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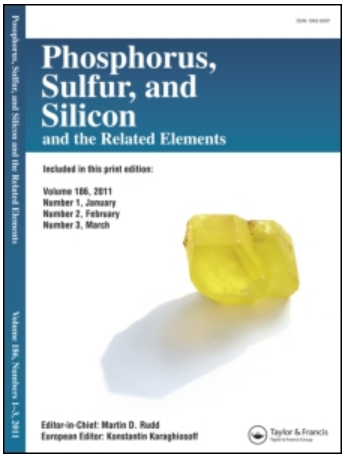

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Studies on Spiroheterocycles, Part III: Synthesis of Diazaspiroundecanetetraone Derivatives Containing Biologically Active Heterocycles

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Studies on Spiroheterocycles, Part III: Synthesis of Diazaspiroundecanetetraone Derivatives Containing Biologically Active Heterocycles

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Barbituric acid ***2*** *upon Michael addition with dibenzal acetones* ***1a–c*** *afforded the corresponding diazaspiro derivatives* ***3a–c****. The base-catalyzed condensation of* ***3a–c*** *with various aromatic aldehydes produces diarylidine derivatives* ***4a–l****. The diarylidene compounds* ***4a–l*** *on condensation with hydrazine, phenyl hydrazine, hydroxylamine, urea, guanidine carbonate, and hydrazine hydrate with acetic acid afforded their respective in situ oxidized products* ***5, 6, 7, 8, 9,*** *and* ***10****. The structures of the compounds are ascertained from their analytical and spectral data. Some of the compounds are screened for their biological activities against E. coli, B. cirroflagellosus, A. niger, and C. albicans.*

Keywords Barbituric acid; diarylidene; dibenzal acetone; spiroheterocycles

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INTRODUCTION

Derivatives of barbituric acid and thiobarbituric acid have attracted the attention of researchers in synthetic organic chemistry, as well as in medicinal chemistry, for a long time due to their exceptionally diverse biological activities, such as fungicidal,[1] sedatives,[2,3] antibacterial,[4] herbicidal,[5] and antiviral,[6] etc. Spiro compounds are found to exhibit various biological activities, such as fungicidal,[7–11] herbicidal,[12] bactericidal,[13,14] anticonvulsant,[15] anti-inflammatory,[16]antianxiety,[17] etc. Keeping in view the above facts, some work has been reported on the synthesis of spiro compounds containing barbiturates/thiobarbiturates

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moieties.[18–30] Reddy et al.[23,24] have synthesized 7,11-diaryl-2,4-diazaspiro[5.5]undecane-1,3,5,9-tetrones, which are found to have good antifungal and antibacterial characteristics. Kokel[25] has reported the synthesis of 4,5-annulated-2-dimethylamino-1,3,8,10-tetraaza-spiro [5.5]-1,4-undecadiene-7,9,11(3H,8H,10H)triones from 2-dimethylaminooxazolo[5,4-d]pyrimidine-4,6-diones. Kotha et al.[26] have synthesized spiro annulated derivatives obtained from the ring closing metathesis of diallylated products, which were obtained from barbituric/thiobarbituric acid and β-dicarbonyl compounds. Shaabani et al.[27,28] have synthesized 3,3-dimethyl-(7*S*,11*R*)-bis(4-methylphenyl)-2,4-dioxa-8,10-diazaspiro[5.5]undecane-1,5,9-triones by the reaction of an aldehyde, urea, and barbituric acid derivatives using microwave irradiation under solvent-free conditions. Jursic and Stevens[29] have reported the synthesis of 5,6-dihydro-1,3-dimethyl-5,6-di [1′,3′-dimethyl-2′,4′,6′-trioxopyrimidin(5′,5′)yl)]furo[2,3-d]uracil. Renard et al.[30] have synthesized spirodeoxyribosylbarbituric acid and spirocyclopentylbarbituric acid in order to evaluate their possible use as building blocks in modified oligonucleotide synthesis. Therefore, the present work describes the synthesis of spiroheterocycles containing barbituric acid moiety.

