

Article

Synthesis and Antifungal Activity of Novel 3-Caren-5-One Oxime Esters

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Abstract: A series of novel 3-caren-5-one oxime esters were designed and synthesized by multi-step reactions in an attempt to develop potent antifungal agents. Two *E-Z* stereoisomers of the intermediate 3-caren-5-one oxime were separated by column chromatography for the first time. The structures of all the intermediates and target compounds were confirmed by UV-Vis, FTIR, NMR, ESI-MS, and elemental analysis. The antifungal activity of the target compounds was preliminarily evaluated by the in vitro method against *Fusarium oxysporum* f. sp. *cucumerinum*, *Physalospora piricola*, *Alternaria solani*, *Cercospora arachidicola*, *Gibberella zeae*, *Rhizoctonia solani*, *Bipolaris maydis*, and *Colleterichum orbicalare* at 50 µg/mL. The target compounds exhibited best antifungal activity against *P. piricola*, in which compounds (Z)-**4r** (R = β-pyridyl), (Z)-**4q** (R = α-thienyl), (E)-**4f'** (R = *p*-F Ph), (Z)-**4i** (R = *m*-Me Ph), (Z)-**4j** (R = *p*-Me Ph), and (Z)-**4p** (R = α-furyl) had inhibition rates of 97.1%, 87.4%, 87.4%, 85.0%, 81.9%, and 77.7%, respectively, showing better antifungal activity than that of the commercial fungicide chlorothanil. Also, compound (Z)-**4r** (R = β-pyridyl) displayed remarkable antifungal activity against all the tested fungi, with inhibition rates of 76.7%, 82.7%, 97.1%, 66.3%, 74.7%, 93.9%, 76.7% and 93.3%, respectively, showing better or comparable antifungal activity than that of the commercial fungicide chlorothanil. Besides, the *E-Z* isomers of the target oxime esters were found to show obvious differences in antifungal activity. These results provide an encouraging framework that could lead to the development of potent novel antifungal agents.

Keywords: 3-carene; 3-caren-5-one; 3-caren-5-one oxime ester; *E-Z* stereoisomer; antifungal activity

1. Introduction

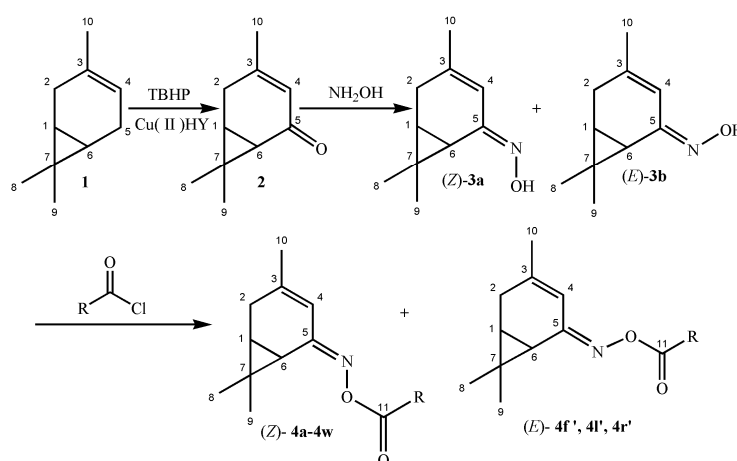
3-Carene, a naturally occurring bicyclic monoterpene containing a carbon-carbon double bond and a gem-dimethylcyclopropane ring, is a constituent of many essential oils and turpentine oils [1,2]. It was reported that the isomeric mixture of 3-carene showed a broad spectrum of activities, such as antimicrobial [3–6], anticancer [6], semiochemical [7,8], antioxidant [6,9], and fumigant activities [10]. Because of its special structure and bioactive activities, screening of structurally modified 3-carene derivatives for their bioactivity has received considerable attention. For instance, stable, potent, and selective sphingosine-1-phosphate receptor 1 (S1P₁) agonists were successively synthesized by using (+)-3-carene as starting material [11]. Ingenol and (+)-phorbol, two crucial natural products with various biological activities, especially anticancer, have been also synthesized from inexpensive (+)-3-carene [12–15]. On the other hand, oxime esters as an important class of bioactive compounds for agrochemical and pharmaceutical use were investigated extensively by chemists. It was reported that oxime esters exhibited insecticidal [16,17], herbicidal [18], antiviral [19], antitumor [20–22], and antibacterial activities [23–25]. For example, a series of 3-ethoxy-4-hydroxybenzaldehyde oxime esters were synthesized and evaluated for their in vitro antifungal activity against three pathogenic fungi and antibacterial activity against three bacterial strains, and the structure-activity

relationship was also preliminarily summarized [26]. In continuation of our interest in the bioactive properties of natural product-based compounds [27–33], a series of novel 3-carene-5-one oxime esters were designed and synthesized by integrating bioactive oxime esters into the skeleton of 3-carene. Structural characterization and antifungal evaluation of all the title compounds were carried out as well. In addition, Cu(II)HY zeolite was first employed as catalyst in the oxidative preparation of 3-carene-5-one, and the *E-Z* stereo-isomers of 3-carene-5-one oxime were also separated for the first time by column chromatography.

2. Results and Discussion

2.1. Synthesis and Characterization

As illustrated in the Scheme 1, 3-carene-5-one (**2**) was prepared by oxidation of 3-carene (**1**, isomeric mixture) using TBHP (*tert*-butyl hydroperoxide) as oxidant in a 30% yield (GC). In this process, Cu(II)HY, in which Cu(II) ions were incorporated into HY zeolite, was chosen as a heterogeneous catalyst to increase the selectivity for **2** due to the shape-selectivity of this mesoporous material [34] and the activation capacity of copper ion to saturated C–H [35–37]. After the reaction was completed, this catalyst could easily be separated from the reaction system by filtration, and could be recycled several times.



Scheme 1. Synthesis of 3-carene-5-one oxime esters (*Z*)-**4a–4w**, and (*E*)-**4f'**, **4l'**, **4r'**. **4a**: R = Ph; **4b**: R = *o*-Cl Ph; **4c**: R = *m*-Cl Ph; **4d**: R = *p*-Cl Ph; **4e**: R = *o*-F Ph; **4f**: R = *p*-F Ph; **4g**: R = *o*-OMe Ph; **4h**: R = *o*-Me Ph; **4i**: R = *m*-Me Ph; **4j**: R = *p*-Me Ph; **4k**: R = 2,4-Cl Ph; **4l**: R = 2,3-Cl Ph; **4m**: R = *p*-CH₂Cl Ph; **4n**: R = cyclopentyl; **4o**: R = cyclohexyl; **4p**: R = α -furyl; **4q**: R = α -thienyl; **4r**: R = β -pyridyl; **4s**: R = α -Cl- β -pyridyl; **4t**: R = *n*-pentyl; **4u**: R = ethyl; **4v**: R = *n*-propyl; **4w**: R = *n*-butyl; **4f'**: R = *p*-F Ph; **4l'**: R = 2,3-Cl; **4r'**: R = β -pyridyl.

3-Carene-5-one oxime (**3**, isomeric mixture) was prepared by oximation of compound **2** with NH₂OH·HCl in a mixed solvent (EtOH:H₂O = 5:1, *v/v*). Sodium acetate was added into the reaction system as an additive to neutralize HCl and form a buffer system. Two stereoisomers, (*Z*)-3-carene-5-one oxime ((*Z*)-**3a**) and (*E*)-3-carene-5-one oxime ((*E*)-**3b**), were isolated from compound **3** (**3a**:**3b** = 7:1, *w/w*, GC). In the ¹H-NMR spectrum of (*Z*)-**3a**, the olefinic proton (C₄-H) in the 3-carene skeleton showed signals at about 5.88 and the signals of the C₆-H appeared at 1.99 ppm. However, the corresponding signals of another isomer (*E*)-**3b** were shifted to 6.65 ppm and 1.50 ppm, respectively (Figure 1). Due to the hydrogen bond interaction of the hydroxyl group oxygen with the olefinic proton (C₄-H) or the C₆-H, the signal of olefinic proton (C₄-H) in the (*E*)-isomer and the signal of the C₆-H in the (*Z*)-isomer shifted to downfield [38]. The structures of the two stereo-isomers were further confirmed by NOESY spectra. In the NOESY spectrum of (*Z*)-**3a**, no peak related to the coupling of hydroxyl hydrogen with C₄-H was observed, while a peak corresponding to this space interaction in (*E*)-**3b** was found (Figure 2).

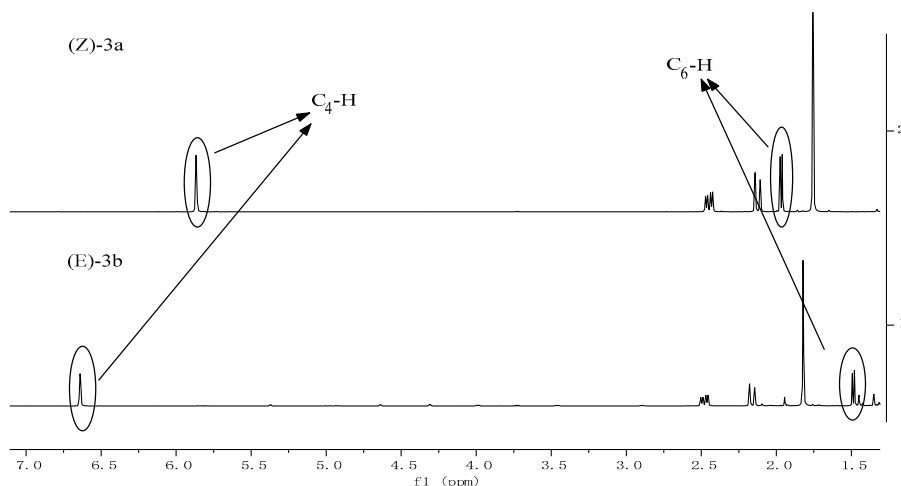


Figure 1. ^1H -NMR spectra of (Z)-3a and (E)-3b.

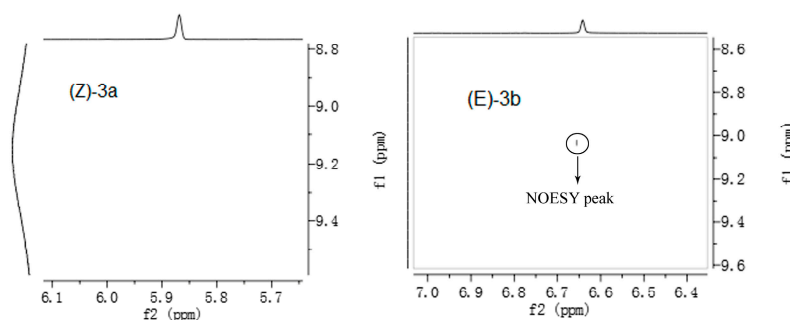


Figure 2. The coupling of $\text{C}_4\text{-H}$ and hydroxyl hydrogen in ^1H - ^1H NOESY spectra.

