Res Chem Intermed
DOI 10.1007/s11164-012-0877-2

Synthesis and spectroscopic studies of some new oxazepine derivatives throughout [2+5] cycloaddition reactions (III)

Alaa J. Mahrath · Saadon A. Aowda · Sabah N. Kamil

Received: 12 September 2012 / Accepted: 17 October 2012

Abstract The present work included condensation reactions of o-tolidine with different aromatic aldehydes in absolute ethanol to give Schiff bases (**w_9–w_{12}**) in high yield which, on reaction with maleic and phthalic anhydride by [2+5] cycloaddition reactions in the presence of suitable solvents, give the corresponding [1,3]oxazepine-4,7-dione (**w_9m–w_{12}m**) and [1,3]oxazepine-1,5-dione (**$w_9$ph–w_{12}ph**), respectively. The structure of the newly synthesized compounds were monitored by TLC and established on the basis of elemental analysis, FT-IR, and ^{1}H NMR.

Keywords Imines · o-Tolidine · 1,3-Oxazepine-4,7-dione

Introduction

o-Tolidine is the derivative of benzidine which belongs to an important group of aromatic compounds containing methyl group in the 3-position of 4,4′-diamino biphenyl [1]. o-Tolidine derivatives possessing diverse biological activities play important roles as versatile building blocks for the synthesis of natural products and biologically active compounds [2–9]. In particular are the formation of imine derivatives, which have great interest due to their proceeding in several important pathway reactions [10–12]. Moreover, the reactions of imine throughout ring

A. J. Mahrath (✉)
Chemistry Department, College of Medicine, Babylon University, Babylon, Iraq
e-mail: aalaamahrath@gmail.com; ajmbioorg@gmail.com

S. A. Aowda
Chemistry Department, College of Science, Babylon University, Babylon, Iraq

S. N. Kamil
Department of Pharmacology, College of Pharmacy, Babylon University, Babylon, Iraq

Published online: 03 November 2012

closing generate a wide range of five-, six-, and seven-member rings of heterocyclic organic molecules, such as 4-thiazolidinone derivatives [13], 1,2-dihydro-1-arylnaphtho[1,2-e][1,3]oxazine-3-one derivatives [14–17], and 1,3-oxazepinediones [14]. Based on these papers, all of these derivatives have attracted considerable attention in drug synthesis and a wide range of pharmaceutical activities for these purposes indicate that the synthesis of these compounds is interesting.

Experimental

Materials and methods

The chemicals used in this work were obtained from B.D.H. and they were all pure grade reagents. All melting points were determined in an open capillary and are uncorrected. The solvents, ethanol, methanol dichloromethane, tetrahydrofuran, ether, and acetone were purified according to the literature [18]. The characterizations of the prepared compounds were accomplished by FT-IR spectra using Perkin Elmer apparatus with a KBr disk and an interval ranging from 450 to 4,400 cm^{-1}. ^1H NMR spectra were obtained using a Bruker 300 MHz spectrometer in Jordanian University and Glasgow University. The samples were in (DMSO–d_6) and $CDCl_3$ with tetramethylsilane (TMS) as the reference. Elemental analysis was carried out using a EuroEA Elemental Analyzer/University of Kufa.

General procedure for the synthesis of imines derivatives ($\mathbf{w_9}$–$\mathbf{w_{12}}$)

A mixture of 1 mmol of o-tolidine (0.21 g) and 2 mmol of substituted aromatic aldehyde were heated in the presence of approximately 10–15 ml of absolute ethanol with drops of glacial acetic acid in a water bath at 70–80 °C for approximately 30–40 min. The process of reaction was followed by TLC. Then, filtration or evaporation of the solvent under reduced pressure was followed by recrystallization from a suitable solvent [19].

Synthesis of N^4,$N^{4'}$-dibenzylidene-3,3′-dimethylbiphenyl-4,4′-diamine ($\mathbf{w_9}$)

2 mmol (0.42 g) of o-tolidine in absolute ethanol was added to 4 mmol (0.4 g) of benzaldehyde in the presence of drops of glacial acetic acid under refluxing for 40 min, yellow precipitate was observed, and then section filtration yielded 65 % with m.p. = 156–158 °C. The IR spectra showed that adsorption bands appeared in the range of 3,004 and 2,901 cm^{-1}, which belong to C–H aromatic and CH_3, respectively, while –C=N appeared at 1,624 cm^{-1}, –C–N appeared at a stretching frequency of 1,167 cm^{-1}, and, besides that, the aromatic C=C appeared at the range 1,417–1,575 cm^{-1}. On the other hand, ^1H NMR in DMSO–d_6 as a solvent showed a sharp singlet at $\delta = 8.40$ ppm (s, 2H, CH–N), (dd, 4H) aromatic at $\delta = 7.76$–7.74 ppm, (dd, 5H) aromatic at $\delta = 7.55$–7.47 ppm, (d, 3H) at $\delta = 7.06$–7.04 ppm, (d, 4H) at $\delta = 6.87$–6.75 ppm, and (s, 6H, $2CH_3$) at $\delta = 2.41$–2.28 ppm. Elemental

analysis confirmed the molecular formula $C_{28}H_{24}N_2$ (calculated/found): C, 86.56/87.12; H, 6.23/6.93; N, 7.21/7.87.

Synthesis of bis(4-(dimethylamino)benzylidene)-3,3′-dimethylbiphenyl-4,4′-diamine (**w_{10}**)

2 mmol (0.42 g) of o-tolidine in absolute ethanol was added to 4 mmol (0.6 g) of N,N-dimethylamino benzaldehyde in the presence of drops of glacial acetic acid under refluxing for 30 min, yellow-orange precipitate was observed, and then section filtration yielded 94 % with m.p. = 256–258 °C. The IR spectra showed stretching absorption bands at 3,010–2,956 cm^{-1}, referring to CH aromatic and aliphatic, respectively, while imines' band appeared at about 1,607 cm^{-1}, C=C appeared in the range 1,521–1,585 cm^{-1}, a medium intensity band appeared at 1,361 cm^{-1} referring to N–CH_3 and at 1,165 cm^{-1} referring to C–N. On the other hand, ^{1}H NMR in $CDCl_3$ as a solvent showed an approximately similar chemical shift of compound **w_9** as follows: at $\delta = 8.43$ ppm (s, 2H, CH=N), $\delta = 7.83$–7.85 ppm (d, 2H, Ar), $\delta = 7.44$–7.49 ppm (m, 4H, Ar), $\delta = 6.88$–7.26 ppm (dd, 8H, Ar), and two sharp singlet peaks at $\delta = 2.45$–2.46 ppm, referring to (6H, 2CH_3–Ar) and (12H, 4CH_3–N). Elemental analysis confirmed the molecular formula $C_{32}H_{34}N_4$ (calculated/found): C, 80.98/81.54; H, 7.22/7.89; N, 11.80/12.49.

