Synthesis and Antibacterial Activity of Oxime Ester Derivatives Containing 16-isopropyl-5,9-dimethyl tetracyclo [10.2.2.0^{1,10}.0^{4,9}] hexadec-15-ene-5,14-Dicarboxyl Group

[1]JIAN LI, [1,2]XIAOPING RAO, [1,2]SHIBIN SHANG*, [1]YANQING GAO AND [1]BINGLEI SONG
[1]*Institute of Chemical Industry of Forestry Products, CAF; Key Lab. of Biomass Energy and Material, Jiangsu Province; National Engineering Lab. for Biomass Chemical Utilization; Key and Lab. on Forest Chemical Engineering, SFA, Nanjing 210042, China.*
[2]*Institute of Forest New Technology, CAF, Beijing 100091, China.*
shangsb@hotmail.com*

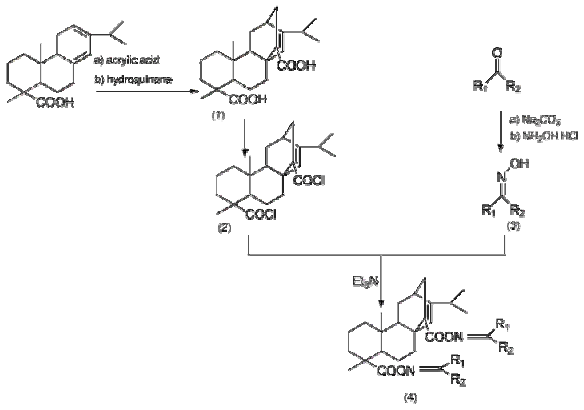
(Received on 17th February.2011, accepted in revised form 7th October, 2011)

Summary: Acrylpimaric acid (16-isopropyl-5,9- dimethyltetracyclo [10. 2. 2. 0^{1,10}.0^{4,9}]hexadec-15-ene-5,14-dicarboxylic acid) was prepared by rosin through Diels-Alder addition reaction, then a series of oxime ester derivatives containing acrylpimaryl (16-isopropyl-5,9-dimethyltetracyclo [10.2.2.0^{1,10}.0^{4,9}]hexadec-15-ene-5,14-dicarboxyl) group were synthesized. Their structures were characterized by IR, ^{1}HNMR, MS, and elemental analysis. The antibacterial activity of these newly synthesized oxime ester derivatives against Gram-negative bacteria and Gram-positive bacteria were also investigated. The results indicate that compounds display extensive anti-bacterial activity against Gram-negative bacteria and Gram-positive bacteria. Especially compounds (4c, 4d, 4f, 4h and 4k) exhibit excellent anti-bacterial activity against Escherichia coli (Gram-negative bacteria). Compared with the diameter of inhibition zone is 9.66mm of the standard compound bromogeramine, which the diameter of inhibition zone is 12.17mm, 10.00mm, 10.33mm, 9.67mm and 9.67mm respectively.

Introduction

As one important natural resource, large amounts of rosin are available in China [1]. Nowadays, rosin and its Diels-Alder adducts have been developed as a feedstock for synthesizing various chemicals and intermediates that are suitable alternative and renewable substitutes for petrochemical-based chemicals [2-4]. For example, acrylpimaric acid (16-isopropyl-5,9- dimethyl-tetracyclo [10.2.2.0^{1,10}.0^{4,9}]hexadec-15-ene-5,14-di-carboxylic acid) with two carboxyl groups is synthesized by reaction of rosin and acrylic acid. This adduct has been used for production of alkyd resins or as a paper sizing agent [5], coatings [6, 7], adhesives [8], surfactant [9] or photoresist [10].

