Selective oxidations by nitrosating agents in liquid and solid acid catalysts

N.C. Marziano*, L. Ronchin, C. Tortato

Chemistry Department, University of Venice, Dorsoduro 2137, 30123 Venice, Italy

Abstract

The oxidative properties of N_2O_3 and NO^+ ion towards methyl or methylene groups of enolizable ketones are tested at 25 °C in homogeneous and heterogeneous acid systems. The results in concentrated aqueous sulphuric acid show that reasonable good yields (∼95%) of benzoylformic acid from acetophenone are obtained at selected acidity ranges. A kinetic study for the conversion reagents–products and a thermodynamic treatment of the rates was also attempted by using the acidity dependence of rates, the equilibria of the reacting species and the departure from the ideality of the catalytic acid system. On the replacement of aqueous acid solutions with solid acids, benzoyl cyanide is instead obtained, with high yields and selectivity over catalysts with suitable acidic properties. Additional studies of different ketones and of certain alcohols are also reported.

© 2004 Published by Elsevier B.V.

Keywords: Oxidation; Nitrosating agents; Acid catalysis

1. Introduction

Acid catalysts, as well known, are important functional materials for the production of a large variety of industrial products. Processes involving conventional acids are typically associated with problems of high toxicity, corrosion, catalyst waste, etc. and their replacement with solid acid catalysts is continuously evolving owing to the need of an ecological approach of catalyst design. A difficulty in the use of solids for a larger impact in industrial applications is the selection of a practical, efficient, selective catalyst and the detailed knowledge of the catalyst itself at each stage of its work. In the study of an acid catalysed system where acid–base equilibria, ionic species and phenomena relating acidity and catalytic reactivity are involved, an improved understanding of acidic properties of medium is also a necessary requirement. New progress in the elucidation of the problems of solid acid materials has been obtained by comparing the equilibria and the reactivity of the specific acid–base pair under investigation in liquid and in solid phase [1–4]. This approach successfully applied for the conversion reagents–products in the nitration of aromatic compounds [2], in the esterification of benzoic and mesitoic acids [3], in the Beckmann rearrangement of ketoximes [4] is now tested in the selective oxidations of methyl and methylene groups of some enolizable ketones using the oxidative properties of N_2O_3 and NO^+ ion. An extension of the studies to certain alcohols is also reported.

2. Experimental

The oxidations were performed at 25 °C in well stirred thermostatted reactors containing weighed amounts of solvent, reagents and catalysts. The progress of reaction and the products obtained were analysed by HPLC and GC–MS. $NaNO_2$ in aqueous sulphuric acid and N_2O_3 in 1,2-dichloroethane have essentially been used as oxidants in the reactions carried out, respectively, in homogeneous and heterogeneous acid systems. The active species of nitrosating agents have been characterised by UV, IR and Raman measurements [5–7]. For instance, N_2O_3 adsorbed on H_2SO_4/SiO_2 exhibit by the Raman spectrum the typical band of NO^+ ion at 2300 cm^{-1} [5]. The concentration of N_2O_3 in the solution (ca. 0.2 mol dm^{-3} of N_2O_3) was measured by UV-Vis spectra [6] and estimated by the

* Corresponding author. Tel.: +39-041-2348626;
fax: +39-041-2348517.
E-mail address: marziano@unive.it (N.C. Marziano).

molar extinction coefficient of N_2O_3 in 1,2-dichloroethane ($\varepsilon = 7.3$ at $\lambda = 700$ nm).

