Organic Chemistry Research

Article

Organic Chemistry Research
www.orgchemres.org

Cite this: *Org. Chem. Res.* **2022**, *Vol. 8,* 16-20.
DOI: 10.22036/org.chem.2023.412000.1291

Oakes-Yavari-Nair (OYN)-based Synthesis of Imidazo[2,1-*b*][1,3]thiazin-7-imines and Imidazo[2,1-*b*][1,3]thiazin-7-amines with Thiohydantoins, Isocyanides, Acetylenedicarboxylates

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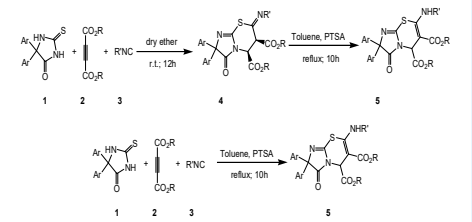
Received: August 16, 2023; Accepted: October 26, 2023

Abstract: Hydantoin and thiohydantoin derivatives are important core moiety in the design and synthesis of heterocyclic compounds as well as medical products with good biological activity. These molecules are useful building blocks for the synthesis of various heterocycles with hypothermic activities, antibacterial, fungicidal activity and other pharmaceuticals properties. The Oakes-Yavari-Nair (OYN) three-component reaction (OYN-3-CRs) of acetylenedicarboxylates, alkyl isocyanides in the presence of 2-thiophenytoins afforded imidazo[2,1-*b*][1,3]thiazines as a imine compounds **4** in which these imines produce target amines **5** in the present of *p*-TsOH catalyst. To choose the best catalyst among various common acidic catalysts, *p*-TsOH has the best yield in the shortest reaction time. Finally the stereochemistry of the Imidazo[2,1-*b*][1,3]thiazin-7-imines was studied by NOE (Nuclear Overhauser Effect) spectra.



Keywords: Hydantoin, NOE spectra, Imidazo thiazines, Heterocyclic compounds, Antibacterial

1. Introduction

5,5-Diaryl-2-thiohydantoins are important core moiety in the design and synthesis of heterocyclic compounds as well as medical products. These molecules and their derivatives are useful building blocks for the synthesis of various heterocycles such as imidazo[2,1-*b*][1,3]thiazines, 4,5-dihydro-2-(methylthio)-5-oxoimidazoles, imidazo[2,1-*b*]thiazoles and imidazo[2,1-*b*]naphtho[1,2-*e*][1,3]thiazin-10-ones.[1-4] These heterocyclic skeletons shows hypothermic activities, antibacterial, fungicidal activity and other pharmaceuticals properties.[5-8]

Multicomponent reactions (MCRs), in which three, four or more compounds react to form a product, where basically all or most of the atoms donate to the newly formed product.[1-8] Oakes-Yavari-Nair isocyanide-based multicomponent reaction (OYN-IMCRs) covers the reactivity of isocyanide and acetylenic ester adducts with NuH (Nu = nucleophiles) or carbonyl functional groups where the NuH can be -NH, -CH, -OH and -SH acids.[9]

1,3-Thiazines are of great interest as biologically active compounds. They have strong analgesic, muscle relaxing, and stimulation of the entire sympathetic system. As a part of our current studies in our laboratory on the development of new routes in hydantoin and thiohydantoin derivatives synthesis,[1-4] herein we report the results of our studies involving the reaction of the zwitterionic intermediates derived from alkyl isocyanides **3** and acetylenic esters **2** with 5,5-diaryl-2-thioxoimidazolidin-4-one **1**, which constitutes a synthesis of 7-alkylamino-3-oxo-2,2-diaryl-2,3-dihydro-5*H*-imidazo[2,1-*b*][1,3]thiazine-5,6-dicarboxylic acid alkyl esters **5** in 80-98% yields (see Scheme 1 and Table 1).

2. Experimental

General

Acetylenic esters and isocyanides were obtained from Fluka and were used without further purification. 5,5-Diaryl-2-thiohydantoins was prepared by known methods.[10-12] Elemental analyses for C, H, N and S were performed using a Heraeus CHN-O-Rapid analyzer. The experimental data were in good agreement with the calculated values. ^{1}H and ^{13}C NMR spectra were measured with a Bruker DRX-300 Avance spectrometer. IR spectra were recorded on a Shimadzu IR-460 spectrometer.

