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CONVERSION OF FATTY ACID FEEDSTOCKS TO 2-OXAZOLINE

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ABSTRACT

A sustainable and clean synthesis of 2-oxazolines from different fatty acids is described in this article. Various small (C6 and C8), medium (C10 and C12) and long chain (C16 and C18) fatty acids were reacted with 2-amino-2-methyl-1-propanol in the presence of Hβ-zeolite under microwave irradiation. The Hβ-zeolite was used both as a catalyst and a support to facilitate the cyclisation and dehydration reactions leading to 2-oxazoline formation. Yields of the corresponding 2-oxazolines were 68%-94%. The work-up and purification method presented here is safe, and high yielding. Experimental results also indicated that smaller aliphatic acids viz, *acetic acid, butyric acid, and valeric acid did not yield the expected products as they are too small to be retained inside the cavity of Hβ-zeolite.*

Keywords: 2-oxazoline, fatty acid, oleochemistry, microwaves, Hβ-zeolite.

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INTRODUCTION

The 2-oxazolines are promising compounds with potential applications in organic synthesis and pharmacology (Grant and Meyers, 1994; Meyers and Mihelich, 1976; Frump, 1971; Reuman and Meyers, 1985). These heterocyclic compounds are used as synthetic intermediates, protecting groups and chiral auxillaries (Grant and Meyers, 1994; Meyers and Mihelich, 1976; Frump, 1971). In addition, these five membered heterocylclic compounds are known as naturally occurring chelators, cytotoxic cyclic-peptides, antimitotic and neuroprotective agents (Grant and Meyers, 1994; Meyers and Mihelich, 1976; Frump, 1971). As reported in the literatures, these compounds are synthesised from N-acyl derivatives of β-hydroxyl amines by heating or using dehydrating agents such as $SOCl_2$, H_2SO_4 or P_2O_5 (Grant and Meyers, 1994; Meyers and Mihelich, 1976; Frump, 1971; Vobruggen and Krolikiewicz, 1993). Other methods include the synthesis of 2-oxazolines from imidate hydrochlorides, orthoesters, imino ether hydrochlorides, aldehydes, carboxylic acids, nitriles and carboxylic esters (Grant and Meyers, 1994; Meyers and Mihelich, 1976; Frump, 1971). Generally, amino alcohols are used as reactants for the synthesis of 2-oxazolines (Grant and Meyers, 1994; Meyers and Mihelich, 1976; Frump, 1971).

In the above context, use of nitrile as starting material requires Lewis acid and proceeds at high temperature with elimination of ammonia (Bolm *et al*., 1991). Also, other methods utilise complex chemical reagents or strong acidic conditions (Bandgar and Pandit, 2003). As most of these reported methods use complex reagents, hazardous chemicals and harsh reaction conditions, there are constant efforts to develop new and simpler routes for the 2-oxazoline synthesis.

Microwave as an unconventional heating source has become widely recognised technology in organic synthesis. Particularly, microwave has solved the problem of long reaction times for the synthesis of 2-oxazolines (Oussaid *et al*., 1995; Marraero-Terrero and Loupy, 1996; Tellado *et al*., 2003; Sharma et al., 2009). Recently, the synthesis of 2-oxazolines from N-acylbenzotriazoles using microwaves has been reported (Katritzky *et al*., 2004). This method needs

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the preparation of starting materials and requires toxic chemicals like $CHCl_3$ and $SOCl_2$ (Katritzky *et al*., 2004).

This work is a continuation of the on-going research on the preparation of value-added compounds from biomass feedstocks (Karmee and Chadha, 2005a, b; Karmee, 2011; 2012; 2013; 2009; 2008; 2014). The objective of this work is to synthesise 2-oxazolines from fatty acids which are readily obtained from food waste, grease, plant oils and animal fats. Along this line, earlier work describe utilisation of oils, fatty acids and glycerol for the synthesis of biodiesel and value-added chemical compounds.

