Esterification of Mixed Carboxylic-fatty Anhydrides Using Amberlyst-15 as Heterogeneous Catalyst

Iteb Trabelsi, Kamel Essid* and Mohamed Hedi Frikha

Laboratory of Physical and Organic Chemistry: Department of Chemistry, Faculty of Sciences in Sfax, TUNISIA

Abstract: The article deals with the use of mixed anhydrides for the synthesis of fatty esters. Both aliphatic and aromatic acids are involved, indicating different behaviors according to the chain length of the aliphatic acid. We describe a novel and efficient method for the synthesis of fatty esters by the esterification reaction of primary, secondary and tertiary alcohols with mixed carboxylic-palmitic anhydrides using resin Amberlyst-15 as heterogeneous acid catalyst. Influence of various reaction parameters such as molar ratio (anhydride/alcohol), catalyst amount, type of alcohol and type of mixed anhydride were studied to optimize the conditions for maximum yield. Among tested anhydrides we quote mainly the 4-chlorobenzoic palmitic anhydride because it was both reactive and selective for the preparation of palmitic acid ester. This anhydride gave a good yield of palmitic ester.

Key words: fatty acid, mixed anhydride, heterogeneous acid catalyst, resin Amberlyst-15, esterification

1 Introduction

The esterification of fatty acid with alcohol under acid catalyst is a reversible reaction limited by the low equilibrium conversion and slow reaction rate¹⁾. To perform high-yielding esterification with equimolar reaction of carboxylic acid and alcohol under mild conditions, activated derivatives of carboxylic acids (carboxylic acid chlorides or anhydrides) have been often employed²⁻⁴⁾. Carboxylic anhydrides in organic chemistry are acylating agents appreciated for their high reactivity compared to carboxylic acids⁵⁾. They are also important classes of chemicals that have been used extensively as synthetic intermediates in the preparation of variety of fine or special chemicals such as amides, esters, peptides, drugs, etc.⁶⁾. Mixed anhydrides obtained from two different carboxylic acids are molecules finding an increasing interest in the chemical industry due to their high reactivity resulting from the difference in pK values of the two moieties in asymmetric molecules^{7,8)}.

The aim of this work is the synthesis of fatty esters from mixed carboxylic fatty anhydrides using heterogeneous acid catalyst. They constitute an important class of useful chemical intermediates in the synthesis of several products⁹⁻¹¹⁾. These compounds are essential chemicals that are widely used in food, pharmaceutical, cosmetic, detergent, plasticizer, lubricant, textile and other industrial applications¹⁰⁻¹⁴⁾.

In a previous work we have prepared mixed carboxylic

fatty anhydrides in organic solvent and in the presence of triethylamine as acid acceptor¹⁵⁾. These mixed anhydrides were prepared from palmitic acid and aliphatic or aromatic carboxylic acid chloride. This work describes a novel and efficient method of synthesis of fatty esters by esterification of mixed carboxylic fatty anhydrides using heterogeneous acid catalyst. We have investigated the reactivity of some carboxylic palmitic anhydrides in the esterification reaction of primary, secondary and tertiary alcohols and in the presence of resin Amberlyst-15. We have optimized the conditions for maximum esterification yields by varying different reaction parameters such as molar ratio (anhydride/alcohol), effect of catalyst amount and type of alcohol.

2 Experimental

2.1 Chemicals

The chemicals purchased from Sigma-Aldrich Company include: Palmitic acid (90%), benzoyl chloride ($\geq 99\%$), 4-chlorobenzoyl chloride (99%), pivaloyl chloride (99%), acetyl chloride (98%), 2-phenylethanol (99%), benzyl alcohol (99.8%), 2-butanol (99%), 2-methyl-2-propanol (99.5%), salicylic acid (99%), triethylamine ($\geq 99.5\%$), hexane ($\geq 95\%$), dichloromethane (99.8%).

Amberlyst-15 was purchased from Fluka and used as re-

*Correspondence to: Kamel Essid, Laboratory of Physical and Organic Chemistry: Department of Chemistry, Faculty of Sciences in Sfax, TUNISIA

E-mail: kamelessid.issat@yahoo.fr

Accepted March 10, 2017 (received for review January 13, 2017)

Journal of Oleo Science ISSN 1345-8957 print / ISSN 1347-3352 online

<http://www.jstage.jst.go.jp/browse/jos/> <http://mc.manuscriptcentral.com/jjocs>

ceived. It is brown-grey solid having the following physical properties: ionic form: hydrogen, matrix: styrene-divinylbenzene, particle size: $<300\ \mu\text{m}$, maximum operating temperature: 120°C , exchange capacity: 4.7 meq/g.

2.2 Preparation of mixed carboxylic-palmitic anhydride

Mixed anhydrides were prepared by reaction between palmitic acid as fatty acid, acid chloride (such as acetyl chloride, pivaloyl chloride, benzoyl chloride and 4-chlorobenzoyl chloride) and triethylamine with the molar ratios 1:1.1:1.1. The reaction proceeded at room temperature for three hours in hexane (50 mL). The obtained crude anhydrides were used in the esterification reaction with different alcohols.

These crude mixed anhydrides were employed directly in the esterification reaction. Their composition was determined by ^1H NMR and resumed in Table 1.

