Available online www.jocpr.com

Journal of Chemical and Pharmaceutical Research, 2014, 6(5):872-879

Research Article

ISSN : 0975-7384
CODEN(USA) : JCPRC5

Synthesis of some new N-saccharin derivatives of possible biological activity

Ahmed Wahed Naser and Aseel Farhan Abdullah

Department of Chemistry, College of Science, University of Baghdad, Baghdad, Iraq

---

ABSTRACT

In the present work a variety of new heterocyclic compounds namely thiazole ,oxazole , oxazoline, cyclicimide, B-lactam and oxazpeine were synthesized using α-(N-saccharin) acetate (1) as a starting material .A series of Schiff bases (3-5) have been synthesized by condensation of α- (N-saccharin)acetohydrazide (2) with various aromatic aldehydes namely p-bromobenzaldehyde, p-chlorobenzaldehyde and p-methoxybenzaldehyde. Cyclization of (3-5) with maleic anhydride, succinic anhydride, phthalic anhydride and chloroacetylchloride gave the corresponding oxazpeine (6-14) and azitidine (15-17) derivatives. Reaction (1) with urea and thiourea gave carbonyl derivative (18) and carbonthioyl derivative (19).Compounds (18, 19) that cyclized either with p-bromophenacyl bromide and p-phenylphenacyl bromide to give the corresponding 1, 3-oxazole (20, 21) and 1, 3 thiazole (22, 23) derivatives. The carboxamide derivatives (24, 25) were obtained by condensation of (2) with phenylisocynate and 1-naphtylisocynate. Compounds (24, 25) that cyclized either p-bromophenacyl bromide or p-phenylphenacyl bromide to give the corresponding oxazoline derivatives (26-29). Reaction (2) with various acid anhydrides namely maleic anhydride, succinic anhydride and phthalic anhydride in presence acetic acid gave the corresponding cyclicimide derivatives (30-32). F.T.IR and $^{1-}$ HNMR were used to characterize the target compounds.

Keywords: oxazole, thiazole, oxazepine, oxazoline, azitidine

INTRODUCTION

Heterocyclic compounds are considered one of important types of organic compounds due to their implication in drugs and industrial studies. [1-5] heterocyclic compounds, any of a major class of organic chemical compounds characterized by the fact that some or all of the atoms in their molecules are joined in rings containing at least one atom of an element other than carbon [6]. Large number of natural products in particular from the marine environment , contain thiazole , and oxazolines heterocycls [7].In many cases, promising antitumor , antibacterial ,antiviral ,antimalaria and antihelmintic activities have been identified for these compounds [8-13]. *B*- Lactams, being a structural unit found in the most widely used antibiotics [14, 15]. *B* -Lactams have been found to act as cholesterol acyltransferase inhibitors [16], thrombin inhibitors [17] and cysteineprotease [18]. Oxazepine compounds have medical and biological important and they have medicinal and pharmaceutical application. Some oxazepine derivatives are considered a medical drug against the disease [19], against anxiety [20] and affecting the nervous center [21].

EXPERIMENTAL SECTION

Melting points were recorder using electrothermal melting point apparatus and were uncorrected. FTIR spectra were run on a Shimadzu FTIR-8400S spectrophotometer. ^{1}H-NMR was recorder on Bruker Ultra Shield, 400MHz, using

$CDCl_3$ or DMSO-d_6 as solvent and TMS as internal standard. Thin-layer chromatography was performed glass plats coated with 0.25 mm layer of silica-gel (Fluka).

Preparation of Schiff Bases Derivatives (3-5)

General procedure: A mixture of compound (2)[22] (0.5gm1.9 mmol.), appropriate aromatic aldehyde namely *p*-bromobenzaldehehayde, *p*-chlorobenzaldehehayde *p*- methoxybenzaldehyde (1.9 mmol.) and few drops of glacial acetic acid in (15ml) ethanol was refluxed for(6 h). The formed precipitate after cooling was filtered, dried and recrystallized from benzene and ethanol (1:1) to give compounds (3-5) respectively.

N-(*p*-bromobenzylidene)-α- (N-saccharin) aceamide (3)

Yield 75%, m.p. 191-193°C, R_f (0.78), IR (KBr) cm^{-1}: 3200(NH), 1683(C=Oamid),1623 (C=N).^{1}H-NMR (DMSO-d_6)δ: 4.3(s, 2H, N-CH_2-), 7.1-8.3(m, 8H, Ar-H), 9.1(s, 1HNH), 11.0(s, 1H, NH=C-).