The target oxime esters were characterized by UV-Vis, IR, ^1H -NMR, ^{13}C -NMR, ESI-MS, and elemental analysis, and all the related spectra can be found in the Supplementary Materials. It was found that the molar extinction coefficient of all target compounds ranged from 3.89 to 4.42 ($\log \epsilon$), implying that a conjugated system existed in these compounds. In the IR spectra, the weak absorption bands at about 3018 cm^{-1} were attributed to the stretching vibrations of the unsaturated C–H in the 3-carene moiety. The strong absorption bands at about 1738 cm^{-1} were assigned to the vibrations of C=O in the ester moiety. The moderate absorption peaks at about 1649 cm^{-1} were due to the vibrations of C=N. In the ^1H -NMR spectra, the protons of benzene ring showed signals at 7.10–8.20 ppm. The olefinic protons of the 3-carene scaffold showed signals at about 6.10 ppm for the (Z)-isomers and the (E)-isomers showed signals at about 6.60 ppm. The protons bonded to the saturated carbons displayed signals in the range of 0.50–3.00 ppm. The ^{13}C -NMR spectra of the target compounds showed peaks for the olefinic carbons of the 3-carene moiety at 117.92–119.05 ppm (C_4) and 147.49–149.74 ppm (C_3) for the (Z)-isomers, however, the corresponding signals for (E)-isomers showed at about 113.20 (C_4) ppm and 153.03 ppm (C_3). The other saturated carbons displayed signals in the region of 13.59–55.94 ppm. The other signal peaks were correlated to the carbons of C=O, C=N, and the benzene ring. The molecular weights of the intermediates and target oxime esters were confirmed by the ESI-MS.

2.2. Antifungal Activity

The antifungal activities of the target compounds (Z)-4a–4w and (E)-4f' were evaluated by in vitro method against fusarium wilt on cucumber (*Fusarium oxysporum* f. sp. *cucumerinum*), speckle on peanut (*Cercospora arachidicola*), apple ring rot (*Physalospora piricola*), tomato early blight (*Alternaria solani*), wheat scab (*Gibberella zeae*), rice sheath blight (*Rhizoeotnia solani*), corn southern leaf blight (*Bipolaris maydis*), and watermelon anthracnose (*Colleterichum orbicalare*) at $50\text{ }\mu\text{g/mL}$. The results are listed in Table 1.

Table 1. Antifungal activity of the target compounds (Z)-4a–4w and (E)-4f' at 50 µg/mL.

Compounds	Relative Inhibition Rate (%) against the Tested Fungi							
	<i>F. oxysporum</i> f. sp. <i>cucumerinum</i>	<i>C. arachidicola</i>	<i>P. piricola</i>	<i>A. solani</i>	<i>G. zeae</i>	<i>R. solani</i>	<i>B. myadis</i>	<i>C. orbicalare</i>
(Z)-4a (R = Ph)	28.8	35.0	69.4	13.7	21.8	0	32.2	43.3
(Z)-4b (R = <i>o</i> -ClPh)	16.3	30.0	0	0	21.8	18.3	23.9	30.5
(Z)-4c (R = <i>m</i> -ClPh)	22.5	0	44.4	0	21.8	17.1	26.7	33.1
(Z)-4d (R = <i>p</i> -ClPh)	28.8	0	28.8	0	19.8	0	29.4	33.1
(Z)-4e (R = <i>o</i> -FPh)	31.9	45.0	41.3	35.9	37.5	35.0	26.7	45.9
(Z)-4f (R = <i>p</i> -FPh)	25.6	15.0	30.7	0.0	15.9	0	26.7	23.8
(Z)-4g (R = <i>o</i> -OMePh)	25.6	0	60.0	21.1	13.9	0	26.7	35.6
(Z)-4h (R = <i>o</i> -MePh)	31.9	50.0	28.8	21.1	29.6	38.6	29.4	43.3
(Z)-4i (R = <i>m</i> -MePh)	19.4	15.0	85.0	0	12.0	0	23.9	0
(Z)-4j (R = <i>p</i> -MePh)	38.1	20.0	81.9	24.8	17.8	0	35.0	53.6
(Z)-4k (R = 2,4-ClPh)	28.8	55.0	16.3	13.7	17.8	18.3	23.9	53.6
(Z)-4l (R = 2,3-ClPh)	25.6	15.0	28.8	17.4	19.8	0	21.1	43.3
(Z)-4m (R = <i>p</i> -CH ₂ ClPh)	56.9	20.0	41.3	0	19.8	0	21.1	40.8
(Z)-4n (R = cyclo-pentyl)	22.5	35.0	0	13.7	19.8	0	23.9	51.0
(Z)-4o (R = cyclo-hexyl)	25.6	30.0	28.8	21.1	15.9	16.0	23.9	40.8
(Z)-4p (R = α -furyl)	60.0	64.5	77.7	53.8	36.5	54.6	43.3	54.4
(Z)-4q (R = α -thienyl)	48.9	37.3	87.4	41.3	33.5	42.1	33.8	48.9
(Z)-4r (R = β -pyridyl)	76.7	82.7	97.1	66.3	74.7	93.9	76.7	93.3
(Z)-4s (R = α -Cl- β -pyridyl)	15.6	37.3	55.2	41.3	54.1	63.6	24.3	21.1
(Z)-4t (R = <i>n</i> -pentyl)	21.1	19.1	58.4	35.0	48.2	67.1	24.3	21.1
(Z)-4u (R = <i>n</i> -ethyl)	15.6	19.1	58.4	28.8	48.2	36.8	29.0	21.1
(Z)-4v (R = <i>n</i> -propyl)	15.6	28.2	32.6	41.3	57.1	54.6	24.3	21.1
(Z)-4w (R = <i>n</i> -butyl)	15.6	19.1	51.9	22.5	18.8	18.9	19.5	21.1
(E)-4f' (R = <i>p</i> -FPh)	60.0	64.5	87.4	53.8	65.9	76.1	76.7	54.4
(Z)-3a	15.6	23.6	51.9	35.0	18.8	24.3	24.3	26.7
(E)-3b	15.6	23.6	51.9	22.5	18.8	27.9	19.5	21.1
2	21.1	19.1	45.5	16.3	24.7	18.9	24.3	15.6
Chlorothanil	100	73.3	75.0	73.9	73.1	96.1	90.4	91.3

It was found that, at 50 $\mu\text{g/mL}$, all the target compounds presented obviously different antifungal activity against the eight tested fungi. Compared with the intermediates **2**, **3a** and **3b**, some of the target compounds showed enhanced activities after esterification. On the whole, most of the target compounds exhibited best antifungal activity against *P. piricola*, in which compounds (Z)-**4r** (R = β -pyridyl), (Z)-**4q** (R = α -thienyl), (E)-**4f'** (R = *p*-F Ph), (Z)-**4i** (R = *m*-Me Ph), (Z)-**4j** (R = *p*-Me Ph), and (Z)-**4p** (R = α -furyl) had inhibition rates of 97.1%, 87.4%, 87.4%, 85.0%, 81.9%, and 77.7%, respectively, showing better antifungal activity than that of the commercial fungicide chlorothanil with the inhibition rate of 75.0%. It was also found that compound (Z)-**4r** (R = β -pyridyl) displayed remarkable antifungal activity against all the tested fungi, with inhibition rates of 76.7%, 82.7%, 97.1%, 66.3%, 74.7%, 93.9%, 76.7% and 93.3%, respectively, showing better or comparable antifungal activity than that of the commercial fungicide chlorothanil. Therefore, compound (Z)-**4r** (R = β -pyridyl) is a lead compound worthy of further investigation. Furthermore, it was found that (E)-isomer **4f'** (R = *p*-F Ph) exhibited much better antifungal activity than the corresponding (Z)-isomer **4f** (R = *p*-F Ph) against all the tested fungi. For instance, (E)-isomer **4f'** (64.5%) showed 4.3 times that of **4f** (Z)-isomer (15.0%) against *C. arachidicola*, and the two isomers displayed 76.1% and 0.0% inhibition rates, respectively, against *R. solani*. The obvious difference in antifungal activity between E-Z isomers is very meaningful and requires further studies in photoisomerization and drug resistance.

3. Experimental Section

3.1. General Information

The GC analysis was performed on an Agilent 6890 GC (Agilent Technologies Inc., Santa Clara, CA, USA) equipped with a HP-1 (30 m, 0.530 mm, 0.88 μm) column. IR spectra were recorded (KBr pellet method) on a Nicolet iS50 FT-IR spectrometer (Thermo Scientific Co., Ltd., Madison, WI, USA). NMR spectra (including $^1\text{H-NMR}$, $^{13}\text{C-NMR}$, NOESY) were recorded in CDCl_3 solvent on a Bruker Avance III HD 600 MHz spectrometer (Bruker Co., Ltd., Zurich, Switzerland) and chemical shifts are expressed in ppm (δ) downfield relative to TMS as an internal standard. MS spectra were obtained by means of the electrospray ionization (ESI) method on TSQ Quantum Access MAX HPLC-MS instrument (Thermo Scientific Co., Ltd., Waltham, MA, USA). Elemental analyses were measured using a PE 2400 II elemental analyzer (Perkin-Elmer Instruments Co., Ltd., USA). The UV spectra were measured on a Shimadzu UV-1800 spectrophotometer (Shimadzu Corp., Kyoto, Japan). Melting points were determined on a MP420 automatic melting point apparatus (Hanon Instruments Co., Ltd., Jinan, China) and were not corrected. Ultrasonic irradiation was carried out on XO-SM50 ultrasonic microwave reaction system (Nanjing Xianou Instrument Manufacturing Co., Ltd., Nanjing, China). 3-Carene (GC purity 98%, isomeric mixture) was provided by Wuzhou Pine Chemicals Co., Ltd. (Wuzhou, Guangxi, China). The 7 Å HY zeolite was purchased from Nankai University Catalyst Co., Ltd. (Tianjin, China). Other reagents were purchased from commercial suppliers and used as received.