2.3 Esterification of alcohols by mixed carboxylic-palmitic anhydrides

The esterification reactions of primary, secondary and tertiary alcohols with crude anhydrides mixtures, were performed in hexane as solvent (25 mL) in the presence of an ion-exchange resin (Amberlyst-15). The esterification reactions were refluxed with stirring for 4 hours. Different initial molar ratios between crude anhydrides and alcohols were employed (1:1, 1:2 and 1:4). The influence of amount in Amberlyst-15 cation resin (exchange capacity: 4.7 meq/g) was investigated. When the reaction was completed, the reaction mixture was filtered and the Amberlyst-15 washed with hexane (20 mL). The solvent was then evaporated to dryness and the crude product was weighed and analysed by IR, ^1H NMR and ^{13}C NMR spectroscopy (Table 2).

2.4 Spectroscopic analysis

The IR analysis was performed using a spectrometer type Perkin Elmer Spectrum version 10 in a wave number range of $500\text{--}4000\ \text{cm}^{-1}$. The ^1H NMR and ^{13}C NMR spectra were carried out at 25°C on a Bruker Avance III HD at a ^1H frequency of 400 MHz and ^{13}C frequency of 100 MHz. Each sample was dissolved in CDCl_3 or in mixture of ($\text{CDCl}_3/\text{DMSO}$).

The ^1H NMR spectral data of the crude product obtained by the esterification of 2 phenyl- ethanol with 4-chlorobenzoic palmitic anhydride (Table 3 entry 2), taken as representative example, are summarized below.

1: 2-phenylethyl palmitate

^1H NMR (400 MHz, CDCl_3 and DMSO) δ 0.83 (t, 3H, CH_3 -), 1.20 (m, 24H, $-\text{C}_{12}\text{H}_{24}-\text{C}_2\text{H}_4\text{CO}-\text{O}-$), 1.46–1.49 (m, 2H, $-\text{CH}_2-\text{CH}_2\text{CO}-\text{O}-$), 2.19 (t, 2H, $-\text{CH}_2-\text{CO}-\text{O}-$), 2.85 (t, 2H, $-\text{CH}_2-\text{CH}_2-\text{O}-$), 4.18 (t, 2H, $-\text{CH}_2-\text{O}-$), 7.14–7.25 (m, 5H, Ar-H).

2: 4-chlorobenzoic acid

^1H NMR (400 MHz, CDCl_3 and DMSO) δ 7.42 (d, $J = 8.4$ Hz, 2H, Ar-H), 7.91 (d, $J = 8.4$ Hz, 2H, Ar-H).

3: 2-phenylethyl 4-chlorobenzoate

^1H NMR (400 MHz, CDCl_3 and DMSO) δ 3.01 (t, 2H, $-\text{CH}_2-\text{CH}_2-\text{O}-$), 4.43 (t, 2H, $-\text{CH}_2-\text{O}-$), 7.14–7.25 (m, 5H, Ar-H), 7.40 (d, $J = 8.4$ Hz, 2H, Ar-H), 7.88 (d, $J = 8.4$ Hz, 2H, Ar-H).

3 Results and discussion

3.1 Esterification of primary and secondary alcohols with crude mixed anhydrides

Mixed anhydrides used in this study were freshly prepared by the action of palmitic acid on aromatic or aliphatic acid chlorides as indicated in Scheme 1⁽⁵⁾.

Table 1 Composition of crude mixture anhydride.

Entry	Crude mixed anhydride	Composition of crude mixture anhydride ^a
1	Benzoic-Palmitic	50.50%: benzoic palmitic anhydride 24.24%: palmitic anhydride 25.25%: benzoic anhydride
2	4-Cl-benzoic-Palmitic	73%: 4-Cl-benzoic palmitic anhydride 19.6%: palmitic anhydride 7.4%: 4-Cl-benzoic anhydride
3	Palmitic-Pivalic	51%: palmitic pivalic anhydride 22%: palmitic anhydride 27%: pivalic anhydride
4	Acetic-Palmitic	84%: acetic palmitic anhydride 13%: palmitic anhydride 3%: acetic anhydride

^a Composition of crude mixture anhydride determined by ^1H NMR.

Table 2 Esterification of primary and secondary alcohols with crude mixed anhydride.