MATERIALS AND METHODS

Materials and Instruments

All acids, zeolite and 2-amino-2-methyl-1-propanol were purchased from local sources. Ethyl acetate used for the extraction purpose was purchased from local solvent suppliers and distilled before its use. Palmitic, stearic, and oleic acid were obtained from *Pongamia* oil and palm oil. Other fatty acids (C6, C8, C10 and C12) were purchared from local commercial sources. All ^1H NMR and ^{13}C NMR were recorded in 400 MHz and 100 MHz Brucker instruments using $CDCl_3$-TMS as a solvent. A modified microwave oven equipped with a reflux condenser was used for all the reactions. The modification of the microwave oven was done according to earlier report in the book, *Microwaves in Organic Synthesis* by A Loupy, p. 872, *Figure 19.12* (Loupy, 2004). The frequency of microwaves was 2.45 GHz. After microwave irradiation, the final temperatures of the reactions were 175°C-190°C.

General Procedure for the Synthesis of 2-Oxazoline Using Hβ-zeolite

One mmol of stearic acid *(Table 1*, entry 6, 284 mg) and 3 mmol of 2-amino-2-methyl-1-propanol (267 mg) were added to a round bottom flask (*Figure 1*). To this mixture Hβ-zeolite (30 mg) was added. Afterwards, it was exposed to microwaves at 360 W for 9 min. The final reaction temperature was 175°C. The reaction was monitored by TLC. After the reaction the resulting mixture was cooled down to room temperature and diluted with ethyl acetate (10 ml). The catalyst was filtered off and the reaction mixture was poured into saturated $NaHCO_3$ solution (5 ml) to ensure the removal of unreacted free acid. Then, the product was extracted using ethyl acetate from aqueous layer. The combined organic layer was dried over sodium sulphate and concentrated under reduced pressure. The obtained residue was purified by a silica column chromatography using pentane: EtOAc (80v: 20v).

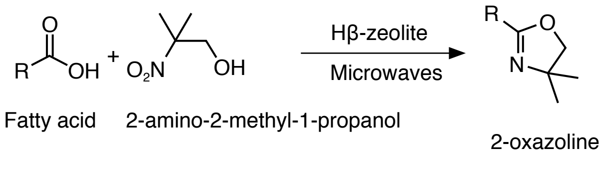


Figure 1. Synthesis of 2-oxazolines from fatty acids.

General Procedure for the Synthesis of 2-Oxazoline in Absence of Hβ-zeolite

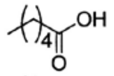
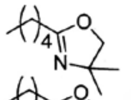
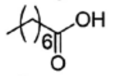
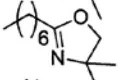
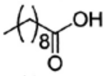
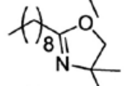
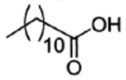
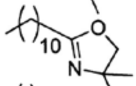
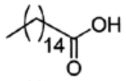
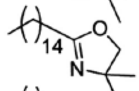
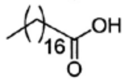
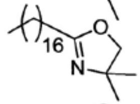
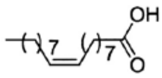
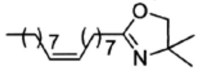
One mmol of stearic acid (*Table 1*, entry 6, 284 mg) and 3 mmol of 2-amino-2-methyl-1-propanol (267 mg) were added to a round bottom flask. Afterwards, it was exposed to microwaves at 360 W for 9 min. The reaction was monitored by TLC. After reaction the obtained mixture was cooled down to room temperature and diluted with ethyl acetate (10 ml). The reaction mixture was poured into saturated $NaHCO_3$ solution (5 ml) to ensure the removal of unreacted free acid. Then the product was extracted using ethyl acetate from the aqueous layer. The combined organic layer was dried over sodium sulphate and concentrated under reduced pressure. The obtained residue was purified by a silica gel column chromatography using pentane: ethyl acetate (80v: 20v) as a solvent system.