Synthesis of bis[4-(diethylamino)benzylidene]-3,3′-dimethylbiphenyl-4,4′-diamine (**w_{11}**)

2 mmol (0.42 g) of o-tolidine in absolute ethanol was added to 4 mmol (0.7 g) of 4-*N*,*N*-diethylamino benzaldehyde in the presence of drops of glacial acetic acid under refluxing for 35 min, yellow bold precipitate was observed, and then section filtration yielded 87 % with m.p. = 174–176 °C. The IR spectra showed stretching absorption bands at 3,103–2,912 cm^{-1}, referring to CH aromatic and aliphatic respectively, while imines' band appeared at about 1,609 cm^{-1}, C=C aromatic appeared in the range 1,587–1,523 cm^{-1}, a medium intensity band appeared at 1,334 cm^{-1} referring to N–CH_3 and at 1,172 cm^{-1} referring to C–N. On the other hand, ^{1}H NMR in DMSO–d_6 as a solvent showed an approximately similar chemical shift of compound **w_{10}** as follows: at $\delta = 8.33$ ppm (s, 2H, CH=N), $\delta = 7.73$–7.75 ppm (d, 2H, Ar), $\delta = 7.38$–7.54 ppm (d, m, 5H, Ar), $\delta = 6.75$–7.066 ppm (dd, 5H, Ar), and two peaks overlapping each other at $\delta = 2.54$–2.11 ppm, referring to (8H, 4CH_2–N) and (6H, 2CH_3–Ar), while (t, 12H, 4CH_3–C) appeared at $\delta = 1.04$–1.29 ppm. Elemental analysis confirmed the molecular formula $C_{36}H_{42}N_4$ (calculated/found): C, 81.47/82.10; H, 7.98/8.62; N, 10.56/11.24.

Synthesis of bis(4-hydroxy-3-methoxy benzylidene) 3,3′dimethyl biphenyl-4,4′-diamine (**w_{12}**)

2 mmol (0.42 g) of o-tolidine in absolute ethanol was added to 4 mmol (0.60 g) of 4-hydroxy 3-methoxy benzaldehyde in the presence of drops of glacial acetic acid

under refluxing for 60 min, a solid yellow mixture was observed after work up, and the section filtration yielded 67 % with m.p. = 199–200 °C. The IR spectra showed stretching absorption broad bands at 3,312 cm^{-1} referring to OH group, 3,018–2,922 cm^{-1} referring to CH aromatic and aliphatic, respectively, while imines' band appeared at about 1,622 cm^{-1}, C=C aromatic appeared in the range 1,429–1,583 cm^{-1}, a medium intensity band appeared at 1,282 cm^{-1} referring to C–O and 1,123 cm^{-1} referring to C–N. On the other hand, ^{1}H NMR in DMSO–d_6 as a solvent showed a chemical shift of compound **w12** as follows: at δ = 9.73–9.82 ppm (s, 2H, OH–Ar), δ = 8.310 ppm (s, 2H, CH–N=), δ = 7.87–7.90 ppm (d, m, 4H, Ar), δ = 7.272–7.67 ppm (m, 4H, Ar), δ = 6.72–6.92 ppm (s, 2H, Ar), and a sharp singlet peak close to DMSO at δ = 2.35 ppm (6H, $2CH_3$–Ar). On the other hand, a sharp singlet peak was observed at δ = 3.73–3.84 ppm (s, $2CH_3O$–). Elemental analysis confirmed the molecular formula $C_{32}H_{34}N_4$ (calculated/found): C, 74.98/75.44; H, 5.87/6.29; N, 5.83/6.51.

Cycloaddition reaction of the imines derivatives with maleic and phthalic anhydride

General procedure

1 mmol of the desired imines (**w9**–**w12**) was dissolved in suitable solvent under N_2 flow, followed by drop wise addition of the cyclic anhydride under refluxing conditions and monitoring with TLC to determine the completion of the reaction. Filtration or evaporation took place under reduced pressure and the yield was dried and recrystallized by a proper solvent.

With maleic anhydride

*Synthesis of 3,3′-(3,3′-dimethylbiphenyl-4,4′-diyl)bis(2-phenyl-2,3-dihydro-1,3-oxazepine-4,7-dione)] (**w9m**)*

Reaction of 1 mmol (0.38 g) of compound **w9** with 2 mmol (0.20 g) maleic anhydride in dry CH_2Cl_2 added drop wise within N_2 flow and stirring under refluxing condition for about 2.5 h. After cooling the reaction mixture, an orange precipitate was observed and section filtration yielded 87.7 % with m.p. = 214–215 °C. The IR spectra showed the following bands: two stretching strong absorption bands at 1,712 and 1,627 cm^{-1} due to (2C=O, ring), 1,489–1,580 cm^{-1} (C=C, aromatic and alkene), 3,051–2,880 cm^{-1} (C–H, aromatic and alkene). ^{1}H NMR clearly showed δ = 8.59 ppm (2H, CH, oxazepine rings), at δ = 7.97–8.0 ppm (m, 4H, Ar), δ = 7.58–7.61 ppm (d, 2H, Ar), δ = 7.4–7.61 ppm (m, 10H, Ar), δ = 7.10–7.21 ppm (dd.4H, 2CH=CH), and at δ = 2.34 (s, 6H, $2CH_3$). Elemental analysis of the molecular formula $C_{36}H_{28}N_2O_6$ of the compound **w9m** (calculated/found): C, 73.96/74.49; H, 4.83/5, 38; N, 4.79/5.40.

*Synthesis of 3,3′-(3,3′-dimethylbiphenyl-4,4′-diyl)bis(2-(4-(dimethylamino)phenyl)-2,3-dihydro-1,3-oxazepine-4,7-dione) (**w$_{10}$m**)*

Reaction of 1 mmol (0.47 g) of compound **w$_{10}$** with 2 mmol (0.20 g) maleic anhydride in dry CH_2Cl_2 added drop wise within N_2 flow and stirring under refluxing condition for about 3.0 h. After cooling the reaction mixture, an orange precipitate was observed and section filtration yielded 89 % with m.p. = 184–186 °C. The IR spectra showed the following bands: two stretching strong absorption bands at 1,712 and 1,642 cm^{-1} due to (2C=O, ring), 1,460–1,539 cm^{-1} (C=C, aromatic and alkene), 3,047–2,895 cm^{-1} (C–H, aromatic and alkene), in addition to stretching frequency at 3,269 cm^{-1} (CH, chiral). ^{1}H NMR clearly showed $\delta = 9.66$ ppm (2H, CH, oxazepine rings), at $\delta = 7$, 25–7, 82 (m, 10H, Ar), at $\delta = 7.10$–7.22 (m, 2H, Ar), $\delta = 6.77$–6.84 ppm (m, 2H, Ar), $\delta = 6.18$–6.34 ppm (d, 2H, alkene), $\delta = 6.59$–6.68 ppm (d, 2H, alkene), at $\delta = 2.81$ ppm (s, $4CH_3$–N–), and at $\delta = 2.30$ (s, 6H, $2CH_3$). Elemental analysis of the molecular formula $C_{40}H_{38}N_4O_6$ of the compound **w$_9$m** (calculated/found): C, 71.63/72.32; H, 5.71/6.37; N, 8.35/8.94.