Typical Procedure for the Preparation of Dimethyl 7-(cyclohexylimino)-3,5,6,7-tetrahydro-3-oxo-2,2-diphenyl-2H- imidazo[2,1-b][1,3]thiazine-5,6-dicarboxylate (exemplified by 4a):

To a magnetically stirred solution of 0.536 g **1a** (2 mmol) and 0.284 g **2a** (2 mmol) in 5 mL ether was added dropwise a solution of 0.218 g **3a** (2 mmol) in 2 mL ether at 5 °C over 10 min. After 12 h stirring at room temperature, the product was filtered and washed with cold ether to give **4a**.

Typical Procedure for the Preparation of 3-Oxo-2,2-diphenyl-7-[(toluene-4-sulfonylmethyl)-amino]-2,3-dihydro-5H-imidazo[2,1-b][1,3]thiazine-5,6-dicarboxylate (exemplified by 5d):

Two-steps method: A solution of 2 mmol of the compound **4** in toluene (3 mL) in the presence of catalytic amount of *p*-TsOH (PTSA) was refluxed for 10 h. The solvent was removed under reduced pressure, and the yellowish oil was separated by silica column chromatography (Merck 230-400 mesh) using hexane/AcOEt (3:1) as eluent to afford pure imidazo thiazines (**5**).

One-step method: To a magnetically stirred solution of 0.536 g **1d** (2 mmol) and 0.340 g **2d** (2 mmol) in 5 mL toluene was added dropwise a solution of 0.390 g **3d** (2 mmol) in 2 mL toluene over 10 min in the presence of catalytic amount of *p*-TsOH. After 10 h stirring under reflux condition, the product **5d** was achieved.

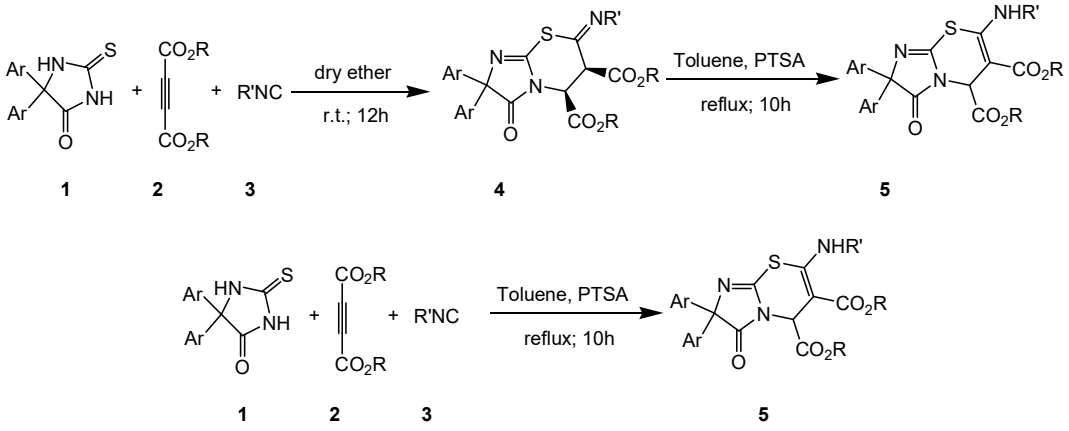
3. Results and Discussion

The reaction of 5,5-diaryl-2-thioxoimidazolidin-4-one **1** with dialkyl acetylenedicarboxylates **2** in the presence of isocyanides proceeded at room temperature in dry diethyl ether, and was complete about 12 hours. ^{1}H and ^{13}C NMR spectra of the crude products clearly indicated the formation of stable dialkyl 7-(alkylimino)-3,5,6,7-tetrahydro-3-oxo-2,2-diaryl-2*H*-imidazo[2,1-*b*][1,3]thiazine-5,6-dicarboxylate **4** (Scheme 1).

The white precipitate **4** left from this stage produce 7-alkylamino-3-oxo-2,2-diaryl-2,3-dihydro-5*H*-imidazo[2,1-*b*][1,3]thiazine-5,6-dicarboxylic acid alkyl esters **5** under reflux condition. In the second method imidazo[2,1-*b*][1,3]thiazines **5** were synthesized directly from 5,5-diaryl-2-thioxoimidazolidin-4-one **1** with dialkyl acetylene-dicarboxylates **2** and isocyanides in the presence of *p*-toluenesulfonic acid (*p*-TsOH) under reflux condition. No other products other than **5** could be detected. The structures of compounds **5a-5h** were deduced from their elemental analyses and IR, ^{1}H and ^{13}C NMR spectra. Any initial fragmentation involves loss from, or complete loss of the side chains and scission of the heterocyclic ring system. The structures of compounds **5** were deduced from ^{1}H and ^{13}C NMR and IR data.