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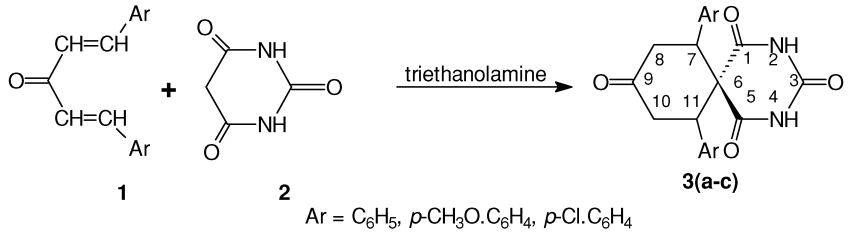
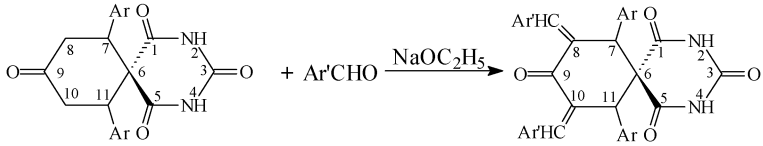
RESULTS AND DISCUSSION

Michael addition of barbituric acid (**2**) with the appropriate divinyl ketone (**1**) in ethanol and triethanolamine yielded the required spiro compounds (**3a–c**) (Scheme 1). The IR spectrum of the spiro compound **3a** (Ar = C_6H_5) shows three carbonyl peaks at 1752, 1711, and 1689 cm^{-1}. The peak at 3256 cm^{-1} corresponds to the -NH groups. The ^1H NMR spectrum of **3a** shows two doublet of doublets center at δ 2.48, δ 3.99 and a triplet center at δ 3.55 corresponding to two equatorial protons at C-8 and C-10, two axial protons at C-7 and C-11, and two



SCHEME 1

axial protons at C-8 and C-10 respectively. The spectrum also shows two broad singlets at δ 11.2 and δ 11.5 for the -NH protons, which is confirmed from an earlier report.[30] The aromatic protons resonate at δ 7.14–7.31 in the form of a multiplet. The ^{13}C NMR spectrum of **3a** shows peaks at δ 173.0, 172.0, 171.0, 59.0, 49.0, and 44.8 corresponding to the carbonyl carbons, spiro carbon, -CH_2, and –CH, respectively. The three very closely spaced peaks due to carbons of the aromatic rings appear in the region δ 128–129. The IR, ^{1}H NMR, and ^{13}C NMR data are in conformity with the proposed structure of the compound as **3a**.



3 (a-c) **4 (a-l)**

Ar = C_6H_5; *p*-$CH_3O.C_6H_4$; *p*-$Cl.C_6H_4$
Ar' = C_6H_5; *p*-$CH_3O.C_6H_4$; *p*-$Cl.C_6H_4$; *p*-$NO_2C_6H_4$

SCHEME 2

The base-catalyzed condensation of the spiro compound **3a–c** with different aldehydes afforded the diarylidene compounds **4(a–l)** (Scheme 2). The IR spectrum of **4a** (Ar = Ar′ = C_6H_5) shows the carbonyl peaks of cyclohexanone ring at 1707 cm^{-1}. The shift of the carbonyl peak to lower frequency may be due to its conjugation with the exocyclic double bond.

The ^{1}H NMR spectrum of **4a** (Ar = Ar' = C_6H_5) shows two protons singlet at δ 3.6 corresponding to the two axial protons at C-7 and C-11.The two doublet of doublet observed in the ^{1}H NMR spectrum of **3a** (Ar = C_6H_5) corresponding to four protons at C-8 and C-10 disappeared in the spectrum of **4a** because of condensation with benzaldehyde at C-8 and C-10. In the ^{13}C NMR spectrum of **4a** (Ar = Ar' = C_6H_5), the absence of the peak at δ 49.0 corresponding to CH_2 group as observed in the spectrum of **3a** and the appearance of a new peak at δ 120.0 in the spectrum of **4a** confirms the formation of dibenzylidene compound.