*Synthesis of 3,3′-(3,3′-dimethylbiphenyl-4,4′-diyl)bis[2-(4-(diethylamino)phenyl)-2,3-dihydro-1,3-oxazepine-4,7-dione] (**w$_{11}$m**)*

Reaction of 1 mmol (0.53) of compound **w$_{11}$** with 2 mmol (0.20 g) maleic anhydride in dry THF added drop wise within N_2 flow and stirring under refluxing condition for about 3.3 h. After cooling the reaction mixture, an orange precipitate was observed and section filtration yielded 55 % with m.p. = 190–192 °C. The IR spectra showed the following bands: two stretching strong absorption bands at 1,716 and 1,640 cm^{-1} due to (2C=O, ring), 1,489–1,591 cm^{-1} (C=C, aromatic and alkene), 3,027–2,847 cm^{-1} (C–H, aromatic and aliphatic), in addition to stretching frequency at 3,275 cm^{-1} (CH, chiral). ^{1}H NMR in DMSO–d_6 clearly showed $\delta = 9.27$ ppm (2H, CH, oxazepine rings), at $\delta = 7.27$–7.89 ppm (m, 14H, Ar), 6.33–6.79 ppm (d, 4H, alkene), at $\delta = 2.12$ ppm (s, $2CH_3$–Ar), at $\delta = 2.50$–2.720 (m, 8H, $4CH_2$–C), and at $\delta = 0.85$–1.23 ppm (t, 12H, $4CH_3$–C). Elemental analysis of the molecular formula $C_{44}H_{46}N_4O_6$ of the compound **w$_9$m** (calculated/found): C, 72.71/73.38; H, 6.38/6.96; N, 7.71/8.31.

*Synthesis of 3,3′-(3,3′-dimethylbiphenyl-4,4′-diyl)bis[2-(4-hydroxy-3-methoxyphenyl)-2,3-dihydro-1,3-oxazepine-4,7-dione] (**w$_{12}$m**)*

Reaction of 1 mmol (0.48) of compound **w$_{12}$** with 2 mmol (0.20 g) maleic anhydride in dry THF added drop wise within N_2 flow and stirring under refluxing condition for about 4 h. After cooling the reaction mixture, an orange precipitate was observed and section filtration yielded 65 % with m.p. = 196–198 °C. The IR spectra showed the following bands: two stretching strong absorption bands at 1,714 and 1,627 cm^{-1} due to (2C=O, ring), 1,448–1,570 cm^{-1} (C=C, aromatic and alkene), 3,041–2,959 cm^{-1} (C–H, aromatic and aliphatic), in addition to stretching frequency at 3,234 cm^{-1} (CH, chiral). ^{1}H NMR in DMSO–d_6 clearly showed

δ = 10.45 ppm (s, 2H, OH, phenolic rings), at δ = 8.72 ppm (2H, chair, oxazepine rings), at δ = 7.97–7, 99 ppm (d, 2H, Ar), at δ = 7.59–7.84 ppm (dd, 4H, Ar), at δ = 7. 49–7.59 ppm (d, 4H, Ar), at δ = 6.31–6.35 and 6.48–6.52 ppm (d, d, 2CH=CH–, alkene), at δ = 3.53 ppm (s, 6H, $2CH_3$–O–Ar), and at δ = 2.28 ppm (s, 6H, $2CH_3$–Ar). Elemental analysis of the molecular formula $C_{38}H_{32}N_2O_{10}$ of the compound **w₉m** (calculated/found): C, 67.45/68.15; H, 4.77/5.31; N, 4.14/4.67.

With phthalic anhydride

*Synthesis of 4,4′-(3,3′-dimethylbiphenyl-4,4′-diyl)bis(3-phenyl-3,4 dihydrobenzo [1,3] oxazepine-1,5-dione) (**w₉ph**)*

Reaction of 1 mmol (0.38 g) of compound **w₉** with 2 mmol (0.30 g) phthalic anhydride in dry dioxan added drop wise within N_2 flow and stirring under refluxing condition for about 3.5 h. After cooling the reaction mixture, an oily product was left, after work up with petroleum ether–hexane, a yellow precipitate was observed, and section filtration yielded 51 % with m.p. = 278–280 °C. The IR spectra showed the following bands: two stretching strong absorption bands at 1,699 and 1,637 cm^{-1} due to (2C=O, ring), 1,488–1,587 cm^{-1} (C=C, aromatic and alkene), 3,026–2,856 cm^{-1} (C–H, aromatic and alkene). ^1H NMR clearly show a chemical shift at δ = 8.38 ppm (s, 3H, Ar), at δ = 7.97 ppm (s, 2H, oxazepine ring), at δ = 7.52–7.58 ppm (m, 7H, Ar), at δ = 7.12–7.18 ppm (m, 7H, Ar), at δ = 6.72–6.73 ppm (dd.6H, Ar), and at δ = 2.36 (s, 6H, $2CH_3$). Elemental analysis of the molecular formula $C_{44}H_{32}N_2O_6$ of the compound **w₉m** (calculated/found): C, 77.18/77.72; H, 4.71/5.43; N, 4.09/4.65.

*Synthesis of 4,4′-(3,3′-dimethylbiphenyl-4,4′-diyl)bis[3-(4-dimethylaminophenyl)-3,4-dihydrobenzo[1,3]oxazepine-1,5-dione] (**w₁₀ph**)*

Reaction of 1 mmol (0.47 g) of compound **w₁₀** with 2 mmol (0.30 g) phthalic anhydride in dry CH_2Cl_2 added drop wise within N_2 flow and stirring under refluxing condition for about 5.0 h. After cooling, the reaction mixture was directly precipitated, after work up with petroleum ether–hexane, a yellow precipitate was observed, and section filtration yielded 65 % with m.p. = 146–148 °C. The IR spectra showed two stretching strong absorption bands at 1,718 and 1,645 cm^{-1} due to (2C=O, ring), 1,489–1,593 cm^{-1} (C=C, aromatic and alkene), 3,016–2,924 cm^{-1} (C–H, aromatic and alkene). ^1H NMR clearly showed the formation of product by a chemical shift at δ = 9.78 ppm (s, 2H, charily), at δ = 8.73 ppm (s, 2H, Ar), at δ = 7.97–7.99 ppm (d, 2H, Ar), at δ = 7.59–7.79 ppm (m, 10H, Ar), at δ = 7.49–7.51 ppm (d, 4H, Ar), at δ = 7.37–7.40 ppm (d.4H, Ar), at δ = 3.49 (s, 12H, $4CH_3$–N), and at δ = 2.27 ppm (s, 6H, $2CH_3$–Ar). Elemental analysis of the molecular formula $C_{48}H_{42}N_4O_6$ of the compound **w₉m** (calculated/found): C, 74.79/75.28; H, 5.49/6.04; N, 7.27/7.81.