Entry ^a	Crude mixed anhydride	Alcohol	IR (C=O, cm ⁻¹)	¹³ C NMR (C=O, ppm)	Crude mixture composition ^b
1	Benzoic-Palmitic	2-Phenyl-ethanol	1697: acid	180.47: palmitic acid	9.16%: palmitic acid
			1727: ester	172.19: benzoic acid	26.40%: benzoic acid
				173.95: 2-phenylethyl palmitate	49.70%: 2-phenylethyl palmitate
				166.61: 2-phenylethyl benzoate	14.74%: 2-phenylethyl benzoate
2		Benzyl	1687: acid	180.77: palmitic acid	50%: palmitic acid
			1730: ester	172.44: benzoic acid	42%: benzoic acid
				173.90: benzyl palmitate	8%: benzyl palmitate
3		2-Butanol	1686: acid	180.36: palmitic acid	48%: palmitic acid
			1733: ester	172.15: benzoic acid	42%: benzoic acid
				173.72: 2-butyl palmitate	10%: 2-butyl palmitate
4	4-Cl-benzoic-Palmitic	2-Phenyl-ethanol	1697: acid	166.94: 4-Cl-benzoic acid	45%: 4-Cl-benzoic acid
			1729: ester	173.13: 2-phenylethyl palmitate	52%: 2-phenylethyl palmitate
					3%: 2-phenylethyl 4-Cl-benzoate
5		Benzyl	1695: acid	175.84: palmitic acid	44%: palmitic acid
			1733: ester	167.38: 4-Cl-benzoic acid	40%: 4-Cl-benzoic acid
				173.43: benzyl palmitate	16%: benzyl palmitate
6		2-Butanol	1689: acid	175.45: palmitic acid	45%: palmitic acid
			1733: ester	167.04: 4-Cl-benzoic acid	41%: 4-Cl-benzoic acid
				173.03: 2-butyl palmitate	14%: 2-butyl palmitate
7 ^c			1695: acid	175.81: palmitic acid	32%: palmitic acid
			1731: ester	167.37: 4-Cl-benzoic acid	37%: 4-Cl-benzoic acid
				173.34: 2-butyl palmitate	31%: 2-butyl palmitate
8	Palmitic-Pivalic	2-Phenyl-ethanol	1700: acid	179.87: palmitic acid	12%: palmitic acid
			1735: ester	184.97: pivalic acid	27%: pivalic acid
				173.96: 2-phenylethyl palmitate	41%: 2-phenylethyl palmitate
				178.60: 2-phenylethyl pivalate	20%: 2-phenylethyl pivalate
9	Acetic-Palmitic	2-Phenyl-ethanol	1700: acid	179.03: palmitic acid	12.84%: palmitic acid
			1739: ester	178.12: acetic acid	1.7%: acetic acid
				173.93: 2-phenylethyl palmitate	42.73%: 2-phenylethyl palmitate
				171.16: 2-phenylethyl acetate	42.73%: 2-phenylethyl acetate

^a NMR samples (entry: 1, 2, 3, 8 and 9) realized in CDCl₃ and NMR samples (entry: 4, 5, 6 and 7) realized in the (CDCl₃/DMSO) mixture.

^b Composition of crude mixture determined by ¹H NMR.

^c The molar ratio (anhydride/alcohol) is (1:4).

The action of crude mixed anhydrides on primary (2-phenylethanol and benzyl alcohol) or secondary (2-butanol) alcohols proceeded in hexane under reflux, in the presence of ion-exchange resin (Amberlyst-15) as heterogeneous catalyst¹⁵. The reaction mixture, consisted of the two acids and two esters, was so complex as shown in **Scheme 2**^{15, 16}.

The esterification reaction was performed with crude mixed aromatic palmitic anhydrides (benzoic palmitic, 4-chlorobenzoic palmitic) and mixed aliphatic palmitic anhydrides (palmitic pivalic and acetic palmitic) on alcohols (2-phenylethanol, alcohol benzyl and 2-butanol) with a

molar ratio (anhydride/alcohol) 1:2 in the presence of 2 g of Amberlyst-15 resin (9.4 meq active sites/1.3 10⁻³ mol of mixture crude anhydride). The structures of the products obtained at the end of reaction were determined by IR and (¹H and ¹³C) NMR analyses and the results are shown in **Table 2**.

Representative IR, ¹³C NMR and ¹H NMR spectra of the crude product, obtained by esterification of 2 phenylethanol with 4-chlorobenzoic palmitic anhydride (**Table 3** entry 2), were taken as representative examples and included respectively in **Figs. 1, 2** and **3**.

The IR spectra showed that all crude products were

Table 3 Effect of Amberlyst-15 catalyst amount.

Entry ^a	Alcohol	Catalyst amount (g)	IR (C=O, cm ⁻¹)	¹³ C RMN (C=O, ppm)	Crude mixture composition ^b	Yield of ester (%)
1	2-Phenyl-ethanol	2	1697: acid 1729: ester	166.94: 4-Cl-benzoic acid 173.13: 2-phenylethyl palmitate	45%: 4-Cl-benzoic acid 52%: 2-phenylethyl palmitate 3% : 2-phenylethyl 4-Cl-benzoate	92.69
2		0.5	1697: acid 1729: ester	166.95: 4-Cl-benzoic acid 173.11: 2-phenylethyl palmitate	43%: 4-Cl-benzoic acid 53%: 2-phenylethyl palmitate 3%: 2-phenylethyl 4-Cl-benzoate	94.47
3		0.25	1697: acid 1729: ester	166.95: 4-Cl-benzoic acid 173.11: 2-phenylethyl palmitate	44%: 4-Cl-benzoic acid 52%: 2-phenylethyl palmitate 4%: 2-phenylethyl 4-Cl-benzoate	92.69
4	Benzyl	2	1695: acid 1733: ester	175.84: palmitic acid 167.38: 4-Cl-benzoic acid 173.43: benzyl palmitate	46%: palmitic acid 40%: 4-Cl-benzoic acid 14%: benzyl palmitate	30.23
5		0.5	1695: acid 1733: ester	174.44: palmitic acid 166.23: 4-Cl-benzoic acid 172.33: benzyl palmitate	25%: palmitic acid 43%: 4-Cl-benzoic acid 32%: benzyl palmitate	69.11
6		0.25	1695: acid 1733: ester	166.77: 4-Cl-benzoic acid 172.86: benzyl palmitate	46%: 4-Cl-benzoic acid 51%: benzyl palmitate 3%: benzyl 4-Cl-benzoate	90.90
7	2-Butanol	2	1689: acid 1733: ester	175.45: palmitic acid 167.04: 4-Cl-benzoic acid 173.03: 2-butyl palmitate	45%: palmitic acid 41%: 4-Cl-benzoic acid 14%: 2-butyl palmitate	30.23
8		0.5	1689: acid 1732: ester	174.89: palmitic acid 166.85: 4-Cl-benzoic acid 172.68: 2-butyl palmitate	26%: palmitic acid 40%: 4-Cl-benzoic acid 34%: 2-butyl palmitate	73.43
9		0.25	1689: acid 1732: ester	175.20: palmitic acid 166.86: 4-Cl-benzoic acid 173.85: 2-butyl palmitate	12 %: palmitic acid 45%: 4-Cl-benzoic acid 42%: 2-butyl palmitate 1% : 2-butyl 4-Cl-benzoate	90.71