Recently, oxime ester and ether derivatives compounds attracted considerable attention to agrochemical and medicinal research, because their excellent bioactivities such as insecticida1 [11, 12], fungicidal activity [13], herbicidal [14, 15], antitumor [16, 17] and antiphytoviral [18, 19]. Since Tranid- the first oxime ester was developed in 1963 [20], a large number of investigations on their synthesis and biological activities have been reported during the last forty years. In this paper, we have synthesized a series of oxime ester derivatives from rosin, and also investigated their antimicrobial activity. This exploration would promote the application of rosin in antimicrobial activity aspects. Synthetic routes and R_1 and R_2 substituted groups of oxime ester derivatives containing acrylpimaryl (16-isopropyl-5,9-dimethyl-tetracyclo [10.2.2.0^{1,10}.0^{4,9}]hexadec-15-ene-5,14-di-carboxyl) group were shown in Scheme 1 and Table-1, respectively.



Scheme 1: Synthetic routes of the target chemicals.

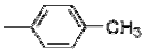
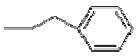
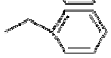
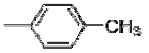
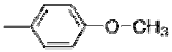
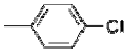
Results and Discussion

Acrylpimaric acid was obtained by the Diels-Alder addition reaction between rosin and acrylic acid. Due to the complexity of the reaction, two isomers were identified using GC. Therefore, further treatment is required. Though there are some purification methods for acrypimaric acid, there are many restrictions, for example, poor separation efficiency [21, 22]. In previous work, we separated

*To whom all correspondence should be addressed.

and purified acrylpimaric acid through ethanol washing efficiently and got one of its isomers, as 16-isopropyl-5,9-dimethyltetracyclo [10.2.2.$0^{1,10}$.$0^{4,9}$] hexadec-15-ene-5,14-dicarboxylic acid, meanwhile its crystal structure was also determined [23, 24].

Table-1: R_1 and R_2 substituted groups of oxime ester derivatives containing acrylpimaryl group.

Compounds	R_1	R_2
4a		H
4b		H
4c		H
4d		
4e		
4f		
4g		
4h		
4i		
4j		
4k		H
4l		

The preparation of compounds (3) is the key step for the synthesis of compounds (4). The yield may be affected by solvent or base [13, 17]. In this paper, diphenyl ketone is selected to optimize the reaction conditions. When sodium carbonate is used for base, ethanol, THF, and acetone have the yield ranging from 86% to 83%, much higher than DMF and Methanol, 75% and 60%, respectively (entries 1, 2, 3, 4 and 9 in Table-2). Sodium carbonate also demonstrates as the best base, compared to sodium hydroxide (50%) and triethylamine (46%) (entries 5, 7 and 9 in Table-2), when ethanol is used as solvent. Therefore, ethanol and sodium carbonate are selected as solvent and base in preparing compounds (3).

Twelve newly synthesized compounds were screened for their antibacterial activity against two kinds of bacteria, namely, Staphylococcus aureus (Gram-positive bacteria) and Escherichia coli (Gram-negative bacteria). Some of them were comparable to standard bromogeramine and Ofloxacin. The antimicrobial action of oxime ester derivatives containing acrylpimaryl group against tested micro-organisms is presented in Table-3. The primary biological test showed that compounds possess good anti-bacterial activity. Among them, compounds (4c, 4d, 4f, 4h and 4k) exhibit anti-bacterial activity against Escherichia coli (Gram-negative bacteria), which the diameter of inhibition zone is 12.17mm, 10.00mm, 10.33mm, 9.67mm and 9.67mm respectively, compared with the 9.66mm of standard compound bromogeramine. In addition, these compounds demonstrate mild antibacterial activity against Staphylococcus aureus (gram-positive bacteria). In contrast, non-modified rosin shows some antibacterial activities over Gram-positive bacteria only [25-28]. The oxime ester derivatives containing acrylpimaryl group show the potential to be a wide-spectrum anti-bacterial agent.

Table-2: Synthesis of benzophenone oxime under various reaction conditions.