*Synthesis of 4,4′-(3,3′-dimethylbiphenyl-4,4′-diyl)bis(3-(4-(diethylamino)phenyl)-3,4-dihydro benzo[1,3]oxazepine-1,5-dione) (**w_{11}ph**)*

Reaction of 1 mmol (0.53 g) of compound **w_{11}** with 2 mmol (0.30 g) phthalic anhydride in dry THF added drop wise within N_2 flow and stirring under refluxing

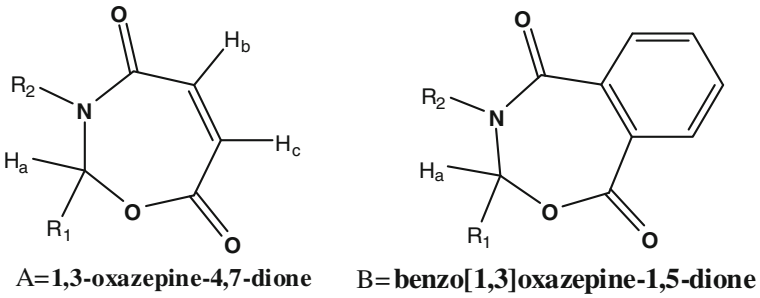
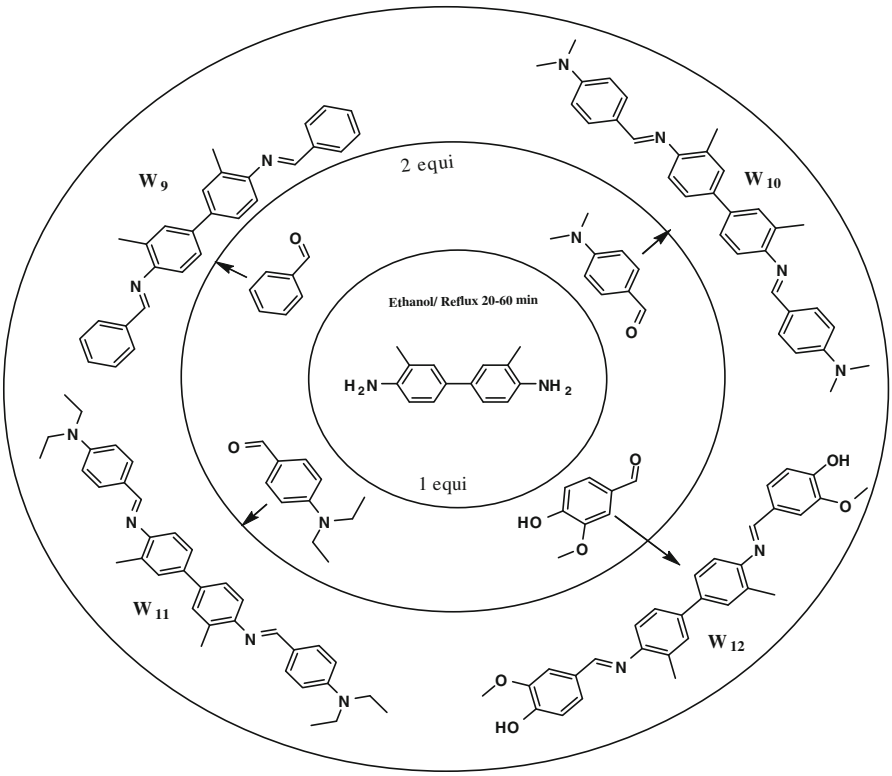


Fig. 1 Two types A and B of [1,3]oxazepine-dione



Scheme 1 Condensation reaction of o-tolidine via aromatic aldehyde in the presence of absolute ethanol and glacial acetic acid under refluxing condition

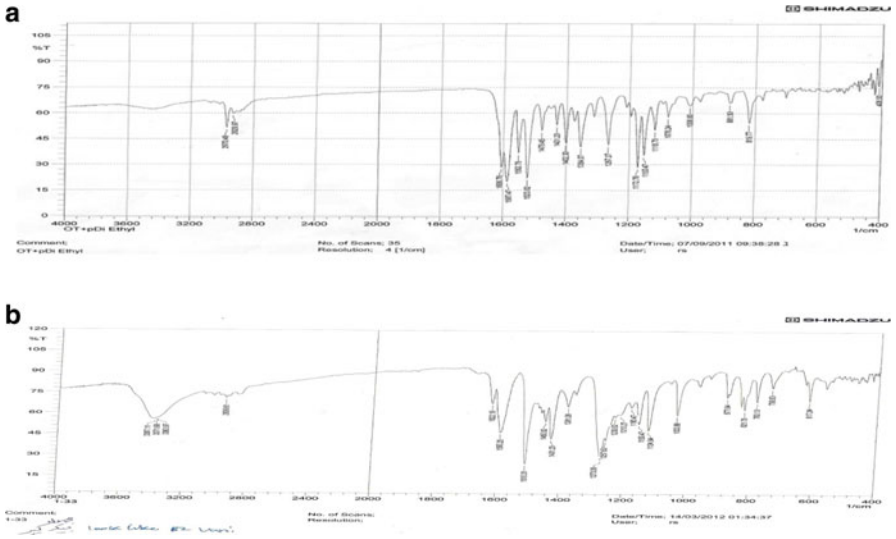


Fig. 2 **a** FT-IR of bis(4-(dimethylamino)benzylidene)-3,3′-dimethylbiphenyl-4,4′-diamine (**w_{10}**), **b** FT-IR of bis[3-methoxy-4-hydroxy benzylidene] 3,3′-dimethylbiphenyl-4,4′-diamine (**w_{12}**)