^a NMR samples realized in the (CDCl₃/DMSO) mixture.

^b Composition of crude mixture determined by ¹H NMR.

Scheme 1 Synthesis of mixed carboxylic-palmitic anhydride.

Scheme 2 Esterification reaction of mixed anhydride with alcohol.

Fig. 1 FT-IR spectrum of the crude product obtained by esterification of 2 phenyl- ethanol with 4-chlorobenzoic-palmitic anhydride (Table 3 entry 2).

Fig. 2 ^{13}C NMR spectrum of the crude product obtained by esterification of 2 phenyl- ethanol with 4-chlorobenzoic-palmitic anhydride (Table 3 entry 2).

mixture of esters and acids. The FT-IR spectrum showed an intense carbonyl stretch at 1700 cm^{-1} that corresponded to carboxylic acid. The presence of broad O-H band of acid in IR spectrum was observed between 2500 and 3000 cm^{-1} . A stretch peak was observed at $(1733\text{--}1739)\text{ cm}^{-1}$ corresponding to ester carbonyl group and C-O band centred on $(1150, 1280)\text{ cm}^{-1}$. Aliphatic C-H band was observed at $(2880\text{--}2970)\text{ cm}^{-1}$.

The analysis by ^{13}C NMR confirmed these remarks. Some ^{13}C NMR spectra showed indeed, 4 peaks relating to a carbonyl ($\text{C}=\text{O}$) in the region $(166\text{--}180\text{ ppm})$, reflecting the presence of mixture of two types of ester and two types of acid (entry 1, 8, 9). Other ^{13}C NMR spectra showed 2 or 3 peaks relating to a carbonyl ($\text{C}=\text{O}$) reflecting the presence of mixture of a single type of ester and two types of acid (entry 2, 3, 5, 6, 7) or the presence of mixture of a single

Fig. 3 ^1H NMR spectrum of the crude product obtained by esterification of 2 phenyl- ethanol with 4-chlorobenzoic-palmitic anhydride (Table 3 entry 2).

type of ester and single type of acid (entry 4).

The ^1H NMR analysis confirmed the presence of mixture of esters and acids in most of crude reaction products. The best yields of 2-phenylethyl palmitate were obtained in the case of mixed aromatic palmitic anhydrides (entry 1: 49.70% and entry 4: 52%). The existence of an electron withdrawing group (Cl) on aromatic ring of mixed anhydride promotes the formation reaction (1) of palmitic acid ester (entry 4: 52%). Similar results were emphasized in the literature. They show that electron-withdrawing groups (Cl, F, NO_2) increase the reactivity of substituted benzoic anhydrides and promote the formation of aliphatic esters^{15, 17–19}. In addition, the formation rate of benzoic ester was much slower than that of aliphatic acid ester when we used the mixed anhydrides as reagents of esterification^{15, 16, 19}. Indeed, the aromatic acid esters were obtained in a low yield in the case of esterification by the mixed aromatic palmitic anhydrides (entry 1: 14.74% and entry 4: 3%). These results indicate that 4-chlorobenzoic palmitic anhydride was more reactive and more selective than benzoic palmitic anhydride in the case of esterification of primary alcohol (2-phenylethanol).

Mixed Aliphatic palmitic anhydrides were less reactive and less selective than their mixed aromatic palmitic anhydrides. The 2-phenylethyl palmitate was obtained with a less yield in the case of palmitic pivalic and acetic palmitic anhydrides (entry 8: 41% and entry 9: 42.73%). we note that the esterification with these anhydrides promotes the

reaction 2 (Scheme 2) and leads to the formation of undesirable ester **C** with important yield (entry 8: 20% and entry 9: 42.73%).