Although the relative configuration of CH-CH in compounds **4** is cis,[1] the distance between these two hydrogens (H_5-H_6) in the compound **4a** is QUOTE, 2.28 Å while the distance between H_6 and Hydrogen in cyclohexyl is QUOTE, 1.75 Å (Figure 1). From the NOE spectra and using the expression $\frac{\mathrm{NOE_{ref}}}{\mathrm{NOE}} = \frac{r_{\mathrm{ref}}^{-6}}{r^{-6}} = \frac{r^{6}}{r_{\mathrm{ref}}^{6}}$, the distance between two hydrogen (r) were calculated.[13] We now report a simple synthetic procedure for the preparation of imidazo[2,1-*b*][1,3]thiazines **5** in the presence of p-TsOH as the catalyst.

To choose the best catalyst among various common acidic catalyst (Table 2), the results showed that *p*-TsOH has the best yield in the shortest reaction time, so that it was selected as catalyst for subsequent experiments.



Scheme 1. Synthesis of Imidazo[2,1-*b*][1,3]thiazines in two-steps method and one-step method, respectively

Table 1. Synthesis of Imidazo[2,1-*b*][1,3]thiazines

Entry	Ar	R	R'	Product	Yield (%)	
					Two-steps	One-pot
1	Ph	Me	Cy	5a	91	90
2	Ph	Et	Cy	5b	97	95
3	Ph	Me	$TsCH_2$	5c	95	95
4	Ph	Et	$TsCH_2$	5d	96	96
5	Ph	Me	^{t}Bu	5e	85	84
6	Ph	Et	^{t}Bu	5f	80	80
7	*p*-Tolyl	Me	Cy	5g	98	97
8	*p*-Tolyl	Et	Cy	5h	87	85

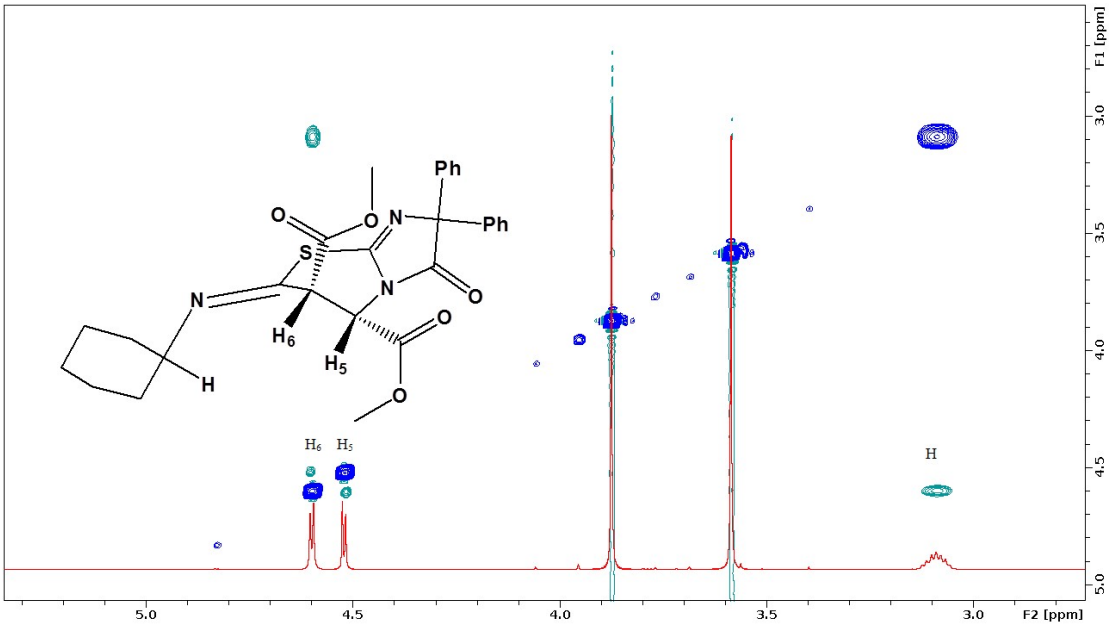
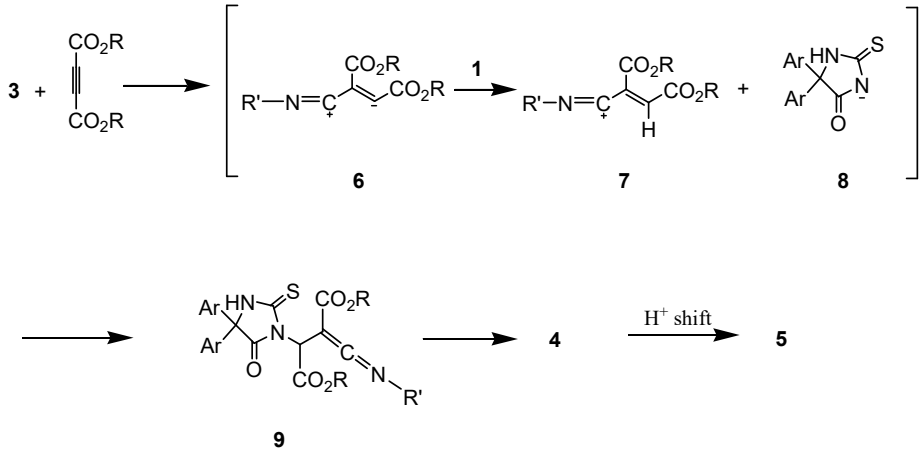