N-(*p*-chlorobenzylidene)-α-(N-saccharin) acetamide (4)

Yield 65%, m.p. 225-228°C, R_f (0.73), IR (KBr) cm^{-1}: 3100(NH), 1690 (C=O amide), 1600(C=N), ^{1}H-NMR (DMSO-d_6)δ: 4.2 (s, 2H,N-CH_2-), 7.3-7.8(m, 8H, Ar-H), 9(s, 1HNH), 11.2(s, 1H, NH=C-).

N-(*p*-mthoxybenzylidene)-α- (N-saccharin) acetamide (5)

Yield 72%, m.p. 175-178°C, R_f (0.69), IR (KBr) cm^{-1}: 3200(NH), 1680 (C=O amide), 1579(C=N). ^{1}H-NMR (DMSO-d_6)δ: 3.3(s, 3H, OCH_3, 4.4(s, 2H, N-CH_2-), 7.0-8.0(m, 8H, Ar-H),9(s, 1HNH), 11.2(s, 1H, NH=C-).

Preparation of Oxazepines Derivatives (6-14)

General procedure: A mixture of compounds (3-5) (5.3 mmol.) and the appropriate acid anhydride namely maleic anhydride succinic anhydride and phthalic anhydride (5.3 mmol.) in (20 ml) T.H.F. was refluxed for 24h. The formed precipitate was filtered, dried and recrystlaized from benzene and ethanol (2:1) to give compounds (6-14) respectively.

2-(*p*-bromophenyl)-3-[α-(N-saccharin) acetamido]-2, 3-dihydro-1, 3-oxazepine- 4-7-dione (6)

Yield 70%, m.p. 124-127°C, R_f (0.79), IR (KBr) cm^{-1}: 3186(NH), 1745(C=O oxazepine ring), 1681(C=O amide),^{1}H-NMR (DMSO-d_6) δ, 4.3(s,2H, NCH_2), 4.9(s,2H,CH=CH), 7-8.3(m,8H, Ar-H), 10.3(s, 1H, C-H oxazepine ring), 11.7 (s, 1H, NH).

2-(*p*-chlorophenyl)-3-[α-(N-saccharin) acetamido]-2,3-dihydro-1,3 –oxazepine - 4,7-dione (7)

Yield 67%, m.p140-143°C, R_f (0.81), IR (KBr) cm^{-1}: 3182(NH), 1749(C=O oxazepine ring), 1681(C=O amide),^{1}H-NMR (DMSO-d_6) δ: 4.0(2H N-CH_2), 5.0(s,2H,CH=CH), 7-8.3(m,8H, Ar-H), 10.3(s, 1H, C-H oxazepine ring), 11.7 (s, 1H, NH).

2-(*p*-methoxyphenyl)-3-[α-(N-saccharin) acetamido]-2, 3-dihydro-1, 3-oxazepine- 4-7-dione (8)

Yield 75%, m.p. 177-179°C, R_f (0.830), IR (KBr) cm^{-1}: 3195(NH), 1745 (C=O oxazepine ring), 1683(C=O amide),^{1}H-NMR (DMSO-d_6) δ 3.2 (s, 3H, OCH_3), 4.3(s,2H, NCH_2), 5.0(s,2H,CH=CH), 6.9-8.0(m, 8H, Ar-H), 10.0(s, 1H, C-H oxazepine ring), 11.3 (s, 1H, NH).

2-(*p*-bromophenyl)-3-[α-(N-saccharin) acetamido]-2, 3, 5, 6--tetrahydro-1, 3-oxazepine- 4-7-dione (9)

Yield 87%, m.p. 196-1198°C, R_f (0.55), IR (KBr) cm^{-1}: 3184(NH), 1751(C=O oxazepine ring), 1674(C=O amide), ^{1}H-NMR (DMSO-d_6) δ 3.5-4.3(m,6H,2CH_2 oxazpeine ring, NCH_2) , 6.8-8.2(m, 8H, Ar-H,), 9.0 (s, 1H, NH),10.0(s, 1H, C-H oxazepine ring).

2-(*p*-chlorophenyl)-3-[α-(N-saccharin) acetamido]-2, 3, 5, 6-tetrahydro-1, 3 –oxazepine - 4, 7-dione (10)

Yield 80%, m.p. 172-174°C, R_f (0.600), IR (KBr) cm^{-1}: 3182(NH), 1749(C=O oxazepine ring), 1670(C=O amide),^{1}H-NMR (DMSO-d_6) δ:,3.7-4.4(m,6H,2CH_2 oxazpeine ring, NCH_2) , 6.8-8.2(m, 8H, Ar-H,), 9.0 (s, 1H, NH),10.0(s, 1H, C-H oxazepine ring).