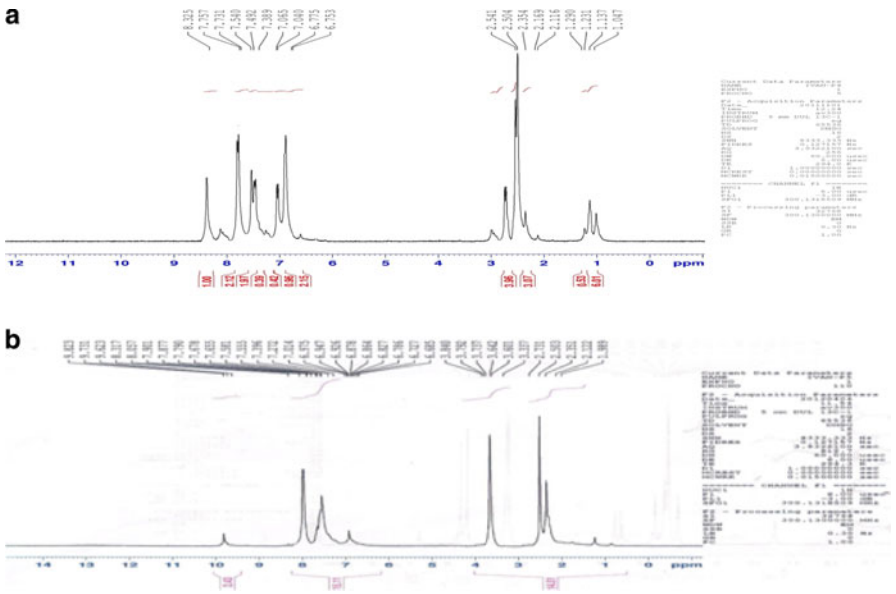
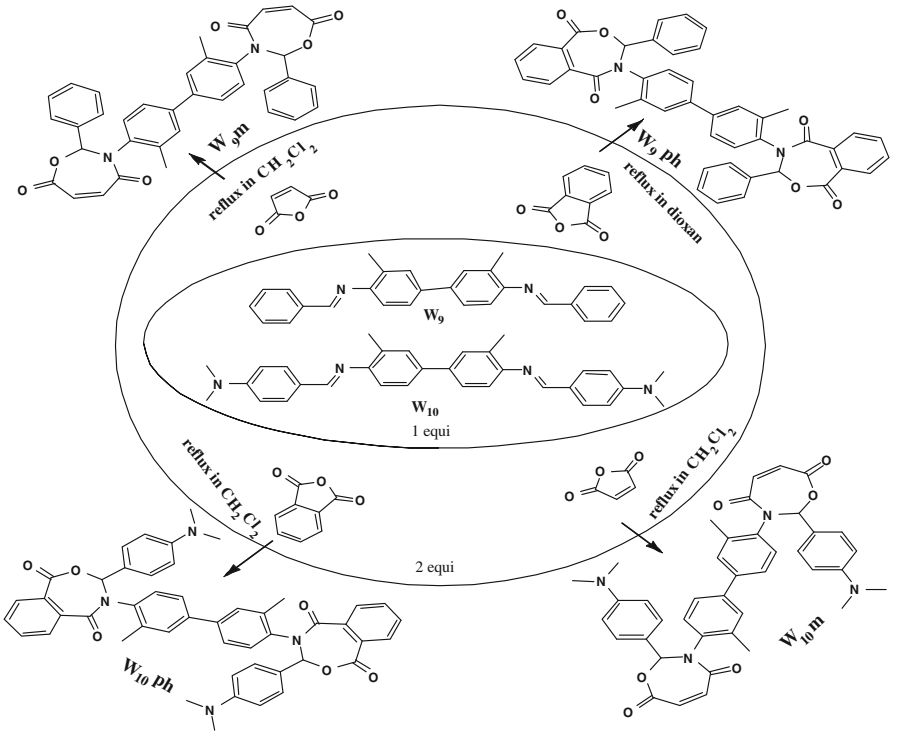


Fig. 3 **a** 1H NMR in DMSO–d_6 of bis(4-(diethylamino)benzylidene)-3,3′-dimethyl biphenyl-4,4′-diamine (**w_{11}**), **b** ^{1}H NMR in DMSO–d_6 of bis[3-methoxy-4-hydroxy benzylidene] 3,3′-dimethylbiphenyl-4,4′-diamine (**w_{12}**)

condition for about 6.0 h. After cooling, the reaction mixture was an oily product, many attempts to solidify the product failed, after work up with hexane, some precipitate was observed, and section filtration yielded 41 % with m.p. = °C. The

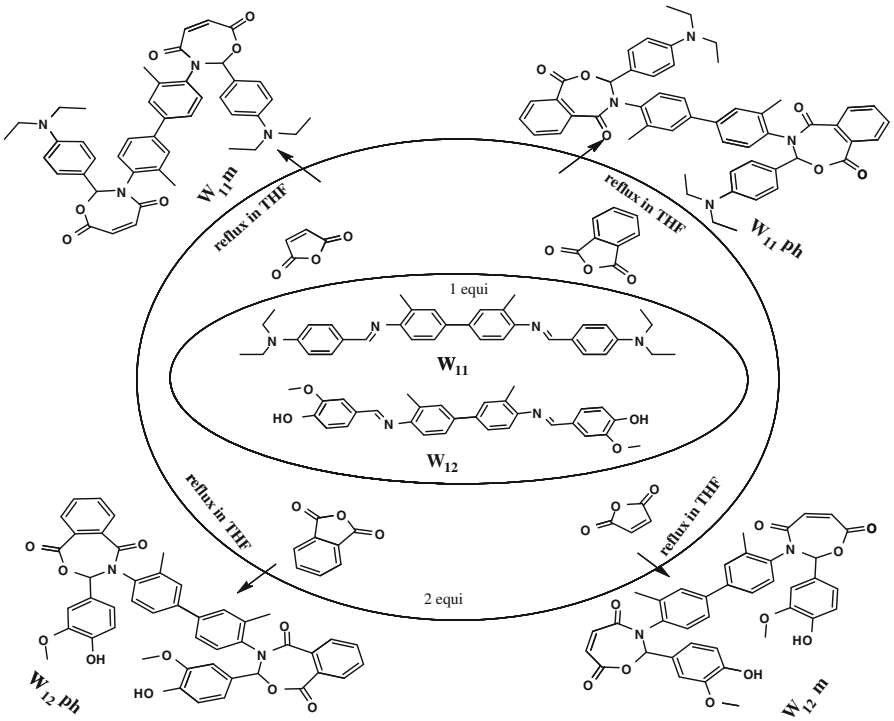


Scheme 2 [2+5] Cycloaddition reactions of imine derivative ($\mathbf{w_9}$, $\mathbf{w_{10}}$) with maleic and phthalic anhydride to afforded ($\mathbf{w_9m}$, $\mathbf{w_9ph}$, $\mathbf{w_{10}m}$, and $\mathbf{w_{10}ph}$)