RESULTS AND DISCUSSION

Fatty acids are converted to fatty acid esters, triglycerides, polymers, triazole, dicarboxylic acids, hydroxyl fatty acids and various other value-added compounds. In particular, 2-oxazolines derived from fatty acids are used as reactive diluents (Berry-Walker *et al*., 2005). In this work, a range of fatty acids (C6-C18) were converted to corresponding 2-oxazolines under microwave irradiation. Initial experimental results revealed that acetic acid (C2) and butyric acid (C4) did not yield the corresponding 2-oxazolines; whereas, the expected 2-oxazoline was obtained for octanoic acid (C8). For the first time a series of 2-oxazolines were synthesised from fatty acids in the presence of Hβ-zeolite and microwaves Hβ-zeolite was found to be a good catalyst and support for this cyclisation reaction. Yield of the corresponding 2-oxazoline was between 68%- 94%.

In order to establish a correlation between chain length of aliphatic carboxylic acid and formation of 2-oxazoline, experiments were performed using hexanoic and valeric acids. Valeric acid did not yield the product while hexanoic acid did. These results suggest that smaller aliphatic acids *viz*. acetic acid, butyric acid, valeric acid are too small to be retained inside the cavity of Hβ-zeolite. Therefore, they cannot establish contact with the active acidic sites of Hβ-zeolite. Different carboxylic acids *viz*. hexanoic acid, octanoic

TABLE 1. SYNTHESIS OF 2-OXAZOLINES FROM VARIOUS FATTY ACIDS

Entry	Fatty acid	2-Oxazoline	Time (min)	Yield (%^{a,b})
1			12	68
2			12	74
3			11	82
4			10	81
5			9	89
6			9	94
7			9	92

Note: ^{a}Isolated yield after column chromatography.
^{b}All compounds were characterised by 1H NMR,13C NMR and ESI-MS.

acid, decanoic acid, dodecanoic acid, hexadecanoic acid, octadecanoic acid and octadecenoic acid gave the corrosponding 2-oxazolines in 68%-94% yield (*Table 1*). A representative spectral characterisation of a fatty acid 2-oxazoline is presented below:

2-Heptadecyl-4, 4-dimethyl-4, 5-dihydro-1, 3 oxazole (Sharma *et al*., 2009), entry 6: yield: 94% (317 mg, white solid): 1H NMR (400 MHz, CDCl3-TMS) δ: 0.89-0.86 (t, J = 6.4 HZ, 3 H), 1.29-1.25 (br.s, 22 H), 1.60 (m, 2 H), 2.25-2.21 (t, J = 8 Hz, 2 H), 3.89 (s, 2 H) ppm; 13C NMR (100 MHz, CDCl3-TMS): δ 14.0, 22.6, 26.2, 28.1, 28.3, 29.1, 29.2, 29.3, 29.4, 29.5, 29.6, 29.7, 31.9, 66.7, 78.8, 166.2 ppm. (ESI-MS) m/z: (M+H)+ 338.34.

Microwave reactions in the presence and absence of Hβ-zeolite were carried out. When stearic acid was reacted with 2-amino-2-methyl-1-propanol for 9 min, 94% of the corrosponding 2-oxazoline was obtained in the presence of Hβ-zeolite; whereas, in the absence of Hβ-zeolite, only 70% of 2-oxazoline was obtained.

However, under similar reaction conditions acetic acid, butyric acid, and valeric acid failed to give the desired products. In the absence of zeolite both long chain and short chain fatty acids gave small quantities of amides as observed by TLC. Along this line, it was already reported that acetic acid and propionic acid did not yield the corresponding 2-oxazolines when another zeolite (Ersorb-4) was used as a catalyst (Cwik *et al*., 2002).