Entry	Solvent	temp./ °C	Base	yield/%
1	THF	25	Sodium carbonate	83
2	Acetone	25	Sodium carbonate	85
3	DMF	25	Sodium carbonate	75
4	Methanol	25	Sodium carbonate	60
5	Ethanol	25	Sodium hydroxide	50
6	Ethanol	reflux	Sodium hydroxide	50
7	Ethanol	25	Triethylamine	46
8	Ethanol	reflux	Triethylamine	46
9	Ethanol	25	Sodium carbonate	86
10	Ethanol	reflux	Sodium carbonate	86

[a] reaction condition: diphenyl ketone (10 mmol), hydroxylammonium (15 mmol), solvent (150 mL), base (50 mmol)

Table-3: Inhibition zone (mean diameter of inhibition/mm) as a criterion of antibacterial activity of the newly synthesized title compounds (256 μg/mL solution in ethanol).

Compound	Escherichia coli (Gram-negative bacteria)	Staphyloccocus aureus (Gram-positive bacteria)
4a	8.00	11.00
4b	8.00	12.00
4c	12.17	13
4d	10.00	12.33
4e	8.00	12.17
4f	10.33	12.00
4g	8.00	12.50
4h	9.67	12.67
4i	9.00	13.00
4j	8.50	13.00
4k	9.67	12.33
4l	9.00	13.00
Bromogeramine	9.66	24.67
Ofloxacin	44.00	23.00

Experimental

Materials and Instruments

Rosin and compound formaldoxime (3a) was obtained from a commercial source and used without further purification. All other chemicals were of reagent grade. The IR spectra were taken on a Nicolet IS10 FT-IR (Nicolet, Madison, USA) spectrophotometer. The ^{1}H NMR spectra were recorded on a Bruker AV-500 (Bruker, Karlsruhe, Germany) nuclear magnetic resonance spectrometer with $CDCl_3$ as solvent and TMS as internal standard. The MS spectra were taken on an Agilent-5973 (Agilent, Santa Clara, USA) spectrophotometer. The

melting points were determined using XT-5 (Saiao, Beijing, China) melting point apparatus. The elemental analysis (C, H, N) was performed on a Vario EL-III (Elementar, Hanau, Germany) elemental analyzer, their results were found to be in good agreement with the calculated values (within ±0.5%). All reactions were traced by the thin layer chromatography (TLC).

General Synthetic Procedure for Acrylpimaric Acid (16-Isopropyl-5,9-dimethyltetracyclo [10.2.2.0^{1,10}.0^{4,9}] hexadec-15-ene-5,14-dicarboxylic Acid) (**1**)

According to the literature [29-31], the gum rosin 1000 g and hydroquinone 5 g were charged to a flask equipped with a stirrer, dropping funnel, N_2 inlet, thermometer, and water trap topped with water cooled condenser. The rosin was heated under a slow stream of nitrogen. Stirring begins after the rosin had melted. The temperature was adjusted to 220 °C and the acrylic acid were added dropwise within 0.3 h. Then the mixture was heated up to 230 °C for a residence time of 4 h and the product were poured out after cooling to 170 °C. The adduct were purified by crystallization with ethanol and sodium salts.

General Synthetic Procedure for Acrylpimaryl Chloride (16-Isopropyl-5,9- dimethyltetracyclo [10.2.2.0^{1,10}.0^{4,9}] hexadec-15-ene-5,14-dicarbonyl chloride (**2**)

In a 250 mL flask with water cooling condenser, thermometer, drying tube and dropping funnel, 20 mmol acrylpimaric acids and 80 mL dichloromethane were stirred magnetically until the solid was dissolved. After that, 50 mmol thionyl chloride were added dropwise through a dropping funnel within 1 h. After refluxing for 4 h at 65 °C, acrylpimaryl chloride was obtained after removing the dichloromethane and excess thionyl chloride under reduced pressure.

GeneralSynthetic Procedure for Oximes (**3**)

To a solution of aldehyde or ketone 0.1 mol and hydroxylammonium 0.15 mol in ethanol 150 mL, sodium carbonate 0.5 mol was added in batch within 30 min at room temperature. Reacting time depends on the monitoring results of TLC. After that the mixture was poured into ice water, the separated solid was washed with water, dried and recrystallized from ethanol to get title compounds (3) with the yield over 85%.