H_2SO_4/ZrO_2, H_2SO_4/TiO_2, H_3PO_4/SiO_2, H_2SO_4/SiO_2–TiO_2, H_2SO_4/SiO_2–ZrO_2 and H_2SO_4/SiO_2 have been used as solid acids. The supports were samples of: SiO_2 (Grace, 90 μm average particle size, 364 m^2/g (S_{BET}), 1.14 ml/g pore volume), TiO_2 (Fluka, 5 m^2/g (S_{BET}), 0.24 ml/g pore volume), ZrO_2 (Fluka, 5 m^2/g (S_{BET}), 0.24 ml/g pore volume) and SiO_2–TiO_2 and SiO_2–ZrO_2 (prepared by polymerisation of $Ti(OPr)_4$ and $Zr(OPr)_4$ (Fluka) over SiO_2). The slurry was stirred for ca. 1 h then, the supernatant solution was removed by filtration and the wet catalyst dried at 105 °C under N_2. The acid percentage composition in the solids after impregnation was determined by potentiometric titrations against standard solutions of NaOH. The meq H^+/g_{cat} of the catalysts are: $H_2SO_4/ZrO_2 = 0.8$, $H_2SO_4/TiO_2 = 0.9$, $H_3PO_4/SiO_2 = 1.7$, H_2SO_4/SiO_2–$TiO_2 = 2.1$, H_2SO_4/SiO_2–$ZrO_2 = 2.3$ and $H_2SO_4/SiO_2 = 8.6$. The samples of H_2SO_4/SiO_2 characterised by XPS measurements shows the presence of the Brönsted acid sites [2,3]. Samples of sulfonated polystyrene ion-exchange resin (Amberlyst-15®) (Aldrich, 37 m^2/g (S_{BET}), 0.21 ml/g pore volume, average pore diameter 20 nm), with 4.7 meq H^+/g_{cat} have also been proved.

The stability of reagents and products was tested in different experimental conditions. Benzoylformic acid was found to be stable in aqueous acid mixtures with or without addition of an excess of oxidant, but can be easily converted to benzoic acid by N_2O_3 in non-aqueous solvents.

Additional experimental observations show that benzoic acid was the main product obtained in the oxidation of acetophenone by H_2O_2 or peroxides carried out in different experimental conditions. 1,2-Dichloroethane was found to be a suitable solvent for heterogeneous reactions because of its not very high empirical solvent polarity parameter ($E_T(30) = 41.9$ kcal/mol), compared to the limiting values of water ($E_T(30) = 63.1$) and cyclohexane ($E_T(30) = 31.2$) [8].

3. Results and discussion

3.1. Results in liquid acid phase: aqueous sulphuric acid

3.1.1. Analysis of products

Concentrated aqueous solutions of strong acids are well-known catalytic mixtures of many processes and the conversion reagents–products observed in the reaction between acetophenone and nitrous acid is now reported using the experimental conditions given in Table 1. The results show that benzoylformic acid (ArCOCOOH) can be easily obtained at 25 °C in the narrow acidity range between 72 and 80 wt.% H_2SO_4 (see Table 1A). In contrary, low conversions of the starting material (∼55%) and low yields

Table 1
Oxidation of ArCOCH$_3$ in H_2SO_4 by HNO_2 at 25 °C

H_2SO_4 (wt.%)	Conversion (%)	Yield (%)			Ratio of ArCOCOOH/ArCOOH
		ArCOCOOH	ArCOOH	Other compounds[a]	
(A) Products of reaction[b]					
64.1	99.5	60.7	10.9	27.9	5.6
71.9	98.8	81.0	12.8	5.0	6.3
74.1	98.1	84.4	12.3	1.4	6.9
77.1	99.9	93.3	6.2	0.4	15
77.2[c]	99.1	94.0	4.8	0.3	19.6
77.4	97.2	83.9	11.4	1.9	7.3
87.2	28.8	9.0	7.6	12.2	1.2
96.0	8.8	1.8	2.5	4.5	0.7
	ArCOCH$_3$ ($\log k_{1obs}$)	ArCOCOOH ($\log k_{1obs}$)	ArCOCH$_3$[d,e] ($\log k_1^*$)	ArCOCOOH[d,f] ($\log k_1^*$)	
(B) Kinetic data[g]					
64.2	−3.02	−3.24	−2.10	−2.33	
68.4	−3.03	−3.28	−2.43	−2.68	
70.9	−3.01	−3.24	−2.59	−2.82	
75.4	−3.16	−3.32	−2.97	−3.13	
77.2	−3.29	−3.36	−3.17	−3.24	
80.8	−3.46	−3.50	−3.41	−3.45	
82.4	−3.51	−3.58	−3.48	−3.55	

