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FATTY ACID DISUBSTITUTED 1, 2, 3-TRIAZOLES: MICROWAVE IRRADIATED SYNTHESIS AND *IN VITRO* EVALUATION OF ANTIMICROBIAL POTENTIAL

Fatima Zohra Abdelhadi-Bessedik[a], Soulef Dib[b], Valérie Rolland [c], Nadia Kambouche[a], Salima Bellahouel-Benzine[a*].

[a]*Laboratoire de Synthèse Organique Appliquée, Département de Chimie, Université Oran1, BP 1524 EL Mnaouer, 31000 Oran, Algérie*
[b]*Laboratoire de Biologie des Microorganismes et de Biotechnologies, Université Oran1, BP 1524 El Mnaouer 31000 Oran, Algérie*
[c]*IBMM UMR 5247 UM-CNRS-ENSCM,Campus Triolet Montpellier, France.*
**E-mail: salimabellahouel@yahoo.fr, bellahouel.salima@univ-oran1.dz*

Abstract
Fatty acid disubstituted 1,2,3-triazoles were prepared under optimum conditions via Huisgen's terminally induced 1,3-dipolar cycloaddition between azide and propargylic acid under microwave irradiationsand then evaluated for their antibacterial and antifungal properties. Use of dimethylformamide as solvent during 3 hours at temperature of 60°C and after 3hours was the best combination to improve reaction yield. Synthesized compounds were obtained with high yields and characterized by spectroscopy ^{1}H and ^{13}C nuclear magnetic resonance NMR, high performance liquid chromatography HPLC and mass spectrometry coupling with liquid chromatography LC-MS, their antibacterial and antifungal activities were studied in vitro using the disc diffusion method. The results showed that the 1,4 isomer is predominant. Activity against two bacterial strains (Gram positive bacteria and Gram negative bacteria) and two fungal strains was discussed. The obtained new triazoles derivatives showed potential activity against assayed bacteria (Escherichia coliATCC 8739,StaphylococcusaureusATCC 6538) and fungal strain CandidaalbicansATTC 1023.

Keywords: Fatty acid1,2,3-triazole, microwave irradiation,(1,3)-dipolar cycloaddition,antibacterial and antifungal activities.

Introduction

The 1H-1,2,3-triazole have been studied for many years as an important class of heterocyclic compounds, and they attract considerable attention of chemists and biologists due to their use on board a range of biological activities. More recently, they had significant interest in the development of novel triazole with anti-inflammatory[i]activity, anti-microbial[ii]activity, anti-bacterial[iii] activity, anti-cancer[iv] and anti-viral[v]as well as activities against several neglected diseases.

1,2,3-triazoles are five-membered rings with three nitrogen atoms in the ring. They are attractive prototypes because of their great stability even in a strong oxidizing and reducing environment and also for their propensity to form a hydrogen bond increasing their solubility which promotes binding to biomolecular targets[vi].

Many synthetic methodologies have been developed for synthesis of the 1,2,3-triazole moiety, the most popular reaction is the 1,3-dipolar cycloaddition[vii] also known as Huisgen's cycloaddition, between azide and terminal alkyne.Theazidedipolarophile is central structural motifs of biological interest when they are coupled to another heterocyclic ring, they show therapeutic potential in different domain.

Under thermal conditions the cycloaddition 1,3-dipolar was not initially often applied in organic synthesis regarding the poor regioselectivity (1,4- and 1,5-disubstituted 1,2,3-triazoles), heating and a long reaction time required for completion[viii]. Because of mentioned reasons,many research groups have showed interested in developing new synthesis methods.

A great number of publications advocated the use of microwave technology in organic synthesis; it has been successfully applied in chemistry since 1975[ix] and a large number of examples have been described in organic synthesis [x]. Several reviews have been published on the application of this technique to cycloaddition reactions[xi]. The use of microwave irradiations has led to the introduction of new concepts in chemistry because of the absorption and transmission energy is completely different compared to conventional heating mode, this can lead to a significantly reduced reaction times improved yields of product, chemioselectivity and regioselectivity[x,xi].