The diarylidene compounds **4(a–l)** upon condensation with hydrazine, phenyl hydrazine, hydroxylamine, urea, guanidine carbonate, and hydrazine hydrate with acetic acid afforded their respective in situ oxidized products **5**, **6**, **7**, **8**, **9**, and **10** (Scheme 3).

The disappearance of the carbonyl frequency at 1707 cm^{-1} in the IR spectra of **5**, **6**, **7**, **8**, **9**, and **10** confirms the installation of pyrazole, phenyl pyrazole, isoxazole, and pyrimidine moieties in **4**. In the case of **8**, a broad band in the region 3300–3400 cm^{-1} is due to the -OH group.

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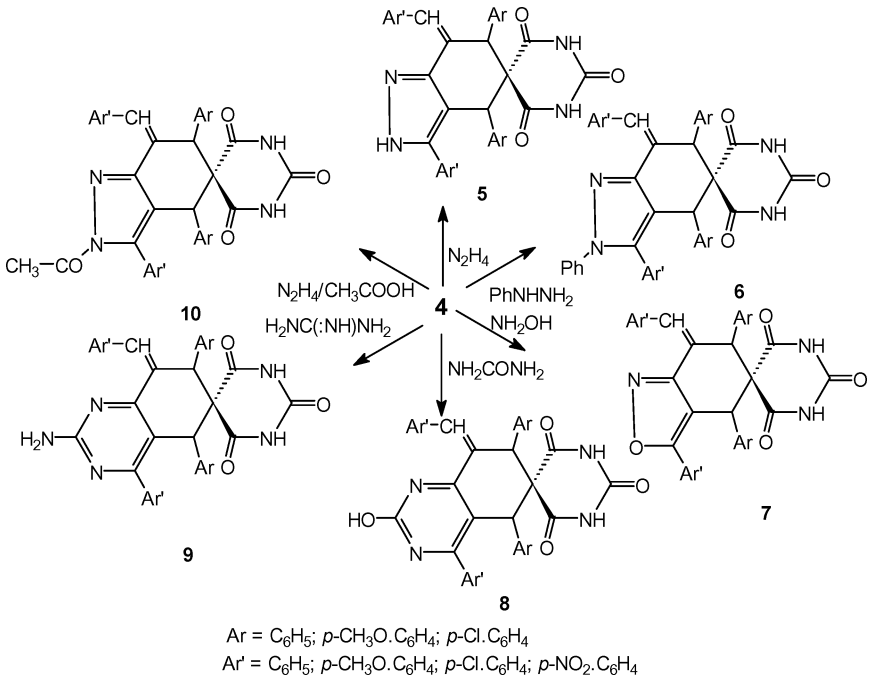

SCHEME 3

The broad band at 3400 cm^{-1} in the IR spectrum of **9** may be attributed to a -NH_2group. The ^1H NMR spectra of the compounds **5–10** display a broad multiplet at δ 6.3–7.6, corresponding to aromatic protons, along with a singlet at δ 3.45–3.76 for the axial protons at $C_7$and C_{11}.

ANTIMICROBIAL ACTIVITY

Antimicrobial activity was carried out against two pathogenic bacteria, *E. coli* and *B. cirroflagellosus*, and *A. niger* and *C. albicans* were the fungal strains. The reference drugs used were Norfloxocin and Griseofalvin, respectively, with DMF as solvent control. The cup-plate method[19–20] was used, and nutrient agar was the culture media. Norfloxocin showed a zone of inhibition of 28 mm against *E. coli* and 25 mm against *B. cirroflagellosus*. Griseofalvin exhibited a zone of 30 mm against both fungi *A. niger* and *C. albicans*. The results of antibacterial and antifungal screening showed that most of the compounds exhibit moderate activity (zone of inhibition 17 to 23 mm) against both bacteria and both fungi, as shown in Table I.

