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Esterification of salicylic acid with methanol/dimethyl carbonate over anion-modified metal oxides

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The esterification of salicylic acid to methyl salicylate over solid acids such as zirconia, alumina and silica and their sulphate, phosphate and borate modified forms, has been studied for the first time in an autoclave under autogenous conditions using methanol and dimethyl carbonate to compare their methylating ability. Metal oxides such as zirconia, alumina and silica as well as their sulphate, phosphate and borate modified forms are effective catalysts for the conversion of salicylic acid to methyl salicylate. Superacid, sulphated zirconia, is the most suitable catalyst due to high yield, selectivity, reusability and the simple method used for the preparation of the catalyst. The percentage yield of methyl salicylate was found to be higher when methanol was used as the methylating agent over these catalysts rather than dimethyl carbonate. Hence, methanol appears to be a better methylating agent compared to dimethyl carbonate in terms of yield as well as atom economy. The influence of reaction temperature, amount of catalyst, duration of reaction and molar ratio of salicylic acid: methanol/dimethyl carbonate has been studied over sulphated zirconia.

Keywords: Esterification, Autogenous conditions, Methanol, Dimethyl carbonate, Methyl salicylate, Isoamyl salicylate, Sulphate-, borate- and phosphate-modified zirconia, Alumina, Silica, Solid acids

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Esterification is an important reaction in organic chemistry used extensively for the synthesis of esters and also as a method for the protection of alcohol and carboxylic acid groups[1-5]. Methyl esters may be prepared by treatment of carboxylic acids with diazomethane[6] but the method is not practical because of its toxicity and the explosive nature of diazomethane, which renders it unsuitable for large-scale conversion. Hence, the strategy of carboxylic acid activation is a preferred route which involves the use of methylating reagents such as $P(OMe)_5$[7], Me_3OBF_4-$^i Pr_2NEt$[8], Me_3SOH[9], Li_2CO_3-MeI[10], CsF-2-fluoropyridinium salt-MeOH[11], *o*-methylcaprolactim at 80˚C for 16 h[12], K_2CO_3-Ph_2S^+ $M_3BF_4^-$CuBr($^i Pr_2NEt$)[13], K_2CO_3-(18-C-6)-Cl_3CO_2Me[14], Cs_2CO_3-(18-C-6)-MeI[8,15], CsF-MeI[16], aqueous K_2CO_3-Bu_4NBr-MeI[17] and Me_4NOH at 260˚C[18]. These methods have limitations, such as, use of costly reagents that are hazardous and/or harsh reaction conditions. The method of reaction of carboxylate anion and Me_2SO_4, has been neglected because of the use of aqueous alkali (leading to side reactions such as hydrolysis of Me_2SO_4 and the ester formed), costly reagents (e.g. Dicyclohexylethy-lamine or DBN) as proton acceptors[19] and stringent reaction conditions. An effective chemoselective protection of carboxylic acids under mild conditions was reported that replaced toxic diazomethane or other costly reagents by $LiOH.H_2O$-Me_2SO_4[20-22]. It is desirable to make the reactions catalytic rather than using stoichiometric amount of base. The reported catalytic procedures for the synthesis of methyl esters recommend the use of sulphuric acid, HCl etc.[24], as catalysts and toxic chemicals like dimethyl sulphate, methyl iodide or diazomethane as methylating agents. Hence, an attempt is made to obtain environmentally benign reagents and catalysts for the conversion of carboxylic acid entity to its ester, by studying the feasibility of substituting toxic methylating agents, like, dimethyl sulphate, methyl iodide etc., with a non-toxic chemical such as dimethyl carbonate (DMC)[26-31], and designing a heterogeneous catalytic system involving the use of safe, active, selective and reusable catalysts such as zeolites, metal oxides, their modified forms etc. There are very few reports on the use of dimethyl carbonate in the esterification of acids[28,32,33]. Lee and Shimizu[28] have reported the reaction of mycophenolic acid with dimethyl carbonate over cesium carbonate catalyst. In this case, both the carboxylic and the hydroxyl groups are methylated. However, when salicylic acid was taken with dimethyl carbonate over zeolite catalyst, exclusive esterification of –COOH group leading to the formation of methyl salicylate was observed[32]. Shieh *et al*.[33] have employed dimethyl carbonate to esterify carboxylic acids using 1,8-diazo bicyclo [5,4,0]undec-7-ene (DBU) as catalyst adopting the microwave irradiation technique. In the light of these data from literature, it is of interest to study the chemoselectivity of dimethyl carbonate in the methylation of salicylic acid over a solid super acid such as SO_4^{2-}/ZrO_2 (SZ), which is known to catalyze a wide variety of industrially important organic synthetic reactions. The derivatives of salicylic acid obtained by methylation are potentially useful chemical intermediates. Methyl salicylate is one of the important esters of salicylic acid[3,4]. In pharmaceuticals, methyl salicylate is used in liniments and ointments for the relief of pain and rheumatic conditions. It is used in confectionaries, dentifrices, cosmetic and perfumes as flavour and fragrance agent. Commercially, it is useful as dye carrier, UV-light stabilizer in acrylic resins, and as chemical intermediate.