In this paper, anefficient and easy cycloaddition 1.3-dipolar has been reportedfor the synthesis of fatty acid disubstituted1,2,3-triazole,under microwave irradiations.

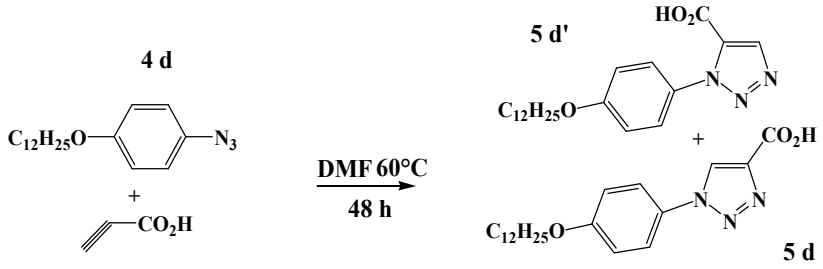
All synthesized compounds were characterized by spectroscopy ^{1}H and ^{13}C nuclear magnetic resonance NMR, high performance liquid chromatography HPLC and mass spectrophotometry coupling with liquid chromatography LC-MS.

In continuation of this work, in vitro evaluation of 1,2,3-triazole compounds antibacterial and antifungal potentialsagainst *Escherichia coli*, *Staphylococcus aureus*, *Candida albicans* and *Aspergilusniger*iscarried out.

Results and discussion

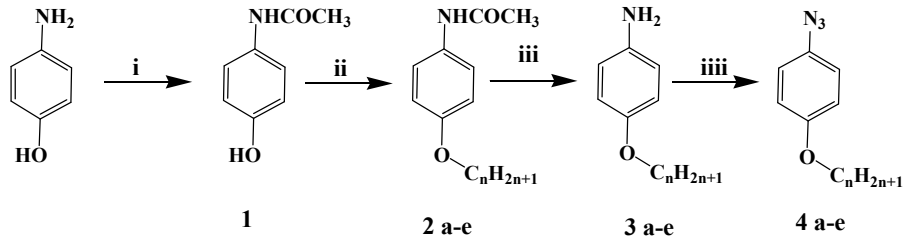
Chemistry

Firstly,the 1H-1,2,3-triazole carboxylic acids were synthetisezedby our teamthrough a 1,3-dipolar cycloaddition between 4-azido-1-dodecyloxybenzene **4d** and propargylic acid, underthermal conditions, using DMF as solvent, after 48 h.Two regioisomers were obtained 1,4- and 1,5- disubstituted 1,2,3-triazole respectively **5d** and **5d'(scheme 1).**



Scheme1: Huisgen's cycloaddition of propargylic acid with substituted azides under thermal conditions

The strategy used to access to the aryl azid (**4a-e)** consists into for steps synthesis (**scheme 2)**: protection of amine function of 4-amino-phenol, etherification of hydroxyl group, deprotection of amine function and azidation of substituted aniline.



Scheme 2: Synthetic pathway of aryl azides **4a-e. (i)** Acetic anhydride, H_2O, 115°C, 24h**. (ii)** $C_nH_{2n+1}Br$ (n= 6,7,8,12,14), K_2CO_3, butanone,80°C,48h. **(iii)** HCl, H_2O,reflux,24h. **(iiii)** HCl, H_2O, $NaNO_2$, NaN_3 , 0-5°C, 2h.

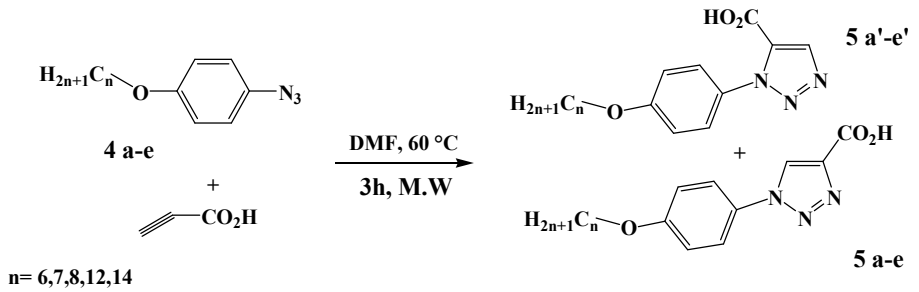
In order to reduce the reaction times, the effect of microwave irradiation on the reactions hasbeen examined. The aryl azides **4d** were simply heated under microwave in the presence of 2 equivalents of propargylic acid, by varying temperature of 60°, 80°, or 100°C, and reaction time 3,6 or 12 hours.The results are shown in **Table 1.**

Table 1: Optimization of operating conditions for the preparation of (**5 d**) and (**5d'**) under microwave irradiations.