2-(*p*-methoxyphenyl)-3-[α-(N-saccharin) acetamido]-2, 3, 5, 6-tetrahydro-1, 3- oxazepine-4 -7-dione (11)
Yield 75%, m.p. 215-218°C, R_f (0.58), IR (KBr) cm^{-1}: 3213(NH), 1743(C=O oxazepine ring), 1679(C=O amide),^{1}H-NMR (DMSO-d_6) δ 3.3 (s, 3H, OCH_3), 3.7-4.4(m,6H,2CH_2 oxazpeine ring, NCH_2), 6.8-8.1(m, 8H, Ar-H), 9.1 (s, 1H, NH),10.2(s, 1H, C-H oxazepine ring).

2-(*p*-bromophenyl)-3-[α-(N-saccharin)acetamido]-2,3-dihydro-benzo[e]-1,3-oxazepine-4-7-dione (12)
Yield 62%, m.p. 205-207°C , R_f (0.47), IR (KBr) cm^{-1}: 3182(NH), 1747 (C=O oxazepine ring), 1679(C=O amide), ^{1}H-NMR (DMSO-d_6) δ:4.5(s,2H,NCH_2),7.0-8.2(m,12H,Ar-H), 9.1 (s, 1H, NH),10.2(s, 1H, C-H oxazepine ring).

2-(*p*-chlorophenyl)-3-[α-(N-saccharin)acetamido]-2,3-dihydro-benzo[e]-1,3-oxazepine-4,7-dione (13)
Yield 62%, m.p. 187-190°C., R_f (0.44), IR (KBr) cm^{-1}: 3184(NH), 1749 (C=O oxazepine ring), 1676(C=O amide), ^{1}H-NMR(DMSO-d_6) δ:4.5(s, 2H, N-CH_2), 7.0-8.2(m, 12H, Ar-H), 9.3 (s, 1H, NH),10.0(s, 1H, C-H oxazepine ring).

2-(*p*-mthoxyphenyl)-3-[α-(N-saccharin)acetamido]-2,3-dihydro-benzo[e]-1,3-oxazepine-4-7-dione (14)
Yield 64%, m.p. 220-222°C, R_f (0.824), IR (KBr) cm^{-1}: 3282(NH), ,1745 (C=O oxazepine ring), 1679(C=O amide), ^{1}H-NMR (DMSO-d_6) δ:3.3(s,3H, OCH_3,4.3(s,2H,NCH_2),7.0-8.2(m,12H,Ar-H), 9.0(s, 1H, CH oxazepine ring),10.0 (s,1H, NH).

Preparation of Azetidinone Derivatives (15-17)
General procedure: A solution of chloroacetyl chloride (1.0 mmol.) in dry dioxane (10 ml) was slowly added to a solution of Schiff base (3-5) (0.5 mmol.) and triethylamine (1.0 mmol.) in (10 ml) dry dioxane at 0 to 5 °C. The reaction mixture was then allowed to warm to room temperature and stirred for 15 h. The precipitate obtained was filtered and recrystallized from hexane and ethylacetate (1:1) to give compounds (15-17) respectively.

3-Chloro-4-(*p*-bromophenyl)-1-[α-(N-saccharin) acetamido] azitidine-2-one (15)
Yield 70%, m.p. 200°C dec., R_f (0.629), IR (KBr) cm^{-1}: 3186(NH), 1747 (C=O lactm ring), ^{1}H-NMR (DMSO-d_6) δ:4.1-4.3(d,d,2H,azitidene ring) 4.6(s, 2H, N-CH_2-)8.0-8.4(m, 8H, Ar-H), , 8.9(s,1H, NH).

3-Chloro-2-(*p*-chlorophenyl)-1-[α-(N-saccharin)acetamido]azitidine-2-one (16)
Yield 75%, m.p. 215°C dec., R_f (0.35), IR (KBr) cm^{-1}: 314(NH), 1747 (C=O lactm ring) . ^{1}H-NMR (DMSO-d_6) δ:, 4.2-4.4(d,d,2H,azitidene ring) 4.6(s, 2H,N-CH_2-), 7.7-.-8.6(m, 8H, Ar-H), 8.9 (s, 1H, NH).

3-Chloro-4-(*p*-methoxyphenyl)-1-[α-(N-saccharin) acetamido] azitidine-2-one (17)
Yield 74%, m.p. 235°C dec., R_f (0.33), IR (KBr) cm^{-1}: 3180(NH), 1745 (C=O lactm ring).^{1}H-NMR (DMSO-d_6) δ:3.3 (s, 3H, OCH_3,4.1-4.3(d,d,2H,azitidene ring) 4.6 (s, 2H,N-CH_2-), 8.0-8.3(m, 8H, Ar-H), 8.9(s,1H, NH).

Preparation of derivatives (18, 19)
General procedure: A mixture of compound (1) (1.1 mmol.) and urea or thiourea (1.1 mmol.) in (15ml) absolute ethanol was refluxed for 12 h. then cooled, the produced precipitate was filtered and recrystallizede from ethanol to give compound (18 and 19) respectively.