General Synthetic Procedure for Oxime Ester Derivatives (**4**)

A solution of above acrylpimaryl chloride in 15 mL CH_2Cl_2 were added dropwise to a solution of 60 mmol oxime and 70 mmol triethylamine in 40 mL CH_2Cl_2 within 30 min at the temperature 0-5 °C. After which time the reaction mixture was allowed to warm to room temperature over 2 h and washed with water, then dried with anhydrous $MgSO_4$. Purification of the residue by silica gel chromatography [v (ethyl acetate)/ v (petroleum ether) =10:1) gave compounds **4a-4l**.

(E)-Acetaldehydeoximyl 16-isopropyl- 5,9-dimethyl-tetracyclo [10.2.2.0^{1,10}.0^{4,9}]hexadec-15-ene-5,14 -dicarboxylate (4a, $C_{27}H_{40}N_2O_4$)

TLC R_f=0.58 [V (ethyl acetate)/ V (petroleum ether)= 10:1) 6.42g (70.4%) 4a, yellow solid. M.p.: 175.0-176.2 °C; IR: $\bar{\nu}$ = 2929, 2861 (-CH_3, -CH_2), 1742 (C=O), 1633 (C=N) cm^{-1}. ^{1}HNMR ($CDCl_3$, 300MHz): δ= 8.35 (S, H, -CH=N-), 8.29 (S, H, -CH=N-), 5.40 (S, H, C=CH-), 2.59 (S, H, =C<u>H</u>-$(CH_3)_2$), 2.34-2.35 (m, H, -CH-C=O-), 1.86-1.91 (S, 3H, -CH-), 1.73-1.77 (m, 6H, C<u>H</u>$_3$-CH=N-), 1.07-1.55 (m, 14H, -CH_2-), 0.65-1.33 (S, 12H, -CCH_3) ppm; MS (ESI (+)) m/s 457 (M+H$^+$). Anal. Calc. for $C_{27}H_{40}N_2O_4$: C, 71.02; H, 8.83; N, 6.13. Found: C, 70.88; H, 8.70; N, 6.50.

(E)-Benzaldehyde Oximyl 16-isopropyl- 5,9-dimethyl-tetracyclo [10.2.2.0^{1,10}.0^{4,9}]hexadec-15-ene-5,14-di-carboxylate (4b, $C_{37}H_{44}N_2O_4$)

TLC R_f=0.65 [V (ethyl acetate)/ V (petroleum ether)= 10:1) 7.63g (65.8%) 4b, white solid. M.p.: 172.9-173.6 °C; IR: $\bar{\nu}$ =2924, 2864 (-CH_3, -CH_2), 1766 (C=O), 1612 (C=N), 756, 695 (Ar-H) cm^{-1}. ^{1}HNMR ($CDCl_3$, 300MHz): δ= 8.39 (S, H, -CH=N-), 8.30 (S, H, -CH=N-), 7.69-7.76 (m, 4H, Ar-H), 7.26-7.47 (m, 6H, Ar-H), 5.40 (S, H, C=CH-), 2.60 (S, H, =C<u>H</u>-$(CH_3)_2$), 2.37-2.47 (m, H, -CH-C=O-), 1.83-1.97 (S, 3H, -CH-), 1.17-1.71 (m, 14H, -CH_2-), 0.63-1.27 (S, 12H, -CCH_3) ppm; MS (ESI (+)) m/s 581 (M+H$^+$). Anal. Calc. for $C_{37}H_{44}N_2O_4$: C, 76.52; H, 7.64; N, 4.82. Found: C, 76.31; H, 8.06; N, 4.60.