3.2. Preparation of Catalyst

Cu(II)HY zeolite catalyst used for the synthesis of 3-carene-5-one was prepared by the incipient wetness method [39]. HY zeolite with pore diameter of 7 Å was dried at 120 °C 3 h under air atmosphere. Then, a solution of $\text{Cu}(\text{NO}_3)_2 \cdot 3\text{H}_2\text{O}$ (5.7 g) in deionized water based on the saturated water absorption amount of the zeolite (10.0 g) was added dropwise to the dried zeolite, with constant stirring and grinding. The resulting mixture was aged for 24 h, and then dried in vacuum at 120 °C for 2 h. The powder sample was calcinated at 550 °C for 4 h under air atmosphere.

3.3. Synthesis of 3-Carene-5-One (**2**)

3-Carene (10 mL, 63 mmol), Cu(II)HY zeolite catalyst (2.7 g) and CH_3CN (20 mL) were mixed and then irradiated under ultrasonic wave for 40 min. When the mixture was heated to 45 °C, a mixed solution of 40 mL *tert*-butyl hydroperoxide (70% in water, wt %) (288 mmol) and 20 mL CH_3CN was

added to the reaction system by the way of constant flowing at a rate of 1 mL/min. Afterwards, the reaction mixture was stirred for 18 h at 45 °C. When the reaction was completed, the reaction mixture was cooled to room temperature and appropriate amount of Na₂S₂O₃ was added into it to destroy the unreacted *tert*-butyl hydroperoxide. The solvent CH₃CN was removed by vacuum distillation, and the residue was then extracted three times with EtOAc. The combined organic phase was washed with saturated sodium chloride and deionized water, respectively, and dried over with anhydrous Na₂SO₄. After the EtOAc was removed in vacuum, the crude product was purified by silica gel column chromatography (EtOAc–petroleum ether = 1:30, *v/v*) to obtain pale yellow liquid compound **2**. Yield 20%. UV-Vis (EtOH) λ_{max} (log ε): 226.50 (4.416) nm; IR (thin film, cm⁻¹): 3029 (w, =C-H), 1655 (s, C=O); ¹H-NMR δ = 5.83 (s, 1H, C₄-H), 2.64 (dd, *J* = 20.4, 8.5 Hz, 1H, C₂-H_a), 2.33 (d, *J* = 20.8 Hz, 1H, C₂-H_b), 1.87 (s, 3H, C₃-CH₃), 1.56 (d, *J* = 7.8 Hz, 1H, C₆-H), 1.45 (t, *J* = 8.0 Hz, 1H, C₁-H), 1.19 (s, 3H, C₇-CH₃), 1.04 (s, 3H, C₇-CH₃); ¹³C-NMR δ = 196.67 (C₅), 158.96 (C₃), 126.40 (C₄), 32.85 (C₆), 28.43 (C₉), 27.87 (C₂), 25.86 (C₁), 23.68 (C₁₀), 22.57 (C₇), 14.38 (C₈); ESI-MS *m/z*: 151.17 [M + H]⁺. Anal. Calcd. For C₁₀H₁₄O (150.22): C, 79.96; H, 9.39. Found: C, 79.85; H, 9.36.

3.4. Synthesis of 3-Carene-5-One Oxime (**3**)

3-Carene-5-one (1.5 g, 10 mmol), NH₂OH·HCl (1.04 g, 15 mmol), and NaOAc (4.08 g, 30 mmol) were dissolved in a mixed solvent (EtOH:H₂O = 5:1, *v/v*). The reaction mixture was stirred at 80 °C for 3 h. The reaction process was monitored by TLC. When 3-carene-5-one was fully reacted, the mixture was cooled to room temperature. After the solvent EtOH was removed by rotary evaporation, the residue was extracted by EtOAc. The separated organic phase was washed with saturated NaCl solution three times, and concentrated under reduced pressure to obtain the crude product, which was purified by silica gel column chromatography using a mixed solvent (EtOAc–petroleum ether = 1:60, *v/v*) as eluent.

(*Z*)-3-Carene-5-one oxime ((*Z*)-**3a**) was obtained as a white needle crystal. Yield 63.5%, m.p.: 96.7–98.1 °C. UV-Vis (EtOH) λ_{max} (log ε): 239.70 (4.28) nm; IR (KBr, cm⁻¹): 3464–3078 (s, br, O-H), 3033 (w, =C-H), 1659 (m, C=N), 1614 (m); ¹H-NMR δ = 9.03 (s, 1H, OH), δ 5.87 (s, 1H, C₄-H), 2.45 (dd, *J* = 20.0, 8.2 Hz, 1H, C₂-H_a), 2.12 (d, *J* = 20.0 Hz, 1H, C₂-H_b), 1.97 (d, *J* = 8.3 Hz, 1H, C₆-H), 1.76 (s, 3H, C₃-CH₃), 1.23 (s, 3H, C₇-CH₃), 1.19 (t, *J* = 8.3 Hz, 1H, C₁-H), 0.89 (s, 3H, C₇-CH₃); ¹³C-NMR δ = 155.00 (C₅), 142.27 (C₃), 119.32 (C₄), 27.97 (C₆), 27.08 (C₉), 23.39 (C₂), 22.37 (C₁), 20.71 (C₁₀), 19.67 (C₇), 14.59 (C₈); ESI-MS *m/z*: 166.14 [M + H]⁺. Anal. Calcd. For C₁₀H₁₅NO (165.23): C, 72.69; H, 9.15; N, 8.48. Found: C, 72.71; H, 9.17; N, 8.49.

(*E*)-3-Carene-5-one oxime ((*E*)-**3b**) was obtained as a white plate-like crystal. Yield 3%, m.p.: 73.5–75.0 °C. UV-Vis (EtOH) λ_{max} (log ε): 235.80 (3.89) nm; IR (KBr, cm⁻¹): 3432–3081 (s, br, O-H), 3015 (w, =C-H), 1644 (m, C=N), 1608 (m); ¹H-NMR δ = 8.98 (s, 1H, OH), 6.64 (s, 1H, C₄-H), 2.48 (dd, *J* = 20.4, 8.0 Hz, 1H, C₂-H_a), 2.16 (d, *J* = 20.5 Hz, 1H, C₂-H_b), 1.82 (s, 3H, C₃-CH₃), 1.49 (d, *J* = 8.7 Hz, 1H, C₆-H), 1.19 (t, *J* = 8.3 Hz, 1H, C₁-H), 1.13 (s, 3H, C₇-CH₃), 0.88 (s, 3H, C₇-CH₃); ¹³C-NMR δ = 152.05 (C₅), 147.32 (C₃), 112.59 (C₄), 28.03 (C₆), 27.71 (C₉), 23.86 (C₂), 23.54 (C₁), 21.82 (C₁₀), 19.61 (C₇), 14.15 (C₈); ESI-MS *m/z*: 166.14 [M + H]⁺. Anal. Calcd. For C₁₀H₁₅NO (165.23): C, 72.69; H, 9.15; N, 8.48. Found: C, 72.60; H, 9.18; N, 8.46.

3.5. General Procedure for Synthesis of 3-Carene-5-One Oxime Esters (*Z*)-**4a–4w**, (*E*)-**4f'**, **4l'**, **4r'**

A solution of acyl chloride (1.2 mmol) in CH₂Cl₂ (3 mL) was added slowly to a solution of (*Z*)- or (*E*)-3-carene-5-one oxime (1 mmol) and triethylamine in CH₂Cl₂ (5 mL) with ice-water cooling. The reaction process was monitored by TLC. Upon completion, 5 mL deionized water was added to the reaction mixture to destroy the unreacted acyl chloride. Then, the organic layer was separated, washed with deionized water three times, and concentrated in vacuum. The crude product was further purified by silica gel chromatography to afford the target compounds (*Z*)-**4a–4w**, and (*E*)-**4f'**, **4l'**, **4r'**.

Only three (*E*)-oxime esters, i.e., (*E*)-**4f'**, **4l'**, **4r'**, were reported in this study because of the very low yield of (*E*)-**3b**.

(*Z*)-3-Caren-5-one *O*-(benzoyl) oxime ((*Z*)-**4a**). Pale yellow solid. Yield: 65.4%, m.p.: 97.4–98.7 °C. UV-Vis (EtOH) λ_{\max} (log ϵ): 257.40 (4.34) nm, 236.70 (4.25) nm; IR (KBr, cm^{-1}): 3069 (w), 3015 (w, Ar-H, =C-H), 1739 (s, C=O), 1658 (m, C=N), 1602 (w), 1581 (s), 1495 (w), 1456 (m, Ar); $^1\text{H-NMR}$ δ = 8.10 (d, J = 7.1 Hz, 2H, C₁₃-H, C₁₇-H), 7.59 (t, J = 7.4 Hz, 1H, C₁₅-H), 7.47 (t, J = 7.8 Hz, 2H, C₁₄-H, C₁₆-H), 6.17 (s, 1H, C₄-H), 2.56 (dd, J = 20.2, 8.4 Hz, 1H, C₂-H_a), 2.21 (d, J = 19.5 Hz, 1H, C₂-H_b), 2.05 (d, J = 8.2 Hz, 1H, C₆-H), 1.85 (s, 3H, C₃-CH₃), 1.34 (d, J = 7.8 Hz, 1H, C₁-H), 1.30 (s, 3H, C₇-CH₃), 0.94 (s, 3H, C₇-CH₃); $^{13}\text{C-NMR}$ δ = 164.12 (C₁₁), 161.89 (C₅), 147.97 (C₃), 133.02 (C₁₅), 129.60 (C₁₂), 129.53 (C₁₃ and C₁₇), 128.49 (C₁₄ and C₁₆), 118.38 (C₄), 28.09 (C₆), 27.15 (C₉), 23.77 (C₂), 23.08 (C₁), 21.68 (C₁₀), 21.32 (C₇), 14.59 (C₈); ESI-MS m/z : 270.09 [M + H]⁺. Anal. Calcd. For C₁₇H₁₉NO₂ (269.34): C, 75.81; H, 7.11; N, 5.20. Found: C, 75.79; H, 7.12; N, 5.21.