Figure 1. The NOE Spectra of **4a**.



Scheme 2. Proposed mechanism

Table 2. Preparation of **5a** by reaction of thiohydantoin, isocyanide and dialkylacetylendicarboxylate in the presence of various catalysts

Entry	Catalyst	Time (h)	Yield (%)
1	*p*-TsOH	10	91
2	CH_3COOH	14	85
3	$AlCl_3$	12	80
4	H_3BO_3	7	45

Although we have not yet established the mechanism of formation of **5** in an experimental manner, a plausible rationalization for the formation of functionalized imidazo[2,1-*b*][1,3]thiazines **5a-5h** is shown in Scheme 2. Presumably, the zwitterionic intermediate,[14,15] formed from **2** and **3**, is protonated by the NH acidic compound **1**. Then, the positively charged ion **6** undergo intramolecular reaction with compounds **7** to produce the ketenimines **8**; which apparently isomerise under the reaction conditions employed to produce **4**. Finally, after a proton shift obtain the final products **5** in excellent yields (Scheme 2).

Dimethyl 7-(cyclohexylimino)-3,5,6,7-tetrahydro-3-oxo-2,2-diphenyl-2H- imidazo[2,1-b][1,3]thiazine-5,6-dicarboxylate (4a):

White powder; mp: 188-190 °C; yield: 0.92 g (91%); IR (KBr) (ν_{max}/cm^{-1}): 1741 and 1735 (C=O), 1447 (C=C); ^{1}H NMR (300 MHz, $CDCl_3$): δ = 0.92 (2H, m, CH_2), 1.08 (4 H, m, $2CH_2$), 1.44 (2H, m, CH_2), 1.55 (2H, m, CH_2), 3.09 (1H, m, CH), 3.58 (3H, s, MeO), 3.87 (3H, s, MeO), 4.51 (1H, d, $^3J_{HH}$ = 3.0 Hz, CH), 4.59 (1H, d, $^3J_{HH}$ = 3.0 Hz, CH), 7.22-7.58 (10H, m, $2C_6H_5$) ppm; ^{13}C NMR (75 MHz, $CDCl_3$): δ = 23.6 (CH_2), 23.7 (CH_2), 25.4 (CH_2), 32.7 (CH_2), 33.1 (CH_2), 42.1 (CH), 44.5 (CH), 53.2 (MeO), 53.6 (MeO), 57.1 (CH), 77.2 (C), 127.5 (2CH), 127.6 (2CH), 127.8 (CH), 128.0 (CH), 128.2 (2CH), 129.9 (2CH), 136.3 (C), 137.9 (C), 138.7 (C),

166.2 (OC=O), 169.2 (OC=O), 178.5 (C=O), 186.3 [NC(S)N] ppm; MS (EI, 70 eV): m/z (%) = 520 (M+, 15), 322 (75), 263 (78), 225 (30), 192 (40), 166 (100), 77 (28), 59 (12); Anal. Calcd. (%) for $C_{28}H_{29}N_3O_5S$ (519.61): C, 64.72; H, 5.63; N, 8.09; S, 6.17. Found: C, 64.83; H, 5.71; N, 7.94; S, 6.08.

