Synthesis of 1,3-dioxolanes catalysed by $AlPO_4$ and $AlPO_4$–Al_2O_3: kinetic and mechanistic studies

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A number of aldehydes and ketones were easily and quantitatively converted to the corresponding 1,3-dioxolanes by the reaction with ethylene glycol over four synthetic amorphous $AlPO_4$ and $AlPO_4$–Al_2O_3 catalysts using acetonitrile as the solvent at different temperatures in the range 30–60 °C without the formation of any by-product. The influence of the number of acid sites on the catalyst surface as well as the substituent effects of different carbonyl compounds studied can be evaluated through several isokinetic parameters obtained owing to the existence of a linear free-energy relationship (LFER). The results obtained account for an intermediate in the transition state whose relative stability is determined by the resonance between the carbonyl group and their substituents, but its evolution is *via* a concerted process in two adsorption–desorption steps.

The acetalization reaction is one of the most reliable and useful ways to protect ketones or aldehydes in the synthesis of multifunctional organic molecules. Thus, the carbonyl functions are generally transformed into suitable acetals or ketals that can be readily cleaved by acidic hydrolysis or directly converted to enamines, enol ethers and silylenol ethers.[1] Compounds bearing *cis*-1,2-diols and *cis*- and *trans*-1,3-diols can be protected as cyclic acetals and ketals. Thus, acetalization is also a reaction of particular importance in carbohydrate chemistry.[2] Furthermore, in addition to their well established role as protective groups or synthetic intermediates, cyclic acetals have served increasingly in recent years as valuable temporary chiral auxiliaries in asymmetric syntheses.[3]

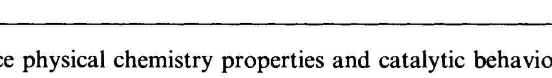
Acetalization of carbonyl compounds is generally carried out under homogeneous conditions in the presence of acid catalysts. Both simple alcohols themselves or formic acid orthoesters can be used for acetal formation in the presence of protic acids such as perchloric or toluenesulfonic acid,[4] as well as Lewis acids such as tellurium(IV) and lanthanum(III) halides.[5] Furthermore, a great variety of techniques based on the acid-catalysed reaction of the respective diol with the carbonyl compound have been developed[6] in the synthesis of cyclic acetals 1,3-dioxanes and 1,3-dioxolanes, respectively.

On the other hand, the use of inorganic solids as catalysts is rapidly increasing, because these reactions often involve milder conditions, easier work-up and higher selectivity than similar homogeneous reactions where it is sometimes rather troublesome to remove the acid catalyst after acetalization and also the application is difficult for the compounds which are unstable in acids. Thus, activated silica gel,[7] alumina,[8] clay minerals such as Kaolin or K-10 Montmorillonite,[9] hydrous zirconium oxide[10] and zeolites[11] were described as efficient heterogeneous catalysts for acetalization as well as for the hydrolytic cleavage of acetals because the former reaction is the exact reverse of acetal formation, all reaction steps being reversible.

In this respect, while the mechanism of the homogeneous acetalization reaction is at present undisputed,[12] the kinetic data for heterogeneous acetal formation are poor. However, the number and relative strength of acid and basic sites of solid catalysts, as well as their textural properties, can play an important role in the reaction mechanism taking into account that the rate-determining step ought to involve surface absorbed species.

In this regard, in a number of papers on amorphous $AlPO_4$ and $AlPO_4$–Al_2O_3 catalysts, dealing with the relation between surface physical chemistry properties and catalytic behaviour, we have shown that they are bifunctional catalysts whose acid and basic sites enable them to be used as heterogeneous catalysts in many selective organic processes. Thus, we have previously reported their use as catalysts for base catalysed condensations in Knoevenagel condensation in a dry medium[13] and in liquid-phase retroaldolization of diacetone alcohol,[14] as well as for the liquid-phase acid-catalysed regioselective ring-opening of 2,3-epoxy esters[15] and Diels–Alder catalysed reactions.[16] Tetrahydropyranylation of alcohols and phenols,[17] as well as acetalization of different carbonyl compounds,[18] were also described. They have also been used as metal supports in the liquid-phase hydrogenation of the double bond of alkenes bearing a variety of organic functions,[19] as well as in a number of gas-phase organocationic reactions.[20]

As part of our work studying the use of synthetic $AlPO_4$ and $AlPO_4$–Al_2O_3 in the field of selective synthetic chemistry which involves acid- and basic-catalysed reactions, the present paper reports on the results obtained in a kinetic study of the heterogeneous liquid–solid catalytic acetalization of different aldehydes and ketones with ethylene glycol affording 1,3-dioxolanes (Scheme 1). Four different $AlPO_4$ and $AlPO_4$–Al_2O_3 catalysts obtained by a sol–gel method with widely varying acid site numbers and acid–base character are used in order to gain information about the mechanism and nature of surface active sites of catalysts in this synthetically important reaction.



Scheme 1

Experimental

Apparatus, materials and kinetics

Acetalization reactions were carried out in a 15 cm^3 silicone-septum sealed vessel, under vigorous shaking (a Vibromatic-384 agitator) and submerged in a water thermostatic bath able to control the reaction temperature with an accuracy of ±0.5 °C. Starting carbonyl compounds and ethylene glycol were commercial pa quality chemicals purchased from Aldrich and Merck and they were all doubly distilled under reduced pressure before use. The acetonitrile solvent (pa 99%, Panreac)

Table 1 Textural and acid–base properties of different $AlPO_4$ and $AlPO_4$–Al_2O_3 catalysts

				Acidity/μmol g^{-1}			Basicity/μmol g^{-1}	
Catalyst	S_{BET}/m^2 g^{-1}	V/cm^3 g^{-1}	d/nm	CHA	PY	AN	BA	PH
AP–E	242	0.52	4.3	789	267	152	266	120
AP–P	228	0.75	6.6	732	227	40	166	56
APAl–E	242	0.55	4.5	298	208	48	577	214
APAl–P	319	0.68	4.2	203	326	32	774	198

was used without further purification. In this respect, some experiments were carried out to test the influence of the purity of solvent and substrates and the results indicated that while the solvent could be used directly, substrates needed at least two distillations to give reproducible results.