4-chlorobenzoic palmitic anhydride remained selective in the esterification reaction of benzyl alcohol giving only benzyl palmitate but with a yield (entry 5: 16%) lower than that recorded in the case of esterification of 2-phenylethanol. Benzoic palmitic anhydride was selective but less reactive than 4-chlorobenzoic palmitic anhydride in the case of esterification by benzyl alcohol (entry 2: 8%).

Mixed Aromatic palmitic anhydrides were selective in the case of esterification by the secondary alcohol (2-butanol) but less reactive. As example the 2-butyl palmitate esterified with 4-chlorobenzoic palmitic anhydride was obtained with a 14% yield (entry 6) and that when anhydride and alcohol were employed in stoichiometric amounts. Improved yield of 2-butyl palmitate (entry 7: 31%) was observed when increasing the molar ratio (anhydride/alcohol) from 1:2 to 1:4. Benzoic palmitic anhydride was selective but less reactive than 4-chlorobenzoic palmitic anhydride in the esterification of 2-bantanol (entry 3: 10%).

The molar compositions of crude products, obtained from ^1H NMR spectra, showed that the amount of palmitic acid ester in the reaction mixtures depended on the nature of alcohol and mixed anhydride used in esterification reaction. To improve the yield of esterification of primary and secondary alcohols, we have varied the molar ratio (anhydride/alcohol) and the amount of catalyst while keeping

Table 4 Theoretical composition in the crude mixture of esterification reaction.

Crude anhydride composition	Theoretical composition of the crude mixture: Esterification by palmitic group
73%: 4-Cl-benzoic palmitic anhydride	9.8%: palmitic acid
19.6%: palmitic anhydride	40.2%: 4-Cl- benzoic acid
7.4%: 4-Cl-benzoic anhydride	46.3 %: palmitic acid ester
	3.7%: 4-Cl-benzoic acid ester

constant the other experimental conditions such as solvent, time reaction and temperature. This study was performed with 4-chlorobenzoic palmitic anhydride as most selective and responsive in the esterification of tested primary and secondary alcohols.

3.1.1 Effect of Amberlyst-15 catalyst amount

To study the effect of resin amount on the yield of palmitic acid esters, the esterification of alcohols (2-phenylethanol, benzyl alcohol and 2-butanol) with 4-chlorobenzoic palmitic anhydride was carried out with a molar ratio (anhydride/alcohol) equal to 1:2 and in the presence of 2 g, 0.5 g and 0.25 g of Amberlyst-15 resin corresponding respectively to the ratios 4, 1 and 0.5 (equivalent of active sites/equivalent of alcohol). The structures of products obtained at the end of reaction were determined by IR and (^1H and ^{13}C) NMR analysis (Table 3).

The yields of palmitic acid esters were calculated by the ratio between the experimental molar percentage of these esters and their theoretical molar percentage directly related to the starting anhydride mixture composition. The theoretical molar compositions were calculated assuming that 4-chlorobenzoic-palmitic anhydride reacted only by its palmitic group, the results of this calculation are shown in Table 4.

It was noted a decrease in the resin amount accompanied by a clear increase in the molar percentage of palmitic acid esters of benzyl alcohol and 2-butanol (entry 6: 90.90% and entry 9: 90.71%).

We note that the selectivity of esterification reaction was not affected by the variation of resin amount because we obtain in all cases a reaction mixture consisting by palmitic acid ester. The resin amount did not affect the composition of reaction mixture in the case of 2-phenylethanol but had a remarkable effect in case of the two other alcohols.

These results are in good agreement with those of literature who show that the presence of wide excess of active sites (with regard to the reactants) can have an inhibitory effect on the rate of esterification reaction. It was shown that the reaction rate of esterification of free fatty acids in olive-pomace oil with ethanol in the presence of macroporous ion exchange resin type SPC118 was maximal for a ratio (active sites/free fatty acids) equal to 1^{20, 21}. We have proven in a previous work realized in our laboratory that when the ratio (active sites/alcohol) was equal or less to 1, the yield was better than if the ratio was greater²¹. This

was probably due to the presence of excess in active sites which caused a decrease in probability of meeting of reactants in the same active site so the yield in product of reaction decreased too^{21, 22}.

3.1.2 Effect of molar ratio (anhydride/alcohol)

We have studied the effect of molar ratio (anhydride/alcohol) on the yield of palmitic acid esters. Esterification was performed by 2-phenylethanol or benzyl as primary alcohols and by 2-butanol as secondary alcohol, with crude mixed 4-Cl-benzoic-palmitic anhydride. The reactions were performed in the presence of 0.5 g of Amberlyst-15 resin. The molar ratios (anhydride/alcohol) were fixed to 1:1, 1:2 and 1:4, corresponding respectively to the reports (equivalent of active sites/equivalent of alcohol) of 2, 1 and 0.5. The structures of the obtained products were determined by IR and (^1H and ^{13}C) NMR analysis and the yields of palmitic acid esters were calculated by the ratio between the experimental molar percentage of these esters and their theoretical molar percentage (Table 5).