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TABLE I Antibacterial and Antifungal Activities of Some Compounds, 4–10

	Zone of inhibition			
Comp. No.	*E. coli*	*B. cirroflagellosua*	*A. niger*	*C. albicaus*
4c	++	++	+	+
4d	+	+	++	++
4g	++	++	++	+++
4h	+	++	++	+
4i	+	+	+	++
4j	+++	++	++	++
4k	++	+++	+	+
4l	+	++	++	+
5a	+	++	++	++
5b	++	++	++	++
5c	++	+	++	+
5g	++	++	+++	+++
5k	++	++	++	+
5l	++	++	++	+
6b	++	+	++	+++
6c	+	++	++	+
6e	++	++	+	++
6g	+++	++	++	++
6j	++	+++	+	+
6k	+	++	++	+
6l	++	+	++	+++
7c	+	++	++	+
7e	++	++	+	++
7g	+++	++	++	++
7i	++	+++	+	+
7j	+	++	++	+
7k	++	+	++	+++
7l	++	++	++	+
8b	++	++	+	++
8c	+++	++	++	++
8g	++	+++	+	+
8i	+	++	++	+
8j	++	+	+	+
8k	++	+++	+	++
8b	++	++	++	+++
8c	+	++	++	+
8g	++	+++	+	+
9b	++	++	++	+++
9c	+	++	++	+
9e	++	++	++	+
9g	+	++	+++	++
9j	++	++	++	+

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TABLE I Antibacterial and Antifungal Activities of Some Compounds, 4–10 *(Continued)*

	Zone of inhibition			
Comp. No.	*E. coli*	*B. cirroflagellosua*	*A. niger*	*C. albicaus*
9k	++	+++	++	+
10e	++	++	+++	+++
10i	++	++	++	++
10j	++	+	++	++
10k	++	++	++	++

(−) = inactive, (+) = weakly active (12–16 mm), (++) = moderately active (17–21 mm), and (+ + +) = highly active (22–30 mm).

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In conclusion, we have developed a convenient synthetic route for the synthesis of a number of spiroheterocycles containing cyclohexane and barbituric acid nuclei. Biologically active moieties such as pyrimidine, pyrazole, and isoxazole have been easily installed onto the spiro framework.

EXPERIMENTAL

The melting points were determined on a Zenith apparatus and are uncorrected. IR spectra were recorded on a Perkins Elmer FT-IR spectrophotometer using KBr disc.[13]C and [1]H NMR spectra were recorded on a Bruker AC 250 MHz NMR spectrometer and were recorded in d6-DMSO, unless otherwise stated. Purity of the products was checked by TLC, using silica gel "G" (BDH) and hexane-ethyl acetate as eluent.

Synthesis of Dibenzylidene Acetone (1a)

To a solution of NaOH (10 g in 100 mL of water) and ethyl alcohol (80 mL), acetone (3 mL, 0.05 mol) was added and stirred for 15 min. Then benzaldehyde (0.1 mol) was added in two phases and stirred for 2 h at 25°C. Yellow crystals thus separated were filtered, washed with water, and crystallized from ethyl acetate. Yield 9 g (73.2%), mp 112°C, mixed mp 112°C.[31] 4,4′-dianisalacetone[32] **1b** and 4,4′-dichlorbenzalacetone[33] **1c** were prepared according to the reported procedure.

Synthesis of 7,11-Diphenyl-2,4-diaza-spiro[5.5]undecane-1,3,5,9-tetraones (3a)