Most reactions between ethylene glycol (10 mol dm^{-3}) and the corresponding carbonyl compounds (10 mmol dm^{-3}) were carried out in 5 cm^3 acetonitrile as solvent (2 mol dm^{-3} reactant concentrations), 0.05 g catalyst with reaction temperatures in the range 30–60 °C. In addition, some sets of reactions with different catalyst weight (0.05–0.4 g) and substrate concentrations (0.5–4 mol dm^{-3}) were carried out in order to determine the limits of diffusion control and reaction orders of reactants, respectively.

Reaction rates were followed by gas chromatographic analysis, GCA (with a 2 m stainless steel column packed with 15% carbowax-20M on Chromosorb GAW DMCS 80/100), analysing the reaction mixtures obtained from the reaction vessel with a syringe [10 μl dose (1 μl = 1 mm^3)] at appropriate time intervals. The initial reaction rates were calculated by taking the initial slope of the plot of the corresponding dioxolane concentration (the reaction product) *versus* time. As these plots were always linear up to 60–70% conversion, the determination was straightforward and reproducible to within *ca.* 8%. In reactions carried out to completion, removal of the solvent yielded the corresponding practically pure 1,3-dioxolane. They were identified by comparison of retention times in GLC with those of authentic samples as well as by their physical and spectral characteristics (bp, FT–IR, ^{1}H NMR and ^{13}C NMR DEPT). No other reaction product was detected in any of the cases.

All acetals obtained can be cleaved to their constituent carbonyl compounds and ethylene glycol by the action of water in the presence of the catalysts studied. Hydrolysis was very easily obtained by refluxing 5 cm^3 of a 2 mol dm^{-3} 1,3-dioxolane solution for 2 h in acetonitrile with 0.05 g of catalyst and 0.9 cm^3 of water.

Catalysts

Four different catalysts have been used, two pure $AlPO_4$ (AP) and two $AlPO_4$–Al_2O_3 (75:25 wt%) (APAl) systems, all obtained according to the sol–gel method previously described.[16–20] Thus, these catalysts were obtained by precipitation from the corresponding $AlCl_3 \cdot 6H_2O$ and H_3PO_4 aqueous solutions (in the adequate molar ratio) by addition of ethene (E) or propylene oxide (P) to an 'end point' pH value of 6.1. After filtering, the samples were dried at 120 °C for 24 h and then the resulting powders screened to < 0.149 mm were calcined at 650 °C for 3 h in a muffle furnace. Their amorphous character was determined by powder X-ray diffraction.

Textural properties of catalysts (surface area, S_{BET}, pore volume, V, and main pore diameter, d), determined according to the BET method[21] from the adsorption–desorption nitrogen isotherms at liquid nitrogen temperature,[20,22] are collected in Table 1. Acid–base properties at room temperature, also collected in Table 1, were determined by a spectrophotometric method[14,23] that allows titration from cyclohexane solutions (spectroscopic grade Merck) of the amount of irreversibly adsorbed cyclohexylamine, CHA, (pK_a = 10.6); pyridine (PY) (pK_a = 5.3) and aniline (AN) (pK_a = 4.6) as well as benzoic acid (BA) (pK_a = 4.19) and phenol (PH) (pK_a = 9.9) employed as titrant agents of acid and basic sites of different strengths, respectively. The monolayer coverage at equilibrium at 25 °C, X_m, is accomplished by applying the Langmuir adsorption isotherm which is assumed to be a measure of the total amount of Lewis and Brønsted acid or basic sites corresponding to the specific pK_a of the base or acid used.

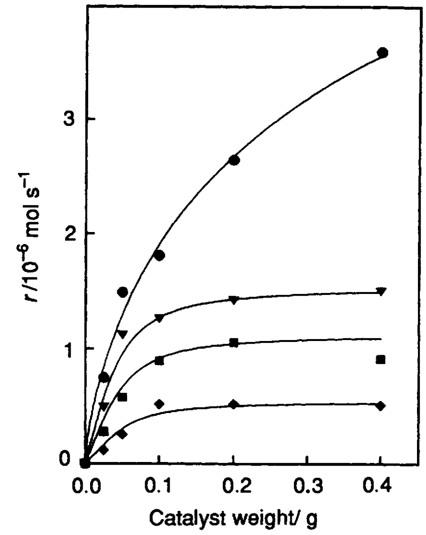


Fig. 1 Influence of weight of catalyst AP–P, w/g on the initial rate of formation of 2-phenyl-1,3-dioxolane, r/μmol s^{-1} g^{-1} at different temperatures: (◆) 30; (■) 40; (▼) 50 and (●) 60 °C

Diffusional limitations

The effect of external diffusion of reactants on reaction rates was checked by lowering the shaking regime from 1000–100 strokes min^{-1}. The reaction rates were independent of the agitation speed above 500 strokes min^{-1}. Furthermore, a linear variation between the weight of the catalyst and the acetalization reaction rate was obtained with different carbonyl compounds in the range of operating variables studied. Thus, reaction rates were directly proportional to the catalyst weight. Results obtained with benzaldehyde and the catalysts AP–P are shown in Fig. 1. The internal diffusion control was excluded by using catalysts with a grain diameter < 0.149 mm. As may be seen in Table 2, where acetalization rates of benzaldehyde are collected with different catalysts of several grain sizes at 60 °C under standard conditions, the internal diffusion operates when the grain size is greater than 0.21 mm. Thus, we have to conclude that under the selected standard conditions, the kinetic data are free from transport influences.