A plausible mechanism for the synthesis of 2-oxazolines from fatty acids is presented in *Figure 2*. The first step for the synthesis is the formation of amides by the dehydration of ammonium salts of aliphatic carboxylic acids (*Figure 2*). Previously, it was reported that the cyclisation leading to 2-oxazoline is possible only in the presence of at least two hydroxyl functional groups in amino alcohols (Tellado *et al*., 2003). When a second hydroxyl group is absent in amino alcohol, *e.g*. 2-amino-2-methyl-1-propanol the

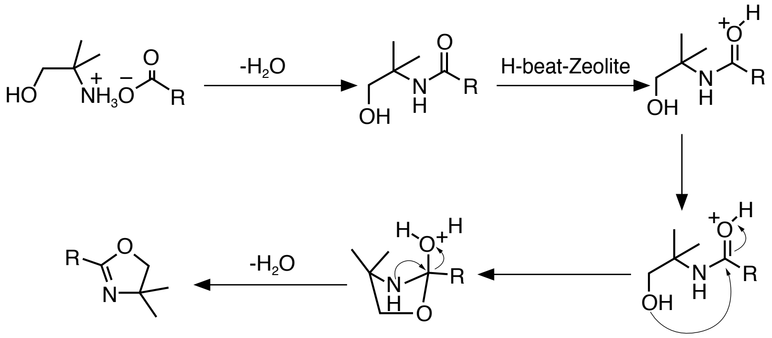


Figure 2. Mechanism of 2-oxazoline formation by the reaction of fatty acid and 2-amino-2-methyl-1-propanol.

condensation require a catalyst to proceed (Tellado *et al*., 2003). In the present case, probably the acidic site of Hβ-zeolite was coordinating with the carbonyl oxygen of the amide; thereby, facilitating the nucleophilic attack of alcohol on the carbonyl carbon of the amide (*Figure 2*). However, on the contrary, Sharma *et al*. (2009) described a method where carboxylic acids were condensed with excess 2-amino-2-methyl-1-propanol to yield 2-oxazolines under microwaves and catalyst-free condition (Sharma *et al*., 2009). Earlier kaolinitic clay and acidic adsorbent Ersorb-4 were used for the synthesis of 2-oxazolines from nitriles (Ganeswara *et al*., 1998) and carboxylic acids (Cwik *et al*., 2002).

CONCLUSION

Small (C6 and C8), medium (C10 and C12) and long (C16 and C18) chain fatty acids were successfully employed for the preparation of corresponding 2-oxazolines. The Hβ-zeolite was used as a catalyst and support to facilitate the cyclisation and dehydration reaction. The work-up and purification method described here is safe, clean, and high yielding. This method can be applied in oleochemical industries for the preparation of 2-oxazolines from oil palm, edible oils, non-edible oils and other feedstocks containing fatty acids.

REFERENCES

BANDGAR, B P and PANDIT, S S (2003). Direct synthesis of 2-oxazolines from carboxylic acids using 2-chloro-4,6-dimethoxy-1,3,5-triazine under mild conditions. *Tetrahedron Lett., 44*: 2331-2333.

BERRY-WALKER, Y; SHEETS, A C and TRUMBO, D L (2005). Use of a fatty acid oxazoline derivative as a reactive diluent. *Surface Coatings International Part B: Coatings Transactions, 88*: 231-316.

BOLM, C; WEICKHARDT, K; ZEHNDER, M and RANFF, T (1991). Synthesis of optically active Bis (2-oxazolines): crystal structure of a 1,2-Bis (2-oxazolinyl)benzene $ZnCl_2$ complex. *Chem Ber., 124*: 1173-1180.

CWIK, A; HELL, Z; HEGEDUS, A; FINTA, Z and HORVATH, Z (2002). A simple synthesis of 2-substituted oxazolines and oxazines. *Tetrahedron Lett., 43*: 3985-3987.

FRUMP, J A (1971). Oxazolines. Their preparation, reactions, and applications. *Chem Rev., 71 (5)*: 483-505.