To a solution of barbituric acid (1.28 gm, 0.01 mol) in 1,4-dioxane (30 mL) and dibenzal acetone (2.34 g, 0.01 mol) in ethanol (30 mL), 10 drops of triethanolamine were added. The mixture was refluxed with stirring for 7 h. The reaction mixture was filtered, cooled, and poured into ice-cold water. The solid so obtained was filtered, dried, and crystallized from acetic acid. Yield 3.2 g (85%), mp 272°C, Anal. Calc. for $C_{21}H_{18}O_4N_2$: C, 66.67; H, 4.76; N, 7.41% Found: C, 66.52; H, 4.92; N, 7.29%. IR: 3256 cm^{-1} (-NH) 1711, 1689 cm^{-1} (C=O); ^1H NMR: δ 2.48 (dd, $J = 15$ Hz, 4Hz, 2H, equatorial-H at C_8 & C_{10}), 3.55 (t, $J = 15$ Hz, 2H, axial-H at C_8 & C_{10}), 3.99 (dd, $J = 15$Hz, 4Hz, 2H, axial-H at C_7 & C_{11}), 7.14–7.31 (m, 10H, Ar-H), 11.2 (bs, 1H, NH), 11.5 (bs, 1H, NH); ^{13}C NMR: (d6-DMSO) δ 44.8, 49.0, 59.0, 128.1, 128.6, 128.8, 137.4, 171.0, 172.0, 173.0.

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Synthesis of 8,10-Dibenzylidene-7-11-diphenyl-2,4-diazaspiro[5.5]undecane-1,3,5,9-tetraones (4a)

A mixture of **3a** (0.362 g, 0.001 mol), $NaOC_2H_5$ (0.002 mol) in ethanol (10 mL), and benzaldehyde (0.21 g, 0.002 mol) was refluxed for 16 h. The reaction mixture was filtered while hot, and then acidified with dil. HCl after cooling. The solid that separated was filtered, washed with cold water, dried, and crystallized from ethanol. Yield 0.53 g (75%), mp 162°C. Anal. Calcd for $C_{35}H_{26}O_4N_2$: C, 78.07; H, 4.83; N, 5.20; % Found: C, 77.86; H, 4.78; N, 5.06; %. IR:1708 cm^{-1} (C = O);^1H NMR: δ 3.6 (s,2H, H at C_7 & C_{11}), 6.8–7.6 (m,22H, Ar-H and =CH), 11.1 (bs, 1H, NH), 11.4 (bs, 1H, NH);^{13}C NMR: (d6-DMSO) δ 46.2, 54.7, 113.4, 120.0, 128.0–133.0 (aromatic carbon), 137.0, 170.0, 170.5, 172.0.

Synthesis of 8′-Benzylidene-1,3,5-trihydro-3′,5′,7′ triphenyl-2,4,6-trioxo-spiro[pyrimidine-5,6′-pyrazolo[3, 4-b]cyclohexane] (5a)

To a solution of **4a** (0.107 g, 0.0002 mol) and hydrazine hydrate (0.01 g, 0.0002 mol) in ethanol (5 mL), two drops of piperidine were added, and the mixture was refluxed on a water bath for 19 h. The reaction mixture was concentrated, cooled, and poured into ice-cold water. The solid that separated was filtered, washed with water, and crystallized from 95% ethanol. Yield 0.08 g (80%), mp 132°C. Anal. Calcd for $C_{35}H_{26}O_3N_4$: C, 76.36; H, 4.73; N, 10.18, Found: C, 76.44; H, 4.75; N, 10.20; %. IR: 3400 cm^{-1}, 1678 cm^{-1}, 1660 cm^{-1}; ^1H NMR: δ 3.62 (s, 2H, H at C_7 & C_{11}),

7.0–7.4 (m, 21H, Ar-H and =CH), 9.8 (bs, 1H, NH), 11.0 (bs, 1H, NH), 11.3 (bs, 1H, NH).

Synthesis of 8′-Benzylidene-1,3,5-trihydro-2′,3′,5′,7′-tetraphenyl-2,4,6-trioxo-spiro[pyrimidine-5,6′-pyrazolo[3,4-b]cyclohexane] (6a)

To a solution of **4a** (0.107 g, 0.0002 mol) and phenyl hydrazine hydrate (0.02 g, 0.0002 mol) in ethanol (5 mL), two drops of piperidine were added, and the mixture was refluxed on a water bath for 16 h. The reaction mixture was concentrated, cooled, and poured into ice-cold water. The solid that separated was filtered, washed with water, and crystallized from ethanol. Yield 0.047 g (75%), mp 166°C. Anal. calcd. for $C_{41}H_{30}O_3N_4$: C, 78.59; H, 4.79; N, 8.95%, Found: C, 78.43; H, 4.62; N, 8.79%. IR: 3300 cm^{-1}, 1660 cm^{-1}, 1674 cm^{-1}, 1600 cm^{-1}; ^{1}H NMR: δ 3.48 (s, 2H, H at C_7 & C_{11}), 6.36–7.55 (m, 26H, Ar-H and =CH).

