3-dioxolane (5a) Procedure at atmospheric pressure: 7.67 g of ethylene glycol (**1**, 124 mmol) and 0.1 g of silica gel are placed in a flask (50 cm^3) equipped with a reflux condenser and the whole is heated at 196 °C for 120 h. After cooling and separating the silica gel by filtration, the residue is treated in the same manner as described above. Diethylene glycol (**2**) was obtained in a yield of 1% (Table 1).

Procedure under pressure: 7.67 g of ethylene glycol (**1**, 124 mmol) and 0.1 g of silica gel are placed in an autoclave (100 cm^3). The sealed reactor is heated to 150 °C for various amounts of time. After cooling and separating the silica gel by filtration, the residue is treated in the same manner as described above. The yields of products **2** and **5a** are listed in Table 1.

Synthesis of 1,3-dioxolanes 5b–5o Ethylene glycol (**1**, 3.41 g, 55 mmol, 36 eq), 1.50 mmol of carbonyl compound **4** (1 eq), and 50 mg (1 eq) or 500 mg (10 eq) of silica are placed in an autoclave (100 cm^3). The sealed reactor is heated for 24 h at various temperatures. After cooling and separating the silica gel by filtration, the residue is treated in the same manner as described above. The yields of dioxolanes are given in Tables 3 and 4.

Synthesis of 1,3-dioxolanes 5b–5o using alumina Ethylene glycol (**1**, 3.41 g, 55 mmol), carbonyl compound **4** (1.50 mmol), and 50 mg of alumina were placed in an autoclave (100 cm^3). The sealed reactor was heated for 24 h at various temperatures. After cooling and separation of the alumina by filtration, the residue was treated in the same manner described above. The isolated yields of dioxolanes are given in Table 3.

Trace amounts of the dioxolanes **5b** and **5c** can be detected in the ^{13}C NMR spectra of the crude reaction mixture by the presence of the low intensity signals corresponding to the C_2–H carbons at 102.51 and 102.45 ppm, respectively.

Synthesis of oxazolidines 7

Synthesis of oxazolidines by silica gel

2-Amino-2-methylpropanol (**6**, 4.89 g, 55 mmol, 8.5 eq), 6.50 mmol of carbonyl compound **4** (1 eq), and 50 mg of silica gel are placed in an autoclave (100 cm^3). The sealed reactor is heated for 24 h at various temperatures. After cooling and separating the silica gel by filtration, the residue is treated in the same manner as described above. The yields of isolated oxazolidines **7** are given in Table 5.

Synthesis of oxazolidines by acid-activated clay

2-Amino-2-methylpropanol (**6**, 4.89 g, 55 mmol, 8.5 eq), 6.50 mmol of carbonyl compound **4** (1 eq), and 50 mg of

H_2-activated clay are placed in an autoclave (100 cm^3). The sealed reactor is heated for 24 h at various temperatures. After cooling and separation of the H_2-clay by filtration, the residue is treated in the same manner as described above. The yields of oxazolidines **7** are given in Table 5.

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