Diethyl 7-(cyclohexylimino)-3,5,6,7-tetrahydro-3-oxo-2,2-diphenyl-2H- imidazo[2,1-b][1,3]thiazine-5,6-dicarboxylate (4b):
White powder; mp: 180-181 °C; yield: 0.90 g (84%); IR (KBr) (ν_{max}/cm^{-1}): 1733 and 1725 (C=O), 1447 (C=C); ^{1}H NMR (300 MHz, $CDCl_3$): δ = 1.02 (2H, m, CH_2), 1.08 (3H, t, Me), 1.17 (4H, m, $2CH_2$), 1.33 (3H, t, Me), 1.50 (4H, m, $2CH_2$), 3.12 (1H, m, CH), 4.00 (1H, dq, $^2J_{HH}$ = 11.1 Hz, $^3J_{HH}$ = 6.9 Hz, CH), 4.20 (1H, dq, $^2J_{HH}$ = 11.1 Hz, $^3J_{HH}$ = 6.9 Hz, CH), 4.31 (2H, qd, $^3J_{HH}$ = 6.9 Hz, $^2J_{HH}$ = 1.2 Hz, CH_2), 4.49 (1H, d, $^3J_{HH}$ = 3.0 Hz, CH), 4.59 (1H, d, $^3J_{HH}$ = 3.0 Hz, CH), 7.21-7.57 (10H, m, $2C_6H_5$) ppm; ^{13}C NMR (75 MHz, $CDCl_3$): δ = 14.3 (Me), 14.4 (Me), 24.5 (CH_2), 24.6 (CH_2), 26.1 (CH_2), 33.5 (CH_2), 33.7 (CH_2), 42.6 (CH), 45.4 (CH), 58.4 (CH), 62.9 (CH_2O), 63.5 (CH_2O), 77.9 (C), 128.5 (2CH), 129.0 (2CH), 131.5 (CH), 132.7 (2CH), 133.2 (2CH), 133.3 (CH), 135.7 (C), 136.2 (C), 137.5 (C), 166.2 (OC=O), 169.1 (OC=O), 172.6 (C=O), 186.9 [NC(S)N] ppm; MS (EI, 70 eV): m/z (%) = 548 (M+, 4), 336 (64), 262 (100), 224 (37), 166 (98), 77 (33); Anal. Calcd. (%) for $C_{30}H_{33}N_3O_5S$ (547.67): C, 65.79; H, 6.07; N, 7.67; S, 5.85. Found: C, 65.70; H, 6.12; N, 7.56; S, 5.98.

Di-tert-butyl 7-(cyclohexylimino)-3,5,6,7-tetrahydro-3-oxo-2,2-diphenyl-2H- imidazo[2,1-b][1,3]thiazine-5,6-dicarboxylate (4c):
White powder; mp: 184-186 °C; yield: 1.00 g (85%); IR (KBr) (ν_{max}/cm^{-1}): 1740 and 1732 (C=O), 1447 (C=C); ^{1}H NMR (300 MHz, $CDCl_3$): δ = 0.92 (2H, m, CH_2), 1.08 (4H, m, $2CH_2$), 1.34 (9H, s, 3Me), 1.44 (2H, m, CH_2), 1.52 (2H, m, CH_2), 1.57 (9H, s, 3Me), 3.08 (1H, m, CH), 4.48 (1H, d, $^3J_{HH}$ = 3.0 Hz, CH), 4.59 (1H, d, $^3J_{HH}$ = 3.0 Hz, CH), 7.10-7.45 (10H, m, $2C_6H_5$) ppm; ^{13}C NMR (75 MHz, $CDCl_3$): δ = 23.6 (CH_2), 23.9 (CH_2), 26.2 (CH_2), 26.4 (Me), 27.8 (Me), 32.7 (CH_2), 33.1 (CH_2), 42.1 (CH), 44.5 (CH), 57.1 (CH), 77.5 (C), 79.0 ($COMe_3$), 79.9 ($COMe_3$), 127.5 (2CH), 127.6 (2CH), 127.8 (CH), 128.1 (CH), 128.3 (2CH), 129.9 (2CH), 136.3 (C), 137.9 (C), 138.7 (C), 166.2 (OC=O), 169.3 (OC=O), 175.6 (C=O), 186.7 [NC(S)N] ppm.