Methyl salicylate is produced synthetically for commercial purposes by the catalytic esterification of salicylic acid with methanol. This process involves the use of sulphuric acid, HCl, $AlCl_3$ etc., (sometimes in stoichiometric amounts) which is undesirable and may be replaced with solid acids that are environmentally benign and can be recycled [34-40]. In this work, the study of methylating ability of dimethyl carbonate and the kinetics involved has been investigated and compared with that of methanol (MeOH). The use of dimethyl carbonate as a methylating reagent requires temperatures above the boiling point of dimethyl carbonate and hence these reactions must be performed under autogenous pressure in an autoclave[33,41-45]. The results of the kinetic study are compared with the respective higher homologues by preparing ethyl salicylate from salicylic acid using ethanol (EtOH)/diethyl carbonate (DEC). Zirconia, alumina and silica have been considered for a general comparative study of amphoteric, basic and acidic metal oxides. The effect of modification of the catalytic activity of zirconia, alumina and silica by the addition of anions such as sulphate, phosphate and borate ions has been compared. A detailed study of this reaction has been made over sulphated zirconia which is considered to be a superacid, and the reaction conditions are optimized.

Experimental Procedure

The commercial forms of zirconium hydroxide was obtained from Aldrich, aluminium hydroxide and precipitated silicic acid from Loba chemie, and concd. sulphuric acid, phosphoric acid and boric acid from sd fine chemicals.

Catalyst preparation

The catalysts, zirconia, alumina and silica and their sulphate, phosphate and borate modified forms, were prepared by following the procedure mentioned hereunder.

Hydrated zirconia, alumina and silica

Hydrated zirconia $Zr(OH)_4.xH_2O$, alumina $Al(OH)_3.xH_2O$ and silica $SiO_2.xH_2O$ were obtained by calcining separately zirconium hydroxide, aluminium hydroxide and silicic acid at 550°C and represented as ZrO_2, Al_2O_3 and SiO_2 respectively.

Modified oxides

A calculated amount of zirconium hydroxide, aluminium hydroxide and silicic acid, was taken before calcination and subjected to impregnation separately with sulphate, phosphate and borate ions. For instance, 1.0 g of each of the samples was treated with 2.0 mL of 1M $H_2SO_4/H_3PO_4/H_3BO_3$ solution and mixed with 3.0 mL of deionized water to form a slurry and stirred for 1 h at room temperature, filtered without washing and dried at 120°C for 12 h, and calcined at 550°C for 4 h. The sulphated oxides were labeled as S-ZrO_2, S-Al_2O_3 and S-SiO_2 (SZ, SAl and SSi in figures). Similarly, the phosphated and borated samples were denoted with a prefix P- and B- respectively.

Catalyst characterization

The BET surface area of the calcined samples was analyzed by nitrogen adsorption at liquid nitrogen temperature using NOVA-1000 high speed gas sorption analyzer version-3.70. Total surface acidity of the samples was measured by *n*-butylamine back titration method using bromothymol blue indicator. Powder XRD patterns were recorded with Seimens-D5005 X-ray diffractometer with a Ni filtrated Cu-Kα radiation (1.5418 Å). The FTIR spectra of all the catalyst samples were obtained from Nicolet instrument by KBr pellet technique.

Catalytic activity studies

Esterification reactions were carried out in a stainless steel autoclave reactor (internal volume: 100

mL) under autogenous pressure at a temperature of 150°C in a hot air oven. The reactant mixture of salicylic acid and methanol/dimethyl carbonate was heated in the autoclave along with the catalyst for a definite period of time. After the stipulated reaction time, the reactor was allowed to cool to room temperature. The unreacted salicylic acid was dissolved in acetone and filtered to separate the catalyst. The filtrate was analyzed by GC (MAPL GC with 2m ss column packed with '10%AT – 1200 + 1% H_3PO_4 on chromosorb W-HP'). The products were identified by comparing with the standards and further confirmed by GC-MS. Blank reactions were also carried out in the absence of a catalyst. The major product was identified as methyl salicylate (MS). Phenol was obtained as a minor product (1-5%) with alumina-based catalysts. The conversion and selectivity were calculated based on the GC results using the following expressions, where the terms in bracket represent the concentration of the various species in the reaction mixture:

$$\text{Conversion of salicylic acid (\%)} = 100 - \frac{100 \times [SA]}{[SA] + [MS] + [Phenol]}$$

$$\text{Yield of methyl salicylate (\%)} = 100 \times \frac{[MS]}{[SA] + [MS] + [Phenol]}$$

$$\text{Selectivity of methyl salicylate (\%)} = 100 \times \frac{[MS]}{[MS] + [Phenol]}$$

Results and Discussion

A systematic study of the esterification of salicylic acid using methanol/dimethyl carbonate in the presence of solid acid catalysts was conducted to check the efficacy and viability of the reaction under different conditions and the percentage yield of methyl salicylate obtained from the reactions, carried out in the autoclave for different durations in the presence of different amounts of the mentioned catalysts at 150°C and is shown in Table 1.