N-(aminocarbonyl) - α - (N-saccharin) acetamide (18)
Yield 70%, m.p. 65-67°C, R_f (0.38), IR (KBr) cm^{-1}: 3294, 3363, 3387(NH_2, NH), 1620, 1670 (2 C=O amide).

N-(aminocarbonothioyl) - α - (N-saccharin) acet amide (19)
Yield 86%, m.p. 70-72°C, R_f (0.32), IR (KBr) cm^{-1}: 3182, 3274, 3382(NH_2, NH), 1704 (C=O amide), 1240(C=S).

Preparation of 1, 3-oxazole derivatives (20, 21)
A mixture of compound (18) (0.16 gm, 0.59 mmol.), p-bromophenacylbromide or *p*-phenylphenacyl bromide (0.59 mmol.) in (20 ml) ethanol was refluxed for 8h. The formed precipitate after cooling was filtered, dried and recrystallized from ethanol to give compounds 20, 21 respectively.

N-[4-(p-bromophenyl)-1, 3-oxazole-2-yl]-α-(N-saccharin) acetamide (20)
Yield 52%, m.p. 72-74°C, R_f (0.31), IR (KBr) cm^{-1}: 3467(NH), 1680 (C=O), 1530(C=N). ^{1}H-NMR (DMSO-d_6) δ:4.6(s,2H,NCH_2),5.49(s,1H,oxazole ring), 7.6-8.4(m,8H,Ar-H),9.4(s,1H,NH).

N-[4-(biphenyl)-1, 3-oxazole-2-yl]-α-(N-saccharin) acetamide (21)
Yield 66%, m.p. 94-96°C, R_f (0.47), IR (KBr) cm^{-1}: 3467(NH), 1680 (C=O) 1530(C=N). ^{1}H-NMR (DMSO-d_6) δ: 4.6(s,2H,NCH_2),5.49(s,1H,oxazole ring), 7.8-8.6(m,13H,Ar-H),9.4(s,1H,NH).

Preparation of 1, 3-thiazole derivatives (22, 23)
Compounds 22 and 23 were prepared by the same method described for the preparation of oxazole derivatives

N-[4-(p-bromophenyl)-1, 3-thiazole-2-yl]-α-(N-saccharin) acetamide (22)
Yield 50%, m.p. 69-72°C, R_f (0.27), IR (KBr) cm^{-1}: 3456(NH), 1681 (C=O), 1540(C=N). ^{1}H-NMR (DMSO-d_6)δ: 4.6(s, 2H, NCH2), 5.0(s, 1H, thiazole ring), 7.6-8.4(m, 8H, Ar-H), 9.2(s, 1H, NH).

N-[4-(biphenyl)-1, 3-thiazole-2-yl]-α-(N-saccharin) acetamide (23)
Yield 63%, m.p. 87-90°C, R_f (0.94), IR (KBr) cm^{-1}: 3448(NH), 1687 (C=O), 1540(C=N). ^{1}H-NMR (DMSO-d_6) δ: 4.6(s,2H,NCH_2),5.0(s,1H,thiazole ring), 7.6-8.4(m,13H,Ar-H),9.0(s,1H,NH).

Preparation of carboxamide derivatives (24, 25)
A mixture of compound (2) (0.9 gm, 3.5 mmol.) and phenylisocynate or 1-naphthylisocynate (3.5 mmol.) in (20 ml) absolute ethanol was refluxed for 8h. The formed precipitate after cooling was filtered, dried and recrystallized from ethanol to give compounds 24, 25 respectively.

2-N- (α -N-saccharin) acetyl-N-phenyl hydrazine carboxamide (24)
Yield 54%, m.p. 122-123°C, R_f (0.63) IR (KBr) cm^{-1}: 3387-3383(bro. NH), 1649, 1668 (2 C=O).

2-N- (α -N-saccharin) acetyl-N-(1-naphthyl) hydrazine carboxamide (25)
Yield 72%, m.p. 137-139°C, R_f (0.67), IR (KBr) cm^{-1}: 3387-3383(NH), 1649, 1668 (2 C=O).

Preparation of oxazoline derivatives (26-29)
A mixture of compound 24 or 25 (0.59 mmol.), *p*-bromophenacylbromide or *p*-phenylphenacyl bromide (0.59 mmol.) in (20 ml) ethanol was refluxed for 8h. The formed precipitate after cooling was filtered, dried and recrystallized from ethanol to give compounds (26-29) respectively

N-[5-(p-bromophenyl)-3-phenyl-2-hydroxy-1,3-oxazol-2-ylidene]-α- (N-saccharin)acetohydrazide (26)
Yield 50%, m.p. 100°C dec. , R_f (0.61), IR (KBr) cm^{-1}: 3346(OH),3195(NH), 1695,1681(C=O),1184(C-O).^{1}H-NMR (DMSO-d_6) δ:4.4(s,2H,NCH_2),7.9-8.4(m,13H, Ar-H),9.9(s,1H,NH), 10.2(s,1H,NH), 10.5. (s, 1H, OH).