Dimethyl 7-(tert-butylimino)-3,5,6,7-tetrahydro-3-oxo-2,2-diphenyl-2H- imidazo[2,1-b][1,3]thiazine-5,6-dicarboxylate (4d):
White powder; mp: 185-187 °C; yield: 0.88 g (89%); IR (KBr) (ν_{max}/cm^{-1}): 1755 and 1741 (C=O), 1447 (C=C); ^{1}H NMR (300 MHz, $CDCl_3$): δ = 0.96 (9H, s, 3Me), 3.65 (3H, s, MeO), 3.87 (3H, s, MeO), 4.45 (1H, d, $^3J_{HH}$ = 3.3 Hz, CH), 4.59 (1H, d, $^3J_{HH}$ = 3.3 Hz, CH), 7.25-7.58 (10H, m, $2C_6H_5$) ppm; ^{13}C NMR (75 MHz, $CDCl_3$): δ = 30.8 (3Me), 42.3 (C), 44.6 (CH), 53.8 (MeO), 54.3 (MeO), 55.2 (CH), 78.2 (C), 127.5 (2CH), 127.8 (2CH), 127.9 (CH), 128.4 (CH), 128.7 (2CH), 130.9 (2CH), 136.0 (C), 136.4 (C), 138.3 (C), 167.3 (OC=O), 168.7 (OC=O), 177.5 (C=O), 187.0 [NC(S)N] ppm.

Diethyl 7-(tert-butylimino)-3,5,6,7-tetrahydro-3-oxo-2,2-diphenyl-2H- imidazo[2,1-b][1,3]thiazine-5,6-dicarboxylate (4e):
White powder; mp:178-180 °C; yield: 0.84 g (81%); IR (KBr) (ν_{max}/cm^{-1}): 1733 and 1725 (C=O), 1447 (C=C); ^{1}H NMR (300 MHz, CDCl3): δ = 0.98 (9H, s, 3Me), 1.17 (3H, t, Me), 1.33 (3H, t, Me), 4.12 (1H, dq, $^2J_{HH}$ = 11.0 Hz, $^3J_{HH}$ = 6.8 Hz, CH), 4.25 (1H, dq, $^2J_{HH}$ = 11.0 Hz, $^3J_{HH}$ = 6.8 Hz, CH), 4.33 (2H, qd, $^3J_{HH}$ = 6.8 Hz, $^2J_{HH}$ = 2.5 Hz, CH_2), 4.43 (1H, d, $^3J_{HH}$ = 3.3 Hz, CH), 4.60 (1H, d, $^3J_{HH}$ = 3.3 Hz, CH), 7.21-7.55 (10H, m, $2C_6H_5$) ppm; ^{13}C NMR (75 MHz, $CDCl_3$): δ = 14.3 (Me), 14.4 (Me), 30.8 (3Me), 42.3 (C), 42.6 (CH), 45.4 (CH), 62.9 (CH_2O), 63.5 (CH_2O), 77.9 (C), 128.5 (2CH), 129.0 (2CH), 133.3 (CH), 131.5 (CH), 132.7 (2CH), 133.2 (2CH), 135.7 (C), 136.2 (C), 137.5 (C), 166.2 (OC=O), 169.1 (OC=O), 172.6 (C=O), 186.9 [NC(S)N] ppm.

Dimethyl 3,5,6,7-tetrahydro-3-oxo-2,2-diphenyl-7-(tosylmethylimino)-2H- imidazo[2,1-b][1,3]thiazine-5,6-dicarboxylate (4f):
White powder; yield: 0.65 g (54%); IR (KBr) (ν_{max}/cm^{-1}): 1750 and 1741 (C=O), 1468 (C=C); ^{1}H NMR (500 MHz, $CDCl_3$): δ = 2.41 (3H, s, Me), 3.77 (3H, s, MeO), 3.84 (3H, s, MeO), 4.50 (1H, d, $^2J_{HH}$ = 15.0 Hz, CH), 4.74 (1 H, d, $^3J_{HH}$ = 2.7 Hz, CH), 4.81 (1H, d, $^3J_{HH}$ = 2.7 Hz, CH), 4.97 (1H, d, $^2J_{HH}$ = 15.0 Hz, CH), 6.91-7.79 (14H, m, $2C_6H_5$, C_6H_4) ppm; ^{13}C NMR (125 MHz, $CDCl_3$): δ = 22.0 (Me), 42.5 (CH), 53.3 (CH), 54.1 (MeO), 54.7 (MeO), 77.8 (C), 90.1 (CH2), 128.2 (2CH), 128.5 (2CH), 128.8 (CH), 129.2 (CH), 129.3 (2CH), 129.7 (2CH), 130.4 (2CH), 131.0 (2CH), 135.6 (C), 135.8 (C), 145.1 (C), 146.2 (C), 165.7 (OC=O), 169.2 (OC=O), 179.3 (C=O), 186.3 [NC(S)N] ppm.