The preliminary investigations revealed selective esterification of salicylic acid leading to the formation of methyl salicylate with all the catalyst samples, ZrO_2, Al_2O_3, SiO_2, and their SO_4^{2-}, PO_4^{3-} and BO_3^{3-} modified forms. The super acid, SO_4^{2-}/ZrO_2, was found to be a highly effective catalyst for this esterification. No methyl salicylate was formed in the absence of the catalysts. The percentage yield of methyl salicylate was found to be higher when methanol was used as the methylating agent rather than dimethyl carbonate. Among the simple oxides, ZrO_2, Al_2O_3 and SiO_2, it is noticed that there is little difference in the catalytic activity for this reaction. The percentage yield of methyl salicylate with the untreated metal oxides, was in the range of 20-30%. The low activity may be attributed to the low total surface acidity of the simple oxides that is in the range of 0.2 to 0.4 $mmolg^{-1}$ (Table 2), obtained form *n*-butylamine back titration method. However, it may be noted that there is no direct correlation between total surface acidity and the catalytic activity of

Table 1—Comparison of the methylating ability of methanol and dimethyl carbonate over ZrO_2, Al_2O_3 and SiO_2 and the modified forms in the esterification of salicylic acid. 1.64 g salicylic acid + 2 mL methanol/5 mL dimethyl carbonate/(molar ratio = 1:5), temperature = 150°C.

Catalyst	Catalyst weight	Reaction time	Percentage yield of methyl salicylate (%)							
			Methanol				Dimethyl carbonate			
			A*	SO_4^{2-}	PO_4^{3-}	BO_3^{3-}	A*	SO_4^{2-}	PO_4^{3-}	BO_3^{3-}
ZrO_2	1 g	8 h	21	81	40	65	19	84	25	52
		12 h	26	89	41	69	22	89	31	58
	2 g	8 h	28	95	48	70	23	95	29	59
		12 h	28	98	52	72	28	96	34	62
Al_2O_3	1 g	8 h	24	59	40	50	22	41	28	36
		12 h	26	62	42	54	24	51	33	39
	2 g	8 h	28	68	44	56	23	58	34	42
		12 h	29	71	48	68	29	68	41	63
SiO_2	1 g	8 h	28	48	39	62	25	42	32	49
		12 h	29	56	44	66	27	55	36	52
	2 g	8 h	30	66	50	70	28	60	41	56
		12 h	31	74	54	74	35	66	50	58

A*: untreated metal oxides.

Table 2—Total surface acidity values of the oxides and their anion modified forms by *n*-butylamine back titration method

Catalyst	Total surface acidity ($mmolg^{-1}$)	Catalyst	Total surface acidity ($mmolg^{-1}$)	Catalyst	Total surface acidity ($mmolg^{-1}$)
ZrO_2	0.20	Al_2O_3	0.44	SiO_2	0.40
S-ZrO_2	1.20	S-Al_2O_3	1.00	S-SiO_2	1.44
P-ZrO_2	0.40	P-Al_2O_3	0.70	P-SiO_2	0.67
B-ZrO_2	0.60	B-Al_2O_3	0.75	B-SiO_2	0.85

Table 3—Acidity distribution of various zirconias determined by NH_3 TPD[46]

Catalyst	Acidity ($mmolg^{-1}$)				
	weak (<100°C)	intermediate (100-200°C)	strong (200-400°C)	very strong (<400°C)	total
ZrO_2	0.0735	-	0.0608	-	0.1343
S-ZrO_2	-	0.2858	0.2529	0.0653	0.6040
P-ZrO_2	0.1290	0.1493	-	-	0.2783
B-ZrO_2	0.1482	0.0822	0.0784	-	0.3030

zirconia, alumina and silica. This implies that the conversion of salicylic acid depends on the type of acid sites and not on the total number of acid sites.