N-[5-(p-biphenyl)-3-phenyl-2-hydroxy-1,3-oxazol-2-ylidene]-α (N-saccharin) acetohydrazide (27)
Yield 53%, m.p. 115°C dec. , R_f (0.65), IR (KBr) cm^{-1}: 3360(OH),3193(NH), 1695,1679(C=O),1184(C-O). ^{1}H-NMR (DMSO-d_6) δ:4.4(s,2H,NCH_2),7.9-8.4(m,18H, Ar-H),9.9(s,1H,NH), 10.2(s,1H,NH), 10.5. (s,1H,OH).

N-[5-(*p*-bromophenyl)-3-(1-naphthyl)-2-hydroxy-1,3-oxazol-2-ylidene]-α- (N-saccharin)acetohydrazide (28)
Yield 52%, m.p. 150°C dec. , R_f (0.70), IR (KBr) cm^{-1}: 3370(OH),3175(NH), 1695,1679(C=O),1184(C-O). ^{1}H-NMR (DMSO-d_6) δ: 4.4(s,2H,NCH_2),7.9-8.4(m,15H, Ar-H),9.9(s,1H,NH), 10.2(s,1H,NH), 10.5. (s,1H,OH).

N-[5-(*p*-piphenyl)-3-(1-naphthyl)-2-hydroxy-1,3-oxazol-2-ylidene]-α (N-saccharin) acetohydrazide (29)
Yield 51%, m.p. 135°C dec. , R_f (0.73), IR (KBr) cm^{-1}: 3360(OH),3188(NH), 1695,1683(C=O),1184(C-O). ^{1}H-NMR (DMSO-d_6) δ:4.4(s,2H,NCH_2),7.9-8.4(m,20H, Ar-H),9.9(s,1H,NH), 10.2(s,1H,NH), 10.5. (s,1H,OH).

Preparation of imides derivatives (30-32)
General procedure: A mixture of compounds (2) (0.5 gm, 2 mmol.) and the appropriate acid anhydride namely maleic anhydride, succinic anhydride and phthalic anhydride (2 mmol.) in (15 ml) acetic acid was refluxed for 24h. The formed precipitate was filtered, dried and recrystlaized from ethanol to give compounds (30-32) respectively

N-[α-(N-saccharin) acetamido] maleimide (30)
Yield 52%, m.p. 228-230°C, R_f (0.55), IR (KBr) cm^{-1}: 3226(NH), 1751(C=O imide) 1660 (C=O amide). ^{1}H-NMR (DMSO-d_6)δ: 4.4 (s, 2H, N-CH_2-), 4.9(s,2H, CH=CH), 7.4-8.4(m, 4H, Ar-H), 11.8(s, 1H, NH).

N-[α-(N-saccharin) acetamido] succinimide (31)
Yield 63%, m.p. 218-220°C, R_f (0.59), IR (KBr) cm^{-1}: 3218(NH), 1741(C=O imide) 1685 (C=O amide). ^{1}H-NMR (DMSO-d_6)δ: 3.2(s, 4H,-CH_2-CH_2-), 4.2 (s, 2H, N-CH_2-), 7.0-7.8(m, 4H, Ar-H), 11.3(s, 1H, NH).