Diethyl 3,5,6,7-tetrahydro-3-oxo-2,2-diphenyl-7-(tosylmethylimino)-2H- imidazo[2,1-b][1,3]thiazine-5,6-dicarboxylate (4g):
White powder; yield: 0.65 g (51%); IR (KBr) (ν_{max}/cm^{-1}): 1747 and 1741 (C=O), 1461 (C=C); ^{1}H NMR (500 MHz, $CDCl_3$): δ = 1.01 (3H, t, Me), 1.38 (3H, t, Me), 2.46 (3H, s, Me), 3.86 (1H, dq, $^2J_{HH}$ = 11.1 Hz, $^3J_{HH}$ = 6.9 Hz, CH), 4.11 (1H, dq, $^2J_{HH}$ = 11.1 Hz, $^3J_{HH}$ = 6.9 Hz, CH), 4.38 (2H, qd, $^3J_{HH}$ = 6.9 Hz, $^2J_{HH}$ = 1.2 Hz, CH_2), 4.48 (1H, d, $^2J_{HH}$ = 15.0 Hz, CH), 4.72 (1H, d, $^3J_{HH}$ = 2.7 Hz, CH), 4.80 (1H, d, $^3J_{HH}$ = 2.7 Hz, CH), 4.88 (1H, d, $^2J_{HH}$ = 15.0 Hz, CH), 6.77-7.85 (14H, m, $2C_6H_5$, C_6H_4) ppm; ^{13}C NMR (125 MHz, $CDCl_3$): δ = 14.1 (Me), 14.4 (Me), 21.8 (Me), 41.4 (CH), 53.8 (CH), 61.7 (CH_2O), 62.2 (CH_2O), 71.6 (C), 90.1 (CH_2), 127.1 (2CH), 128.3 (2CH), 128.4 (CH), 129.2 (CH), 129.3 (2CH), 129.8 (2CH), 130.6 (2CH), 130.9 (2CH), 134.8 (2CH), 135.5 (C), 136.9 (C), 145.2 (C), 153.4 (C), 163.9 (OC=O), 165.8

(OC=O), 177.3 (C=O), 185.6 [NC(S)N] ppm.

Dimethyl 7-(cyclohexylimino)-3,5,6,7-tetrahydro-3-oxo-2,2-dip-tolyl-2H- imidazo[2,1-b][1,3]thiazine-5,6-dicarboxylate (4h):
White powder; mp: 173-175 °C; yield: 0.91 g (85%); IR (KBr) (ν_{max}/cm^{-1}): 1741 and 1735 (C=O), 1447 (C=C); ^{1}H NMR (300 MHz, $CDCl_3$): δ = 0.92 (2H, m, CH_2), 1.08 (4H, m, $2CH_2$), 1.44 (2H, m, CH_2), 1.55 (2H, m, CH_2), 2.34 (3H, s, Me), 2.35 (3H, s, Me), 3.09 (1H, m, CH), 3.58 (3H, s, MeO), 3.87 (3H, s, MeO), 4.51 (1H, d, $^3J_{HH}$ = 3.0 Hz, CH), 4.59 (1H, d, $^3J_{HH}$ = 3.0 Hz, CH), 7.22-7.58 (8H, m, $2C_6H_4$) ppm; ^{13}C NMR (75 MHz, $CDCl_3$): δ = 21.5 (Me), 21.6 (Me), 23.6 (CH_2), 23.7 (CH_2), 25.4 (CH_2), 32.7 (CH_2), 33.1 (CH_2), 42.1 (CH), 44.5 (CH), 53.2 (MeO), 53.6 (MeO), 57.1 (CH), 77.2 (C), 126.9 (2CH), 127.0 (2CH), 127.7 (2CH), 130.4 (2CH), 130.5 (C), 132.4 (C), 136.2 (C), 140.3 (C), 140.4 (C), 166.2 (OC=O), 169.2 (OC=O), 178.5 (C=O), 186.2 [NC(S)N] ppm.