4-Methylbenzaldehyde Oximyl 16-isopropyl- 5,9-di-methyltetracyclo [10.2.2.0^{1,10}.0^{4,9}]hexadec-15-ene-5,14-dicarboxylate (4c, $C_{39}H_{48}N_2O_4$)

TLC R_f=0.39 [V (ethyl acetate)/ V (petroleum ether)= 10:1) 9.48g (78.0%) 4c, white solid. M.p.: 108.9-110.3 °C; IR: $\bar{\nu}$= IR (cm^{-1}): 2932, 2867 (-CH_3, -CH_2), 1743 (C=O), 1607 (C=N), 812 (Ar-H) cm^{-1}. ^{1}HNMR ($CDCl_3$, 300MHz): δ= 8.35 (S, H, -CH=N-), 8.26 (S, H, -CH=N-), 7.58-7.65 (m, 4H,

Ar-H), 7.17-7.26 (m, 4H, Ar-H), 5.40 (S, H, C=CH-), 2.60 (S, H, =C<u>H</u>-$(CH_3)_2$), 2.36-2.38 (m, H, -CH-C=O-), 2.17 (m, 6H, CH_3-Ar), 1.82-1.85 (m, 3H, -CH-), 1.05-1.78 (m, 14H, $-CH_2-$), 0.65-1.56 (S, 12H, $-CCH_3$) ppm; MS (ESI (+)) m/s 631($M+Na^+$). Anal. Calc. for $C_{39}H_{48}N_2O_4$: C, 76.94; H, 7.95; N, 4.60. Found: C, 76.46; H, 8.41; N, 4.45.

Propan-2-one Oximyl 16-isopropyl- 5,9-dimethyltetracyclo [10.2.2.0^{1,10}.0^{4,9}]hexadec-15-ene-5,14-dicarboxylate (4d, $C_{29}H_{44}N_2O_4$)

TLC R_f=0.67 [V (ethyl acetate)/ V (petroleum ether)= 10:1) 7.68g (79.4%) 4d, white solid. M.p.: 87.1-87.5 °C; IR: $\bar{\nu}$= IR (cm^{-1}): 2927, 2865 ($-CH_3$, $-CH_2$), 1734 (C=O), 1642 (C=N) cm^{-1}. ^{1}HNMR ($CDCl_3$, 300MHz): δ= 5.38-5.40 (m, H, C=CH-), 2.52-2.57 (m, H, =C<u>H</u>-$(CH_3)_2$), 2.33-2.37 (m, H, -CH-C=O-), 2.03-2.17 (S, 3H, -CH-), 1.67-2.06 (S, 12H, N=C-$(CH_3)_2$), 1.03-1.57 (m, 14H, $-CH_2-$), 0.61-1.14 (S, 12H, $-CCH_3$) ppm; MS (ESI (+)) m/s 485 ($M+H^+$). Anal. Calc. for $C_{29}H_{44}N_2O_4$: C, 71.87; H, 9.15; N, 5.78. Found: C, 71.79; H, 9.46; N, 5.48.

(E)-Acetophenone Oximyl 16-isopropyl- 5,9-dimethyltetracyclo [10.2.2.0^{1,10}.0^{4,9}]hexadec-15-ene-5,14-dicarboxylate (4e, $C_{27}H_{40}N_2O_4$)

TLC R_f=0.45 [V (ethyl acetate)/ V (petroleum ether)= 10:1) 10.21g (84%) 4e, white solid. M.p.: 167.3-168.9 °C; IR: $\bar{\nu}$= 2931, 2869 ($-CH_3$, $-CH_2$), 1743 (C=O), 1612 (C=N), 754, 689 (Ar-H) cm^{-1}. ^{1}HNMR ($CDCl_3$, 300MHz): δ= 7.70-7.76 (m, 4H, Ar-H), 7.36-7.49 (m, 6H, Ar-H), 5.41 (S, H, C=CH-), 2.55 (S, H, =C<u>H</u>-$(CH_3)_2$), 2.36-2.47 (m, H, -CH-C=O-), 1.83-1.99 (S, 3H, -CH-), 1.56 (S, 6H, N=C-CH_3), 0.97-1.53 (m, 14H, $-CH_2-$), 0.99-1.44 (S, 12H, $-CCH_3$) ppm; MS (ESI (+)) m/s 609 ($M+H^+$). Anal. Calc. for $C_{27}H_{40}N_2O_4$: C, 76.94; H, 7.95; N, 4.60. Found: C, 77.26; H, 7.68; N, 4.65.