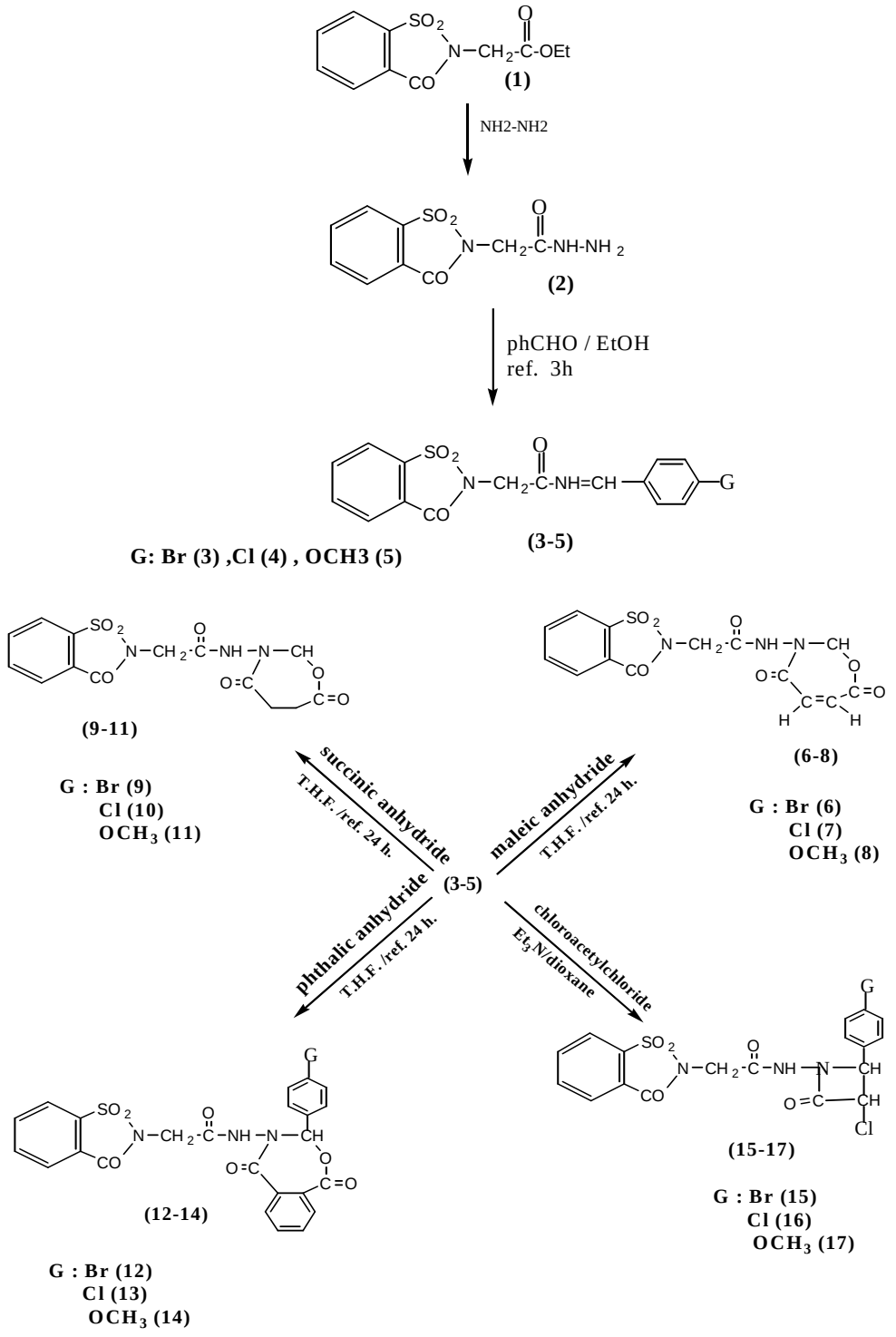
N-[α-(N-saccharin) acetamido] phthalimide (32)
Yield 65%, m.p. 235-237°C, R_f (0.62), IR (KBr) cm^{-1}: 3220(NH), 1741(C=O imide) 1665 (C=O amide). ^{1}H-NMR (DMSO-d_6)δ: 4.4 (s, 2H, N-CH_2-), 7.5-8.2(m, 8H, Ar-H), 11.1(s, 1H, NH).