Results

Reaction orders

The reactions were first-order with respect to the concentrations of ethylene glycol and carbonyl compound at every

Table 2 Influence of the grain diameter of different catalysts, $\bar{d}$, on the initial reaction rate of formation of 2-phenyl-1,3-dioxolane, r, at 60 °C under standard conditions

	$[r/\mu\mathrm{mol\ s^{-1}\ g^{-1}}]$			
$\bar{d}$/mm	AP–E	AP–P	APAl–E	APAl–P
$\bar{d} < 0.149$	34.2	15.3	10.6	6.0
$0.149 > \bar{d} > 0.105$	38.5	18.5	12.1	6.9
$0.105 > \bar{d} > 0.074$	37.4	17.6	12.4	6.9
$0.074 > \bar{d} > 0.053$	38.8	18.0	11.8	6.9
$0.053 > \bar{d} > 0.037$	38.3	18.1	11.9	6.9
$0.037 > \bar{d}$	22.4	8.9	6.2	4.2

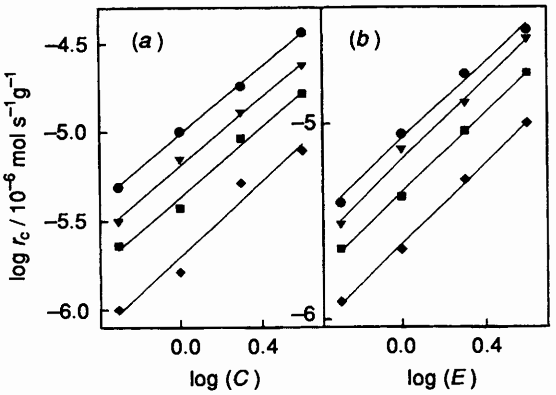


Fig. 2 Dependence of acetalization reaction rate ($r/\mu\mathrm{mol\ s^{-1}\ g^{-1}}$) on the concentration of reactants under standard conditions and different temperatures: (◆) 30; (■) 40; (▼) 50 and (●) 60 °C. (*a*) Initial concentration of ethylene glycol, [E] = 2 mol dm^{-3}; (*b*) initial concentration of benzaldehyde, [B] = 2 mol dm^{-3}.

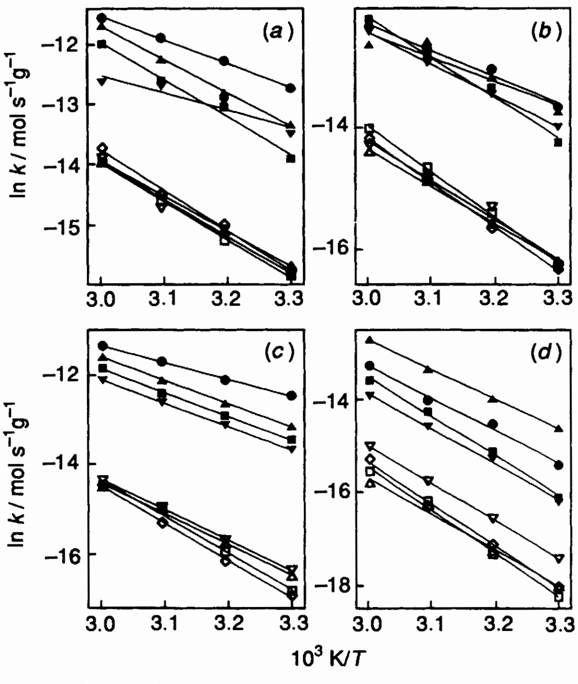


Fig. 3 Arrhenius plots for the acetalization reaction under standard conditions of different carbonyl compounds R–CO–R′ with different catalysts: (*a*) AP–E; (*b*) AP–P; (*c*) APAl–E and (*d*) APAl–P. (●) R = Ph, R′ = H; (▼) R = Pr^{i}CH, R′ = H; (■) R = CH$_2$=CH, R′ = H; (▲) R = PhCH=CH, R′ = H; (▽) R = Et, R′ = Me; (□) R = Pr, R′ = Me; (△) R = PrCH$_2$, R′ = Me; (◇) R = Bu, R′ = Me

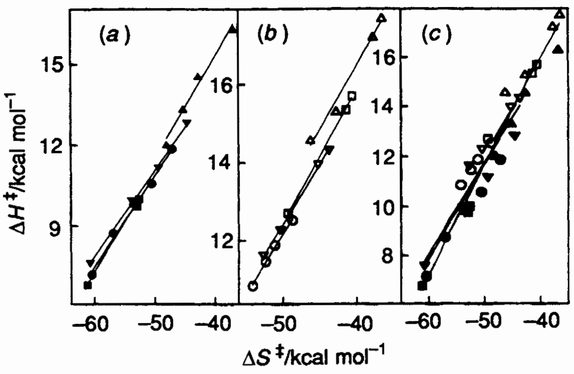


Fig. 4 Compensation effect between $\Delta H^{\ddagger}$ and $\Delta S^{\ddagger}$ values in Table 3 for different catalysts by separately plotting (*a*) aldehydes: (●) AP–E; (▼) AP–P; (●) APAl–E; (▲) APAl–P; (*b*) ketones: (○) AP–E; (▽) AP–P; (□) APAl–E; (△) APAl–P; (*c*) all carbonyl compounds together

studied temperature (30, 40, 50 and 60 °C) for all catalysts and different carbonyl compounds studied. They were determined in different reaction sets, always using 0.05 g catalyst under standard conditions, from the dependence of the acetalization reaction on the concentration of carbonyl compounds (0.5–4 mol dm^{-3}) as well as from the dependence of reaction rate on the concentration of ethylene glycol (0.5–4 mol dm^{-3}). In the former sets, ethylene glycol concentration was a fixed constant at 2 mol dm^{-3} and in the latter sets, it was always 2 mol dm^{-3} concentration of every carbonyl compound studied. Results obtained with benzaldehyde and AP–P catalysts are shown in Fig. 2.