We note that the selectivity of esterification reaction was not affected by the variation of molar ratio (anhydride/alcohol) because we have obtained in all cases a reaction mixture consisting by the palmitic acid ester. It should be noted that any increase in the molar ratio (anhydride/alcohol) was accompanied by an increase in the molar percentage of palmitic acid ester for the three alcohols. Palmitic acid was totally esterified from a molar ratio (anhydride/alcohol) 1:2 in the case of 2-phenylethanol. Palmitate 2-phenylethyl was obtained with a yield of 94.47% (entry 2). In the case of esterification of the two other alcohols, it was necessary to increase the molar ratio (anhydride/alcohol) beyond 1:2 to improve the yield in palmitic acid esters. For a molar ratio (anhydride/alcohol) equal to 1:4, with benzyl alcohol and 2-butanol, a yield of 90% was reached. This improvement was attributed mainly to the displacement of chemical equilibrium of esterification reaction when we increased the concentration of one of the two reactants and also to the decrease of ratio (equivalent of active sites/equivalent of alcohol) which passed from 2 to 0.5.

It was clear, in light of these results that mixed 4-chlorobenzoic palmitic anhydride had good reactivity and high selectivity for esterification of primary and secondary alcohols. Experimental conditions used in the initial moment were essentially related to the amount of ion exchange

Table 5 Effect of molar ratio (anhydride/alcohol).

Entry ^a	Alcohol	Molar rapport (anhydride/alcohol)	IR (C=O, cm ⁻¹)	¹³ C RMN (C=O, ppm)	Crude mixture composition ^b	Yield of ester (%)
1	2-Phenyl-ethanol	1:1	1697: acid 1729: ester	174.87: palmitic acid 166.70: 4-Cl-benzoic acid 172.87: 2-phenylethyl palmitate	10%: palmitic acid 44%: 4-Cl-benzoic acid 43 %: 2-phenylethyl palmitate 3%: 2-phenylethyl 4-Cl-benzoate	92.87
2		1:2	1697: acid 1729: ester	166.95: 4-Cl-benzoic acid 173.11: 2-phenylethyl palmitate	43%: 4-Cl-benzoic acid 53%: 2-phenylethyl palmitate 3%: 2-phenylethyl 4-Cl-benzoate	94.47
3	Benzyl	1:1	1695: acid 1733: ester	174.83: palmitic acid 166.67: 4-Cl-benzoic acid 172.73: benzyl palmitate	42%: palmitic acid 40%: 4-Cl-benzoic acid 18%: benzyl palmitate	38.87
4		1:2	1695: acid 1733: ester	174.44: palmitic acid 166.23: 4-Cl-benzoic acid 173.33: benzyl palmitate	25%: palmitic acid 43%: 4-Cl-benzoic acid 32%: benzyl palmitate	69.11
5		1:4	1695: acid 1733: ester	166.91: 4-Cl-benzoic acid 173.02: benzyl palmitate	47%: 4-Cl-benzoic acid 50%: benzyl palmitate 3%: benzyl 4-Cl-benzoate	89.12
6	2-Butanol	1:1	1686: acid 1733: ester	175.08: palmitic acid 166.7: 4-Cl-benzoic acid 172.77: 2-butyl palmitate	30%: palmitic acid 50%: 4-Cl-benzoic acid 20%: 2-butyl palmitate	43.19
7		1:2	1689: acid 1732: ester	174.89: palmitic acid 166.85: 4-Cl-benzoic acid 172.68: 2-butyl palmitate	26%: palmitic acid 40%: 4-Cl-benzoic acid 34%: 2-butyl palmitate	73.43
8		1:4	1689: acid 1732: ester	175.24: palmitic acid 167: 4-Cl-benzoic acid 172.95: 2-butyl palmitate	13%: palmitic acid 42%: 4-Cl-benzoic acid 43%: 2-butyl palmitate 2%: 2-butyl 4-Cl-benzoate	92.87

^a NMR samples realized in the (CDCl₃/DMSO) mixture.^b Composition of crude mixture determined by ¹H NMR.

resin catalyst (Amberlyst-15) and to the molar ratios of reactants. Excellent yields of esterification of primary and secondary alcohols were reached when a molar ratio (equivalent of active sites/equivalent of alcohol) was equal or less to 1 and molar ratio of reactants (anhydride/alcohol) equal or greater than 1:2.

3.2 Esterification of tertiary alcohols with crude mixed anhydrides

Preliminary tests of esterification of tertiary alcohols (2-methyl-2-propanol and salicylic acid) were realized with crude mixed anhydrides. The molar ratio of reactants (anhydride/alcohol) was fixed to 1:2 and the quantity of Amberlyst-15 resin to 0.5 g (ratio (equivalent active sites/equivalent alcohol) equal to 1). The reaction with 2-methyl-2-propanol was carried out in hexane and that of salicylic acid, non soluble in hexane, was carried out in dichloromethane. The structures of products obtained at the end of reaction were determined by IR, ¹³C NMR and ¹H NMR

analysis (Table 6).

We note that all mixtures obtained at the end of reactions did not contain any traces of ester and anhydrides used as reactants were completely converted to their corresponding acids. We assume that this behavior is due to the sterical hindrance that impedes the access towards the reaction center, or in some cases the access is limited, that makes the reaction rate very slow compared with normal-chain alcohols²³.

4 Conclusion

In the present work, we have investigated the reactivity of some mixed anhydrides of palmitic acid in the esterification reaction of primary, secondary and tertiary alcohols and in the presence of resin Amberlyst-15 as heterogeneous catalyst. We have optimized the conditions for maximum yields of esterification by varying different reac-

Table 6 Esterification of tertiary alcohols with crude mixed anhydrides.