RESULTS AND DISCUSSION

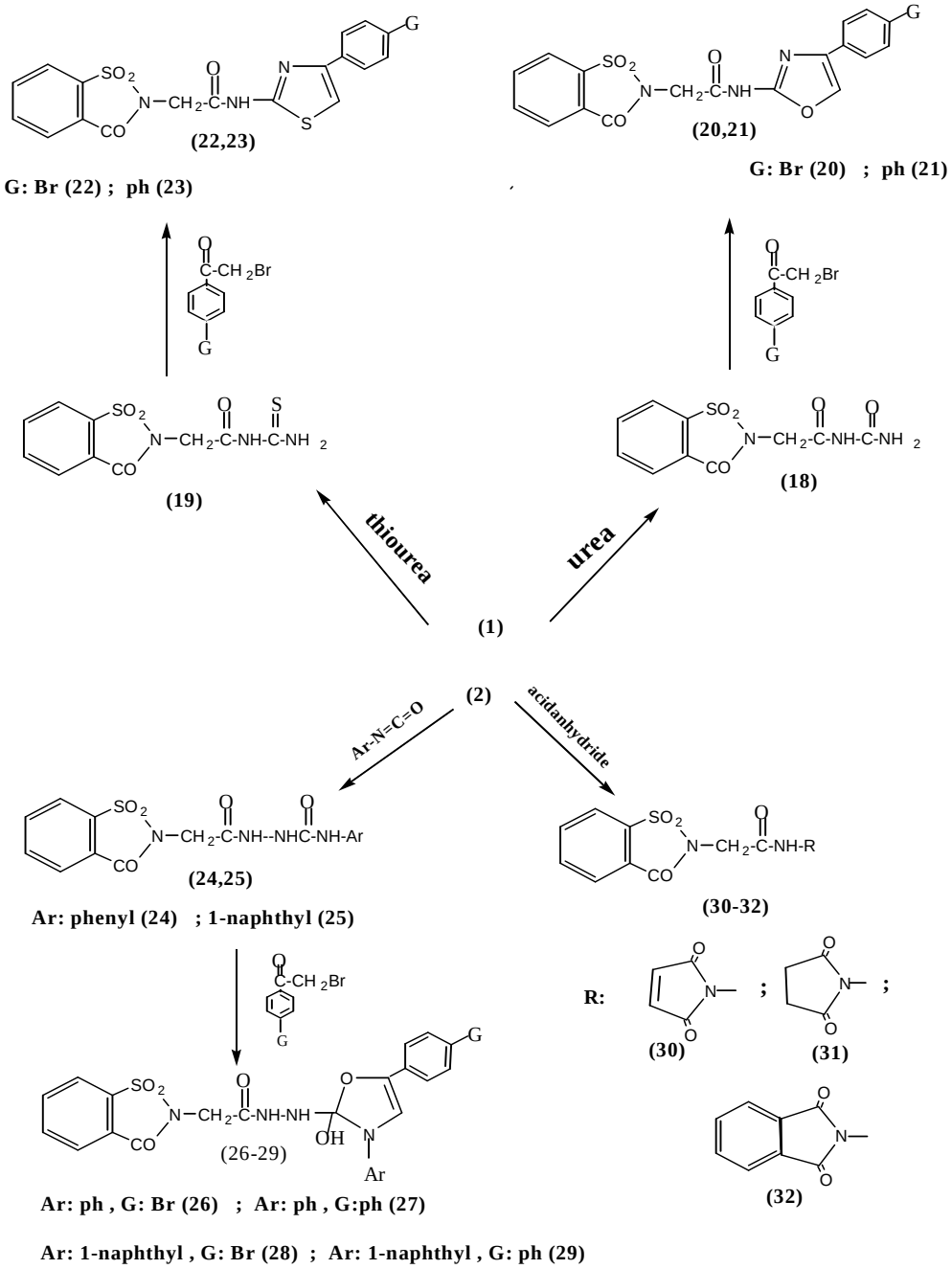
α- (N-saccharin)acetohydrazide (2) was chosen as a starting material for the synthesis of all derivatives (3-32).To get a new series of Schiff-bases (3-5) it was of interest to condense compound (2) with different aromatic aldehydes namely p-bromobenzaldehyde , *p*-chlorobenzaldehyde and *p*-methoxybenzaldehyde with few drops of glacial acetic acid to give the corresponding Schiff-bases (3-5) respectively. The I.R. and ^{1}H-NMR spectrum of formed Schiff bases showed the presence of(C=N) band at 1550-1630 cm^{-1} and a singlet signal for azomethine (CH=N) at 10.7-11.2 ppm. Oxazepine derivatives (6-14) (scheme 1) were prepared by the refluxing of Schiff bases with different acid anhydride namely maleic anhydride succinic anhydride and phthalic anhydride in dry THF for 24h. I.R. and ^{1}H-NMR spectrum of oxazepine derivatives showed many characteristic absorption bands such as (NH) at 3186-3282 cm^{-1}, (C=O oxazepine ring) 1643-1751 $cm^{-1}$and singlet signal for(CH oxazepine ring) at 10-10.3 ppm. Monocyclic *β*-lactams (15-17) (scheme 1) were prepared by the reaction of imines (3-5) with chloroacetyl chloride in dry dioxane in the presence of trimethyl amine via a [2+2] cyclo addition reaction [(23)]. The I.R. spectrum of formed azetidineones showed the presence of *β*-lactam carbonyl absorption at 1774 cm^{-1} while the ^{1}H-NMR spectrum showed doublet- doublet signal at 4.0-4-3 ppm assigned to (CH) protons of β-lactam ring at positions 3 and 4 .

Also cyclization of N-(aminocarbonyl)- α -(N-saccharin)acetamide (18) and N-(aminocarbonothioyl)- α -(N-saccharin)acet amide (19) with *p*-bromophenacylbromide or *p*-phenylphenacyl bromide give the corresponding 1,3-oxazole (20,21) and 1,3 thiazole (22,23) derivatives(scheme 2). The I.R. and ^{1}H-NMR spectrum of these derivatives showed presence of NH band at 3448-3467 cm^{-1}, C=O amid band at 1680-1687 cm^{-1} and C=N band at 1530-1540 cm^{-1} and a singlet signal at 5.49 ppm and 5.0 ppm witch due to (CH) proton for oxazole ring and thiazole ring respectively.