[a] Not identified products.
[b] Ratio of [ArCOCH$_3$]:[HNO$_2$] = 1:6; conversion and yields of products after 24 h analysed by HPLC.
[c] By using the ratios of ArCOCH$_3$:HNO$_2$ of 1:1, 1:1.5, 1:2, the conversion and the yields of ArCOCOOH are <10%.
[d] $\log k_1^* = \log\{k_{1obs}(1 + [B]/[BH^+])\}$.
[e] Plot of $\log k_1^*$ vs. Mc (in H_2SO_4) (intercept = $\log k_1^\circ = -0.3$, slope = 0.51).
[f] Plot of $\log k_1^*$ vs. Mc (in H_2SO_4) (intercept = $\log k_1^\circ = -0.3$, slope = 0.55).
[g] [ArCOCH$_3$] = 0.0422 mol dm^{-3}; [HNO$_2$] = 0.2582 mol dm^{-3}; ratio = 1:6.

of ArCOCOOH (∼9%) are observed by using nitrosylsulphuric acid (NOHSO$_4$) in CH$_3$COOH or in (CH$_3$CO)$_2$O. The improvement of the results by a suitable oxidant in strong acidic media suggests that reactive ionic species formed by protonation of the reagents in appropriate acidity ranges lead to an energetically favourite pathway but that the efficiency of the species is related to acidity of medium.

From investigations of equilibria in aqueous acid solutions it is known that acetophenone is half-protonated at ∼75% H$_2$SO$_4$ (PhCOCH$_3$ + H$^+$ ⇌ [PhC(OH)CH$_3$]$^+$) [9–12]. Nitrous acid is half-protonated at ∼58% H$_2$SO$_4$ [13–17] and is converted into NO$^+$ by a protonation–dehydration equilibrium (HONO+H$^+$ ⇌ NO$^+$+H$_2$O). In the range between 65 and 80 wt.% H$_2$SO$_4$, where HNO$_2$ is almost fully converted into NO$^+$, the ratios [PhC(OH)CH$_3$]$^+$/[PhCOCH$_3$] appear to be the main factors affecting the results. Further details of the process are investigated using ketones with alkyl chains longer than methyl, or benzylacetone (PhCH$_2$CH$_2$COCH$_3$) with methyl and methylene groups in an α-position to a carbonyl group, or cyclohexanone as sample of cyclic ketones. The results show that the side-chain oxidation is particularly successful for substrates with one site of attack or for substrates with equivalent sites of oxidation.

3.1.2. Kinetic analysis

The results obtained by following the variations of acetophenone and benzoylformic acid with time show that the reaction is first order in ketone, with decreasing rate constants (log k_{1obs}) as the acid concentration increases (see Table 1B). The separation of solvent effects involved in the equilibria of reagents from solvent effects involved in the kinetic behaviour was also attempted by using the acidity dependence of rates and the protonation equilibrium of acetophenone (equilibrium (1)) described by thermodynamic equations (2) and (3). Mc(B*) or "activity coefficient function" defined by Eq. (4) is a measure of the deviations from the ideality of the acid system under investigation [1,18,19]:

$$B + H^+ \rightleftharpoons BH^+ \tag{1}$$

$$pK_{BH^+} = \log\frac{[BH^+]}{[B]} - \log[H^+] - \log\left(\frac{f_B f_{H^+}}{f_{BH^+}}\right) \tag{2}$$

$$pK_{BH^+} = \log\frac{[BH^+]}{[B]} - \log[H^+] + n_b\, Mc(B^*) \tag{3}$$

$$-\log\left(\frac{f_{B^*} f_{H^+}}{f_{B^*H^+}}\right) = Mc(B^*) \tag{4}$$
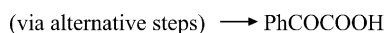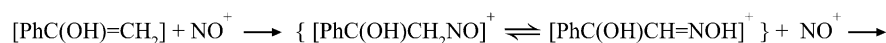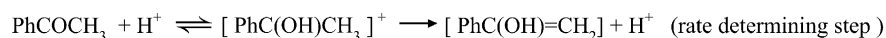
In Table 1B the log k_1^* rate constants obtained from the corresponding log k_{1obs} are also reported. The new values are related to the stoichiometric and to the effective concentrations of reacting species by Eq. (5) rewritten as (6), on the assumption of a reaction by the [BH$^+$] species:

$$\text{Rate} = k_{1obs}([B] + [BH^+])_{st} = k_1^*([BH^+])_{sol} \tag{5}$$

$$k_{1obs}\left(1 + \frac{[B]}{[BH^+]}\right) = k_1^* \tag{6}$$

In addition, the linear relationship observed on the plot log k_1^* versus Mc allows one to obtain, by the intercept, the log k_1° rate constants referred to water as standard state.

The log $k_1^\circ = -0.3$ observed in the reaction between acetophenone and NO$^+$ in aqueous sulphuric acid was found to be equal to the value estimated by an analogous procedure in the detritiation and iodination of acetophenone carried out in concentrated aqueous strong acids [12,20]. From the new thermodynamic observations it follows that the reaction between an electrophilic species and acetophenone, taken as example of an enolizable ketone, proceed through a common rate-determining deprotonation, related to activation of the methyl group in α-position to the carbonyl group (Scheme 1). The addition of NO$^+$ ion to enol form of ketone is the likely sequence of nitrosation after the rate-determining step, but the description of the subsequent trend appears to be complicated because of the equilibria, reactivity and interactions of the new compound in the reaction mixture; i.e. between the nitrosated compound and NO$^+$ or between the nitrosated compound and the high acidic medium.

Experimental evidences for the involvement of α-nitroso-acetophenone as an intermediate are in Table 2 where the conversion of α-nitroso-acetophenone (now used as starting material) to benzoylformic acid with and without NO$^+$ ion, in different acidity ranges, is tested. Additional data obtained in the conversion of phenylglyoxal (PhCOCHO → PhCOCOOH) in analogous experimental conditions are enclosed.

3.2. Results in solid acid phase: supported acids and sulphonated ion-exchange resins

In Table 3 the oxidation of acetophenone by N$_2$O$_3$ over solid acids with different meq H$^+$/g$_{cat}$ and different structures is reported. Benzoyl cyanide (PhCOCN) rather than benzoylformic acid was now the main product, with conversion and yields suitable for synthetic applications (ca. 95%) by using Amberlyst-15® as catalyst.

PhCOCH$_3$ + H$^+$ ⇌ [PhC(OH)CH$_3$]$^+$ ⟶ [PhC(OH)=CH$_2$] + H$^+$ (rate determining step)

[PhC(OH)=CH$_2$] + NO$^+$ ⟶ { [PhC(OH)CH$_2$NO]$^+$ ⇌ [PhC(OH)CH=NOH]$^+$ } + NO$^+$ ⟶

(via alternative steps) ⟶ PhCOCOOH

Scheme 1.

Table 2
Reactivity of α-NO-acetophenone and phenylglyoxal in H_2SO_4 with and without HNO_2 at 25 °C[a,b]

Reagents	H_2SO_4 (wt.%)	Conversion (%)	Yield (%)	
			ArCOCOOH	ArCOOH
α-NO-acetophenone	52	2	<0.1	<0.1
α-NO-acetophenone (+NO[+])	52	99	35	45
α-NO-acetophenone	76	47	–	14
α-NO-acetophenone (+NO[+])	77	99	85	2.5
α-NO-acetophenone	96	99	<0.1	98
Phenylglyoxal	52	–		
Phenylglyoxal (+NO[+])	52	96	95	≈1
Phenylglyoxal	77	–		
Phenylglyoxal (+NO[+])	77	99	95	≈1

[a] Conversion and yields after 24 h (data obtained by HPLC).
[b] Ratio of reagents is 1:4.