Entries	Conditions	T(° C)	time (h)	Yields 5d (%)	Yields 5d' (%)
1	Thermal condition	60	48h	74	11
2			3	70	15
3	M.W	60	6	62	24
4			12	71	28
5			3	65	25
6	M.W	80	6	71	20
7			12	57	34
8			3	73	16
9	M.W	100	6	62	29
10			12	83	12

Where as good results were obtained 70% of (**5d**) just after 3h (**Table 1: entry 2**) comparing with thermal conditions 74% after 48h (**Table 1: entry 1**), this reaction was not regioselective: two regioisomers were obtained with always the higher percentage for the 1,4 isomer.

The reaction conditions were carried out, the same reactions have been realizedby changing length of the fatty chain (**Table 2: entries 1.2.3.4.5**). It observed that this parameter have no influence on yields.The best result is obtained with by chain of 8 carbones (**5 c**) 83%.
(**scheme 3**)



Scheme3: Effect of the length of fatty chains in the synthesis of 1,4 and 1,5 isomers of 1-(4-(dodecyloxy) phenyl)-1-H-[1,2,3]-triazole-carboxylic acid.

Table 2: Yields of 1.4- and 1.5- disubstitued 1,2,3-triazoles **(5 a-e) (5 a'-e').**

Entries	Products	Yields (%)
1	**5a**	70
	5a'	18
2	**5b**	68
	5b'	18
3	**5c**	**83**
	5c'	17
4	**5d**	70
	5d'	15
5	**5e**	68
	5e'	31

Biology

The results obtained on antibacterial and antifungal evaluation of synthesized compounds are presented in **Tables 3 and 4**.

Table 3: Results of antibacterial evaluation of the compounds, after 24h.

Bacterial strains	***Escherichia coli*ATCC 8739**	***Staphylococcus aureus* ATCC 6538**
Compound	**Inhibition zones diameter (mm)**	
	0.01mole/L	**0.01mole/L**
5a	23.1	16.3
5b	16.5	16.3
5c	16	15.2
5d	12.6	12.5
5e	11.6	10.6
5a'	11.1	12.6
DMSO	7.8	8.3

NB : Inhibition zones are including the disc diameter (6mm).

Table 4: Results of antifungal evaluation of the compounds, after 72h.

Fungal strains	***Candida albicans* ATTC 10231**	***Aspergillus niger* ATTC 16404**
Compound	**Inhibition zones diameter (mm)**	
	0.01mole/L	**0.01mole/L**
5a	17	6
5b	11.6	**6**
5c	11.5	6
5d	11.8	6
5e	10.6	6
5a'	12.3	6
DMSO	8.16	6

NB : Inhibition zones are including the disc diameter (6mm).

All tested products are highly active against the Gram negative bacteria *Escherichia coli* ATCC 8739 and Gram positive bacteria *Staphylococcus aureus* ATCC 6538.Generally, this activity depends on the length of the fatty chain of triazole derivatives and on the position of the acid function of the product used.

An exception to this trend is noted for products **5a**, **5b** and **5c** which showed a relatively good effect on bacteria; among these three products, the **5a** was the most reactive on bacteria. For this reason, the **5 a'** substituted in position 1.5 was chosen in order to expect the influence of the position of acid function on the activity.Compound **5a'** shows a weak activity compared to **5a** compound, it can be explained by the stability of the molecule.

Escherichia coli ATCC 8739 is more sensitive than other microbial strains and shows important inhibition zones. It is well known that Gram negative bacteria are generally resistant to antibiotics and drugs[xii–xiv]. Described compounds could be good candidates against this pathogenic Gram-negative bacterium.