Dimethyl 7-(cyclohexylimino)-3,5,6,7-tetrahydro-3-oxo-2,2-diphenyl-2H- imidazo[2,1-b][1,3]thiazine-5,6-dicarboxylate (5a):
White powder; mp: 185-186 °C; yield: 0.91 g (90%); IR (KBr) (ν_{max}/cm^{-1}): 1741 and 1735 (C=O), 1447 (C=C); ^{1}H NMR (300 MHz, $CDCl_3$): δ = 0.92 (2H, m, CH_2), 1.08 (4H, m, $2CH_2$), 1.44 (2H, m, CH_2), 1.55 (2H, m, CH_2), 3.09 (1H, m, CH), 3.58 (3H, s, MeO), 3.87 (3H, s, MeO), 5.10 (1H, S, CH), 7.22-7.58 (10H, m, $2C_6H_5$) ppm; ^{13}C NMR (75 MHz, $CDCl_3$): δ = 23.6 (CH_2), 23.7 (CH_2), 25.4 (CH_2), 32.7 (CH_2), 33.1 (CH_2), 44.1 (CH), 53.2 (MeO), 53.6 (MeO), 57.1 (CH), 77.2 (C), 127.5 (2CH), 127.6 (2CH), 127.8 (CH), 128.0 (CH), 128.2 (2CH), 129.9 (2CH), 136.3 (2C), 137.9 (C), 138.7 (C), 139.7 (C), 166.2 (OC=O), 169.2 (OC=O), 178.5 (C=O), 186.3 [NC(S)N] ppm; Anal. Calcd. (%) for $C_{28}H_{29}N_3O_5S$ (519.61): C, 64.72; H, 5.63; N, 8.09; S, 6.17. Found: C, 64.81; H, 5.73; N, 7.92; S, 6.12.

Diethyl 7-(cyclohexylimino)-3,5,6,7-tetrahydro-3-oxo-2,2-diphenyl-2H- imidazo[2,1-b][1,3]thiazine-5,6-dicarboxylate (5b):
White powder; mp: 178-179 °C; yield: 0.89 g (86%); IR (KBr) (ν_{max}/cm^{-1}): 1733 and 1725 (C=O), 1447 (C=C); ^{1}H NMR (300 MHz, $CDCl_3$): δ = 1.02 (2H, m, CH_2), 1.08 (3H, t, Me), 1.17 (4H, m, $2CH_2$), 1.33 (3H, t, Me), 1.50 (4H, m, $2CH_2$), 3.12 (1H, m, CH), 4.00 (1H, dq, $^2J_{HH}$ = 11.1 Hz, $^3J_{HH}$ = 6.9 Hz, CH), 4.20 (1H, dq, $^2J_{HH}$ = 11.1 Hz, $^3J_{HH}$ = 6.9 Hz, CH), 4.31 (2H, qd, $^3J_{HH}$ = 6.9 Hz, $^2J_{HH}$ = 1.2 Hz, CH_2), 5.11 (1H, S, CH), 7.21-7.57 (10H, m, $2C_6H_5$) ppm; ^{13}C NMR (75 MHz, $CDCl_3$): δ = 14.3 (Me), 14.4 (Me), 24.5 (CH_2), 24.6 (CH_2), 26.1 (CH_2), 33.5 (CH_2), 33.7 (CH_2), 44.1 (CH), 58.4 (CH), 62.9 (CH_2O), 63.5 (CH_2O), 77.9 (C), 128.5 (2CH), 129.0 (2CH), 131.5 (CH), 132.7 (2CH), 133.2 (2CH), 133.3 (CH), 135.7 (C), 136.2 (2C), 137.5 (C), 139.7 (C), 166.2 (OC=O), 169.1 (OC=O), 172.6 (C=O), 186.9 [NC(S)N] ppm; Anal. Calcd. (%) for $C_{30}H_{33}N_3O_5S$ (547.67): C, 65.79; H, 6.07; N, 7.67; S, 5.85. Found: C, 65.72; H, 6.11; N, 7.58; S, 5.93.

4. Conclusions

In conclusion, we have developed a simple and useful method for the synthesis of functionalized imidazo[2,1-*b*][1,3]thiazines in two methods. The present method carries the advantage that not only is the reaction performed under mild conditions, but also the starting materials and reagents can be mixed without any activation or modification.

Declaration of Interests

The author declare that he has no known competing financial interests or personal relationships that could have appeared to influence the work reported in this paper.

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