Table 3
Oxidation of acetophenone by N_2O_3 over solid acid catalysts at 25 °C[a]

Catalyst	meq H^+/g$_{cat}$	Ratio of $ArCOCH_3$/N_2O_3	Conversion (%)	Yield (%)		Other product[b]
				ArCOCN	ArCOOH	
HPMo/SiO$_2$[c]	–	1:1	31	2	24	5
H_2SO_4/ZrO$_2$	0.8	1:1	5	1	2	2
H_2SO_4/TiO$_2$	0.9	1:1	19	16	2	1
H_3PO_4/SiO$_2$	1.7	1:1	47	34	8	5
H_3PO_4/SiO$_2$	1.7	1:4	91	63	10	18
Amberlyst-15®	4.7	1:1	29	11	2	16
Amberlyst-15®	4.7	1:4	>99	95	2	2
H_2SO_4/SiO$_2$	8.6	1:1	68	55	10	3
H_2SO_4/SiO$_2$	8.6	1:4	>99	81	18	1

[a] Solvent = 1,2-dichloroethane; $[N_2O_3]$ = $[ArCOCH_3]$ = 0.2 M; reaction volume = 10 ml; catalyst = 0.6 g; reaction time = 24 h.
[b] Products identified in part.
[c] HPMo: phosphomolybdic acid 1%.

Table 4
Oxidation of alcohols[a] by N_2O_3 over solid acid catalysts at 25 °C[b]

Catalysts	meq H^+/g$_{cat}$	Ratio of alcohols/N_2O_3	Conversion (%)	Yield of cyclohexanone (%)	Reaction time (h)
Cyclohexyl alcohol					
–		1:4	40	1[c]	24
H_3PO_4/SiO$_2$	1.7	1:1	38	27[c,d]	24
Amberlyst-15®	4.7	1:1	82	71[c,d]	24
H_2SO_4/SiO$_2$	8.6	1:1	62	50[c,d]	0.5
H_2SO_4/SiO$_2$	8.6	1:4	<99	92[d]	2
H_2SO_4/SiO$_2$	8.6	1:4	<99	85[d]	24

				Yield (%)		Reaction time (h)
				ArCHO	ArCOOH	
Benzyl alcohol						
–	–	1:4	35	24[c]	–	24
H_3PO_4/SiO$_2$	1.7	1:4	95	85[c]	10	24
Amberlyst-15®	4.7	1:4	>99	99	–	24
H_2SO_4/SiO$_2$	8.6	1:1	>99	57	42	24

[a] From 1-octanol; iso-butanol; n-butanol over Amberlyst-15®, mixtures of acids, ketones and aldehydes are detected.
[b] Solvent = 1,2-dichloroethane; [alcohol] = 0.05–0.2 M; $[N_2O_3]$ = 0.2 M; reaction volume = 10 ml; catalyst = 0.5 g.
[c] The ester of nitrous acid, by GC–MS, has been detected as intermediate.
[d] 2-Nitro-cyclohexanone has been detected.

Benzoyl cyanide from α-nitroso-acetophenone is also observed in the reactions over solid catalysts carried out with and without addition of N_2O_3. The yields are of 65 and 5%, respectively.

It is suggested that the remarkable change of the products is essentially related to the solvent effect, mainly to the change from aqueous to non-aqueous solvent, the latter employed in the reactions conducted in the solid phase. These observations are in accordance with the conversion acetophenone → benzoyl cyanide observed in the oxidation of acetophenone by N_2O_3 using trifluoromethanesulphonic acid and *p*-toluene-sulfonic acid as catalysts (yields of 86 and 57%, respectively) and 1,2-dichloroethane as solvent.

The different stabilities of benzoylformic acid in aqueous and non-aqueous solvent seems to be an additional factor affecting the conversion reagents–products. Benzoylformic acid was found to be stable in aqueous acid mixtures with or without addition of an excess of oxidant, but can be easily converted to benzoic acid by N_2O_3 in non-aqueous solvents. Phenylglyoxal behaves similarly by the sequence (PhCOCHO → PhCOCOOH → PhCOOH).

The results in Table 4 show that the oxidative properties of N_2O_3 can be properly used for the conversion of cyclohexyl and benzyl alcohol to cyclohexanone and benzaldehyde at 25 °C over solid acid catalysts in non-aqueous solvents. It avoids the usual acid catalysed oxidation of alcohols with chromium compounds [21].