The heterocyclic compounds tested *in vitro* against both fungal strains are moderately active on the growth of yeast *Candida albicans*ATTC 10231. On the other hand, they showed no activity against the filamentous fungi *Aspergillus niger*ATTC 16404.

Microbial inhibition was due to the nature of the heterocyclic triazole derivative which contains a long electron donor fatty chain. Electron donor groups have been recognized to increase the electron density that makes the product effective against microorganisms[xv].

A remarkable differences of activity for all tested products was due to the length of the fatty chain,the activity increases when the length is decreased, this is can be explained by the steric hindrance.

The weak antifungal activity and sometimes deficiency are probably due to the resistance of fungal strains[xvi]**.**

Experimental section

Materiel

All starting materials, solvents and culture media for the antimicrobial evaluation (Nutrient agar, Nutrient broth, Mueller-Hinton and Sabouraud) used in the present work were purchased from Sigma-Aldrich, and were used without any further purification.

Chemistry

Thin layer chromatography TLC was performed on ready made silica gel plates Merck 60F254 to examine the completion of reactions and visualization was achieved under ultraviolet UV254 light. Melting points (°C) of the synthesized compounds were obtained using BUCHI510 capillary apparatus and were uncorrected. The ^{1}H and ^{13}C NMR spectra were recorded at 400 MHz on BRUKER AC400 instrument; chemical shifts are quoted in parts per million and were referenced to the residual solvent peak. The following abbreviations used: s, singlet; d, doublet; t, triplet; q, quartet; m, multiple. Coupling constants were reported in Hertz (Hz). Analytic HPLC were performed by AGILENT 1220 using linear gradient of ACN in H_2O with 0.1% TFA in 10 min at 214nm with 5µl/min flow rate. LC-MS: identification was by electrospray on HPLC waters ALLIANCE2690.The microwave used is dedicated to synthesis Biotage Inititiator Microwave synthesizer producing controlled radiation at 2450MHz (parameter fixed hold-time actived).

Synthesis

General procedure for the synthesis of aryl azide :

The starting reagents **4 a-e** were prepared according to the literature procedures for aryleazide[xvii].

General procedure for the synthesis of 1-(4-(alkyloxy) phenyl)-1-H-[1,2,3]-triazole-carboxylic acid:

4-Azido-1-alkyloxybenzene **4a–e** (1 equiv,1.65mmol) and propargyl acid (2 equiv, 3.3 mmol) were dissolved in 3 ml of DMF. The mixture were added in a microwave reactor (2-5ml) of volume at 60°C for 3 h. After solvent evaporation, the residue was washed with diethyl ether to yield the desired 1,4-regioisomer (**5a–e**). The 1,5-regioisomer (**5a'-e'**) can be isolated by evaporation of the filtrate and trituration of the obtained solid in hexane.

In the following section were presented the HPLC, LC-MS and ^{1}H, ^{13}C NMR characterization of only the 1,4 and 1,5 regioisomer triazole derivatives (**5 a-e**) (**5a'-e'**).

1-(4-(hexyloxy)phenyl)-1-H-[1,2,3]-triazol-1-yl-4-carboxylic acid (5a)

White solid, m.p:130°C, yield: 70% ; ^{1}H NMR (400 MHz, DMSO d^6):δ= 0.90 (t, ^{3}J = 6.75 Hz,3H, CH_3), 1.32-1.45 (m, 6H, $CH_3(\underline{CH_2})_3$), 1.72-1.77 (m, 2H, $\underline{CH_2}CH_2O$), 4.05 (t, ^{3}J = 6.5 Hz, 2H, CH_2O), 7.14 (d,^{3}J = 9.06 Hz, 2H, Ar–H), 7.86 (d, ^{3}J = 9.06 Hz, 2H, Ar–H), 9.28 (s, 1H, H-triazole); ^{13}C NMR (126MHz, DMSO d^6):δ= 14.38, 22.55, 25.64, 29, 31.45, 68.44, 115.82, 122.61, 127.31, 129.86, 140.96, 159.56, 162.07; tr: 4.62 min (ACN / H_2O-0.1% TFA, 10min at 214nm); MS (ESI): m/z 290 $[M+H]^+$, 312 $[M+Na]^+$.