IR spectra showed the following bands: two stretching strong absorption bands at 1,718 and 1,645 cm^{-1} due to (2C=O, ring), 1,481–1,595 cm^{-1} (C=C, aromatic and alkene), 3,006–2,854 cm^{-1} (C–H, aromatic and alkene), and a strong absorption band at 1,361 cm^{-1} (–C–N–) bond. ^1H NMR clearly showed a chemical shift at $\delta = 9.73$ ppm (s, 2H, charily), at $\delta = 8.05$–8.31 ppm (s, 2H, Ar), at $\delta = 7.66$–7.87 ppm (m, 4H, Ar), at $\delta = 7.55$–7.58 ppm (d, 10H, Ar), at $\delta = 7.27$–7.39 ppm (d.4H, Ar), at $\delta = 6.92$–7.02 ppm (d, 2H, Ar), at $\delta = 3.13$–3.20 ppm (m, 8H, $4CH_2$–C), at $\delta = 2.35$ ppm (s, 6H, $2CH_3$–Ar), and at $\delta = 1.57$–1.62 ppm (q, 12H, $4CH_3$–C). Elemental analysis of the molecular formula $C_{52}H_{50}N_4O_6$ of the compound $\mathbf{w_9m}$ (calculated/found): C, 75.52/76.16; H, 6.09/6.53; N, 6.77/7.29.

Synthesis of 4,4′-(biphenyl-4,4′-diyl)bis(3-(4-hydroxy-3-methoxyphenyl)-3,4-dihydro benzo [1,3]oxazepine-1,5-dione) ($\mathbf{w_{12}ph}$)

Reaction of 1 mmol (0.48 g) of compound $\mathbf{w_{12}}$ with 2 mmol (0.30 g) phthalic anhydride in dry THF added drop wise within N_2 flow and stirring under refluxing condition for about 3.5 h. After cooling, the reaction mixture was an oily product, after work up with n-hexane, an orange-yellow precipitate was observed, and section filtration yielded 45 % with m.p. = 185 °C. The IR spectra showed the



Scheme 3 [2+5] Cycloaddition reaction of imine derivatives ($\mathbf{w_{11}}$, $\mathbf{w_{12}}$) with maleic and phthalic anhydride to afforded ($\mathbf{w_{11}m}$, $\mathbf{w_{11}ph}$, $\mathbf{w_{12}m}$, and $\mathbf{w_{12}ph}$)

following bands: two stretching strong absorption bands at 1,697 and 1,658 cm^{-1} due to (2C=O, ring), 1,452–1,590 cm^{-1} (C=C, aromatic and alkene), 3,038–2,926 cm^{-1} (C–H, aromatic and alkene), and a strong absorption band at 1,301 cm^{-1} (C–O–C). ^{1}H NMR clearly showed a chemical shift at $\delta = 9.93$ ppm (s, 2H, HO–phenolic), at $\delta = 8.74$ ppm (s, 2H, oxazepine ring), at $\delta = 8.38$ ppm (d, 2H, Ar), at $\delta = 7.65$–7.94 ppm (t, 10H, Ar), at $\delta = 7.35$–7.52 ppm (dd.4H, Ar), at $\delta = 7.13$ (s, 2H, Ar), at $\delta = 6.93$–7.06 ppm (s, 2H, Ar), at $\delta = 3.35$ ppm (s, 6H, $2CH_3O$–Ar), and at $\delta = 2.35$ ppm (s, 6H, $2CH_3$–Ar). Elemental analysis of the molecular formula $C_{46}H_{36}N_2O_{10}$ of the compound $\mathbf{w_9m}$ (calculated/found): C, 71.13/71.79; H, 4.67/5.16; N, 3.61/4.21.

Results and discussion

It's well known that [1,3]oxazepine-4,7-dione or -1,5-dione (Fig. 10 are heterocyclic seven-membered rings containing nitrogen, oxygen, and two carbonyl groups. When R1 and R2=H, the component (A) is known as 2,3-dihydro-1,3-oxazepine-4,7-dione, whilst B is known as 3,4-dihydrobenzo1,3-oxazepine-1,5-dione. Many researchers have investigated these types of heterocyclic compounds due to their important class, which have a variety of biological applications [20–22]. In recent

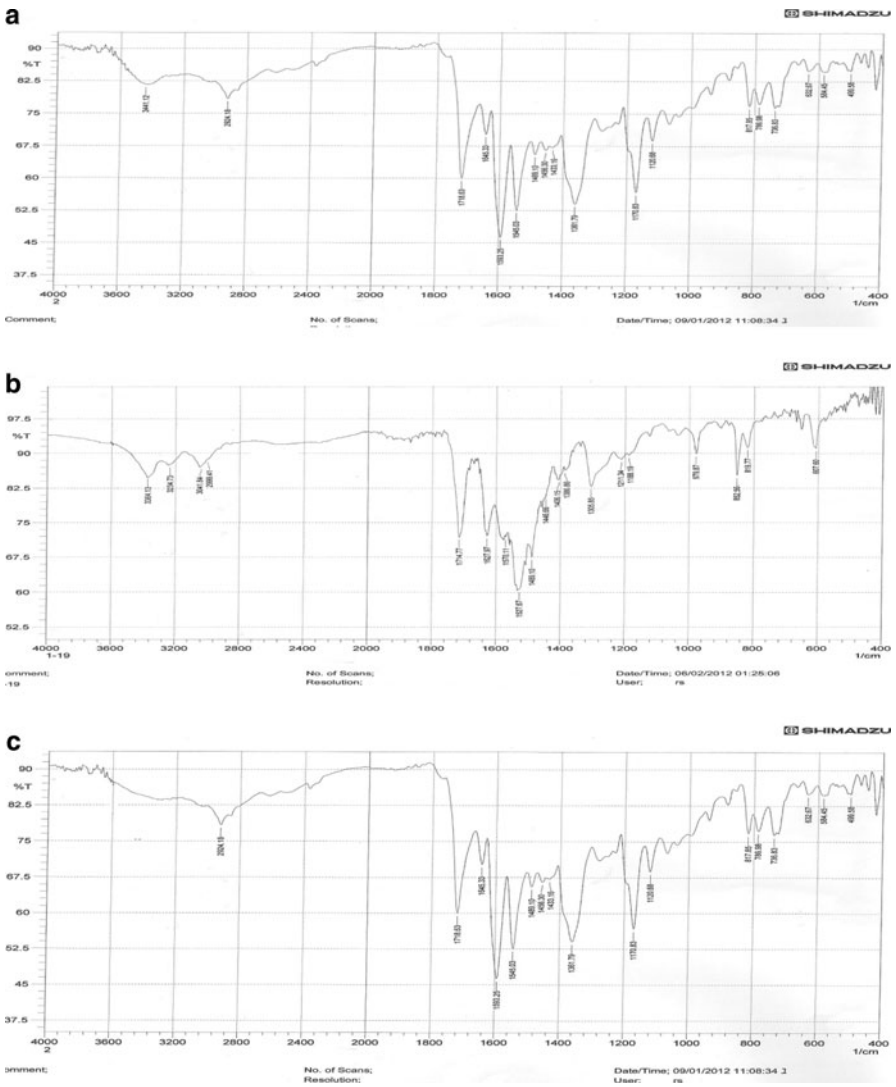


Fig. 4 **a** FT-IR of bis(4-(dimethylamino)benzylidene)-3,3′-dimethylbiphenyl-4,4′-diamine (**w_{10}**), **b** FT-IR of 3,3′-(3,3′-dimethylbiphenyl-4,4′-diyl)bis[2-(4-hydroxy-3-methoxyphenyl)-2,3-dihydro-1,3-oxazepine-4,7-dione] (**w_{12}m**), **c** FT-IR of (3.2) synthesis of 4,4′-(3,3′-dimethylbiphenyl-4,4′-diyl)bis[3-(4-(dimethylamino)phenyl)-3,4-dihydrobenzo[1,3]oxazepine-1,5-dione] (**w_{10}ph**)