Effect of modification of simple metal oxides with anions

The percentage yield of methyl salicylate was compared with total surface acidity obtained by *n*-butyl amine back titration method for the various simple oxides and their modified forms (Table 1 and 2). It is observed that, among the modified samples, the sulphated forms provide better yields compared to the phosphated and borated forms, and between the phosphated and borated forms, the catalytic activity is higher with the borated samples. It may be observed that there is a similar relationship between the percentage yield of methyl salicylate and total surface acidity, irrespective of the methylating agents used, and the zirconia-based samples have greater catalytic activity as compared to the alumina-based and silica-based catalytic reactions. This is a clear indication that the acid sites on zirconia-based catalysts are stronger than those on alumina or silica based catalysts. Also, the percentage yield over sulphated-silica exhibiting the highest total surface acidity is not the maximum, which augments the observation that it is the strength of the acidic sites that determines the catalytic activity rather than the total number of acid sites. To identify the type of acid sites responsible for the conversion of salicylic acid in this reaction, the reported values from the ammonia-TPD measurements of zirconia[46] and its sulphate, phosphate and borate modified forms were analyzed (Table 3) and a direct relationship was found to exist between the conversion of salicylic acid and the acidity, especially in the strong acid region. The higher activity of the borated samples may be attributed to the presence of ‘strong’ acid sites, which are absent in phosphated samples, as determined by NH_3-TPD measurements (Table 3). The ‘very strong’ and ‘superacid’ sites present in sulphated zirconia may be playing a major role in this reaction considering the fact that those zeolites having ‘strong’ acid sites and much larger surface area have lesser activity[32]. To probe this matter further, the catalytic activity of ZrO_2-based samples were compared with the acidity of the sites of different range of acid-strengths and it was conferred that ‘intermediate to strong’ acid sites may be responsible for high catalytic activity based on the following observations: (i) borated samples exhibit greater catalytic activity than expected, because of the presence of ‘strong’ acid sites which are absent in phosphated samples, (ii) sulphated zirconia shows exceptionally high catalytic activity because of the presence of ‘very strong’ and perhaps, super acidic- sites which are absent in the other samples.

Optimization of reaction conditions

Effect of reaction temperature, amount of catalyst and duration of reaction

The reaction between salicylic acid and methanol/dimethyl carbonate was carried out in the temperature range of 100 to 165°C and the results are given in the Table 4. As the temperature is increased, the percentage yield of methyl salicylate also increased. The effect of the amount of the various catalysts on the yield of the reaction between salicylic acid and methanol/dimethyl carbonate was studied,

Table 4—Effect of reaction temperature on the esterification of SA with MeOH / DMC. Molar ratio of SA: MeOH/ DMC = 1:5, duration of reaction = 4 h, amount of S-ZrO_2, = 0.5 g.

Temperature (^{o}C)	Yield of methyl salicylate (%) MeOH	DMC
100	40	18
110	50	22
120	55	28
135	60	32
150	64	49
165	66	50

Table 5—Effect of amount of S-ZrO_2 on the esterification of SA with MeOH / DMC for different durations of reaction. Molar ratio of SA: MeOH/ DMC = 1:5, reaction temperature = 150°C.

Salicylic acid + MeOH/DMC	Weight of catalyst (g)	Yield of methyl solicylate (%) 4 h	6 h	8 h
MeOH	0.5	49	59	62
	1	74	75	81
	2	76	89	95
	3	85	99	99
DMC	0.5	49	50	51
	1	59	68	84
	2	73	81	95
	3	82	86	99

and the results are shown in Table 5. The amount of the catalyst was varied between 0.5 and 3 g, keeping the molar ratio of salicylic acid to methanol/dimethyl carbonate at 1:5 and the reaction temperature at 150˚C for various reaction times (4, 6 and 8 h). With methanol, the reaction goes to completion within 6 h with 3 g of sulphated zirconia. With dimethyl carbonate, it takes 8h for the reaction to reach completion with same amount of same catalyst. Greater the amount of catalyst, faster is the approach to completion of the reaction. As the amount of catalyst increases in the reaction system, the number of active sites increases, thereby, increasing the yield of the reaction. Thus, it may be observed that the selectivity towards the formation of methyl salicylate does not decrease with increase in the amount of the catalyst as well as duration of reaction. The selectivity towards methyl salicylate was 100% and no *o*-methylation was observed. The catalyst, sulphated zirconia, recovered from the reaction mixture after filtration was calcined and reused for the same reaction. The reusability was tested for 3 cycles and there was only 3% reduction in the yield of methyl salicylate. The effect of duration of reaction on the conversion of salicylic acid over sulphated zirconia