1-(4-(hexyloxy)phenyl)-1-H-[1,2,3]-triazol-1-yl-5-carboxylic acid (5a')

Brown solid, m.p: 68°C, yield:18% ; ^{1}H NMR (400 MHz, DMSO d^6):δ= 0.90 (t, ^{3}J = 6.75 Hz, 3H, CH_3), 1.29-1.45 (m, 6H, $CH_3(\underline{CH_2})_3$), 1.71-1.78 (m, 2H, $\underline{CH_2}CH_2O$), 4.05 (t, ^{3}J = 6.5 Hz, 2H, CH_2O), 7.3 (d, ^{3}J = 8.2 Hz, 2H, Ar–H), 7.44 (d, ^{3}J = 8.6 Hz, 2H, Ar–H), 8.7 (s, 1H, H-triazole); ^{13}C NMR (126MHz, DMSO d^6): δ = 14.38, 22.55, 25.64, 29.04, 31.45, 68.37, 115.25, 122.59, 127.51, 129.28, 136.85, 159.65, 162.75; tr : 4.37min (ACN / H_2O-0.1% TFA, 10min at 214nm); MS (ESI): m/z 290 $[M+H]^+$, 312 $[M+Na]^+$.

1-(4-(heptyloxy)phenyl)-1-H-[1,2,3]-triazol-1-yl-4-carboxylic acid (5b)

White solid, m.p: 145°C, yield:68%; ^{1}H NMR (400 MHz, DMSO d^6):δ= 0.88 (t, ^{3}J = 6.9 Hz, 3H, CH_3), 1.29-1.45 (m, 8H, $CH_3(\underline{CH_2})_3$), 1.72-1.76 (m, 2H, $\underline{CH_2}CH_2O$), 4.05 (t, ^{3}J = 6.5 Hz, 2H, CH_2O), 7.14 (d, ^{3}J = 9.06 Hz, 2H, Ar–H), 7.86 (d, ^{3}J = 9.06 Hz, 2H, Ar–H), 9.27 (s, 1H, H-triazole); ^{13}C NMR (126MHz, DMSO d^6):δ= 14.41, 22.51, 25.90, 28.96, 31.70, 68.44,

115.81, 122.64, 127.31, 129.87, 140.98, 159.56, 162.06; tr : 5.02 min (ACN / H_2O-0.1% TFA, 10min at 214nm); MS (ESI): m/z 304 $[M+H]^+$, 327 $[M+Na]^+$.

1-(4-(heptyloxy)phenyl)-1-H-[1,2,3]-triazol-1-yl-5-carboxylic acid (5b')

Brown solid , m.p: 70°C, yield: 18%; ^{1}H NMR (400 MHz, DMSO d^6):δ = 0.90 (t, ^{3}J = 6.75 Hz, 3H, CH_3), 1.30-1.43 (m, 8H, $CH_3(\underline{CH_2})_3$), 1.71-1.78 (m, 2H, $\underline{CH_2}CH_2O$), 4.05 (t, ^{3}J = 6.5 Hz, 2H, CH_2O), 7.05 (d, ^{3}J = 8.9 Hz, 2H, Ar–H), 7.46 (d, ^{3}J = 8.6 Hz, 2H, Ar–H), 8.17 (s, 1H, H-triazole); ^{13}C NMR (126MHz, DMSO d^6): δ = 14.38, 22.55, 25.64, 29, 31.45, 68.44, 115.82, 122.61, 127.31, 129.86, 140.96, 159.56, 162.07; tr : 4.77min (ACN / H_2O-0.1% TFA, 10min at 214nm); MS (ESI): m/z 304 $[M+H]^+$, 327 $[M+Na]^+$.