(*Z*)-3-Caren-5-one *O*-(2-chlorobenzoyl) oxime ((*Z*)-**4b**). White solid. Yield: 74.0%, m.p.: 116.3–117.8 °C. UV-Vis (EtOH) λ_{\max} (log ϵ): 253.50 (4.23) nm. IR (KBr, cm^{-1}): 3048 (w), 3012 (w, Ar-H, =C-H), 1726 (s, C=O), 1652 (m, C=N), 1581 (m), 1464 (w, Ar); $^1\text{H-NMR}$ δ = 7.88 (dd, J = 7.8, 1.6 Hz, 1H, C₁₇-H), 7.47 (dd, J = 8.0, 1.4 Hz, 1H, C₁₄-H), 7.44 (td, J = 8.1, 7.6, 1.6 Hz, 1H, C₁₅-H), 7.35 (td, J = 7.6, 1.4 Hz, 1H, C₁₆-H), 6.14 (s, 1H, C₄-H), 2.54 (dd, J = 20.3, 8.3 Hz, 1H, C₂-H_a), 2.21 (d, J = 20.3 Hz, 1H, C₂-H_b), 2.08 (d, J = 8.1 Hz, 1H, C₆-H), 1.85 (s, 3H, C₃-CH₃), 1.29 (t, J = 8.2 Hz, 1H, C₁-H), 1.22 (s, 3H, C₇-CH₃), 0.94 (s, 3H, C₇-CH₃); $^{13}\text{C-NMR}$ δ = 164.06 (C₁₁), 162.31 (C₅), 148.35 (C₃), 133.30 (C₁₂), 132.55 (C₁₅), 131.70 (C₁₃), 130.91 (C₁₇), 130.03 (C₁₄), 126.67 (C₁₆), 118.22 (C₄), 28.08 (C₆), 27.21 (C₉), 23.77 (C₂), 23.13 (C₁), 21.98 (C₁₀), 21.43 (C₇), 14.56 (C₈); ESI-MS m/z : 304.07 [M + H]⁺. Anal. Calcd. For C₁₇H₁₈ClNO₂ (303.78): C, 67.21; H, 5.97; N, 4.61. Found: C, 67.25; H, 5.93; N, 4.62.

(*Z*)-3-Caren-5-one *O*-(3-chlorobenzoyl) oxime ((*Z*)-**4c**). White solid. Yield: 80.3%, m.p.: 137.3–138.1 °C. UV-Vis (EtOH) λ_{\max} (log ϵ): 259.90 (4.08) nm, 229.80 (4.07) nm; IR (KBr, cm^{-1}): 3084 (w), 3024 (w, Ar-H, =C-H), 1741 (s, C=O), 1652 (m, C=N), 1581 (m), 1491 (w, Ar); $^1\text{H-NMR}$ δ = 8.07 (s, 1H, C₁₃-H), 7.98 (d, J = 7.8 Hz, 1H, C₁₇-H), 7.56 (d, J = 8.0 Hz, 1H, C₁₅-H), 7.42 (t, J = 7.9 Hz, 1H, C₁₆-H), 6.16 (s, 1H, C₄-H), 2.57 (dd, J = 20.3, 8.4 Hz, 1H, C₂-H_a), 2.22 (d, J = 20.3 Hz, 1H, C₂-H_b), 2.02 (d, J = 8.2 Hz, 1H, C₆-H), 1.86 (s, 3H, C₃-CH₃), 1.35 (t, J = 8.4 Hz, 1H, C₁-H), 1.32 (s, 3H, C₇-CH₃), 0.94 (s, 3H, C₇-CH₃). $^{13}\text{C-NMR}$ δ = 162.94 (C₁₁), 162.32 (C₅), 148.54 (C₃), 134.66 (C₁₂), 133.07 (C₁₅), 131.31 (C₁₄), 129.85 (C₁₆), 129.65 (C₁₃), 127.62 (C₁₇), 118.12 (C₄), 28.03 (C₆), 27.16 (C₉), 23.80 (C₂), 23.11 (C₁), 21.80 (C₁₀), 21.35 (C₇), 14.59 (C₈); ESI-MS m/z : 304.05 [M + H]⁺. Anal. Calcd. For C₁₇H₁₈ClNO₂ (303.78): C, 67.21; H, 5.97; N, 4.61. Found: C, 67.23; H, 5.98; N, 4.60.

(*Z*)-3-Caren-5-one *O*-(4-chlorobenzoyl) oxime ((*Z*)-**4d**). White solid. Yield: 78.6%, m.p.: 149.9–151.3 °C. UV-Vis (EtOH) λ_{\max} (log ϵ): 258.80 (4.32) nm, 245.90 (4.32) nm; IR (KBr, cm^{-1}): 3066 (w), 3024 (w, Ar-H, =C-H), 1736 (s, C=O), 1659 (m, C=N), 1596 (m), 1578 (m), 1486 (m, Ar); $^1\text{H-NMR}$ δ = 8.03 (d, J = 8.4 Hz, 2H, C₁₃-H, C₁₇-H), 7.45 (d, J = 8.4 Hz, 2H, C₁₄-H, C₁₆-H), 6.16 (s, 1H, C₄-H), 2.56 (dd, J = 20.2, 8.3 Hz, 1H, C₂-H_a), 2.22 (d, J = 20.3 Hz, 1H, C₂-H_b), 2.01 (d, J = 8.1 Hz, 1H, C₆-H), 1.85 (s, 3H, C₃-CH₃), 1.34 (t, J = 8.2 Hz, 1H, C₁-H), 1.29 (s, 3H, C₇-CH₃), 0.94 (s, 3H, C₇-CH₃); $^{13}\text{C-NMR}$ δ = 163.34 (C₁₁), 162.15 (C₅), 148.32 (C₃), 139.52 (C₁₅), 130.88 (C₁₂), 128.89 (C₁₃, C₁₄), 128.02 (C₁₅), 118.22 (C₃), 28.10 (C₆), 27.15 (C₉), 23.79 (C₂), 23.13 (C₁), 21.77 (C₁₀), 21.32 (C₇), 14.58 (C₈); ESI-MS m/z : 304.04 [M + H]⁺. Anal. Calcd. For C₁₇H₁₈ClNO₂ (303.78): C, 67.21; H, 5.97; N, 4.61. Found: C, 67.23; H, 5.95; N, 4.63.

(*Z*)-3-Caren-5-one *O*-(2-fluorobenzoyl) oxime ((*Z*)-**4e**). White solid. Yield: 76.9%, m.p.: 128.7–131.2 °C. UV-Vis (EtOH) λ_{\max} (log ϵ): 257.60 (4.29) nm, 224.70 (4.29) nm; IR (KBr, cm^{-1}): 3057 (w), 3009 (w, Ar-H, =C-H), 1736 (s, C=O), 1650 (m, C=N), 1608 (m), 1575 (m), 1486 (m), 1453 (m, Ar); $^1\text{H-NMR}$ δ = 8.07 (td, J = 7.5, 1.8 Hz, 1H, C₁₇-H), 7.57–7.52 (m, 1H, C₁₅-H), 7.25 (td, J = 7.7, 1.1 Hz, 1H, C₁₆-H), 7.16 (ddd, J = 10.7, 8.3, 0.9 Hz, 1H, C₁₄-H), 6.15 (s, 1H, C₄-H), 2.55 (dd, J = 20.3, 8.4 Hz, 1H, C₂-H_a), 2.21 (d, J = 20.3 Hz, 1H, C₂-H_b), 2.12 (d, J = 8.1 Hz, 1H, C₆-H), 1.85 (s, 3H, C₃-CH₃), 1.31 (t, J = 7.9 Hz, 1H, C₁-H), 1.26 (s, 3H, C₇-CH₃), 0.93 (s, 3H, C₇-CH₃). $^{13}\text{C-NMR}$ δ = 162.29 (C₁₁), 160.83 (C₅), 148.32 (C₃),

134.61 (C₁₅), 134.55 (C₁₇), 132.63 (C₁₆), 124.13 (C₁₂), 118.23 (C₄), 117.02 (C₁₃), 116.87 (C₁₄), 27.90 (C₆), 27.24 (C₉), 23.78 (C₂), 23.13 (C₁), 21.88 (C₁₀), 21.45 (C₇), 14.56 (C₈); ESI-MS *m/z*: 288.08 [M + H]⁺. Anal. Calcd. For C₁₇H₁₈FNO₂ (287.33): C, 71.06; H, 6.31; N, 4.87. Found: C, 71.10; H, 6.30; N, 4.85.

(*Z*)-3-Caren-5-one *O*-(4-fluorobenzoyl) oxime ((*Z*)-4f). White solid. Yield: 65.2%, m.p.: 133.2–135.0 °C. UV-Vis (EtOH) λ_{max} (log ε): 257.00 (4.29) nm, 229.10 (4.26) nm; IR (KBr, cm⁻¹): 3041 (w), 3018 (w, Ar-H, =C-H), 1748 (s, C=O), 1659 (m, C=N), 1602 (m), 1581 (m), 1507 (m, Ar); ¹H-NMR δ: 8.11 (dd, *J* = 8.9, 5.4 Hz, 2H, C₁₃-H, C₁₇-H), 7.15 (t, *J* = 8.7 Hz, 2H, C₁₄-H, C₁₆-H), 6.16 (s, 1H, C₄-H), 2.56 (dd, *J* = 20.3, 8.4 Hz, 1H, C₂-H_a), 2.22 (d, *J* = 20.3 Hz, 1H, C₂-H_b), 2.02 (d, *J* = 8.2 Hz, 1H, C₆-H), 1.85 (s, 3H, C₃-CH₃), 1.34 (t, *J* = 8.2 Hz, 1H, C₁-H), 1.30 (s, 3H, C₇-CH₃), 0.94 (s, 3H, C₇-CH₃); ¹³C-NMR δ: 166.63 (C₁₁), 164.95 (C₅), 163.23 (C₁₅), 162.01 (C₁₂), 148.19 (C₃), 132.07 (C₁₃ or C₁₇), 132.01 (C₁₃ or C₁₇), 118.27 (C₄), 115.79 (C₁₄ or C₁₆), 115.64 (C₁₄ or C₁₆), 28.11 (C₆), 27.15 (C₉), 23.78 (C₂), 23.12 (C₁), 21.73 (C₁₀), 21.32 (C₇), 14.59 (C₈); ESI-MS *m/z*: 288.07 [M + H]⁺. Anal. Calcd. For C₁₇H₁₈FNO₂ (287.33): C, 71.06; H, 6.31; N, 4.87. Found: C, 71.03; H, 6.29; N, 4.86.