years, great attention has been paid toward the formation of oxazepine rings [23, 24], due to the importance of these compounds as pharmaceutical drugs and in biological systems. Our interest was in regard to the modification of oxazepine rings throughout changes in R_1 and R_2 in the 2 and 3 positions, and these changes might cause variations in their biologic applications. Therefore, we start to create an imine derivative by using selective aldehyde with o-tolidine under condensation reactions

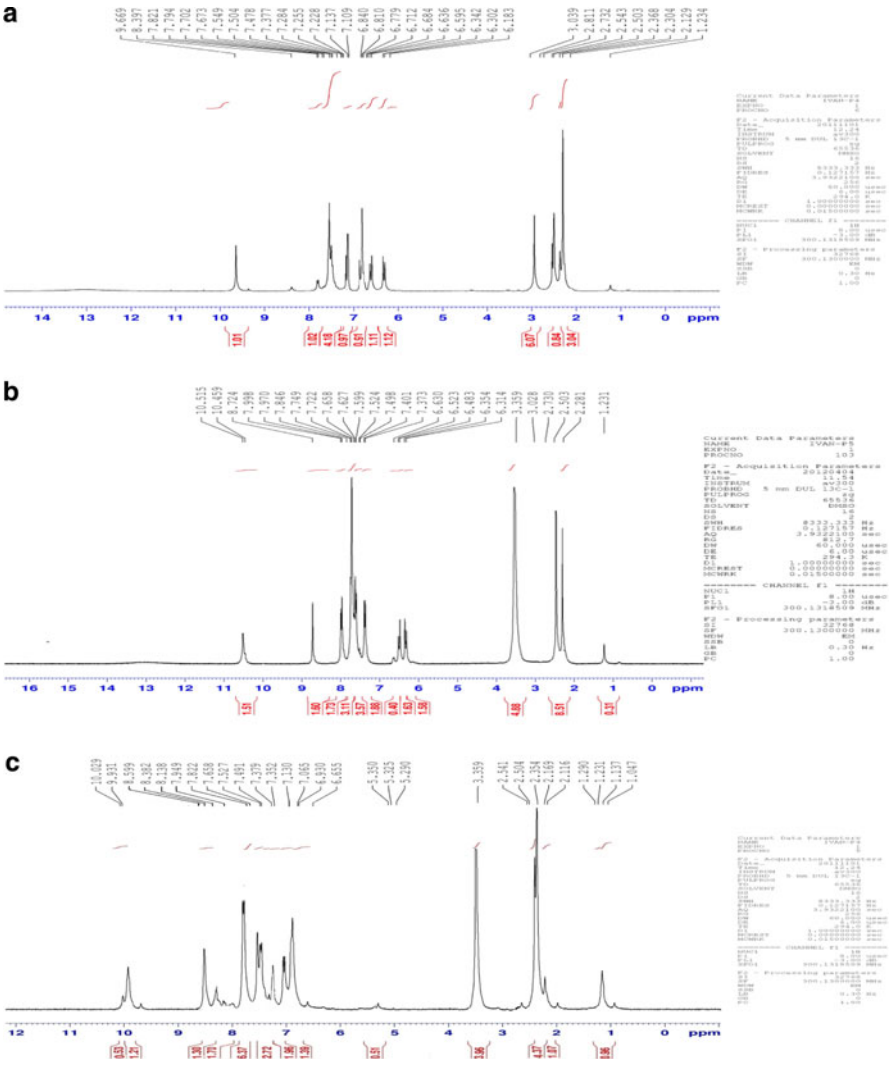


Fig. 5 **a** 1H NMR in DMSO–d_6) bis[4-(dimethylamino)benzylidene]-3,3′-dimethylbiphenyl-4,4′-diamine (**w_{10}**), **b** ^{1}H NMR in DMSO–d_6 of 3,3′-(3,3′-dimethylbiphenyl-4,4′-diyl)bis[2-(4-hydroxy-3-methoxyphenyl)-2,3-dihydro-1,3-oxazepine-4,7-dione] (**w_{12}m**), **c** ^{1}H NMR in DMSO–d_6 of 4,4′-(biphenyl-4,4′-diyl)bis(3-(4-hydroxy-3-methoxyphenyl)-3,4-dihydro benzo [1,3]oxazepine-1,5-dione) (**w_{12}ph**)

(Scheme 1). All the imines derivatives were monitored by TLC and identified by FT-IR, ^{1}H NMR, and elemental analysis, with recall to FT-IR spectra in the KBr disk. In the first stage, the imines derivatives (**w_9–w_{12}**), which were formed by condensation reactions, were proved according to the disappearance of –NH_2 absorption bands in the range 3,465–3,250 cm^{-1}, which belonged to asymmetric and symmetric stretching frequencies and the appearance of the sharp (strong–medium)

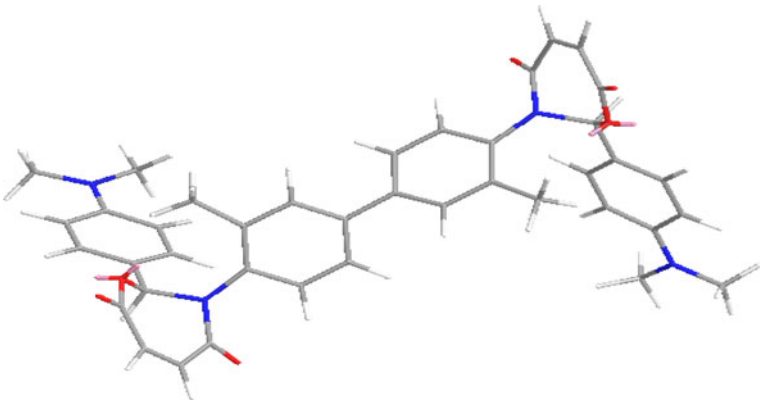


Fig. 6 The default structure of (**w_{10}m**) compound in 3D view (*blue color* N, *red color* O, *white color* H). (Color figure online)