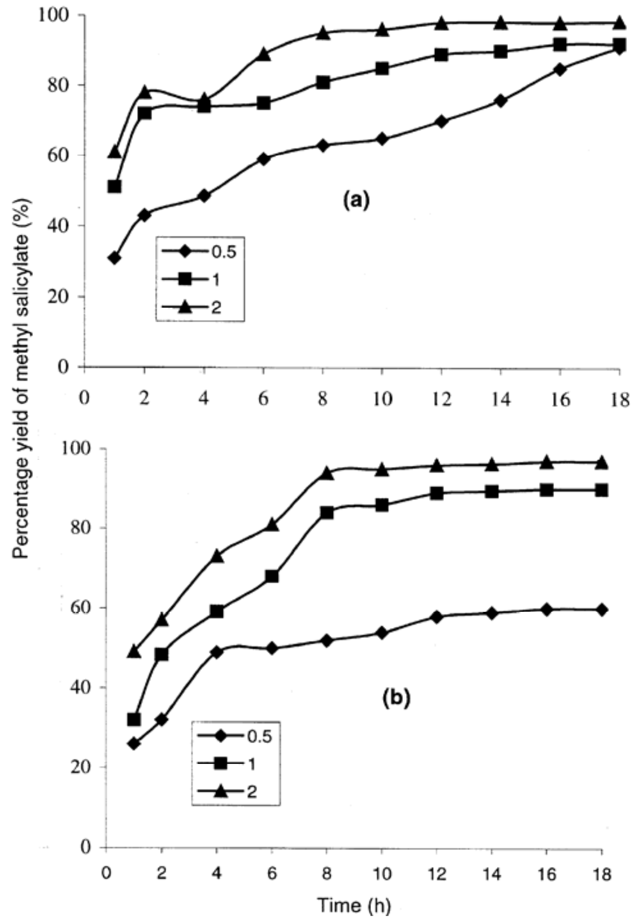


Fig. 1(a-b)—Percentage yield of methyl salicylate from salicylic acid and methanol /dimethyl carbonate and the effect of time for various amounts of catalyst (0.5, 1 and 2 g) over S-ZrO_2, temperature = 423 K. Molar ratio of salicylic acid : MeOH/DMC = 1:5 (a) methanol (b) dimethyl carbonate

was studied and the results are presented as plots of percentage yield of salicylic acid versus duration of reaction for different amounts of catalysts in Fig. 1(a-b). The graphs depict that irrespective of the amount of catalyst taken, the percentage yield of methyl salicylate (MS) formed, increased initially with time and then remained almost constant for longer reaction times. When 2 g of the catalyst is taken, the curve plateaus, and the reaction reaches almost to completion in 12 h, with dimethyl carbonate as well as methanol. When the amount of catalyst is less than 2 g, the reaction does not reach completion even after 18 h. The percentage yield of methyl salicylate after 18 h is 64% and 91.6% with dimethyl carbonate and methanol respectively for 0.5 g of the catalyst. These results, once again, bring out the fact that methanol is a better methylating agent than dimethyl carbonate in the presence of sulphated zirconia. Dimethyl carbonate requires longer reaction times to form as much methyl salicylate as obtained using methanol. One possible reason could be that the number of dimethyl carbonate molecules that approach the active sites available on the catalyst surface, is less than those of methanol molecules in the respective systems at any instant of time due to the bulkiness of dimethyl carbonate molecule. Also, during the course of the reaction with dimethyl carbonate, the by-products formed are CO_2 and methanol, other than the major product methyl salicylate. Thus, in the high-pressure conditions prevailing in the autoclave, the possibility of the acidic CO_2 and methanol molecules formed during the reaction approaching the active sites inhibits the approach of dimethyl carbonate molecules towards the active sites at any instant. This inhibiting factor does not exist in the reaction system using methanol because, other than the major product methyl salicylate, there is only one by-product, water. This effect is compounded as the duration of reaction increases, because the number of by-product molecules formed in the dimethyl carbonate system increases proportionately with time. This explains why the percentage yield of methyl salicylate is better with methanol rather than dimethyl carbonate as the methylating agent.

A significant observation is that the percentage yield of methyl salicylate increased continuously with time when methanol is the reactant. When dimethyl carbonate is the reactant, the percentage yield of methyl salicylate does increase continuously with time, but the curve almost flattens after 8 h as observed in Fig. 1b. In the reaction with dimethyl carbonate, it is expected that along with dimethyl carbonate, the by-product methanol generated during the course of reaction would also participate in the reaction, thereby, increasing the yield of methyl salicylate, with a consequent increase in the slope of the reaction after a certain period of reaction time. However, what is observed is contrary to the expectations, the generation of methanol in the reaction mixture does not lead to a corresponding increase in the amount of methyl salicylate formed. Thus, it may be concluded that the bulkiness of dimethyl carbonate may be an inhibiting factor for this reaction. The approach of the by-product methanol towards the active sites is probably hindered by the larger dimethyl carbonate molecules. Thus, methanol is a good methylating agent in the absence of dimethyl carbonate in the reaction system. In the reaction in which methanol is taken as the methylating agent, the by-product generated during the course of the reaction is water. Due to the high-pressure conditions prevailing in the autoclave at temperatures well above the boiling point of water, it is possible that water does not deactivate the catalyst. This would explain the observation that, with methanol, the reaction yield increases continuously with time.