(*Z*)-3-Caren-5-one *O*-(2-methoxybenzoyl) oxime ((*Z*)-4g). White solid. Yield: 65.0%, m.p.: 123.9–125.5 °C. UV-Vis (EtOH) λ_{max} (log ε): 254.50 (4.38) nm; IR (KBr): 3054 (w), 3006 (w, Ar-H, =C-H), 1724 (s, C=O), 1656 (m, C=N), 1599 (m), 1581 (m), 1489 (m), 1462 (m, Ar); ¹H-NMR δ = 7.85 (dd, *J* = 7.7, 1.8 Hz, 1H, C₁₇-H), 7.48 (td, *J* = 9.0, 8.2, 1.8 Hz, 1H, C₁₅-H), 7.04–6.99 (m, 1H, C₁₆-H), 7.01–6.97 (m, 1H, C₁₄-H), 6.15 (s, 1H, C₄-H), 3.89 (s, 3H, O-CH₃), 2.53 (dd, *J* = 20.2, 8.3 Hz, 1H, C₂-H_a), 2.20 (d, *J* = 20.2 Hz, 1H, C₂-H_b), 2.08 (d, *J* = 8.1 Hz, 1H, C₆-H), 1.84 (s, 3H, C₃-CH₃), 1.29 (t, *J* = 8.1 Hz, 1H, C₆-H), 1.23 (s, 3H, C₇-CH₃), 0.93 (s, 3H, C₇-CH₃); ¹³C-NMR δ = 164.58 (C₁₁), 161.72 (C₅), 158.98 (C₁₃), 147.53 (C₃), 133.45 (C₁₅), 131.79 (C₁₇), 120.20 (C₁₂), 119.68 (C₁₆), 118.58 (C₄), 111.97 (C₁₄), 55.94 (C₁₈), 28.17 (C₆), 27.21 (C₉), 23.73 (C₂), 23.21 (C₁), 21.70 (C₁₀), 21.30 (C₇), 14.56 (C₈); ESI-MS *m/z*: 300.01 [M + H]⁺. Anal. Calcd. For C₁₇H₂₁NO₂ (299.36): C, 72.22; H, 7.07; N, 4.68. Found: C, 72.17; H, 7.04; N, 4.71.

(*Z*)-3-Caren-5-one *O*-(2-methylbenzoyl) oxime ((*Z*)-4h). White solid. Yield: 65%, m.p.: 64.7–67.5 °C. UV-Vis (EtOH) λ_{max} (log ε): 255.80 (4.42) nm; IR (KBr, cm⁻¹): 3048 (w), 3015 (w, Ar-H, =C-H), 1748 (s, C=O), 1653 (m, C=N), 1605 (w), 1581 (m), 1486 (w), 1453 (m, Ar); ¹H-NMR δ = 7.92 (d, *J* = 6.8 Hz, 1H, C₁₇-H), 7.42 (t, *J* = 7.5 Hz, 1H, C₁₅-H), 7.28 (d, *J* = 7.6 Hz, 1H, C₁₆-H), 7.26 (d, *J* = 7.5 Hz, 1H, C₁₄-H), 6.16 (s, 1H, C₄-H), 2.66 (s, 3H, C₁₃-CH₃), 2.54 (dd, *J* = 20.6, 8.7 Hz, 1H, C₂-H_a), 2.20 (d, *J* = 20.3 Hz, 1H, C₂-H_b), 2.00 (d, *J* = 8.2 Hz, 1H, C₆-H), 1.85 (s, 3H, C₃-CH₃), 1.30 (t, *J* = 8.2 Hz, 1H, C₁-H), 1.25 (s, 3H, C₇-CH₃), 0.94 (s, 3H, C₇-CH₃); ¹³C-NMR δ = 165.43 (C₁₁), 161.56 (C₅), 147.75 (C₃), 140.06 (C₁₃), 131.95 (C₁₅), 131.67 (C₁₂), 130.30 (C₁₇), 129.17 (C₁₄), 125.70 (C₁₆), 118.49 (C₄), 28.08 (C₆), 27.13 (C₉), 23.74 (C₂), 23.02 (C₁), 21.72 (C₁₀ and C₁₈), 21.41 (C₇), 14.61 (C₈); ESI-MS *m/z*: 284.12 [M + H]⁺. Anal. Calcd. For C₁₈H₂₁NO₂ (283.36): C, 76.29; H, 7.47; N, 4.94. Found: C, 76.21; H, 7.50; N, 4.90.

(*Z*)-3-Caren-5-one *O*-(3-methylbenzoyl) oxime ((*Z*)-4i). White solid. Yield: 70.0%, m.p.: 131.8–133.2 °C. UV-Vis (EtOH) λ_{max} (log ε): 258.30 (4.31) nm; IR (KBr, cm⁻¹): 3054 (w), 3021 (w, Ar-H, =C-H), 1736 (s, C=O), 1650 (m, C=N), 1572 (m), 1453 (m, Ar); ¹H-NMR δ = 7.93 (s, 1H, C₁₃-H), 7.89 (d, *J* = 7.6 Hz, 1H, C₁₇-H), 7.39 (d, *J* = 7.6 Hz, 1H, C₁₅-H), 7.35 (t, *J* = 7.6 Hz, 1H, C₁₆-H), 6.16 (s, 1H, C₄-H), 2.56 (dd, *J* = 19.9, 8.1 Hz, 1H, C₂-H_a), 2.41 (s, 3H, C₁₄-CH₃), 2.21 (d, *J* = 20.3 Hz, 1H, C₂-H_b), 2.05 (d, *J* = 8.2 Hz, 1H, C₆-H), 1.85 (s, 3H, C₃-CH₃), 1.33 (t, *J* = 8.3 Hz, 1H, C₁-H), 1.31 (s, 3H, C₇-CH₃), 0.94 (s, 3H, C₇-CH₃); ¹³C-NMR δ = 164.29 (C₁₁), 161.83 (C₅), 147.93 (C₃), 138.29 (C₁₄), 133.80 (C₁₅), 130.22 (C₁₂), 129.48 (C₁₃), 128.36 (C₁₆), 126.58 (C₁₇), 118.39 (C₄), 28.03 (C₆), 27.15 (C₉), 23.78 (C₂), 23.02 (C₁), 21.62 (C₁₈), 21.35 (C₁₀), 21.31 (C₇), 14.60 (C₈); ESI-MS *m/z*: 284.13 [M + H]⁺. Anal. Calcd. For C₁₈H₂₁NO₂ (283.36): C, 76.29; H, 7.47; N, 4.94. Found: C, 76.25; H, 7.49; N, 4.92.

(*Z*)-3-Caren-5-one *O*-(4-methylbenzoyl) oxime ((*Z*)-4j). White solid. Yield: 75.3%, m.p.: 125.9–127.6 °C. UV-Vis (EtOH) λ_{max} (log ε): 259.30 (4.38) nm; IR (KBr, cm⁻¹): 3066 (w), 3033 (w, Ar-H, =C-H), 1742 (s, C=O), 1656 (m, C=N), 1617 (m), 1572 (m), 1510 (m), 1450 (m, Ar); ¹H-NMR δ = 7.99 (d, *J* = 8.2 Hz, 2H, C₁₃-H, C₁₇-H), 7.27 (d, *J* = 6.5 Hz, 2H, C₁₄-H, C₁₆-H), 6.16 (s, 1H, C₄-H), 2.55 (dd, *J* = 20.2, 7.7 Hz, 1H, C₂-H_a), 2.42 (s, 3H, C₁₅-CH₃), 2.21 (d, *J* = 20.3 Hz, 1H, C₂-H_b), 2.04 (d, *J* = 8.2 Hz, 1H, C₆-H), 1.84

(s, 3H, C₃-CH₃), 1.32 (t, *J* = 8.0 Hz, 1H, C₁-H), 1.29 (s, 3H, C₇-CH₃), 0.94 (s, 3H, C₇-CH₃). ¹³C-NMR δ = 164.23 (C₁₁), 161.72 (C₅), 147.80 (C₃), 143.75 (C₁₅), 129.57 (C₁₂), 129.21 (C₁₃ and C₁₇), 126.78 (C₁₄ and C₁₆), 118.44 (C₄), 28.07 (C₆), 27.15 (C₉), 23.76 (C₂), 23.05 (C₁), 21.70 (C₁₈), 21.63 (C₁₀), 21.32 (C₇), 14.59 (C₈); ESI-MS *m/z*: 284.17 [M + H]⁺. Anal. Calcd. For C₁₈H₂₁NO₂ (283.36): C, 76.29; H, 7.47; N, 4.94. Found: C, 76.32; H, 7.45; N, 4.93.

(*Z*)-3-Caren-5-one *O*-(2,4-dichlorobenzoyl) oxime ((*Z*)-4k). White solid. Yield: 65.0%, m.p.: 82.0–83.0 °C. UV-Vis (EtOH) λ_{max} (log ε): 249.50 (4.30) nm; IR (KBr, cm⁻¹): 3087 (w), 3018 (w, Ar-H, =C-H), 1736 (s, C=O), 1653 (m, C=N), 1587 (m), 1545 (m), 1468 (m), 1450 (m, Ar); ¹H-NMR δ = 7.85 (d, *J* = 8.4 Hz, 1H, C₁₇-H), 7.50 (d, *J* = 2.0 Hz, 1H, C₁₄-H), 7.34 (dd, *J* = 8.4, 2.0 Hz, 1H, C₁₆), 6.13 (s, 1H, C₄-H), 2.55 (dd, *J* = 20.6, 8.7 Hz, 1H, C₂-H_a), 2.21 (d, *J* = 20.3 Hz, 1H, C₂-H_b), 2.05 (d, *J* = 8.1 Hz, 1H, C₆-H), 1.85 (s, 3H, C₃-CH₃), 1.30 (t, *J* = 8.0 Hz, 1H, C₁-H), 1.22 (s, 3H, C₇-CH₃), 0.93 (s, 3H, C₇-CH₃). ¹³C-NMR δ = 163.20 (C₁₁), 162.44 (C₅), 148.59 (C₃), 138.35 (C₁₅), 134.38 (C₁₃), 132.79 (C₁₂), 130.86 (C₁₇), 128.34 (C₁₄), 127.16 (C₁₆), 118.10 (C₄), 28.10 (C₆), 27.20 (C₉), 23.78 (C₂), 23.16 (C₁), 22.04 (C₁₀), 21.48 (C₇), 14.56 (C₈); ESI-MS *m/z*: 338.06 [M + H]⁺. Anal. Calcd. For C₁₇H₁₇Cl₂NO₂ (338.23): C, 60.37; H, 5.07; N, 4.14. Found: C, 60.30; H, 5.11; N, 4.17.