Accordingly, the kinetic equation for the heterogeneous reaction system under study can be written as eqn. (1) where

$$r = wk[\mathrm{C}][\mathrm{E}] \qquad (1)$$

reaction rate, r is directly proportional to the rate constant, k, the catalyst weight, w, and to the concentrations of reactants, ethylene glycol, E, and carbonyl compound, C, respectively. Accordingly, an adequate representation of the transition state may be obtained[24] from the equilibrium of both reactants absorbed on the surface active sites of catalysts.

Kinetic rate constants

The results obtained with different catalysts and different carbonyl compounds in the temperature range studied are shown in Fig. 3. The straight lines obtained allow us to apply the Arrhenius equation to k values obtaining the corresponding values of apparent activation energies, E_a, and Arrhenius constants, ln A, collected in Table 3. Furthermore, the Eyring equation also evaluates the temperature dependence of reaction rate constants in terms of transition state theory by separating enthalpy, $\Delta H^{\ddagger}$, and entropy, $\Delta S^{\ddagger}$, components. Their corresponding values, obtained by plotting ln ($k\ T^{-1}$) *vs.* T^{-1} are also shown in Table 3. In dealing with $\Delta H^{\ddagger}$ and $\Delta S^{\ddagger}$, it is necessary to point out that their values relate only the activated complex to the reactants so that they represent the additional enthalpy and entropy component of the activated complex relative to the reactants and they are not relevant to the products.

Discussion

Compensation effects

Fig. 4 shows how the kinetic parameters $\Delta H^{\ddagger}$ against $\Delta S^{\ddagger}$ in Table 4 fit straight lines for every carbonyl compound with the four studied catalysts. This enthalpy–entropy relationship may be ascribed to the existence of a linear free energy relationship (LFER) [(eqn. (2)] known as the 'compensation effect' or 'isokinetic relationship' (IKR) 25 although the most habitual

$$\Delta G^{\ddagger} = -\theta R \ln K^{\ddagger} = \Delta H^{\ddagger} - \theta \Delta S^{\ddagger} \qquad (2)$$

Table 3 Apparent activation energies, E_a/kcal mol^{-1}, Arrhenius constants, ln A, activation enthalpies, $\Delta H^\ddagger$/kcal mol^{-1} and activation entropies, $\Delta S^\ddagger$/cal mol^{-1} K^{-1} with their respective standard deviations, for the catalysts and different substrates R–CO–R′

Substrate			[Catalyst]			
R	R′	Activation parameter	AP–E	AP–P	APAl–E	APAl–P
Ph	H	E_a	7.8 ± 0.2	8.2 ± 0.6	7.4 ± 0.3	14.0 ± 0.9
		ln A	0.3 ± 0.3	0.2 ± 0.9	0.1 ± 0.4	7.9 ± 1.4
		$\Delta H^\ddagger$	7.2 ± 0.2	7.6 ± 0.6	6.8 ± 0.2	13.3 ± 0.9
		$\Delta S^\ddagger$	−60.4 ± 0.8	−60.8 ± 1.8	−61.2 ± 0.8	−45.3 ± 2.8
Pr^{i}CH	H	E_a	9.4 ± 0.5	10.6 ± 0.2	10.5 ± 0.1	15.2 ± 0.6
		ln A	2.1 ± 0.9	3.7 ± 0.2	3.8 ± 0.0	9.2 ± 1.0
		$\Delta H^\ddagger$	8.7 ± 0.5	9.9 ± 0.2	9.9 ± 0.1	14.6 ± 0.6
		$\Delta S^\ddagger$	−56.9 ± 1.7	−53.8 ± 0.5	−53.5 ± 0.3	−42.8 ± 2.0
CH$_2$=CH	H	E_a	12.5 ± 1.0	13.4 ± 1.0	10.7 ± 0.3	16.9 ± 0.7
		ln A	7.0 ± 1.5	8.2 ± 1.6	4.3 ± 0.5	12.1 ± 1.1
		$\Delta H^\ddagger$	11.9 ± 1.0	12.8 ± 1.0	10.1 ± 0.3	16.3 ± 0.7
		$\Delta S^\ddagger$	−47.1 ± 3.0	−44.6 ± 3.1	−52.5 ± 0.9	−36.8 ± 2.1
PhCH=CH	H	E_a	11.2 ± 0.2	11.8 ± 0.2	10.4 ± 0.2	12.7 ± 0.3
		ln A	5.3 ± 0.3	5.9 ± 0.4	4.1 ± 0.3	6.6 ± 0.4
		$\Delta H^\ddagger$	10.7 ± 0.2	11.1 ± 0.2	9.7 ± 0.2	12.1 ± 0.3
		$\Delta S^\ddagger$	−50.5 ± 0.7	−49.3 ± 0.7	−52.8 ± 0.7	−48.0 ± 0.8
Et	Me	E_a	12.1 ± 1.3	12.9 ± 1.4	13.3 ± 0.3	15.9 ± 0.1
		ln A	4.4 ± 2.1	5.4 ± 2.2	5.9 ± 0.5	9.2 ± 1.5
		$\Delta H^\ddagger$	11.5 ± 1.3	12.3 ± 1.4	12.7 ± 0.3	15.3 ± 0.1
		$\Delta S^\ddagger$	−52.4 ± 4.1	−50.4 ± 0.9	−49.3 ± 0.9	−42.8 ± 0.1
Pr	Me	E_a	12.5 ± 0.5	14.9 ± 0.4	16.0 ± 1.1	18.3 ± 1.1
		ln A	5.0 ± 0.7	8.7 ± 0.6	9.9 ± 1.8	12.3 ± 1.7
		$\Delta H^\ddagger$	11.9 ± 0.4	14.3 ± 0.4	15.3 ± 1.1	17.7 ± 1.9
		$\Delta S^\ddagger$	−51.1 ± 1.4	−43.8 ± 1.2	−41.4 ± 3.6	−36.5 ± 3.5
Pr^{i}CH$_2$	Me	E_a	11.5 ± 0.3	12.2 ± 0.4	13.4 ± 0.7	15.2 ± 1.7
		ln A	3.5 ± 0.4	4.2 ± 0.7	5.8 ± 1.1	7.4 ± 1.9
		$\Delta H^\ddagger$	10.9 ± 0.3	11.6 ± 0.4	12.7 ± 0.7	14.6 ± 1.2
		$\Delta S^\ddagger$	−54.1 ± 0.9	−52.7 ± 1.4	−49.5 ± 2.3	−46.3 ± 3.7
Bu	Me	E_a	13.2 ± 0.8	14.6 ± 0.4	16.3 ± 0.6	17.8 ± 0.9
		ln A	6.2 ± 1.3	7.9 ± 0.7	10.3 ± 0.9	11.7 ± 1.4
		$\Delta H^\ddagger$	12.5 ± 2.6	13.9 ± 0.4	15.7 ± 0.6	17.2 ± 0.9
		$\Delta S^\ddagger$	−48.7 ± 2.6	−45.3 ± 1.3	−40.6 ± 1.8	−37.7 ± 2.7