4-Phenylbutan-2-one Oximyl 16-isopropyl- 5,9-dimethyltetracyclo [10.2.2.0^{1,10}.0^{4,9}]hexadec-15-ene-5,14-dicarboxylate (4f, $C_{43}H_{56}N_2O_4$)

TLC R_f=0.48 [V (ethyl acetate)/ V (petroleum ether)= 10:1) 11.28g (85%) 4f, yellow solid. M.p.: 56.0-56.6 °C; IR: $\bar{\nu}$= IR (cm^{-1}): 2927, 2864 ($-CH_3$, $-CH_2$), 1750 (C=O), 1642 (C=N), 746, 699 (Ar-H) cm^{-1}. ^{1}HNMR ($CDCl_3$, 300MHz): δ= 7.03-7.30 (m, 10H, Ar-H), 5.36 (S, H, C=CH-), 4.17 (m, 4H, $-CH_2$-Ar), 2.61 (S, H, =C<u>H</u>-$(CH_3)_2$), 2.33-2.43 (m, H, -CH-C=O-), 1.61-1.97 (m, 3H, -CH-), 1.55 (S, 6H, N=C-CH_3), 0.98-1.48 (m, 18H, $-CH_2-$), 0.57-1.19 (S, 12H, $-CCH_3$) ppm; MS (ESI (+)) m/s 687 ($M+Na^+$). Anal. Calc. for $C_{43}H_{56}N_2O_4$: C, 77.67; H, 8.49; N, 4.21. Found: C, 77.57; H, 8.50; N, 4.30.

1,3-Diphenylpropan-2-one Oximyl 16-isopropyl-5,9-dimethyltetracyclo [10.2.2.0^{1,10}.0^{4,9}]hexadec-15-ene-5,14-dicarboxylate (4g, $C_{53}H_{60}N_2O_4$)

TLC R_f=0.40 [V (ethyl acetate)/ V (petroleum ether)= 10:1) 9.46g (60%) 4g, yellow liquid. IR: $\bar{\nu}$= (cm^{-1}): 2926, 2864 ($-CH_3$, $-CH_2$), 1748 (C=O), 1634 (C=N), 752, 699 (Ar-H) cm^{-1}. ^{1}HNMR ($CDCl_3$, 300MHz): δ= 7.19-7.29 (m, 20H, Ar-H), 5.38 (S, H, C=CH-), 2.88 (m, 8H, $-CH_2$-Ar), 2.83-2.95 (m, H, =C<u>H</u>-$(CH_3)_2$), 2.61-2.73 (m, H, -CH-C=O-), 2.28-2.40 (S, 3H, -CH-), 1.06-1.99 (m, 14H, $-CH_2-$), 0.62-1.17 (S, 12H, $-CCH_3$) ppm; MS (ESI (+)) m/s 811($M+Na^+$). Anal. Calc. for $C_{53}H_{60}N_2O_4$: C, 80.67; H, 7.66; N, 3.55. Found: C, 80.55; H, 7.59; N, 3.60.

1-P-Tolylethanone Oximyl 16-isopropyl-5,9-dimethyltetracyclo [10.2.2.0^{1,10}.0^{4,9}]hexadec-15-ene-5,14-dicarboxylate (4h, $C_{41}H_{52}N_2O_4$)

TLC R_f=0.39 [V (ethyl acetate)/ V (petroleum ether)= 10:1) 10.80g (85%) 4h, white solid. M.p.: 78.9-80.1 °C; IR: $\bar{\nu}$= 2929, 2864 ($-CH_3$, $-CH_2$), 1748 (C=O), 1602 (C=N); 815 (Ar-H) cm^{-1}. ^{1}HNMR ($CDCl_3$, 300MHz): δ= 7.64 (t, J=8.2Hz, 4H, Ar-H), 7.15-7.26 (m, 4H, Ar-H), 5.42 (S, H, C=CH-), 2.60 (S, H, =C<u>H</u>-$(CH_3)_2$), 2.31-2.37 (m, H, -CH-C=O-), 2.17 (m, 6H, CH_3-Ar), 1.63-1.67(S, 3H, -CH-), 1.58 (S, 6H, N=C-CH_3), 1.05-1.57 (m, 14H, $-CH_2-$), 0.67-1.28 (S, 12H, $-CCH_3$) ppm; MS (ESI (+)) m/s 659($M+Na^+$). Anal. Calc. for $C_{41}H_{52}N_2O_4$: C, 77.32; H, 8.23; N, 4.40. Found: C, 77.84; H, 8.40; N, 4.10.