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Synthesis of 8′-Benzylidene-1,3,5-trihydro-3′,5′,7′-trihenyl-2,4,6-trioxo-spiro[pyrimidine-5,6′-isoxazole[3,4-b]cyclohexane] (7a)

To a mixture of **4a** (0.107 g, 0.0002 mol) and hydroxylamine hydrochloride (0.12 g, 0.0002 mol) in ethanol (5 mL), a few drops of KOH (2%) were added and refluxed on a steam bath for 15 h. The reaction mixture was concentrated, cooled, and poured into ice-cold water. The solid was filtered, washed with water, and crystallized from ethanol. Yield 0.071 g (65%), m.p.132°C. Anal. calcd. for $C_{35}H_{25}O_4N_3$: C,76.23; H, 4.54; N, 7.62 %, Found: C, 76.31; H, 4.80; N, 7.80%. IR: 1674 cm^{-1},1662 cm^{-1}, 1578 cm^{-1}, 1382 cm^{-1}; ^{1}H NMR: δ 3.68 (s,2H, H at C_7 & C_{11}), 6.40–7.61 (m, 21H, Ar-H, =CH), 11.0 (bs, 2H, NH).

Synthesis of 9′-Benzylidene-1,3,5,-trihydro-2′-hydroxy-4′,6′,8′-triphenyl-2,4,6,-trioxo-5-spiro[pyrimidine-5,7′-pyrimido[5,6-b]cyclohexane] (8a)

To a mixture of **4a** (0.107 g. 0.0002 mol) and urea (0.012g, 0.0002 mol) in ethanol (5 mL), 5 drops of conc. HCl was added and refluxed on a steam bath for 18 h. The reaction mixture was cooled and neutralized with 5% NaOH solution. The solid product was filtered, washed several times with water, and crystallized from acetic acid. Yield 0.083 g (72%),

mp 162 °C. Anal. calcd. for $C_{36}H_{26}O_4N_4$: C, 74.74; H, 4.50; N, 9.69%, Found: C, 74.52; H, 4.38; N, 9.48%. IR: 3300–3400 cm^{-1} (broad), 1695 cm^{-1}, 1660 cm^{-1}, 1590 cm^{-1}; ^1H NMR: δ 3.66 (s, 2H, H at C_7 & C_{11}), 6.47–7.22 (m, 21H, Ar-H and =CH), 9.2 (bs, 1H, -OH), 11.2 (bs, 2H, NH).

Synthesis of 2′-Amino-9′-benzylidene-1,3, 5-trihydro-4′,6′,8′-triphenyl -2,4,6-trioxo-spiro[pyrimidine-5,7′-pyrimido[5,6-b]cyclohexane] (9a)

To a refluxing solution of **4a** (0.107 g, 0.0002 mol) and guanidine carbonate (0.036 g, 0.0002 mol) in ethanol (5 mL), a few drops of 40% NaOH were added, and the mixture was refluxed for 16 h. The reaction mixture was cooled and acidified with dil. acetic acid. The solid so obtained was filtered, washed with water, and crystallized from acetic acid. Yield 0.086 g (75%), mp 178°C. Anal. Calcd. for $C_{36}H_{27}O_3N_5$: C, 74.87; H, 4.68; N,12.13%, Found: C, 74.51; H, 4.57; N, 12.07%. IR: 3400 cm^{-1}, 1667 cm^{-1}, 1660 cm^{-1}, 1584 cm^{-1}, ^1H NMR: δ 3.68 (s, 2H, H at C_7 & C_{11}), 6.38–7.31 (m, 21H, Ar-H and =CH), 8.3 (s, 2H, NH_2), 11.1 (bs, 2H,NH).