Table 4 Values of isokinetic parameters for substrates (R–CO–R′): ln α_s and θ_s^a, obtained from the representation of ln A *vs.* E_a, and θ_s^b, $\Delta G_s^\ddagger$ and ln $K_s^\ddagger$, obtained from the representation of $\Delta H^\ddagger$ *vs.* $\Delta S^\ddagger$. Uncertainties are determined by their respective standard deviation.

Substrate						
R	R	ln α_s	θ_s^a/K	θ_s^b/K	$\Delta G_s^\ddagger$/kcal mol^{-1}	ln $K_s^\ddagger$
Ph	H	−9.7 + 0.7	403 ± 24	404 ± 37	31.6 ± 2.1	−39.6 ± 4.5
Pr^{i}CHCH	H	−8.9 ± 0.5	424 ± 14	419 ± 14	32.5 ± 0.7	−39.2 ± 1.5
CH$_2$=CH	H	−8.6 ± 0.9	408 ± 21	402 ± 21	30.9 ± 2.3	−38.9 ± 2.3
PhCH=CH	H	−6.4 ± 1.5	492 ± 61	472 ± 60	34.6 ± 3.0	−37.0 ± 5.7
Et	Me	−10.8 ± 0.1	404 ± 2	401 ± 2	32.5 ± 0.4	−40.9 ± 0.2
Pr	Me	−10.5 ± 1.5	402 ± 30	393 ± 30	31.8 ± 1.3	−40.9 ± 3.6
Pr^{i}CH$_2$	Me	−8.7 ± 1.2	474 ± 39	463 ± 38	35.9 ± 2.0	−39.2 ± 3.9
Bu	Me	−9.5 ± 0.9	423 ± 19	418 ± 19	32.9 ± 0.8	−39.7 ± 2.0

representation is given in eqn. (3) where $\Delta G^\ddagger$ is the activation

$$\ln A = \ln \alpha + E_a/\theta R \qquad (3)$$

free energy of the activated complex and $K^\ddagger$, its equilibrium constant, R is the gas constant and θ, the isokinetic temperature at which identical values for the reaction rate constant $k = \alpha$ are obtained. Thus, the values of isokinetic parameters for each substrate R–CO–R′ (θ_s, ln α_s, $\Delta G_s^\ddagger$ and ln $K_s^\ddagger$) were obtained from slopes and intercepts eqns. (2) and (3) and collected in Table 4.

On the other hand, from the same activation parameters collected in Table 3, a series of common isokinetic parameters are obtained for every catalyst (θ_c, ln α_c, $\Delta G_c^\ddagger$ and ln $K_c^\ddagger$), on plotting $\Delta H^\ddagger$ *vs.* $\Delta S^\ddagger$ and ln A *vs.* E_a for every catalyst with the eight substrates studied as shown in Fig. 4(*c*). However, better correlations may be obtained by separately plotting aldehydes and ketones [Fig. 4(*a*) and (*b*)], as can be seen in Table 5, where the corresponding isokinetic parameters of catalysts obtained from both sets of carbonyl compounds are also present.

In this respect, if an IKR holds for a reaction series exhibiting a similar $\Delta G^\ddagger$ value throughout the experimental temperature range, a common transition state intermediate can be expected.[26] Thus, the similar $\Delta G_c^\ddagger$ values collected in Table 5 indicate that a similar common interaction mechanism should be considered in the acetalization of aldehydes and ketones, in spite of the possible existence of specific characteristics in every case, as it is detected in Fig. 4.

The compensation effects obtained cannot be ascribed to a false correlation caused by a scatter of data because the θ values obtained are out of the range of temperatures covered by the experimental measurements.[27] In fact, always $\theta > T_{exp}$, so that, according to the classification of Blackadder and

Table 5 Values of isokinetic parameters of each catalyst obtained with aldehydes, with ketones and all together. Ln α_c and θ_c^a, obtained from the representation of ln A *vs.* E_a, and θ_c^b, $\Delta G_c^‡$ and ln $K_c^‡$, obtained from the representation of $\Delta H^‡$ *vs.* $\Delta S^‡$. Uncertainties are determined by their respective standard deviation.