(*Z*)-3-Caren-5-one *O*-(2,3-dichlorobenzoyl) oxime ((*Z*)-4l). Yellow liquid. Yield: 60.7%. UV-Vis (EtOH) λ_{max} (log ε): 254.19 (4.16) nm, 224.42 (4.28) nm; IR (thin film, cm⁻¹): 3076 (w), 3014 (w, Ar-H, =C-H), 1750 (s, C=O), 1653 (m, C=N), 1581 (m), 1560 (w), 1516 (w), 1447 (m, Ar); ¹H-NMR δ = 7.71 (dd, *J* = 7.8, 1.6 Hz, 1H, C₁₇-H), 7.62 (dd, *J* = 8.0, 1.6 Hz, 1H, C₁₅-H), 7.30 (t, *J* = 7.9 Hz, 1H, C₁₆-H), 6.13 (s, 1H, C₄-H), 2.55 (dd, *J* = 21.1, 8.3 Hz, 1H, C₂-H_a), 2.21 (d, *J* = 21.1 Hz, 1H, C₂-H_b), 2.02 (d, *J* = 8.1 Hz, 1H, C₆-H), 1.85 (s, 3H, C₃-CH₃), 1.30 (t, *J* = 8.0 Hz, 1H, C₁-H), 1.22 (s, 3H, C₇-CH₃), 0.94 (s, 3H, C₇-CH₃). ¹³C-NMR δ = 164.70 (C₁₁), 163.64 (C₅), 149.74 (C₃), 135.48 (C₁₂), 134.17 (C₁₅), 133.69 (C₁₄), 132.38 (C₁₃), 130.37 (C₁₇), 128.32 (C₁₆), 119.05 (C₄), 29.11 (C₆), 28.21 (C₉), 24.78 (C₂), 24.20 (C₁), 23.08 (C₁₀), 22.36 (C₇), 15.56 (C₈); ESI-MS *m/z*: 337.99 [M - H]⁻. Anal. Calcd. For C₁₇H₁₇Cl₂NO₂ (338.23): C, 60.37; H, 5.07; N, 4.14. Found: C, 60.40; H, 5.09; N, 4.15.

(*Z*)-3-Caren-5-one *O*-(4-chloromethylbenzoyl) oxime ((*Z*)-4m). White solid. Yield: 78%, m.p.: 121.9–123.2 °C. UV-Vis (EtOH) λ_{max} (log ε): 258.00 (4.23) nm, 238.50 (4.31) nm; IR (KBr, cm⁻¹): 3039 (w), 3009 (w, Ar-H, =C-H), 1748 (s, C=O), 1653 (m, C=N), 1611 (m), 1575 (m), 1516 (w), 1426 (m, Ar); ¹H-NMR δ = 8.09 (d, *J* = 8.3 Hz, 2H, C₁₃-H, C₁₇-H), 7.50 (d, *J* = 8.2 Hz, 2H, C₁₄-H, C₁₆-H), 6.16 (s, 1H, C₄-H), 4.63 (s, 2H, C₁₈-H), 2.56 (dd, *J* = 20.3, 8.3 Hz, 1H, C₂-H_a), 2.22 (d, *J* = 20.3 Hz, 1H, C₂-H_b), 2.03 (d, *J* = 8.1 Hz, 1H, C₆-H), 1.85 (s, 3H, C₃-CH₃), 1.34 (t, *J* = 8.2 Hz, 1H, C₁-H), 1.30 (s, 3H, C₇-CH₃), 0.94 (s, 3H, C₇-CH₃); ¹³C-NMR δ = 163.66 (C₁₁), 162.08 (C₅), 148.22 (C₃), 142.39 (C₁₅), 130.63 (C₁₂), 129.97 (C₁₃, C₁₇), 128.62 (C₁₄, C₁₆), 118.27 (C₄), 45.36 (C₁₈), 28.10 (C₆), 27.16 (C₉), 23.78 (C₂), 23.12 (C₁), 21.75 (C₁₀), 21.34 (C₇), 14.59 (C₈); ESI-MS *m/z*: 318.10 [M + H]⁺. Anal. Calcd. For C₁₈H₂₀ClNO₂ (317.81): C, 68.03; H, 6.34; N, 4.41. Found: C, 68.00; H, 6.35; N, 4.43.

(*Z*)-3-Caren-5-one *O*-cyclopentylcarbonyl oxime ((*Z*)-4n). White solid. Yield: 64.5%, m.p.: 58.0–60.2 °C. UV-Vis (EtOH) λ_{max} (log ε): 241.40 (4.19) nm; IR (KBr, cm⁻¹): 3030 (w, =C-H), 1757 (s, C=O), 1653 (m, C=N); ¹H-NMR δ = 6.07 (s, 1H, C₄-H), 2.89 (p, *J* = 8.0 Hz, 1H, C₁₂-H), 2.51 (dd, *J* = 20.3, 8.4 Hz, 1H, C₂-H_a), 2.17 (d, *J* = 20.3 Hz, 1H, C₂-H_b), 1.94 (tt, *J* = 12.5, 6.8 Hz, 4H, C₁₃-H₂, C₁₆-H₂), 1.89 (d, *J* = 8.2 Hz, 1H, C₆-H), 1.81 (s, 3H, C₃-CH₃), 1.78–1.72 (m, 2H, C₁₄-2H), 1.62 (dt, *J* = 8.9, 4.2 Hz, 2H, C₁₅-H), 1.27 (t, *J* = 8.3 Hz, 1H, C₁-H), 1.23 (s, 3H, C₇-CH₃), 0.89 (s, 3H, C₇-CH₃). ¹³C-NMR δ = 174.14 (C₁₁), 161.27 (C₅), 147.49 (C₃), 118.48 (C₄), 42.99 (C₁₂), 30.08 (C₁₃), 30.02 (C₁₆), 28.02 (C₆), 27.12 (C₉), 25.86 (C₁₄ and C₁₅), 23.71 (C₂), 22.97 (C₁), 21.50 (C₁₀), 21.04 (C₇), 14.56 (C₈); ESI-MS *m/z*: 262.13 [M + H]⁺. Anal. Calcd. For C₁₆H₂₃NO₂ (261.36): C, 73.53; H, 8.87; N, 5.36. Found: C, 73.51; H, 8.89; N, 5.37.

(*Z*)-3-Caren-5-one *O*-cyclohexylcarbonyl oxime ((*Z*)-4o). White solid. Yield: 64.8%, m.p.: 81.4–82.5 °C. UV-Vis (EtOH) λ_{max} (log ε): 243.60 (4.29) nm; IR (KBr, cm⁻¹): 3027 (w, =C-H), 1753 (s, C=O), 1650 (m, C=N); ¹H-NMR δ = 6.07 (s, 1H, C₄-H), 2.54–2.44 (m, 2H, C₂-H_a, C₁₂-H), 2.17 (d, *J* = 20.3 Hz, 1H, C₂-H_b), 1.98 (s, 2H, C₁₃-H), 1.89 (d, *J* = 8.2 Hz, 1H, C₆-H), 1.81 (s, 3H, C₃-CH₃), 1.78 (dd, *J* = 9.1, 3.9 Hz, 2H,

C₁₇-H), 1.57 (q, *J* = 11.7 Hz, 2H, C₁₅-H), 1.37–1.25 (m, 5H, C₁-H, C₁₄-H, C₁₆-H), 1.23 (s, 3H, C₇-CH₃), 0.89 (s, 3H, C₇-CH₃); ¹³C-NMR δ = 173.30 (C₁₁), 161.43 (C₅), 147.52 (C₃), 118.47 (C₄), 42.54 (C₁₂), 29.10 (C₁₃), 29.03 (C₁₇), 28.03 (C₆), 27.11 (C₉), 25.77 (C₁₄), 25.48 (C₁₅), 25.43 (C₁₆), 23.70 (C₂), 22.97 (C₁), 21.50 (C₁₀), 21.04 (C₇), 14.55 (C₈); ESI-MS *m/z*: 276.22 [M + H]⁺. Anal. Calcd. For C₁₇H₂₅NO₂ (275.39): C, 74.14; H, 9.15; N, 5.09. Found: C, 74.16; H, 9.12; N, 5.06.

(*Z*)-3-caren-5-one *O*-α-furylcarbonyl oxime ((*Z*)-4p). White solid. Yield: 82.0%, m.p.: 114.7–115.6 °C. UV-Vis (EtOH) λ_{max} (log ε): 268.90 (4.28) nm; IR (KBr, cm⁻¹): 3110 (m), 3006 (w, =C-H), 1754 (s, C=O), 1653 (m, C=N); ¹H-NMR δ = 7.65–7.61 (m, 1H, C₁₅-H), 7.22 (d, *J* = 3.5 Hz, 1H, C₁₃-H), 6.55 (dd, *J* = 3.5, 1.7 Hz, 1H, C₁₄-H), 6.13 (s, 1H, C₄-H), 2.55 (dd, *J* = 20.3, 8.3 Hz, 1H, C₂-H_a), 2.21 (d, *J* = 20.3 Hz, 1H, C₂-H_b), 2.02 (d, *J* = 8.1 Hz, 1H, C₆-H), 1.84 (s, 3H, C₃-CH₃), 1.33 (t, *J* = 8.1 Hz, 1H, C₁-H), 1.28 (s, 4H, C₇-CH₃), 0.93 (s, 3H, C₇-CH₃). ¹³C-NMR δ = 162.13 (C₁₁), 156.70 (C₅), 148.25 (C₃), 146.63 (C₁₂), 143.61 (C₁₅), 118.14 (C₄), 117.95 (C₁₃), 111.84 (C₁₄), 28.00 (C₆), 27.19 (C₉), 23.77 (C₂), 23.15 (C₁), 21.78 (C₁₀), 21.22 (C₇), 14.54 (C₈); ESI-MS *m/z*: 260.07 [M + H]⁺. Anal. Calcd. For C₁₅H₁₇NO₃ (259.30): C, 69.48; H, 6.61; N, 5.40. Found: C, 69.50; H, 6.58; N, 5.41.

(*Z*)-3-Caren-5-one *O*-α-thienylcarbonyl oxime ((*Z*)-4q). White solid. Yield: 75.5%, m.p.: 108.4–109.3 °C. UV-Vis (EtOH) λ_{max} (log ε): 278.80 (4.30) nm, 253.90 (4.36) nm; IR (KBr, cm⁻¹): 3116 (w), 3018 (w, =C-H), 1739 (s, C=O), 1650 (m, C=N); ¹H-NMR δ = 7.91 (dd, *J* = 3.8, 1.2 Hz, 1H, C₁₃-H), 7.59 (dd, *J* = 5.0, 1.2 Hz, 1H, C₁₅-H), 7.15 (dd, *J* = 4.9, 3.8 Hz, 1H, C₁₄-H), 6.14 (s, 1H, C₄-H), 2.55 (dd, *J* = 20.6, 8.7 Hz, 1H, C₂-H_a), 2.21 (d, *J* = 21.1 Hz, 1H, C₂-H_b), 2.03 (d, *J* = 8.1 Hz, 1H, C₆-H), 1.85 (s, 3H, C₃-CH₃), 1.33 (d, *J* = 8.1 Hz, 1H, C₆-H), 1.31 (s, 3H, C₇-CH₃), 0.93 (s, 3H, C₇-CH₃). ¹³C-NMR δ = 161.82 (C₁₁), 159.90 (C₅), 148.19 (C₃), 133.81 (C₁₂), 132.45 (C₁₃), 132.18 (C₁₅), 127.84 (C₁₄), 118.15 (C₄), 28.00 (C₆), 27.16 (C₉), 23.78 (C₂), 23.03 (C₁), 21.70 (C₁₀), 21.29 (C₇), 14.57 (C₈); ESI-MS *m/z*: 276.06 [M + H]⁺. Anal. Calcd. For C₁₅H₁₇NO₂S (275.37): C, 65.43; H, 6.22; N, 5.09. Found: C, 65.45; H, 6.21; N, 5.10.