4. Conclusions

Analysis of the results from a practical point of view shows that in aqueous acidic media the conversion PhCOCH$_3$ → PhCOCOOH can be easily obtained in the reaction between acetophenone and a nitrosating agent. The experimental trend observed as the acid concentration increases suggests two main experimental conditions: (i) an excess of the nitrosating agent to ensure high conversions and yields of the product; (ii) suitable acidity ranges of acidic mixtures in order to obtain reactive ionic species from the reagents (i.e. $[PhC(OH)CH_3]^+$, $[NO^+]$).

Strong interactions between ionic species and acidic medium, suitable to decrease the efficiency of the reacting species, are also to be avoided being additional factors affecting the results in very concentrated acid solutions. The new methodology appears to be a promising alternative to the conventional procedures where the oxidants most often used are potassium permanganate, chromic acid, nitric acid, etc. [22].

In non-aqueous solvents, the conversion PhCOCH$_3$ → PhCOCN is observed by an acid catalysed reaction between acetophenone and a nitrosating agent carried out under homogeneous and heterogeneous phase. The use of Amberlyst-15® in aprotic solvents as reaction media appears to be of practical synthetic applications. In analogous experimental conditions cyclohexyl and benzyl alcohols can be easily converted to cyclohexanone and benzaldehyde.

References

[1] N.C. Marziano, C. Tortato, L. Ronchin, C. Bianchi, Catal. Lett. 56 (1998) 159.
[2] N.C. Marziano, C. Tortato, L. Ronchin, F. Martini, C. Bianchi, Catal. Lett. 58 (1999) 81.
[3] N.C. Marziano, C. Tortato, L. Ronchin, C. Bianchi, Catal. Lett. 64 (2000) 15.
[4] N.C. Marziano, L. Ronchin, C. Tortato, Unpublished results.
[5] J.D.S. Goulden, D.J. Millen, J. Chem. Soc. (1950) 2620.
[6] J. Mason, J. Chem. Soc. (1959) 1288.
[7] M. Mochida, B.J. Finlayson-Pitt, J. Phys. Chem. A 104 (2000) 8038.
[8] C. Reichardt, Solvent Effect in Organic Chemistry, Verlag Chemie, New York, 1979.
[9] L.A. Flexer, L.P. Hammett, A. Dingwall, J. Am. Chem. Soc. 57 (1935) 2103.
[10] C.C. Greig, C.D. Johnson, J. Am. Chem. Soc. 90 (1968) 6453.
[11] G.C. Levy, J.D. Cargioli, W. Racela, J. Am. Chem. Soc. 92 (1970) 6238.
[12] D.W. Earls, J. Chem. Soc., Perkin Trans. 2 (1976) 1641.
[13] K. Singer, P.A. Vamplew, J. Chem. Soc. (1956) 3971.
[14] N.S. Bayliss, D.W. Watts, Aust. J. Chem. 9 (1956) 319.
[15] F. Seel, R. Winkler, Z. Phys. Chem. NF 25 (1960) 217.
[16] N.S. Bayliss, R. Dingle, D.W. Watts, R.J. Wilkie, Aust. J. Chem. 16 (1963) 933.
[17] K.H. Becker, J. Kleffmann, R. Kunrtenbach, P. Wiesen, J. Phys. Chem. 100 (1996) 14984.
[18] N.C. Marziano, A. Tomasin, C. Tortato, P. Isandelli, J. Chem. Soc., Perkin Trans. 2 (1998) 2535.
[19] N.C. Marziano, A. Tomasin, C. Tortato, J.M. Zaldivar, J. Chem. Soc., Perkin Trans. 2 (1998) 1973.
[20] L. Zucker, L.P. Hammett, J. Am. Chem. Soc. 61 (1939) 2791.
[21] J. March, Advanced Organic Chemistry, Reaction, Mechanisms, and Structure, 3rd ed., Wiley, New York, 1985, p. 1057.
[22] A.H. Haines, Methods for the Oxidation in Organic Compounds, Academic Press, London, 1985, Chapter 2.