Catalyst	Substrate	ln α	θ_c^a/K	θ_c^b/K	$\Delta G_c^‡$/kcal mol^{-1}	ln $K_c^‡$
AP–E	Aldehydes	-11.3 ± 0.8	346 ± 19	340 ± 19	27.9 ± 1.0	-41.4 ± 2.7
	Ketones	-15.2 ± 0.8	312 ± 13	307 ± 14	27.5 ± 0.7	-45.3 ± 2.4
	All together	-8.3 ± 2.2	456 ± 80	380 ± 67	30.6 ± 3.5	-40.8 ± 8.6
AP–P	Aldehydes	-12.7 ± 0.5	324 ± 10	321 ± 10	27.1 ± 0.5	-42.7 ± 1.6
	Ketones	-15.7 ± 0.5	310 ± 7	309 ± 8	27.9 ± 0.4	-45.6 ± 1.3
	All together	-9.7 ± 2.0	408 ± 54	367 ± 49	30.1 ± 2.4	-41.5 ± 6.5
APAl–E	Aldehydes	-10.1 ± 0.9	375 ± 25	668 ± 25	29.3 ± 1.4	-40.4 ± 3.4
	Ketones	-14.1 ± 0.4	338 ± 6	334 ± 6	29.2 ± 0.3	-44.2 ± 1.0
	All together	-7.8 ± 1.0	466 ± 34	447 ± 33	34.0 ± 1.7	-38.5 ± 3.4
APAl–P	Aldehydes	-10.4 ± 1.9	384 ± 37	373 ± 36	30.2 ± 1.6	-41.0 ± 4.5
	Ketones	-15.6 ± 2.3	331 ± 29	323 ± 28	29.4 ± 1.2	-46.0 ± 4.4
	All together	-7.8 ± 2.8	459 ± 74	399 ± 64	31.6 ± 2.7	-40.8 ± 7.5

Hinshelwood,[28] the acetalization reaction of carbonyl compounds under the present experimental conditions ought to be considered 'enthalpy controlled'. Thus, using eqns. (2) and (3)

$$k = (kT/h)\exp[(\Delta H^‡/R)(1/\theta - 1/T) - (\Delta G^‡/R\theta)] \quad (4)$$

$$k = \alpha \exp[(E_a/R)(1/\theta - 1/T)] \quad (5)$$

we can obtain Eyring and Arrhenius expressions as a function of the isokinetic parameters, where k and h are Boltzmann's and Planck's constants. Here we can see that in 'enthalpy controlled' processes (as in the present case where $\theta > T_{exp}$) the reactions with lower E_a (or $\Delta H^‡$) exhibit higher reaction rates. In 'entropy controlled' reactions (where $\theta < T_{exp}$) the opposite is true.

Based on these results, the influence of catalysts as well as the effects of different substituents in the carbonyl group on the acetalization rate can be evaluated through the activation parameters (E_a, ln A, $\Delta H^‡$ and $\Delta S^‡$) collected in Table 3 and the isokinetic parameters (θ, ln α, $\Delta G^‡$ and in $K^‡$) in Tables 4 and 5. Therefore, the isokinetic parameters of catalysts and substrates can provide a more general measurement of the reactivity characteristic of a series of related reactions with respect to the effects of substituents and catalysts.

Catalyst characterization. Nature of surface active sites

In order to determine the potential influence of textural and acid–base properties of different solids on their catalytic behaviour, a correlation matrix using all the data in Tables 1 and 5 was built and the results obtained in the regression analysis of the well correlated parameter pairs are shown in Table 6, where the corresponding correlation coefficients and significance levels are also indicated.

According to the results in Table 6, the isokinetic parameters of catalysts θ_c and $\Delta G_c^‡$, obtained separately for aldehydes and ketones, are well correlated with the number of acid sites titrated with CHA as well as with the basic sites titrated with BA. It is also interesting to note that there is no correlation when isokinetic parameters are obtained from all carbonyl compounds. This clearly indicates that in spite of a common acetalization mechanism for all the carbonyl compounds, there are also some differences (probably of a quantitative character) between aldehydes and ketones with respect to the catalytic effects of surface active sites. Thus, negative values of slopes with CHA indicate, according to eqns. (4) and (5), that a high number of acid sites titrated with CHA promote and increase in catalytic activity although this effect is comparatively more pronounced in aldehydes than in ketones owing to the lower values in the slopes of the former with respect to the latter (Fig. 5).

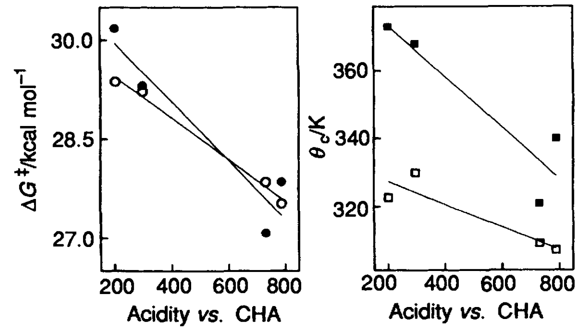


Fig. 5 Correlation between the isokinetic parameters of catalysts θ_c and $\Delta G_c^‡$ and the number of acid sites titrated with cyclohexylamine (CHA)

Positive values of slopes in the correlations with BA should indicate a negative influence of basic sites in the acetalization reaction. However this correlation could be obtained as a consequence of the existence of another negative correlation (shown at the bottom of Table 6) between the number of acid sites titrated with CHA and those basic sites titrated with BA in the catalysts studied. In order to confirm this possibility, some poisoning experiments were developed. Thus, while the addition of the amount of CHA shown in Table 1 for each catalyst to the reaction vessel is able to inactivate the catalyst, the presence of the corresponding amount of BA only promotes a very slight decrease in the reaction rate. This leads us to conclude that acid sites (even those of the lowest strength able to adsorb a very strong base such as CHA, with pK_a = 10.6) are solely responsible for the catalytic action of solids.