Moreover, reaction of (2) with phenylisocynate or 1-naphthylisocynate gave the corresponding carboxamide derivatives (24, 25) which cyclized with *p*-bromophenacylbromide or *p*-phenylphenacyl bromide give the corresponding oxazoline derivatives (26-29). The I.R. spectrum of formed these derivatives showed the presence of (OH) at 3346-3370 cm^{-1} ,(NH) at 3157-3193 cm^{-1} and (C=C) at 1589-1602 cm^{-1}while the ^{1}H-NMR spectrum showed singlet signals at 9.9 ppm , 10.2 ppm and10.5 ppm due to NH-CH, NH-C=O and –OH respectively. Imides derivatives (24-32) were prepared by the refluxing of (2) with different acid anhydride namely maleic anhydride succinic anhydride and phthalic anhydride in acetic acid. The I.R. spectrum of formed these derivatives showed the presence of (NH) at 3218-3226 cm^{-1},(C=O imide) at 1741-1751 $cm^{-1}$and (C=O amide) at 1660-1685) cm^{-1},while the ^{1}H-NMR spectrum showed singlet signals for(–N-CH_2) at 4.2-4.4 ppm, (NH) at 11.1-11.8 ppm , (CH=CH imide ring) at 4.9 ppm and (-CH_2-CH_2- imide ring) at 3.2 ppm.



Scheme 1: synthetic rout for the prepration of compounds (3-17)



Scheme 2: Synthetic rout for the prepration of compounds (18-32)

REFERENCES

[1] H. Kumar; Karvekar; *E. J. Chem.*,(**2010**), 7(2), 636.
[2] M. EL-Zahar; S. Abd EL-Karim; M. Haiba; *World J. Chem*., (**2009**), 4**(**2), 1949
[3[G. Kraus-Berthier; M.Malivet; *Clin. Cancer Res*., (**2001**), **7**, 2573.
[4] R. Rajendra; K.Kumar; *Sci. Pharm*., (**2009**), 7, 19.
[5] K. Fahed; H. Hussein; *Int. J.Chem.Tech Res*., (**2013**), 6,292.
[6] H. yaIc; K. Loses; *J.Med. Chem*., (**1966**), 9, 478.

[7] D. Davyt; G. Serra; *Mar*. *drugs*, (**2010**), 8, 2755.
[8] H. Zhang; Y.Mei; K. Du; X .Cao; P. Zhang; *Molecules*, (**2013**), 18, 13425.
[9] N. Desai ;V. Joshi ; K. Rajpara ; H. Vaghani ; H. Satodiya ;*J. Fluor.Chem*., (**2012**),142, 67
[10] H. Karda ; B. Acharya; B. Sathe ; M. Kaushik ; *Med. Chem.*, (**2008**),17,19.
[11] A. Khalaf; *Molecules*; (**2009**), 14, 2431.
[12] H. Matsuzaki;I. Takuchi; Y. Hamad; K. Hatano; *Chem. Pharm. Bull*, (**2000**), 4,755.
[13] J. Barradas;M. Errea; N .Accorso ; C. Sepulveda; *Eur. J. Med.Chem*., (**2011**),46,259.
[14] A. Jarrahpour; E. Ebrahimi; *Molecules*, (**2010**), 15,515.
[15] I. Cooper; R. Grigg; W. Maclauchlan; M. Thornton; V. Sridharance; Chem *Commun.* , (**2002**), 1372.
[16] S. Dugar; N. Clader;J. Vizziano ;M.Huie ;M. Compton ; D. Davis ; *Bioorg Med. Chem.lett*., (**1996**), 6, 1271.
[17] W. Han; A. Trehan; J. Wright; M. Federici; S. Seiler; *Bioorg. Med.Chem*. (**1995**), 3, 1123.
[18] N. Zhou ;D.guo ;G.Thomas; A. Reddy; J. Kaleta ; R. Micetich ; *Bioorg. Med. Chem. Let*., (**2003**), 13, 139.
[19] B. Hue;B. Palomba; M. Giacordy; R. Alric ; P. Prtit; *Ther. Manit*. , (**1998**), 20, 335.
[20] S. Kapur;R.Cho; C. Jones; G. Mckay ; R. Zipursky ;*Biol. Psychol* , (**1999**),45, , 1217 .
[21] H. Takeuchi ; S. Ykota ; S. Shimada; Y. Ottani ;S. Miura ; H. Kubo ; *Curr. Ther. Rer. Chin. Exp*., (**1993**), 53, 427.
[22] R. Mohammed; *MSc. Thesis College of Science*, Al-NahrainUniversity, (**2004**), 34.
[23] A. Anwar; K.Kamel; M.Mohammed; *Acta. Pol. Pharm.Res*., (**2009**), 6,279.