1-(4-(octyloxy)phenyl)-1-H-[1,2,3]-triazol-1-yl-4-carboxylic acid (5c)

White solid, m.p: 149°C, yield:83%; ^{1}H NMR (400 MHz, DMSO d^6):δ= 0.88 (t, ^{3}J = 6.9 Hz, 3H, CH_3), 1.28-1.45 (m, 10H, $CH_3(\underline{CH_2})_3$), 1.72-1.78 (m, 2H, $\underline{CH_2}CH_2O$), 4.06(t, ^{3}J = 6.5 Hz, 2H, CH_2O), 7.14 (d, ^{3}J = 9.06 Hz, 2H, Ar–H), 7.86 (d, ^{3}J = 9.06 Hz, 2H, Ar–H), 9.25 (s, 1H, H-triazole); ^{13}C NMR (126MHz, DMSO d^6):δ= 14.38, 22.52, 25.92, 29.11, 31.68, 68.49, 115.85, 122.66, 127.28, 129.88, 140.97, 159.60, 162.03; tr : 5.38 min (ACN / H_2O-0.1% TFA, 10min at 214nm); MS (ESI): m/z 318 $[M+H]^+$, 340 $[M+Na]^+$.

1-(4-(octyloxy)phenyl)-1-H-[1,2,3]-triazol-1-yl-5-carboxylic acid (5c')

Brown solid, m.p: 74°C, yield:17%; ^{1}H NMR (400 MHz, DMSO d^6):δ = 0.90 (t,^{3}J = 6.75 Hz, 3H, CH_3), 1.29-1.46 (m, 10H, $CH_3(\underline{CH_2})_3$), 1.72-1.78 (m, 2H, $\underline{CH_2}CH_2O$), 4.05 (t, ^{3}J = 6.5 Hz, 2H, CH_2O), 7.06 (d, ^{3}J = 8.9 Hz, 2H, Ar–H), 7.46 (d, ^{3}J = 8.6 Hz, 2H, Ar–H), 8.17 (s, 1H, H-triazole); ^{13}C NMR (126MHz, DMSO d^6): δ = 14.40, 22.56, 25.94, 29.17, 31.46, 68.41, 115.21, 122.53, 127.30, 129.86, 141.15, 159.68, 162.44; tr : 5.16 min (ACN / H_2O-0.1% TFA, 10min at 214nm); MS (ESI): m/z 318 $[M+H]^+$, 340 $[M+Na]^+$.

1-(4-(dodecyloxy) phenyl)-1-H-[1,2,3]-triazol-1-yl-4-carboxylic acid (5d)

White solid, m.p: 153°C,yield: 70%; ^{1}H NMR (400 MHz, DMSO d^6):δ= 0.85 (t, ^{3}J = 6.7 Hz, 3H, CH_3), 1.25-1.43 (m, 18H, $CH_3(\underline{CH_2})_3$), 1.70-1.77 (m, 2H, $\underline{CH_2}CH_2O$), 4.04 (t, ^{3}J = 6.5 Hz, 2H, CH_2O), 7.13 (d, ^{3}J = 9. Hz, 2H, Ar–H), 7.86 (d, ^{3}J = 6.1 Hz, 2H, Ar–H), 9.21 (s, 1H, H-triazole); ^{13}C NMR (126MHz, DMSO d^6):δ= 14.42, 22.5, 25.90, 29.21, 31.76, 68.43, 115.82, 122.62, 127.29, 129.87, 140.97, 159.56, 162.07; tr : 6.77 min (ACN / H_2O-0.1% TFA, 10min at 214nm); MS (ESI): m/z 374 $[M+H]^+$, 396 $[M+Na]^+$.

1-(4-(dodecyloxy)phenyl)-1-H-[1,2,3]-triazol-1-yl-5-carboxylic acid (5d')

Yield:15%, brown solid, M.p: 80°C; ^{1}H NMR (400 MHz, DMSO d^6):δ= 0.90 (t, ^{3}J = 6.75 Hz, 3H, CH_3), 1.23-1.40 (m, 18H, $CH_3(\underline{CH_2})_3$), 1.69-1.74 (m, 2H, $\underline{CH_2}CH_2O$), 4.05 (t, ^{3}J = 6.5 Hz, 2H, CH_2O), 7.03 (d, ^{3}J = 8.9 Hz, 2H, Ar–H), 7.42 (d, ^{3}J = 8.9 Hz, 2H, Ar–H), 8.16 (s, 1H, H-triazole); ^{13}C NMR (126MHz, DMSO d^6): δ = 14.40, 22.56, 25.96, 29, 33.45, 69.13, 114.77, 122.36, 127.66, 129.71, 137.96, 158.68, 159.92; tr : 6.53min (ACN / H_2O-0.1% TFA , 10 min at 214nm); MS (ESI): m/z 374 $[M+H]^+$, 396 $[M+Na]^+$.