(*Z*)-3-Caren-5-one *O*-β-pyridylcarbonyl oxime ((*Z*)-4r). Brown solid. Yield: 80.0%, m.p.: 97.0–98.7 °C. UV-Vis (EtOH) λ_{max} (log ε): 262.60 (4.18) nm, 223.80 (4.14) nm; IR (KBr, cm⁻¹): 3065 (w), 3039 (w, =C-H), 1743 (s, C=O), 1655 (m, C=N); ¹H-NMR δ = 9.28 (s, 1H, C₁₃-H), 8.81 (d, *J* = 4.8 Hz, 1H, C₁₄-H), 8.38 (d, *J* = 7.9 Hz, 1H, C₁₆-H), 7.45 (dd, *J* = 7.9, 4.9 Hz, 1H, C₁₅-H), 6.16 (s, 1H, C₄-H), 2.57 (dd, *J* = 20.3, 8.4 Hz, 1H, C₂-H_a), 2.23 (d, *J* = 20.3 Hz, 1H, C₂-H_b), 2.03 (d, *J* = 8.1 Hz, 1H, C₆-H), 1.86 (s, 3H, C₃-CH₃), 1.36 (t, *J* = 8.3 Hz, 1H, C₁-H), 1.31 (s, 3H, C₇-CH₃), 0.95 (s, 3H, C₇-CH₃). ¹³C-NMR δ = 162.88 (C₁₁), 162.48 (C₅), 153.47 (C₃), 150.53 (C₁₄), 148.73 (C₁₃), 137.20 (C₁₆), 125.72 (C₁₂), 123.55 (C₁₅), 118.06 (C₄), 28.15 (C₆), 27.18 (C₉), 23.81 (C₂), 23.21 (C₆), 21.94 (C₁₀), 21.34 (C₇), 14.58 (C₈); ESI-MS *m/z*: 271.14 [M + H]⁺. Anal. Calcd. For C₁₆H₁₈N₂O₂ (270.33): C, 71.09; H, 6.71; N, 10.36. Found: C, 71.06; H, 6.70; N, 10.38.

(*Z*)-3-Caren-5-one *O*-(2-chloropyridylcarbonyl) oxime ((*Z*)-4s). Brown solid. Yield: 82.4%, m.p.: 107.1–109.4 °C. UV-Vis (EtOH) λ_{max} (log ε): 257.50 (4.28) nm, 229.10 (4.15) nm; IR (KBr, cm⁻¹): 3051 (w), 3018 (w, =C-H), 1736 (s, C=O), 1650 (m, C=N); ¹H-NMR δ = 8.55 (dd, *J* = 4.8, 2.0 Hz, 1H, C₁₄-H), 8.23 (dd, *J* = 7.7, 2.0 Hz, 1H, C₁₆-H), 7.38 (dd, *J* = 7.7, 4.8 Hz, 1H, C₁₅-H), 6.13 (s, 1H, C₄-H), 2.56 (dd, *J* = 20.7, 8.7 Hz, 1H, C₂-H_a), 2.22 (d, *J* = 21.1 Hz, 1H, C₂-H_b), 2.08 (d, *J* = 8.1 Hz, 1H, C₆-H), 1.86 (s, 3H, C₃-CH₃), 1.32 (t, *J* = 8.0 Hz, 1H, C₁-H), 1.24 (s, 3H, C₇-CH₃), 0.94 (s, 3H, C₇-CH₃). ¹³C-NMR δ = 163.05 (C₁₁), 162.81 (C₅), 151.91 (C₃), 149.48 (C₁₄), 149.00 (C₁₃), 140.74 (C₁₆), 126.97 (C₁₂), 122.24 (C₁₅), 117.92 (C₄), 28.11 (C₆), 27.23 (C₉), 23.80 (C₂), 23.23 (C₆), 22.20 (C₁₀), 21.46 (C₇), 14.56 (C₈); ESI-MS *m/z*: 305.03 [M + H]⁺. Anal. Calcd. For C₁₆H₁₇ClN₂O₂ (304.77): C, 63.05; H, 5.62; N, 9.19. Found: C, 63.01; H, 5.63; N, 9.21.

(*Z*)-3-Caren-5-one *O*-*n*-hexanoyl oxime ((*Z*)-4t). Yellow liquid. Yield: 63.5%. UV-vis (EtOH) λ_{max} (log ε): 241.80 (4.23) nm; IR (thin film, cm⁻¹): 1766 (s, C=O), 1659 (m, C=N), 763 (m), 751 (m, -(CH₂)_{*n*}, *n* > 4); ¹H-NMR δ = 6.06 (s, 1H, C₄-H), 2.51 (dd, *J* = 20.3, 8.3 Hz, 1H, C₂-H_a), 2.45 (t, *J* = 7.5 Hz, 2H, C₁₂-H), 2.18 (d, *J* = 20.3 Hz, 1H, C₂-H_b), 1.90 (d, *J* = 8.2 Hz, 1H, C₆-H), 1.82 (s, 3H, C₄-CH₃), 1.72 (q, *J* = 7.4 Hz, 2H, C₁₃-H), 1.36 (dt, *J* = 7.1, 4.4 Hz, 4H, C₁₄-H, C₁₅-H), 1.28 (d, *J* = 8.6 Hz, 1H, C₁-H), 1.23 (s, 3H, C₇-CH₃), 0.91 (d, *J* = 7.1 Hz, 3H, C₁₆-H), 0.89 (s, 3H, C₇-CH₃). ¹³C-NMR δ = 171.52 (C₁₁), 161.20 (C₅), 147.60

(C₃), 118.45 (C₄), 33.33 (C₁₂), 31.32 (C₁₃), 28.02 (C₆), 27.13 (C₉), 24.76 (C₁₄), 23.70 (C₂), 23.03 (C₁), 22.31 (C₇), 21.59 (C₁₀), 21.00 (C₁₅), 14.53 (C₈), 13.91 (C₁₆); ESI-MS *m/z*: 264.20 [M + H]⁺. Anal. Calcd. For C₁₆H₂₅NO₂ (263.38): C, 72.96; H, 9.57; N, 5.32. Found: C, 72.92; H, 9.60; N, 5.31.

(*Z*)-3-Caren-5-one *O*-*n*-propionyl oxime ((*Z*)-4u). Yellow liquid. Yield: 66.3%. UV-Vis (EtOH) λ_{max} (log ε): 242.00 (4.35) nm; IR (thin film, cm⁻¹): 1765 (s, C=N), 1655 (m, C=N); ¹H-NMR δ = 6.06 (s, 1H, C₄-H), 2.55–2.47 (m, 3H, C₂-H_a, C₁₂-H), 2.18 (d, *J* = 20.3 Hz, 1H, C₂-H_b), 1.90 (d, *J* = 8.2 Hz, 1H, C₆-H), 1.82 (s, 3H, C₃-CH₃), 1.29–1.24 (m, 4H, C₁-H, C₁₃-3H), 1.23 (s, 3H, C₇-CH₃), 0.89 (s, 3H, C₇-CH₃); ¹³C-NMR δ = 172.19 (C₁₁), 161.23 (C₅), 147.61 (C₃), 118.43 (C₄), 28.01 (C₆), 27.14 (C₉), 26.69 (C₁₂), 23.70 (C₂), 23.04 (C₁), 21.59 (C₁₀), 20.97 (C₇), 14.52 (C₈), 9.21 (C₁₃); ESI-MS *m/z*: 222.17 [M + H]⁺. Anal. Calcd. For C₁₃H₁₉NO₂ (221.30): C, 70.56; H, 8.65; N, 6.33. Found: C, 70.59; H, 8.64; N, 6.34.

(*Z*)-3-Caren-5-one *O*-*n*-butanoyl oxime ((*Z*)-4v). Yellow liquid. Yield: 65.7%. UV-Vis (EtOH) λ_{max} (log ε): 243.60 (4.19) nm; IR (thin film, cm⁻¹): IR (KBr, cm⁻¹): 1757 (s, C=O), 1653 (m, C=N); ¹H-NMR δ = 6.06 (d, *J* = 0.9 Hz, 1H, C₄-H), 2.51 (dd, *J* = 20.3, 8.3 Hz, 1H, C₂-H_a), 2.44 (t, *J* = 7.3 Hz, 2H, C₁₂-H), 2.17 (d, *J* = 20.3 Hz, 1H, C₂-H_b), 1.90 (d, *J* = 8.2 Hz, 1H, C₆-H), 1.81 (s, 3H, C₃-CH₃), 1.75 (ddd, *J* = 14.8, 7.4, 2.7 Hz, 2H, C₁₃-H), 1.27 (t, *J* = 8.2, 1H, C₁-H), 1.23 (s, 3H, C₇-CH₃), 1.01 (t, *J* = 7.4 Hz, 3H, C₁₄-H), 0.89 (s, 3H, C₇-CH₃). ¹³C-NMR δ = 171.33 (C₁₁), 161.21 (C₅), 147.62 (C₃), 118.44 (C₄), 35.22 (C₁₂), 28.01 (C₆), 27.13 (C₉), 23.70 (C₂), 23.03 (C₁), 21.58 (C₁₀), 21.00 (C₇), 18.54 (C₁₃), 14.52 (C₈), 13.76 (C₁₄); ESI-MS *m/z*: 236.19 [M + H]⁺. Anal. Calcd. For C₁₄H₂₁NO₂ (235.32): C, 71.46; H, 8.99; N, 5.95. Found: C, 71.44; H, 8.97; N, 5.93.