Influence of molar ratio of salicylic acid: methanol/ dimethyl carbonate

The reaction was carried out using different molar ratios of salicylic acid: methanol/dimethyl carbonate over sulphated zirconia and the results are given in Table 6. The optimum molar ratio of salicylic acid: dimethyl carbonate/methanol was found to be 1:6 in the range considered in this study. The percentage yield of methyl salicylate increased from 66 to 80% on varying the salicylic acid: methanol ratio from 1:4 to 1:6, when heated with 1 g of the catalyst 4 h at 150^{o}C. With dimethyl carbonate, under the same conditions, the percentage yield of methyl salicylate increased from 49 to 70%. Thus, it is observed that as the amount of methanol/dimethyl carbonate is increased in the reaction mixture, the conversion of salicylic acid also increases. Since, this is a reversible reaction, it is quite an expected observation that the forward reaction is favoured by taking one of the reactants in large excess. When the amount of methanol/dimethyl carbonate in the reaction mixture is less, some salicylic acid molecules may have remained undissolved as crystals and are not exposed to the active sites on the catalysts or the activated methanol/dimethyl carbonate molecule. However when the amount of methanol/dimethyl carbonate in the reaction mixture is increased, it functions as a solvent to dissolve salicylic acid to form a homogeneous phase wherein all the salicylic acid molecules can freely access the active sites.

Table 6—Effect of molar ratio on the esterification of SA with MeOH/DMC over S-ZrO_2. Catalyst weight = 1 g, duration of reaction = 4 h, MeOH = 2 mL, DMC = 5 mL.

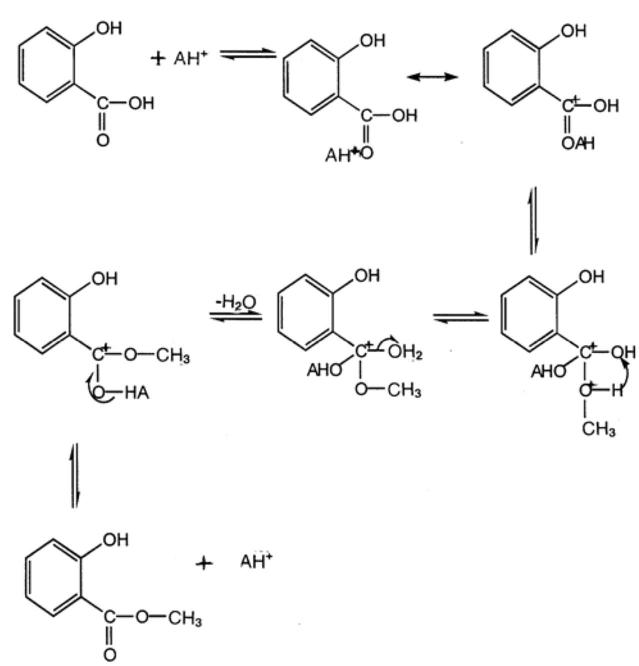
Salicylic acid (g)	Molar ratio SA:MeOH/DMC	Yield of methyl salicylate (%)	
		SA + MeOH	SA + DMC
2.05	1:4	66.0	49.0
1.64	1:5	73.8	59.1
1.37	1:6	80.0	70.0

Kinetics and mechanism of salicylic acid conversion using methanol and dimethyl carbonate

In the esterification of salicylic acid using methanol/dimethyl carbonate, the salicylic acid conversion increases with increase in the amount of the catalyst. This suggests that the transfer of reactants from the liquid phase to the catalyst phase is not a rate limiting step, implying the rate is independent of the catalyst mass[47]. The near linear character of the plot on sulphated zirconia for the reaction of salicylic acid with methanol/dimethyl carbonate indicated a first order dependence of the rate of the reaction on salicylic acid concentration. The rate constants obtained from the slopes of the plots of -ln(1-conv) versus duration of reaction are given in Table 7. The energy of activation (E_a) for the reaction was calculated for the two methylating agents and they were found to be 2.5 and 4 kcal for methanol and dimethyl carbonate respectively. The energy of activation is less in the methanol system indicating that the reaction is more facile with methanol than with dimethyl carbonate over sulphated zirconia. This observation, along with the fact that methanol esterifies salicylic acid in the absence of a catalyst, though to a small extent, while dimethyl carbonate does not, suggests that the mechanisms by which esterification takes place in the two cases are different. Also, another significant point that has to be borne in mind while suggesting the mechanism is, that, when dimethyl carbonate is the methylating agent, methanol is formed as one of the by-products. Though methanol itself is an esterifying agent there is no corresponding increase in formation of methyl salicylate during the course of reaction between salicylic acid and dimethyl carbonate. This is in spite of the fact, that, methanol is more reactive than dimethyl carbonate with salicylic acid over sulphated zirconia. This points to a mechanism wherein dimethyl carbonate gets more easily adsorbed over sulphated zirconia compared to methanol, though its size leads to steric hindrance which reduces the number of effective collisions leading to lesser salicylic acid conversion. The mechanism of the esterification of salicylic acid with methanol over sulphated zirconia (Scheme 1) is expected to be similar to the conventional mechanism involving the nucleophilic attack on the carboxyl oxygen by methanol[32,48]. The resulting loss of water would give the methyl ester. The active acidic site on the catalyst facilitates the formation of the carbocation and removal of OH^- from the carboxylic group. This is possible even in the absence of a catalyst, though to a small extent. On the other hand, the mechanism involving dimethyl carbonate would be different as no reaction takes place in the absence of the catalyst. A mechanism for the alkylation of phenol with dimethyl carbonate was proposed by Beutel[49], wherein the dimethyl carbonate is activated on a Lewis acid site by its carbonyl oxygen and phenol on an adjacent Lewis base site by H-bonding. Jyothi *et al.*[50] have proposed a similar mechanism for the alkylation of catechol by dimethyl carbonate over hydrotalcites. These have been proposed for the alkylation reactions of dimethyl carbonate considering the participation of both the acidic and the basic sites on the catalyst. Based on these informations, the following mechanism was proposed for the esterification reaction using dimethyl carbonate[32]. Dimethyl carbonate is adsorbed on the acid site of sulphated zirconia through its carbonyl carbon to form an activated complex. Through a series of steps