1-(4-(tetradecyloxy) phenyl)-1-H-[1,2,3]-triazol-1-yl-4-carboxylic acid (5e)

White solid, m.p: 155°C, yield:68%; ^{1}H NMR (400 MHz, DMSO d^6):δ= 0.86 (t, ^{3}J = 6.9 Hz, 3H, CH_3), 1.24-1.40 (m, 22H, $CH_3(\underline{CH_2})_3$), 1.67-1.77 (m, 2H, $\underline{CH_2}CH_2O$), 4.05 (t, ^{3}J = 6.5 Hz, 2H, CH_2O), 7.21 (d, ^{3}J = 8.8 Hz, 2H, Ar–H), 7.93 (d, ^{3}J = 8.7 Hz, 2H, Ar–H), 9.35 (s, 1H, H-triazole); ^{13}C NMR (126MHz, DMSO d^6):δ= 14.43, 22.56, 25.90, 29.32, 31.76, 68.42,

115.81, 122.61, 127.24, 129.87, 141.13, 159.54, 162.09; tr : 7.54min (ACN / H_2O-0.1% TFA, 10 min at 214nm); MS (ESI): m/z 402 $[M+H]^+$,424 $[M+Na]^+$.

1-(4-(tetradecyloxy)phenyl)-1-H-[1,2,3]-triazol-1-yl-5-carboxylic acid (5e')

Brown solid, m.p: 92°C, yield: 31%; ^{1}H NMR (400 MHz, DMSO d^6):δ= 0.84 (t,^{3}J = 6.75 Hz, 3H, CH_3), 1.28-1.50 (m, 22H, $CH_3(\underline{CH_2})_5$), 1.78-1.81 (m, 2H, $\underline{CH_2}CH_2O$), 4.02 (t,^{3}J = 6.72 Hz, 2H, CH_2O), 7.1 (d^3J = 8.8 Hz, 2H, Ar–H,), 7.83 (d, ^{3}J = 8.8 Hz, 2H, Ar–H), 8.8 (s, 1H, H5-triazole); ^{13}C NMR (126MHz, DMSO d^6):δ= 14.40, 22.57, 25.61, 29.35, 31.77, 70.29, 115.20, 122.52, 127.37, 130.49, 136.85, 159.47, 162.22 ; tr : 6.87min (ACN / H_2O-0.1% TFA, 10 min at 214nm); MS (ESI): m/z 402 $[M+H]^+$, 424 $[M+Na]^+$.

Biology

The synthesized 1,4 and 1,5 disubstituted 1,2,3-triazole (**5 a-e)** and (**5 a'**) were evaluated for their *in vitro* antimicrobial potential against one Gram positive bacterial strain *Staphylococcus aureus* ATCC 6538, one Gram negative bacterial strain *Escherichia coli* ATCC 8739, and two fungal strains *Candida albicans* ATCC 10231 and *Aspergillus niger*ATTC 16404. Evaluation of antimicrobial activity was determined using the disc diffusion method[xviii,xix].

Inoculum preparation

The bacterial strains were grown overnight at 37°C in Nutrient agar, while fungal strains were grown at 25°C in Sabouraud for 72h. Inoculum for the assays was prepared by inoculating colonies from the agar plate culture into 10 mL of Nutrient broth and then incubated at 37°C (24h) for bacterial strains and at 25°C (72h) for fungal strains. After growing, the microbial suspensions were standardized to 10^8 CFU/mL for bacterial strains (using the 0.5 Mc Farland turbidity standards) and 10^5 cells/mL for fungal strains (using the Thoma cell counting chamber).