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Synthesis of 2′-Aceto-8′-benzelidene-1,3,5-trihydro-3′,5′,7′-triphenyl-2,4,6-trioxo-spiro[pyrimidine-5,6′-pyrazole[3,4-b]cyclohexane] (10a)

A solution of **4a** (0.107 g, 0.0002 mol) and hydrazine hydrate (0.01 g, 0.0002 mol) in acetic acid (5mL) was refluxed for 10 h. The reaction mixture was concentrated, cooled, and poured into ice-cold water. The solid so obtained was filtered, dried, and crystallized from acetic acid. Yield 0.080 g (68%), m.p 145°C. Anal. calcd. for $C_{37}H_{28}O_4N_4$: C,75.00; H, 4.72; N, 9.45%, Found: C,74.79; H, 4.68; N, 9.31%. IR: 3300 cm^{-1}, 1687 cm^{-1}, 1660 cm^{-1}, 1590 cm^{-1}; ^1H NMR: δ 2.6 (s, 3H, CH_3CO-), 3.64 (s, 2H, H at C_7 & C_{11}), 6.41–7.28 (m, 21H, Ar-H and =CH), 11.1 (bs, 2H, NH).

The syntheses of all other derivatives such as **3b–c**, **4b–l**, **5b–l**, **6b–l**, **7b–l**, **8b–l**, **9b–l**, and **10 b–l** were carried out according to the detailed procedure presented for the representative compounds above. The spectral data of the compounds corroborate the proposed structures. However, their physical and analytical data have been given in Table II.

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TABLE II Physical and Analytical Data