Entry ^a	Crude mixed anhydride	Alcohol	IR (C=O, cm ⁻¹)	¹³ C RMN (C=O, ppm)	Crude mixture composition ^b
1	Benzoic-Palmitic	2-Methyl-2-propanol	1684: acid	180.74: palmitic acid 172.4: benzoic acid	51%: palmitic acid 49%: benzoic acid
2		Salicylic acid	1682: acid	181.05: palmitic acid 172.57: benzoic acid 175.37: salicylic acid	25%: palmitic acid 25%: benzoic acid 50%: salicylic acid
3	4-Cl-benzoic-Palmitic	2-Methyl-2-propanol	1686: acid	174.91: palmitic acid 166.92: 4-Cl-benzoic acid	60%: palmitic acid 40%: 4-Cl-benzoic acid
4		Salicylic acid	1686: acid	175.02: palmitic acid 166.90: 4-Cl-benzoic acid 172.52: salicylic acid	25%: palmitic acid 25%: 4-Cl-benzoic acid 50%: salicylic acid
5	Palmitic-Pivalic	2-Methyl-2-propanol	1697: acid	180.60: palmitic acid 185.66: pivalic acid	50%: palmitic acid 50%: pivalic acid
6		Salicylic acid	1695: acid	180: palmitic acid 185.59: pivalic acid 175: salicylic acid	25%: palmitic acid 25%: pivalic acid 50%: salicylic acid
7	Acetic-Palmitic	2-Methyl-2-propanol	1696: acid	180.16: palmitic acid 178: acetic acid	80%: palmitic acid 20%: acetic acid
8		Salicylic acid	1695: acid	180: palmitic acid 178: acetic acid 175: salicylic acid	33%: palmitic acid 17%: acetic acid 50%: salicylic acid

^a NMR samples (entry: 1, 2, 5, 6, 7 and 8) realized in CDCl₃ and NMR samples (entry: 3 and 4) realized in the (CDCl₃/DMSO) mixture.

^b Composition of crude mixture determined by ¹H NMR.

tion parameters such as molar ratio (anhydride/alcohol), effect of catalyst amount and type of alcohol.

Among tested anhydrides we quote mainly 4-chlorobenzoic palmitic anhydride because it was both reactive and selective for the preparation of palmitic acid ester. Mixed aromatic palmitic anhydrides were selective in the case of esterification by secondary alcohol (2-butanol) but less reactive.

It was noted that a decrease in the resin amount was accompanied by a clear increase in the molar percentage of palmitic acid ester of benzyl alcohol and 2-butanol which means important yields of these esters. Any increase in the molar ratio of (anhydride/alcohol) was accompanied by an increase in the molar percentage of palmitic acid ester for the three alcohols (2-phenylethanol or benzyl alcohol as primary alcohols and by 2-butanol as a secondary alcohol). The palmitic acid was totally esterified from a molar ratio (anhydride/alcohol) 1:2 in the case of 2-phenylethanol. In the case of esterification of the two other alcohols, it was necessary to increase the molar ratio (anhydride/alcohol) beyond 1:2 to improve the yield of palmitic acid ester. This improvement was attributed mainly to the displacement of chemical of esterification reaction equilibrium when we increase the concentration of one of the two reactants and

also to the decrease of ratio (equivalent of active sites/equivalent of alcohol) which passed from 2 to 0.5. The reaction between prepared mixed anhydrides with some tertiary alcohols did not contain traces of ester and the anhydrides used as reactants were completely converted to their corresponding acids.

Actually we are studying the synthesis of sugar esters by the esterification reaction of sugar with mixed carboxylic-palmitic anhydrides using resin Amberlyst-15 as heterogeneous acid catalyst. Sugar esters are nonionic surfactants. Their potential applications extend from human food to drugs formulation and biochemical studies. The most studied methods were the biotechnological ways using enzyme as a catalyser.

References

- 1) Sun, H.B.; Hua, R.; Yin, Y. ZrOCl₂·8H₂O: An efficient, cheap and reusable catalyst for the esterification of acrylic acid and other carboxylic acids with equimolar amounts of alcohols. *Molecules* **11**, 263-271 (2006).
- 2) Shiina, I.; Kubota, M.; Oshiumi, H.; Hashizume, M. An effective use of benzoic anhydride and its derivatives