(Z)-1-(4-Methoxyphenyl) Ethanone oximyl 16-isopropyl-5,9-dimethyltetracyclo [10.2.2.0^{1,10}.0^{4,9}]hexadec-15-ene -5,14-dicarboxylate (4i, $C_{41}H_{52}N_2O_4$)

TLC R_f=0.49 [V (ethyl acetate)/ V (petroleum ether)= 10:1) 12.02g (90%) 4i, white solid. M.p.: 74.8-75.2 °C; IR: $\bar{\nu}$= 2925, 2864 ($-CH_3$, $-CH_2$), 1749 (C=O), 1605 (C=N), 831 (Ar-H) cm^{-1}. ^{1}HNMR ($CDCl_3$, 300MHz): δ= 7.71 (t, J=8.7Hz, 4H, Ar-H), 6.88 (t, J=9.0Hz, 4H, Ar-H), 5.42 (S, H, C=CH-), 3.82 (m, 6H, CH_3-O-), 2.62 (S, H, =C<u>H</u>-$(CH_3)_2$), 2.42-2.50 (m, H, -CH-C=O-), 2.33(d, J=13Hz, 3H, -CH-), 2.30 (S, 6H, N=C-CH_3), 1.05-1.54 (m, 14H, $-CH_2-$), 0.67-1.28 (S, 12H, $-CCH_3$) ppm; MS (ESI (+)) m/s 691($M+Na^+$). Anal. Calc. for $C_{41}H_{52}N_2O_4$: C, 73.62; H, 7.84; N, 4.19. Found: C, 74.05; H, 7.98; N, 4.03.

(Z)-1- (4-Chlorophenyl) Ethanone Oximyl 16-isopropyl-5,9-dimethyltetracyclo[10.2.2.0^{1,10}.0^{4,9}] hexadec-15-ene-5,14-dicarboxylate(4j, $C_{39}H_{46}Cl_2N_2O_4$)

TLC R_f=0.40 [V (ethyl acetate)/ V (petroleum ether)= 10:1) 11.22g (83%) 4j, white solid, M.p.: 85.7-86.6 °C; IR: $\bar{\nu}$ = 2929, 2865 (-CH_3, -CH_2), 1753 (C=O), 1614 (C=N), 829 (Ar-H) cm^{-1}. ^{1}HNMR ($CDCl_3$, 300MHz): δ= 7.66-7.72 (m, 4H, Ar-H), 7.32-7.39 (m, 4H, Ar-H), 5.42 (S, H, C=CH-), 2.54 (S, H, =C<u>H</u>-$(CH_3)_2$), 2.42-2.49 (m, H, -CH-C=O-), 2.31-2.36(S, 3H, -CH-), 1.54 (S, 6H, N=C-CH_3), 1.05-1.50 (m, 14H, -CH_2-), 0.67-1.29 (S, 12H, -CCH_3) ppm; MS (ESI9 (+)) m/s 699(M+Na$^+$). Anal. Calc. for $C_{39}H_{46}Cl_2N_2O_4$: C, 69.12; H, 6.84; N, 4.13. Found: C, 68.80; H, 6.92; N, 3.89.