(*Z*)-3-Caren-5-one *O*-*n*-pentanoyl oxime ((*Z*)-4w). Yellow liquid. Yield: 60.0%. UV-Vis (EtOH) λ_{max} (log ε): 243.40 (4.32) nm; IR (thin film, cm⁻¹): 1769 (s, C=O), 1656 (m, C=N), 763 (m), 733 (m, -(CH₂)_{*n*}, *n* ≥ 4); ¹H-NMR δ = 6.06 (s, 1H, C₄-H), 2.51 (dd, *J* = 20.3, 7.7 Hz, 1H, C₂-H_a), 2.46 (t, 2H, C₁₂-H), 2.18 (d, *J* = 19.6 Hz, 1H, C₂-H_b), 1.90 (d, *J* = 8.2 Hz, 1H, C₆-H), 1.81 (s, 3H, C₃-CH₃), 1.73–1.68 (m, 2H, C₁₃-H), 1.41 (dt, *J* = 14.8, 7.4 Hz, 2H, C₁₄-H), 1.27 (t, *J* = 8.5 Hz, 1H, C₁-H), 1.23 (s, 3H, C₇-CH₃), 0.94 (t, *J* = 7.4 Hz, 3H, C₁₅-H), 0.89 (s, 3H, C₇-CH₃). ¹³C-NMR δ = 171.51 (C₁₁), 161.20 (C₅), 147.61 (C₃), 118.44 (C₄), 33.06 (C₁₂), 28.02 (C₆), 27.13 (C₉, C₁₃), 23.70 (C₂), 23.03 (C₁), 22.29 (C₇), 21.59 (C₁₀), 21.01 (C₁₄), 14.53 (C₈), 13.72 (C₁₅); ESI-MS *m/z*: 250.08 [M + H]⁺. Anal. Calcd. For C₁₅H₂₃NO₂ (249.35): C, 72.25; H, 9.30; N, 5.62. Found: C, 72.23; H, 9.31; N, 5.60.

(*E*)-3-Caren-5-one *O*-(4-fluorobenzoyl) oxime ((*E*)-4f'). Pale yellow liquid, yield: 60.0%. UV-Vis (EtOH) λ_{max} (log ε): 256.00 (3.97) nm, 229.70 (4.21) nm; IR (thin film, cm⁻¹): 3078, 3009 (w, Ar-H, =C-H), 1748 (s, C=O), 1679 (m, C=N); ¹H-NMR δ = 8.11 (dd, *J* = 8.8, 5.5 Hz, 2H, C₁₃-H, C₁₇-H), 7.15 (t, *J* = 8.6 Hz, 2H, C₁₄-H, C₁₆-H), 6.61 (s, 1H, C₄-H), 2.58 (dd, *J* = 20.7, 8.0 Hz, 1H, C₂-H_a), 2.27 (d, *J* = 20.7 Hz, 1H, C₂-H_b), 1.91 (s, 3H, C₃-CH₃), 1.84 (d, *J* = 8.6 Hz, 1H, C₆-H), 1.33 (d, *J* = 8.0 Hz, 1H, C₁-H), 1.19 (s, 3H, C₇-CH₃), 0.94 (s, 3H, C₇-CH₃); ¹³C-NMR δ 166.60 (C₁₁), 164.92 (C₅), 163.10 (C₁₅), 159.43 (C₁₂), 152.56 (C₃), 132.06 (C₁₃ or C₁₇), 125.84 (C₁₃ or C₁₇), 115.72 (C₁₄ or C₁₆), 115.58 (C₁₄ or C₁₆), 113.16 (C₄), 28.12 (C₆), 28.01 (C₉), 24.23 (C₂), 23.77 (C₁), 22.35 (C₁₀), 20.57 (C₇), 14.13 (C₈); ESI-MS *m/z*: 288.16 [M + H]⁺. Anal. Calcd. For C₁₇H₁₈FNO₂ (287.33): C, 71.06; H, 6.31; N, 4.87. Found: C, 71.02; H, 6.32; N, 4.85.

(*E*)-3-Caren-5-one *O*-(2, 3-dichlorobenzoyl) oxime ((*E*)-4i'). Yellow liquid. Yield: 60.8%. UV-Vis (EtOH) λ_{max} (log ε): 253.00 (4.26) nm; IR (thin film, cm⁻¹): 3071, 3009 (w, Ar-H, =C-H), 1759 (s, C=O), 1649 (m, C=N); ¹H-NMR δ = 7.67 (dd, *J* = 7.7, 1.5 Hz, 1H, C₁₇-H), 7.61 (dd, *J* = 8.0, 1.5 Hz, 1H, C₁₅-H), 7.30 (t, *J* = 7.9 Hz, 1H, C₁₆-H), 6.58 (s, 1H, C₄-H), 2.57 (dd, *J* = 20.8, 8.1 Hz, 1H, C₅-H_a), 2.26 (d, *J* = 20.8 Hz, 1H, C₅-H_b), 1.87 (s, 3H, C₃-CH₃), 1.82 (d, *J* = 8.5 Hz, 1H, C₆-H), 1.35 (t, *J* = 8.3 Hz, 1H, C₁-H), 1.19 (s, 3H, C₇-CH₃), 0.93 (s, 3H, C₇-CH₃); ¹³C-NMR δ = 163.37 (C₁₁), 159.97 (C₂), 153.10 (C₃), 134.40 (C₁₂), 133.00 (C₁₅), 132.86 (C₁₄), 131.27 (C₁₃), 129.12 (C₁₇), 127.32 (C₁₆), 113.42 (C₄), 28.11 (C₁), 28.01 (C₉), 24.17 (C₅), 23.67 (C₆), 22.47 (C₁₀), 20.68 (C₇), 14.11 (C₈); ESI-MS *m/z*: 337.83 [M - H]⁻. For C₁₇H₁₇Cl₂NO₂ (338.23): C, 60.37; H, 5.07; N, 4.14. Found: C, 60.39; H, 5.06; N, 4.13.

(*E*)-3-Caren-5-one *O*-β-pyridylcarbonyl oxime ((*E*)-4r'). White solid. Yield 78.3%, m.p.: 108.5–109.3 °C. UV-Vis (EtOH) λ_{max} (log ε): 262.50 (4.07) nm, 223.40 (4.12) nm; IR (KBr, cm⁻¹): 3092, 3057 (w, Ar-H,

=C-H), 1750 (s, C=O), 1635 (m, C=N); $^1\text{H-NMR}$ δ = 9.29 (s, 1H, C₁₃-H), 8.80 (d, J = 4.8 Hz, 1H, C₁₄-H), 8.38 (d, J = 7.9 Hz, 1H, C₁₆-H), 7.45 (dd, J = 8.3, 5.2 Hz, 1H, C₁₅-H), 6.63 (s, 1H, C₄-H), 2.60 (dd, J = 20.8, 8.1 Hz, 1H, C₂-H_a), 2.29 (d, J = 20.8 Hz, 1H, C₂-H_b), 1.92 (s, 3H, C₃-CH₃), 1.84 (d, J = 8.5 Hz, 1H, C₃-CH₃), 1.36 (t, J = 8.2 Hz, 1H, C₁-H), 1.20 (s, 3H, C₇-CH₃), 0.95 (s, 3H, C₇-CH₃); $^{13}\text{C-NMR}$ δ = 162.71 (C₁₁), 159.90 (C₅), 153.42 (C₃), 153.19 (C₁₄), 150.55 (C₁₃), 137.24 (C₁₆), 125.77 (C₁₂), 123.51 (C₁₅), 113.03 (C₄), 28.15 (C₆), 28.01 (C₉), 24.24 (C₂), 23.74 (C₆), 22.43 (C₁₀), 20.68 (C₇), 14.13 (C₈); ESI-MS m/z : 270.96 [M + H]⁺. Anal. Calcd. For C₁₆H₁₈N₂O₂ (270.33): C, 71.09; H, 6.71; N, 10.36. Found: C, 71.11; H, 6.69; N, 10.37.

3.6. Antifungal Activity Test

Antifungal activity of the target compounds was performed in vitro method [40]. The tested compound was dissolved in acetone. Sorporl-144 (200 $\mu\text{g}/\text{mL}$) emulsifier was added to dilute the solution to 500 $\mu\text{g}/\text{mL}$. Then, 1 mL solution of the tested compound was poured into a culture plate, and then 9 mL PSA culture medium was added to obtain the flat containing 50 $\mu\text{g}/\text{mL}$ tested compound. A bacterium tray of 5-mm diameter cut along the external edge of the mycelium was transferred to the flat containing the tested compound and put in equilateral triangular style in duplicate. Later, the culture plate was cultured at 24 ± 1 °C and the expanded diameter of the bacterium tray was measured after 48 h and compared with that treated with aseptic distilled water to calculate the relative inhibition percentage:

$$\text{Relative inhibitory rate (\%)} = (CK - PT)/CK \times 100\%$$

where CK is the extended diameter of the circle of mycelium during the blank assay and PT is the extended diameter of the circle of mycelium during testing.

4. Conclusions

Twenty-four novel 3-carene-5-one oxime esters were designed, synthesized, characterized, and evaluated for their antifungal activity. As a result, at 50 $\mu\text{g}/\text{mL}$, the target compounds exhibited best antifungal activity against *P. piricola*, in which compounds (Z)-**4r**, (Z)-**4q**, (E)-**4f'**, (Z)-**4i**, (Z)-**4j**, and (Z)-**4p** had inhibition rates of 97.1%, 87.4%, 87.4%, 85.0%, 81.9% and 77.7%, respectively, showing better antifungal activity than that of the commercial fungicide chlorothanil. Also, compound (Z)-**4r** displayed remarkable antifungal activity against all the tested fungi, with inhibition rates of 76.7%, 82.7%, 97.1%, 66.3%, 74.7%, 93.9%, 76.7% and 93.3%, respectively, showing better or comparable antifungal activity than that of the commercial fungicide chlorothanil. Thus, compound (Z)-**4r** is a lead compound worthy of further investigation. Besides, *E-Z* isomers of the target oxime esters were found to show obvious difference in antifungal activity. It is very meaningful and requires further studies in photoisomerization and drug resistance.

Supplementary Materials: Supplementary materials are available online.

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Author Contributions: Min Huang carried out the experimental work, participated in the discussion of biological activities, and wrote the paper; Wen-Gui Duan and Gui-Shan Lin constructed the target compound structure, designed the experimental scheme, directed and supervised the whole experimentation, discussed the biological activities, and revised the paper; Kun Li explored the preparation of 3-carene-5-one; Qiong Hu participated in the discussion of biological activities.

Conflicts of Interest: The authors declare no conflict of interest.

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Sample Availability: Samples of the compounds **2**, (*Z*)-**3a**, (*E*)-**3b**, (*Z*)-**4a–4w**, and (*E*)-**4f'**, **4l'**, **4r'** are available from the authors.



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