With respect to the nature of active acid sites, we have to consider that Lewis acid sites become Brønsted ones when they adsorb a water molecule. Thus, with independence of the initial nature of acid sites spectroscopically titrated (PY and CHA are able to be chemisorbed on both type of acid sites), they must operate as Brønsted acid sites. Finally, textural properties (S_{BET}, V and d) do not seem to exert any influence on the catalytic behaviour of solids studied under the present experimental conditions if we take into account the absence of correlations obtained.

Structure–activity relationship

The existence of an LFER also manifests itself in the correlation between the isokinetic parameters of substrates and σ parameters of the substituents[29] within the context of the Yukawa–Tsuno equation[30] [eqn. (6)], a modification of the standard

$$\log(k/k^\circ) = \rho\sigma + \rho(r)(\sigma^+ - \rho) \quad (6)$$

Hammett equation,[31] which takes into account the extent of an

Table 6 Regression coefficients from the correlation obtained between some surface properties of the catalysts in Table 1 and the isokinetic parameters of catalysts in Table 5, according to the general expression $y = ax + b$, as well as the corresponding correlation coefficients, r, and significance levels

y	x	$a/10^{-3}$	b	r	Significance (%)
$\Delta G^{\ddagger}_{c}$ (aldehydes)	CHA	−4.4	30.9	0.945	95
θ^{a}_{c} (aldehydes)	CHA	−8.5	400.0	0.917	92
θ^{b}_{c} (aldehydes)	CHA	−7.6	388.7	0.920	92
$\Delta G^{\ddagger}_{c}$ (ketones)	CHA	−3.2	30.1	0.996	99
θ^{a}_{c} (ketones)	CHA	−4.3	344.7	0.933	93
θ^{b}_{c} (ketones)	CHA	−3.8	337.4	0.877	88
$\Delta G^{\ddagger}_{c}$ (aldehydes)	BA	5.0	26.4	0.994	100
θ^{a}_{c} (aldehydes)	BA	95.2	314.8	0.971	97
θ^{b}_{c} (aldehydes)	BA	84.2	313.0	0.965	97
$\Delta G^{\ddagger}_{c}$ (ketones)	BA	3.2	27.1	0.935	94
θ^{a}_{c} (ketones)	BA	42.7	303.9	0.871	87
θ^{b}_{c} (ketones)	BA	35.3	302.6	0.771	77
BA	CHA	−900	903.1	0.962	96
BA/S_{BET}	CHA/S_{BET}	−600	3.0	0.969	97

Table 7 Results obtained by the application of the Yukawa–Tsuno equation to the isokinetic parameters of aldehydes by using Taft resonance effect parameters σ^{-}, in the usual way: isokinetic parameter = $\rho_{o}\sigma + \rho_{o}(r^{-})\ (\sigma^{-} - \sigma)$; as well as the correlation coefficient, r, and significance levels

Isokinetic parameter	ρ_o	(r^{-})	r	Significance (%)
$\Delta G^{\ddagger}$	−29.5	0.7	0.931	64
ln $K^{\ddagger}$	−18.6	0.9	0.994	89
θ_s	−597.0	0.8	0.980	80

Table 8 Results obtained by the application of the Yukawa–Tsuno equation to the isokinetic parameters of ketones by using Taft resonance effect parameters σ^{+}, in the usual way: isokinetic parameter = $\rho_{o}\sigma + \rho_{o}(r^{+})\ (\sigma^{+} - \sigma)$; as well as the correlation coefficient, r, and significance levels

Isokinetic parameter	ρ_o	(r^{+})	r	Significance (%)
$\Delta G^{\ddagger}$	−21.3	0.7	0.999	96
ln $K^{\ddagger}$	−26.3	0.3	0.922	61
θ_s	−524.2	0.5	0.996	91

additional resonance contribution throughout the values of (r), by employing a two parameter correlation. A large (r) value corresponds to a reaction with a large resonance contribution, whereas when (r) is zero the equation is identical to the original Hammett equation.[31] Eqn. (6) contains one set of resonance constants, σ^{+}, for electron-donating substituents. However, when there is direct conjugation with an electron-rich centre, an equation analogous to eqn. (5) ought to be employed replacing σ^{+} with σ^{-}, a set of resonance constants for electron-withdrawing substituents. Thus, the σ^{+} values reflect direct resonance interaction between a substituent, R, acting as an electron donor and a cationic reaction centre, while the σ^{-} set indicates a direct resonance interaction of R with an electron-rich reaction site. Results obtained by using substituent constant values (σ, σ^{+} and σ^{-}, respectively) recently surveyed by Taft[29] and the isokinetic parameters of aldehyde and ketone substrates (Table 4) are collected in Tables 7 and 8.

According to the results, we may assume the validity of the treatment in which the isokinetic parameters are used instead of reaction rates, the kinetic parameters usually employed. This assumption implies a recognition of the variable extent of resonance participation in the reaction mechanism according to the values of (r^{+}) and (r^{-}) other than zero. Here there are again clear differences between aldehydes and ketones because in the former case the fit is obtained with σ^{-} while in the latter with σ^{+}. This fact could account for differences in the nature of the reaction centre (anionic or cationic) where the R substituent is influential although the negative and positive values obtained in (r^{+}) and (r^{-}) may not comply with this explanation.