Table 7—Reaction rate constant for esterification of salicylic acid with MeOH/DMC over sulphated zirconia

Methylating agent	Reaction temperature	Rate constant k (min^{-1})	Reaction temperature	Rate constant k (min^{-1})
MeOH	110°C	1.8×10^{-3}	135˚C	2.2×10^{-3}
DMC	110°C	0.8×10^{-3}	135˚C	1.1×10^{-3}



Scheme 1—Mechanism of esterification of salicylic acid with methanol over protonic acid sites

Table 8—Reaction rate constant for esterification of salicylic acid with EtOH/DEC over sulphated zirconia.

Ethylating agent	Reaction temperature (˚C)	Rate constant k (min^{-1})
EtOH	110	0.7×10^{-3}
	135	1.2×10^{-3}
DEC	110	0.2×10^{-3}
	135	1.0×10^{-3}

involving the nucleophilic attack from salicylic acid and subsequent loss of methanol, the formation of methyl salicylate takes place. CO_2 is evolved by the decomposition of the carbonic acid type complex in the final step.

Reactions with higher homologues (ethanol and diethyl carbonate)

To verify the comparative alkylating ability of dialkyl carbonates and the corresponding alcohols, a pair of ethylating agents, ethanol (EtOH) and diethyl carbonate (DEC) was considered. The esterification of salicylic acid was carried out over sulphated zirconia under similar conditions. The effect of amount of catalyst on the esterification of salicylic acid over ethanol was studied. It was seen that, when the amount of catalyst was increased, the conversion to ethyl salicylate also increased. Ethyl salicylate was formed exclusively under various conditions with ethanol as well as diethyl carbonate. Ethanol is found to be a better alkylating agent than diethyl carbonate which concurs with the comparative alkylating ability of methanol and dimethyl carbonate. The rate constants calculated from the slopes of the plots of -ln(1-conv) versus duration of reaction are given in Table 8. The energy of activation for the ethylation of salicylic acid with ethanol and diethyl carbonate was calculated using Arrhenius equation and found to be 6.7 and 20 kcal respectively. The percentage yield of the ethyl ester is much lesser than that of the methyl ester which may be due to greater steric hindrance of the higher homologues.

Conclusion

From the detailed studies on the esterification of salicylic acid using methanol and dimethyl carbonate, it may be concluded that methanol can be used to exclusively esterify salicylic acid to its methyl ester over metal oxides. Though dimethyl carbonate is selective in converting salicylic acid to methyl salicylate, the yield is low and is not favourable in terms of atom economy. Thus, metal oxides such as alumina, silica and zirconia as well as their sulphate, phosphate and borate modified forms are effective catalysts for the conversion of salicylic acid to methyl salicylate. The 'intermediate to strong' acid sites are found to be responsible for the catalytic activity of these catalysts. From the values of rate constants and energy of activation, it is quite clear that the superacid, sulphated zirconia, is a good catalyst for this reaction which has high yield, selectivity, reusability and a simple method of preparation of the catalyst.