GANESWARA, G K; DESHPANDE, V. H; LALITHAMBIKA, M; RAVINDRANATHAN, T and BEDEKAR, A V (1998). Natural kaolinitic clay catalyzed conversion of nitriles to 2-oxazolines. *Tetrahedron Lett., 39*: 459-462.

GRANT, T G and MEYERS, A I (1994). The chemistry of 2-oxazolines (1985-present). *Tetrahedron, 50*: 2297-2360.

KARMEE, S K and CHADHA, A (2005a). Rapid and simple method of monoacylation of polyols by β-ketoesters using microwave irradiation. *Synth Commun., 35*: 1151-1160.

KARMEE, S K (2011). The synthesis, properties, and applications of ascorbyl esters. *Lipid Technol., 23 (10)*: 227-229.

KARMEE, S K (2012). A two step chemo-enzymatic method for the synthesis of fatty acid ascorbyl esters. *J. Oil Palm Res. Vol. 24*: 1518-1523.

KARMEE, S K (2014). Lipase catalyzed synthesis of fatty acid methyl esters from crude *Pongamia* oil. *Energy Sources, Part A: Recovery, Utilization, and Environmental Effects*. In press, DOI: 10.1080/15567036.2011.572131.

KARMEE, S K (2013). A chemo-enzymatic reaction sequence for the synthesis of dihydroxyacetone phosphate stock material. *Synth Commun., 43*: 450-455.

KARMEE, S K (2008). Lipase catalyzed synthesis of surfactants from biomass derivatives. *Biofuels Bioprod Bioref, 2 (2)*: 144-154.

KARMEE, S K (2009). Biocatalytic synthesis of ascorbyl esters and their biotechnological applications. *Appl Microbiol Biotechnol., 81(6)*: 1013-1022.

KARMEE, S K and CHADHA, A (2005b). Preparation of biodiesel from crude oil of *Pongamia pinnata. Bioresource Technology, 96*: 1425-1429.

KATRITZKY, A R; CAI, C; SUJUKI, K and SINGH, S K (2004). Facile syntheses of oxazolines and thiazolines with N-acylbenzotriazoles under microwave irradiation. *J. Org. Chem., 69*: 811-814.

LOUPY, A (2004). *Microwaves in Organic Synthesis*. John Wiley & Sons, Germany.

MARRAERO-TERRERO, A L and LOUPY, A (1996). Synthesis of 2-oxazolines from carboxylic acids and α,α,α-Tris(hydroxymethyl) methylamine under microwaves in solvent-free conditions. *Synlett., 245*.

MEYERS, A I and MIHELICH, E D (1976). The synthetic utility of 2-oxazolines. *Angew Chem Int Ed Engl., 15*: 270-281.

OUSSAID, B; BERLAN, J; SOUFIAOUI, M and GARRIGUES, B (1995). Improved synthesis of oxazoline under microwave irradiation. *Synth Commun., 25*: 659-665.

REUMAN, M and MEYERS, A I (1985). The synthetic utility of oxazolines in aromatic substitution. *Tetrahedron, 41*: 837-860.

SHARMA, R; VADIVEL, S K; DUCLOS, JR R I and MAKRIYANNIS, A (2009). Open vessel mode microwave-assisted synthesis of 2-oxazolines from carboxylic acids. *Tetrahedron Lett., 50*: 5780-5782.

TELLADO, F G; LOUPY, A; PETIT, A and TERRERO, A L M (2003). Solvent-free microwave-assisted efficient synthesis of 4,4-disubstituted 2-oxazolines. *Eur J Org Chem.*: 4387-4391.

VOBRUGGEN, H and KROLIKIEWICZ, K (1993). A simple synthesis of Δ2-oxazines, Δ2-oxazines, Δ2-thiazolines and 2-substituted benzoxazoles. *Tetrahedron, 49*: 9353-9372.