- for the synthesis of carboxylic esters and lactones: a powerful and convenient mixed anhydride method promoted by basic catalysts. *J. Org. Chem.* **69**, 1822-1830 (2004).
- 3) Chakraborti, A.K.; Shivani, S. Magnesium bistrifluoromethanesulfonimide as a new and efficient acylation catalyst. *J. Org. Chem.* **71**, 5785-5788 (2006).
- 4) Firouzabadi, H.; Iranpoor, N.; Farahi, S. Solid trichlorotitanium(IV) trifluoromethanesulfonate $\text{TiCl}_3(\text{OTf})$ catalyzed efficient acylation of $-\text{OH}$ and $-\text{SH}$: Direct esterification of alcohols with carboxylic acids and transesterification of alcohols with esters under neat conditions. *J. Mol. Catal. A: Chem.* **289**, 61-68 (2008).
- 5) Peydecastaing, J.; Vaca-Garcia, C.; Borredon, E. Consecutive reactions in an oleic acid and acetic anhydride reaction medium. *Eur. J. Lipid Sci. Technol.* **111**, 723-729 (2009).
- 6) Hu, Y.L.; Zhao, X.E.; Lu, M. Efficient and convenient synthesis of symmetrical carboxylic anhydrides from carboxylic acids with sulfated zirconia by phase transfer catalysis. *Bull. Chem. Soc. Ethiop.* **25**, 255-262 (2011).
- 7) Arni, P.C.; Gray, J.D.; Scougall, R.K. Chemical modification of wood. I. Use of trifluoroacetic anhydride in the esterification of wood by carboxylic acids. *J. Appl. Chem.* **11**, 157-163 (1961).
- 8) Peydecastaing, J.; Vaca-Garcia, C.; Borredon, E. Linear anhydrides and carboxylic acids. *Chromatographia* **68**, 685-688 (2008).
- 9) Chemat, F.; Poux, M.; Galema, S.A. Esterification of stearic acid by isomeric forms of butanol in a microwave oven under homogeneous and heterogeneous reaction conditions. *J. Chem. Soc. Perkin. Trans. 2*, 2371-2374 (1997).
- 10) Brahmkhatri, V.; Patel, A. Esterification of lauric acid with butanol-1 over $\text{H}_3\text{PW}_{12}\text{O}_{40}$ supported on MCM-41. *Fuel* **102**, 72-77 (2012).
- 11) De Paiva, E.J.M.; Corazza, M.L.; Sierakowski, M.R.; Wärmã, J.; Murzin, D.Y.; Wypych, F.; Salmi, T. Influence of two different alcohols in the esterification of fatty acids over layered zinc stearate/palmitate. *Bioresour. Technol.* **193**, 337-344 (2015).
- 12) Zaidi, A.; Gainer, J.L.; Carta, G.; Mrani, A.; Kadiri, T.; Belarbi, Y.; Mir, A. Esterification of fatty acids using nylon immobilized lipase in n-hexane: kinetic parameters and chain length effects. *J. Biotechnol.* **93**, 209-216 (2002).
- 13) Peng, L.; Philippaerts, A.; Ke, X.; Van Noyen, J.; De Clippel, F.; Tendeloo, G.V.; Jacobs, P.A.; Sels, B.F. Preparation of sulfonated ordered mesoporous carbon and its use for the esterification of fatty acids. *Catal. Today* **150**, 140-146 (2010).
- 14) Martínez, M.; Oliveros, R.; Aracil, J. Synthesis of bio-surfactants: enzymatic esterification of diglycerol and oleic acid. 1. Kinetic modeling. *Ind. Eng. Chem. Res.* **50**, 6609-6614 (2011).
- 15) Trabelsi, I.; Essid, K.; Frikha, M.H. Synthesis of mixed anhydrides of fatty acids: Stability and reactivity. *Ind. Crop. Prod.* **97**, 552-557 (2017).
- 16) Peydecastaing, J.; Vaca-Garcia, C.; Borredon, E. Bi-acylation of cellulose: determining the relative reactivities of the acetyl and fatty-acyl moieties. *Cellulose* **18**, 1015-1021 (2011).
- 17) Ishihara, K.; Kubota, M.; Kurihara, H.; Yamamoto, H. Scandium trifluoromethanesulfonate as an extremely active lewis acid catalyst in acylation of alcohols with acid anhydrides and mixed anhydrides. *J. Org. Chem.* **61**, 4560-4567 (1996).
- 18) Shiina, I. An effective method for the synthesis of carboxylic esters and lactones using substituted benzoic anhydrides with Lewis acid catalysts. *Tetrahedron* **60**, 1587-1599 (2004).
- 19) Shiina, I.; Kubota, M.; Oshiumi, H.; Hashizume, M. An effective use of benzoic anhydride and its derivatives for the synthesis of carboxylic esters and lactones: a powerful and convenient mixed anhydride method promoted by basic catalysts. *J. Org. Chem.* **69**, 1822-1830 (2004).
- 20) Frikha, M.H.; Ben Zina, M.; Gabsi, S. Esterification of free fatty acids in olive oil with methanol or ethanol: inhibiting effect of alcohol. *Bull. Soc. Chim. Fr.* **133**, 875-879 (1996).
- 21) Frikha, M.H.; Ben Zina, M.; Salem, M. Esterification kinetic equation of free fatty acids of degraded olive oil with ethanol at a temperature higher than that of azeotrope. *Entropie* **206**, 48-54 (1997).
- 22) Bouguerra Neji, S.; Trabelsi, M.; Frikha, M.H. Esterification of fatty acid over Tunisian acid activated clay: kinetic study. *J. Oleo Sci.* **60**, 293-299 (2011).
- 23) Stavarache, C.; Vinatoru, M.; Nishimura, R.; Maeda, Y. Fatty acids methyl esters from vegetable oil by means of ultrasonic energy. *Ultrason. Sonochem.* **12**, 367-72 (2005).