References

1 *Edu Chem*, 62 (1997) 34.
2 Haslam E, *Tetrahedron*, 36 (1980) 2409.
3 Sartori G & Maggi R, *Chem Rev*, 106 (2006) 1077.
4 *Dictionary of Organic Compounds*, 6th edn (Chapman & Hall, London), 5 (1998) 4400.
5 Vane J R & Botting R M (Eds), *Aspirin and other Salicylates*, 1st edn (Chapman & Hall, London), 1992, 115.
6 March J, *Advanced Organic Chemistry* (Wiley Eastern Limited, New Delhi), 1992.
7 Furniss B R, Hannaford A J, Rogers V, Smith P W G & Tatchell A R, *Vogel's Text Book of Practical Organic Chemistry* (Longman, London), 1996.
8 Denney D B, Meli R & Pendse A D, *J Org Chem*, 43 (1978) 4672.
9 Greene T W & Wuts P G M, *Protective Groups in Organic Synthesis* 2nd edn (John Wiley, New York), 1991.
10 Yamaguchi K, Tanabe K & Kinoshita M, *J Org Chem*, 44 (1979) 638.
11 Ballini R & Carotti A, *Synth Commun*, 13 (1983) 1197.
12 Shoda S & Mukaiyama T, *Chem Lett*, (1980) 391.
13 Mohacsi E, *Synth Commun*, 12 (1982) 453.
14 Badet B, Julia M, Ramirez-Munoz M & Sarrazin C A, *Tetrahedron*, 39 (1983) 3111.
15 Renga J M & Wang P C, *Synth Commun*, 14 (1984) 77.
16 Krutius O & Eremeev A V, *Chem Abstr*, 110 (1989) 114583n.
17 Sato T, Otera J & Nazaki H, *J Org Chem*, 57 (1992) 2166.
18 Puntambekar H M, Naik D G & Kapadi A H, *Indian J Chem*, 32B (1993) 793.
19 Uchamma S, Nakano R & Machida A, *Chem Abstr*, 123 (1995) 9171x.
20 Bhatia V G, Shaikh A S, Tongare D B & Balasubramaniyan V, *Indian J Chem*, 21B (1982) 259.
21 Hoobler M A, Bergbreiter D E & Newcomb M, *J Am Chem Soc*, 100 (1978) 8182.
22 Ho G J & Mathre D J, *J Org Chem*, 60 (1995) 2271.
23 Meyers A I, Snyder E S & Ackerman J J H, *J Am Chem Soc*, 100 (1978) 8186.
24 Basak A, Nayak M K & Chakraborti A K, *Tetrahedron Lett*, 39 (1998) 4883.
25 Wagner R B & Zook K H (Eds), *Synthetic Organic Chemistry* (Wiley, New York), 1953.
26 R A Sheldon, *J Chem Technol Biotechnol*, 68 (1997) 381.
27 Ono Y, *Catal Today*, 35 (1997) 15.
28 Ono Y, *Appl Catal, A: Gen*, 155 (1997) 133.
29 Lee Y & Shimizu I, *Synlett*, 10 (1998) 1063.
30 Selva M, Bomben A & Tundo A, *J Chem Soc, Perkin Trans*, 1 (1997) 1041.

31 Batistuta F M, Campelo J M, Garcia A, Luna D, Marinas J M, Romero A A & Urbano M R, *React Kinet Catal Lett*, 62 (1997) 47.

32 Sreekumar K, Jyothi T M, Mathew T, Talawar M B, Sugunan S & Rao B S, *J Mol Catal*, 159 (2000) 327.

33 (a)Kirumakki S R, Nagaraju N, Murthy K V V S B S R & Narayanan S, *Appl Catal, A*; Gen, 226 (2002) 175. (b) Kirumakki S R, Nagaraju N, Chary K V R & Narayanan S, *Appl Catal, A*; Gen 248 (2003) 161.

34 Shieh W C, Dell S & Repic O, *Tetrahedron Lett*, 43 (2002) 5607.

35 Nagaraju N, Peeran M & Devaprasad, *React Kinet Catal Lett*, 61 (1997) 155.

36 D'Souza J & Nagaraju N, *Indian J Chem*, 40 B (2001) 266.

37 Narayanan S & Sulthana A, *Appl Catal, A:* Gen, 167 (1998) 103.

38 Narayanan S & Deshpande K, *Appl Catal*, A: Gen, 199 (2000) 1.

39 Narayanan S & Murthy K V V S B S R, *Appl Catal. A*: Gen, 213 (2001) 273.

40 Sen S E, Smith S M & Sulivan K A, *Tetrahedron*, 55 (1998) 12657.

41 Perosa A, Selva M, Tundo A & Zordan F, *Synlett*, 1 (2000) 227.

42 Selva M, Bomben A & Tundo P, *J Chem Soc*, *Perkin Trans*, 1 (1997) 1041.

43 Selva M, Tundo P & Perosa A, *J Org Chem*, 66 (2001) 677.

44 Bomben A, Marques C A, Selva M & Tundo P, *Tetrahedron*, 51 (1995) 11573.

45 Selva M, Marques C & Tundo P, *J Chem Soc, Perkin Trans*, 1 (1994) 1323.

46 Tundo P, Trotta F & Moraglio G, *J Chem Soc, Perkin Trans*, 1 (1989) 1070.

47 Kumbhar P S, Yadav V M & Yadav G D, in *Chemically Modified Oxide Surfaces* edited by D E Leyden & W T Collins (Gordon and Breach), 1989.

48 Bossaert W D, De Vos D E, Van Rhijn W M, Grobet P J & Jacobs P A, *J Catal*, 182 (1999) 156.

49 Chakraborti A K, Basak A & Grover V, *J Org Chem*, 64 (1999) 8014.

50 Beutel T, *J Chem Soc, Faraday Trans*, 94 (1998) 985.

51 Jyothi T M, Raja T, Talawar M D & Rao B S, *Appl Catal*, A: Gen, 211 (2001) 41.