Antimicrobial evaluation

Each microbial suspension was spread over the surface of Muller-Hinton plates and Sabouraud plates, for bacterial and fungal strains, respectively. The plates containing discs (6mm Ø, Whatman No. 3) impregnated with 10 µL of compound solutions (prepared by dilution in sterile DMSO to attain the final concentration of 0.01mole/L). The plates were then incubated at 37°C (24h) for bacterial strains and at 25°C (72h) for fungal strains. The results were expressed in term of inhibition zones diameter. All tests were performed in triplicates. Solvent (DMSO) was used as a negative control against microbial strains.

Conclusion

An easy and efficient cycloaddition 1.3-dipolar of aryl azide with propargyl acid for the synthesis of fatty acid disubstituted 1.2.3-triazole, assisted by microwave were carried out under mild reaction conditions in a lower time and producing good yields.

Only the compounds (**5a-e and 5a'**) showed an activity towards the pathogenic microorganisms: *E. coli* ATCC 8739, *S. aureus* ATCC 6538 and *C.albicans* ATTC 10231 except with the fungal strain of *Aspergillus niger*ATTC 16404.

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Conflict of interests
No conflict of interests is declared by the authors.

References
i. S. Haider, M. S. Alam, H. Hamid, S. Shafi, A. Nargotra, P. Mahajan, S. Nazreen, A. M. Kalle, C. Kharbanda, Y. Ali, A. Alam, and A. K. Panda, Eur. J. Med. Chem. **70**, 579 (2013).
ii. C. P. Kaushik, K. Kumar, S. K. Singh, D. Singh, and S. Saini, Arab. J. Chem. **9**, 865 (2016).
iii. C. Bengtsson, A. E. G. Lindgren, H. Uvell, and F. Almqvist, Eur. J. Med. Chem. **54**, 637 (2012).
iv. R. M. Kumbhare, T. L. Dadmal, R. Pamanji, U. B. Kosurkar, L. R. Velatooru, K. Appalanaidu, Y. K. Rao, and J. V. Rao, Med. Chem. Res. **23**, 4404 (2014).
v. D. G. Piotrowska, J. Balzarini, and I. E. Głowacka, Eur. J. Med. Chem. **47**, 501 (2012).
vi. W. S. Horne, M. K. Yadav, C. D. Stout, and M. R. Ghadiri, J. Am. Chem. Soc. **126**, 15366 (2004).
vii. R. Huisgen, Angew. Chemie **2**, 633 (1963).
viii. R. Huisgen, G. Szeimies, and L. Möbius, Chem. Ber. **100**, 2494 (1967).
ix. A. Loupy, *Wave-Material Interactions, Microwave Technology and Equipment.In Microwaves in Organic Synthesis*, Wiley-VCH: (2002).
x. A. Hoz, A. Diaz-Ortiz, and A. Moreno, Curr. Org. Chem. **8**, 903 (2005).
xi. S. Zeghada, G. Bentabed-Ababsa, A. Derdour, S. Abdelmounim, L. R. Domingo, J. A. Sáez, T. Roisnel, E. Nassar, and F. Mongin, Org. Biomol. Chem. **9**, 4295 (2011).
xii. K. Poole, Curr. Opin. Microbiol. **4**, 500 (2001).
xiii. M. T. Roe and S. D. Pillai, Poult. Sci. **82**, 622 (2003).
xiv. R. Gómez-Lus, Int. Microbiol. **1**, 279 (1998).
xv. N. C. Desai, N. Bhatt, and H. Somani, Med. Chem. Res. **24**, 258 (2014).
xvi. H. A. Torres, R. Y. Hachem, R. F. Chemaly, D. P. Kontoyiannis, and I. I. Raad, Lancet Infect. Dis. **5**, 775 (2005).
xvii. S. Benallou, S. Saidi-Besbes, E. Grelet, A. Bentaleb, A. Elaissari, G. Agusti, and A. Derdour, Liq. Cryst. **43**, 505 (2016).
xviii. M. Balouiri, M. Sadiki, and S. K. Ibnsouda, J. Pharm. Anal. **6**, 71 (2016).
xix. A. W. Bauer. W. M. M . Kirby, J. C. Sherris, M. Turck, Am. J. Clin. Pathol. **45**, 493 (1966).

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