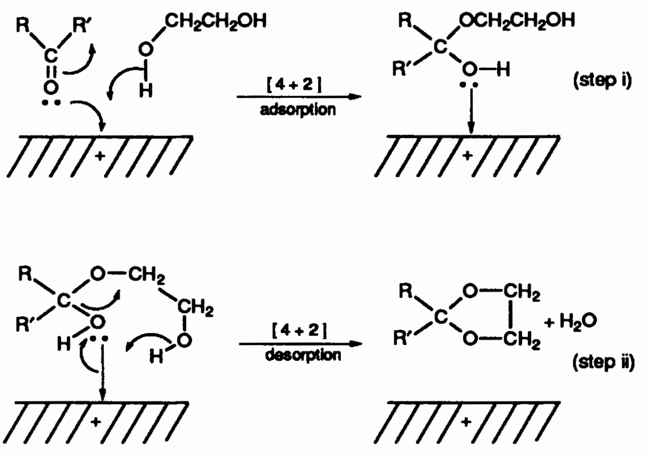
In this respect, in the homogeneous hydrolysis process of acetophenone dimethyl ketals,[32] the application of the Yukawa–Tsuno equation gave (r^{+}) = 0.35, a positive value, contrary to what was obtained here. However, a negative value of the sensitivity coefficient, $\rho = -2.0$ (as obtained here in both cases for the three isokinetic parameters) is associated with a mechanism which proceeds *via* the pre-equilibrium formation of an oxocarbenium ion. In fact, these negative values of ρ indicate an activating effect of the electron-releasing R (and R′) groups.

Reaction mechanism

The results obtained here account for an intermediate in the transition state whose relative stability is determined by the extension of the resonance between the carbonyl group and R and R′ substituents. However, under the present experimental conditions the reaction mechanism in the heterogeneous phase, could be better accounted for through a 'concerted process' that takes into account the experimental results obtained here. Thus, the nature of the catalytic active sites (acid sites of very low strength) led us to assume the output of some cationic intermediate species under the mild reaction conditions used here to be very improbable and nonsensical. Besides, the kinetic parameters in Table 3, where the $\Delta S^{\ddagger}$ (and ln A) values are largely independent of reaction rates (Fig. 3) while the changes in the energy term $\Delta H^{\ddagger}$ (and E_a) are reflected in these values because $\Delta H^{\ddagger}$ values are considerably (13–11 kcal mol^{-1}) larger than those of $\Delta S^{\ddagger}$ (0.05–0.06 kcal mol^{-1} K^{-1}). In addition, the negative values of $\Delta S^{\ddagger}$ indicate that, on going from the ground state to the transition state, an extensive restriction in the degree of freedom must be considered.

This highly ordered transition state is consistent with a reaction mechanism whose slowest step is the stabilization and immobilization of reactant molecules on catalyst active sites. With respect to this, the reaction rate is proportional to the quantity of adsorbed reactant molecules, and the reverse reaction is negligible. Besides, the relatively low $\Delta H^{\ddagger}$ values (with respect to those obtained in a process developed through a zwitterionic mechanism[33]) appear to be consistent with a concerted evolution in the limiting adsorption step, which also must be associated with the low values of $\Delta S^{\ddagger}$.

On the basis of these results, we may consider a concerted evolution in two adsorption–desorption steps (Scheme 2), where the hemiacetal (or hemiketal) is developed by a [4 + 2]



Scheme 2

concerted sigmatropic addition of the hydroxy group of alcohol to the carbonyl group through its adsorption on the acid sites (step *i*). Desorption of the hemiacetal (or hemiketal) through another [4 + 2] concerted sigmatropic movement produces 1,3-dioxolane and a water molecule (step *ii*). Thus, step *i* could be described as a [4 + 2] cycloaddition reaction where the dienophile is the O–H σ bond and the diene resembles an adsorbed 1,3-dipolar species which is constituted by the C=O π bond and a non-bonded electron pair of the oxygen atom where $4e^-$ are distributed along three atoms, two corresponding to the carbonylic bond and the other to the electron deficient atom (acid site) on the catalyst surface.

Consequently, the transfer of the electron pair of oxygen in the adsorption process (step *i*) and its recovery during the desorption (step *ii*) through the action of the acid sites on the catalyst surface removes the symmetry restrictions imposed by the Woodward–Hoffman rules and leads directly to 1,3-dioxolane formation. Thus, here we have to consider necessarily the existence of only hemiacetal as the adsorbed species on the catalyst surface which was never detected in the reaction product analysis. In this connection, its detection in solution necessarily ought to exclude the validity of the proposed reaction mechanism.

Whether or not the new bonds in the concerted mechanism are simultaneously formed is an open question because the concerted character of the acetalization process must be considered according to the terminology proposed by Dewar[34] which considers the difference between concerted reactions (each of which takes place in a single step) and a synchronous one (a concerted reaction where all the bond-breaking and bond-making processes take place in parallel).

Conclusions

From this study we can conclude that the acetalization reaction of carbonyl compounds on $AlPO_4$ and $AlPO_4$–Al_2O_3 catalysts with a high number of surface acid sites exhibits an IKR or 'compensation effect' which manifests itself through a linear relationship between the activation parameters $\Delta H^{\ddagger}$ and $\Delta S^{\ddagger}$ owing to the existence of an LFER. As a consequence, it is possible to obtain a series of isokinetic parameters (θ, ln α, $\Delta G^{\ddagger}$ and ln $K^{\ddagger}$) that provide a more general measurement of the reactivity characteristic of a series of related reactions and/or catalysts, especially θ and $\Delta G^{\ddagger}$, owing to the fact that they are parameters directly related to the kinetic reaction constant values, k, but they can also be regarded as independent of temperature (while ln $K^{\ddagger}$ and ln α represents the values of the equilibrium constant of the activated complex and the reactivity, respectively, at the θ temperature). Valuable information is also obtained on the reaction mechanism because, if an IKR holds for a reaction series, a single common interaction mechanism can be expected. Consequently, the method that makes use of a LFER that is still the most practical for predicting substituent effects for homogeneous reactions in liquid solutions,[35] may constitute a useful technique when applied to an heterogeneous process through IKR, for measuring not only structure–reactivity correlations, but also for obtaining data specifically concerning the catalytically active part of the catalysts as well as the reaction mechanism.

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