Cyclohexanone Oximyl 16-isopropyl-5,9-dimethyl-tetracyclo [10.2.2.0^{1,10}.0^{4,9}]hexadec-15-ene-5,14-dicarboxy- late (4k, $C_{35}H_{52}N_2O_4$)

TLC R_f=0.58 [V (ethyl acetate)/ V (petroleum ether)= 10:1) 9.59g (85%) 4k, white solid, M.p.: 61.9-62.1 °C; IR: $\bar{\nu}$ = 2930, 2861 (-CH_3, -CH_2), 1744 (C=O), 1639 (C=N) cm^{-1}. ^{1}HNMR ($CDCl_3$, 300MHz): δ= 5.37 (S, H, C=CH-), 2.47-2.66 (S, H, =C<u>H</u>-$(CH_3)_2$), 2.23-2.48 (m, H, -CH-C=O-), 1.93-1.97 (S, 3H, -CH-), 1.21-1.85 (m, 34H, -CH_2-), 0.62-1.05 (S, 12H, -CCH_3) ppm; MS (ESI (+)) m/s 565 (M+H$^+$). Anal. Calc. for $C_{35}H_{52}N_2O_4$: C, 74.43; H, 9.28; N, 4.96. Found: C, 73.99; H, 9.24; N, 4.48.

Benzophenone Oximyl 16-isopropyl-5,9-dimethyl-tetracyclo [10.2.2.0^{1,10}.0^{4,9}]hexadec-15-ene-5,14-dicarboxylate (4l, $C_{49}H_{52}N_2O_4$)

TLC R_f=0.49 [V (ethyl acetate)/ V (petroleum ether)= 10:1) 12.44g (85%) 4l, white solid, M.p.: 71.8-72.1°C; IR: $\bar{\nu}$ = 2928, 2863 (-CH_3, -CH_2), 1754 (C=O), 1667 (C=N), 775, 695 (Ar-H) cm^{-1}. ^{1}HNMR ($CDCl_3$, 300MHz): δ= 7.46-7.57 (m, 8H, Ar-H); 7.25-7.40 (m, 12H, Ar-H); 5.29 (S, H, C=CH-); 2.50 (S, H, =C<u>H</u>-$(CH_3)_2$); 2.31-2.40 (m, H, -CH-C=O-); 2.16 (S, 3H, -CH-); 0.96-1.54 (m, 14H, -CH_2-); 0.48-1.32 (S, 12H, -CCH_3); MS (ESI (+)) m/s 733 (M+H$^+$). Anal. Calc. for $C_{49}H_{52}N_2O_4$: C, 80.30; H, 7.15; N, 3.82. Found: C, 79.98; H, 7.26; N, 4.05.

Antibacterial Activity

The antibacterial activity of chemicals was estimated by a disc paper method. Test chemicals were dissolved in ethanol and sterile water to get a solution of a concentration of 256 μg/mL. As test species, Staphylococcus aureus (gram-positive bacteria) and Escherichia col (Gram-negative bacteria) were cultivated in beef extract-peptone for 1 week. After that, a small amounts of (1 scratch ~ 2 scratch) fresh bacteria from the culture medium were added into the culture solution, and in turn 10 fold dilute the solution to a concentration of (5.0 ~ 10.0) × 10^6 (CFU) mL^{-1}, 1mL above bacterial solution was evenly coated on 90 mm plate of beef extract peptone medium. 6 mm diameter sterile filter paper was dipped in the solution of chemicals for 10 minutes, then taken out and placed on the plate. The inhibition zones were measured in mm at the end of an incubation period of 24 h. Standard compounds bromogeramine and ofloxacin were measured alone. All experiments were conducted in triplicate to be positive at a given concentration [32-34].

Conclusion

The energy crisis has resulted in a serious strain on the prospects for petrochemicals. Rosin is an important nature renewable substitute for petrochemical-based chemicals, we use it for synthesizing a series of oxime ester derivatives containing acrylpimaryl group and estimating their antibacterial activity. The biological assay results indicated that compounds display extensive anti-bacterial activity against Gram-negative bacteria and Gram-positive bacteria. Especially, compounds (4c, 4d, 4f, 4h and 4k) exhibited remarkable anti-bacterial activity against Escherichia coli (Gram-negative bacteria), compared with standard compound bromogeramine. Further investigation of this type of compound is also in progress now.

Acknowledgement

We are grateful to the Forestry Commonwealth Industry Special Foundation of China (No.200704008) for financial support.

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