intense azomethane (C=N–) group in the stretching frequency range at 1,606–1,624 cm^{-1}, as shown in Fig. 2a, b. On the other hand, ^{1}H NMR in DMSO–d_6 as a solvent confirmed the generation of these compounds, as shown in Fig. 3a, b. For compound **w_{10}**, it is obvious that the methyl group appeared in triplet at $\delta = 2.35$ ppm, and a sharp singlet peak appeared at $\delta = 8.32$ ppm, which belonged to 2CH of azomethane groups. This proton was deshielded due to the effect of nitrogen azomethane and aromatic ring. The rest of the signals at $\delta = 6.75$–7.75 ppm refer to the aromatic protons with details. Also, elemental analysis gave matching values for the calculated and found molecular formulas of each compound. The second stage involved a coupling reaction between azomethane group (imines derivatives) and two carbonyl groups throughout the [2+5] cycloaddition reaction (concerted reaction) (Schemes 2 and 3). This type of reaction afforded a seven-membered ring of 1,3-oxazepine-4,7-dione and 1,3-oxazepine-1,5-dione derivatives (Fig. 1). These molecules are easily identified by two major observations: firstly, in FT-IR data, two different stretching frequencies of (C=O) groups in the oxazepine ring which appear at approximately 1,716 and 1,642 cm^{-1}, respectively, and (CH, chiral) appears at $\geq$3,200 cm^{-1} (Fig. 4a, b0; secondly, in ^{1}H NMR, more than one proton can be distinguished: highly deshielding proton (Fig. 1) (H_a) observed at a singlet peak at chemical shift $\delta \geq 8.50$ ppm and alkenes' protons in the same Fig. 1 (H_b and H_c) in 1,3-oxazepine 4,7-dione observed at a lower chemical shift (as a doublet to doublet signal at approximately $\delta = 6.34$–6.53 ppm) than aromatic protons (Fig. 5a–c) [25]. Also, elemental analysis of the prepared compounds (**w_9m**–**w_{12}m**) and (**$w_9$ph**–**w_{12}ph**) were in relative agreement with the calculated value. On the other hand, the geometry of oxazepine derivatives were identified by the ChemDraw software program, version 10.2008. The default structure of the **w_{10}m** compound in Fig. 6 in the 3D view shows the orientation of oxazepine rings in the perpendicular of plane of symmetry of the biphenyl molecule, which give an indication that there is no steric factor or hindrance between CH_3 at the biphenyl molecule and protons of the oxazepine ring.

References

1. K.H. Park, J.S. Kang, J. Org. Chem. **62**, 3794 (1997)
2. P. Rajaguru, L.J. Fairbairn, J. Ashby, M.A. Willington, S. Turner, L.A. Woolford, N. Chinnasamy, J.A. Rafferty, Mutat. Res. **444**, 1 (1999)
3. E.A.J. Al-Mulla, N.A.B. Ibrahim, K. Shameli, M.B. Ahmad, W.M.Z.W. Yunus, Res. Chem. Intermed. doi: 10.1007/s11164-012-0687-6 (2012) (Online First article)
4. N. Christian, B. Markus, G. Reiner, S. Hans-Werner, J. Mater. Chem. **16**, 34 (2006)
5. E.A.J. Al-Mulla, N.A.B. Ibrahim, I.H.T Al-Karkhi, K. Shameli, M. Zidan, M.B. Ahmad, W.M.Z.W. Yunus, Res. Chem. Intermed. doi: 10.1007/s11164-012-0745-0 (2012) (Online First article)
6. B. Pelcman, M. Almeida, M. Katevics, P. Nilsson, W. Schaal, K. Olofsson, Biolipox AB, Patent WO 2010/29300, 2010
7. K. Sharad, A. Preeti, A. Rameshwar, J. Indian Chem. Soc. **84**, 801 (2007)
8. E.A.J. Al-Mulla, J. Oleo Sci. **60**, 41 (2011)
9. F.J. Cervantes, J.E. Enriquez, E. Galindo-Petatan, H. Arvayo, E. Razo-Flores, J.A. Field, Chemosphere **68**(6), 1082 (2007)
10. A.A. Ahmed, S.A. BenGuzzi, J Sci Appl **2**, 83 (2008)
11. A.J. Mahrath, A. Saadon, A.S.N. Kamil, J Babylon University **20**, 8 (2012)
12. A.J. Mahrath, A. Saadon, A.S.N. Kamil, J Babylon University **21**, 11 (2012)
13. M.C. Sharma, D.V. Kohli, Sharma Smita, A.D. Kohli, Der Pharmacia Sinica **1**, 58 (2010)
14. A.H. Ahangar, G.H. Mahdavinia, K. Marjani, A. Hafezian, J. Iran. Chem. Soc. **7**, 770 (2010)
15. A.H. Kategaonkar, S.S. Sonar, K.F. Shelke, B.B. Shingate, M.S. Shingare, Org. Commun **13**, 1 (2010)
16. S. Tumtin, I.T. Phucho, A. Nongpiur, R. Nongrum, J.N. Vishwakarma, B. Myrboh, R.L. Nongkhlaw, J. Heterocyclic Chem. **47**, 125 (2010)
17. Y.G. Yeap, A.T. Mohammad, H. Osman, J. Mol. Struc. **982**, 33 (2010)
18. W.L.F. Armarego, C.L.L. Chai, *Purification of Laboratory Chemicals*, 5th edn. (Elsevier Science, New York, 2003)
19. K. Santosh, Niranjan, K.C. Chaluvaraju, C.M. Jamakhandi, K. Dayanand, J. Curr. Pharm. Res. **1**, 39 (2010)
20. F. Aiello, A. Garofalo, F. Grande, G. Ragno, R. Dayan, N. Neamati, Bio. Med. Chem. **12**, 4459 (2004)
21. K. Audouze, E.Q. Nielsen, D. Peters, J. Med. Chem. **47**, 3089 (2004)
22. P.P.M.A. Dols, B.J.B. Folmer, H. Hamersma, C.W. Kuil, H. Lucas, L. Ollero, J.B.M. Rewinkel, P.H.H. Hermkens, Bioorg. Med. Chem. Lett. **18**, 1461 (2008)
23. K. Bajaja, Archana, A. Kumar, Eur. J. Med. Chem. **39**, 369 (2004)
24. A. Kamal, V. Tekumalla, P. Raju, V.G.M. Naidu, P.V. Dawin, R. Sistla, Bioorganic Med. Chem. Lett. **18**, 3769 (2008)
25. A.T. Mohammad, H. Osman, G.Y. Yeap, Aust. J. Basic Appl. Sci. **5**, 192 (2011)