Comp. No.	21Ar	Ar′	Mp (°C)	Mol. Formula	Yield in %	C % Cal. (Found)	H %Cal. (Found)	N % Cal. (Found)
3b	*p*-OCH_3. C_6H_4	–	205	$C_{23}H_{22}O_6N_2$	69	65.40 (65.28)	5.21 (5.13)	6.63 (6.55)
3c	*p*-Cl. C_6H_4	–	238	$C_{21}H_{16}O_4N_2Cl_2$	58	58.60 (58.44)	3.72 (3.66)	6.51 (6.48)
4b	C_6H_5	*p*-OCH_3. C_6H_4	120	$C_{37}H_{30}O_6\ N_2$	72	74.25 (74.15)	5.02 (5.31)	4.68 (4.48)
4c	C_6H_5	*p*-Cl. C_6H_4	140	$C_{35}H_{24}O_4N_2Cl_2$	68	69.19 (69.02)	3.95 (4.03)	4.61 (4.49)
4d	C_6H_5	*p*-NO_2. C_6H_4	259	$C_{35}H_{24}\ O_8N_4$	49	66.88 (66.73)	3.82 (4.07)	8.92 (8.79)
4e	*p*-OCH_3. C_6H_4	C_6H_5	172	$C_{37}H_{30}\ O_6N_2$	57	74.25 (74.11)	5.02 (5.13)	4.68 (4.59)
4f	*p*-OCH_3. C_6H_4	*p*-OCH_3. C_6H_4	82	$C_{39}H_{34}O_8N_2$	46	71.12 (71.03)	5.17 (5.23)	4.26 (4.09)
4g	*p*-OCH_3. C_6H_4	*p*-Cl. C_6H_4	95	$C_{37}H_{28}\ O_6N_2Cl_2$	58	66.57 (66.48)	4.20 (4.12)	4.20 (4.09)
4h	*p*-OCH_3. C_6H_4	*p*-NO_2. C_6H_4	265	$C_{37}H_{28}\ O_{10}N_4$	67	64.53 (64.39)	4.07 (4.13)	8.14 (8.03)
4i	*p*-Cl. C_6H_4	C_6H_5	135	$C_{35}H_{24}O_4N_2Cl_2$	69	69.19 (69.03)	3.95 (4.05)	4.61 (4.49)
4j	*p*-Cl. C_6H_4	*p*-OCH_3. C_6H_4	110	$C_{37}H_{28}\ O_6N_2Cl_2$	78	66.57 (66.38)	4.20 (4.37)	4.20 (4.11)
4k	p-Cl. C_6H_4	*p*-Cl. C_6H_4	121	$C_{35}H_{22}O_4N_2Cl_4$	77	62.13 (62.08)	3.25 (3.38)	4.14 (4.06)
4l	*p*-Cl. C_6H_4	*p*-NO_2. C_6H_4	257	$C_{35}H_{22}\ O_8N_4Cl_2$	65	60.26 (60.13)	3.16 (3.42)	8.03 (7.95)
5b	C_6H_5	*p*-$OCH_3C_6H_4$	108	$C_{37}H_{30}O_5N_4$	54	72.79 (72.68)	4.92 (5.03)	9.18 (9.03)
5c	C_6H_5	*p*-ClC_6H_4	145	$C_{35}H_{24}O_3N_4Cl_2$	67	67.85 (67.73)	3.88 (3.74)	9.05 (8.91)
5d	C_6H_5	*p*-$NO_2C_6H_4$	162	$C_{35}H_{24}O_7N_6$	69	65.63 (65.72)	3.75 (3.82)	13.13 (13.01)
5e	*p*-$OCH_3C_6H_4$	C_6H_5	134	$C_{37}H_{30}O_5N_4$	73	72.79 (72.67)	4.92 (5.09)	9.18 (9.06)
5f	*p*-$OCH_3C_6H_4$	*p*-$OCH_3C_6H_4$	90	$C_{39}H_{34}O_7N_4$	71	69.85 (69.73)	5.07 (5.11)	8.36 (8.22)
5g	*p*-$OCH_3C_6H_4$	*p*-ClC_6H_4	102	$C_{37}H_{28}O_5N_4Cl_2$	56	65.39 (65.21)	4.12 (4.32)	8.25 (8.11)
5h	*p*-$OCH_3C_6H_4$	*p*-$NO_2C_6H_4$	165	$C_{37}H_{28}O_9N_6$	76	63.43 (63.21)	4.00 (4.15)	12.00 (11.89)
5i	*p*-ClC_6H_4	C_6H_5	151	$C_{35}H_{24}O_2N_4Cl_2$	68	67.85 (67.69)	3.88 (4.02)	9.05 (8.94)
5j	*p*-ClC_6H_4	*p*-$OCH_3C_6H_4$	148	$C_{37}H_{28}O_5N_4Cl_2$	48	65.39 (65.27)	4.12 (4.01)	8.25 (8.19)
5k	*p*-ClC_6H_4	*p*-ClC_6H_4	132	$C_{35}H_{22}O_3N_4Cl_4$	50	61.22 (61.13)	3.21 (3.15)	8.16 (8.01)
5l	*p*-Cl. C_6H_4	*p*-$NO_2C_6H_4$	250	$C_{35}H_{22}O_7N_6Cl_2$	57	59.24 (59.14)	3.10 (3.17)	11.85 (11.69)
6b	C_6H_5	*p*-$OCH_3C_6H_4$	102	$C_{43}H_{34}O_5N_4$	53	75.22 (75.13)	4.96 (5.07)	8.16 (8.03)
6c	C_6H_5	*p*-ClC_6H_4	91	$C_{41}H_{28}O_3N_4Cl_2$	62	70.79 (70.64)	4.03 (4.19)	8.06 (7.96)

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6d	C_6H_5	p-$NO_2C_6H_4$	131	$C_{41}H_{28}O_7N_6$	61	68.72 (68.63)	3.91 (4.06)	11.73 (11.61)
6e	p-OCH_3 C_6H_4	C_6H_5	95	$C_{43}H_{34}O_5N_4$	57	75.22 (75.13)	4.96 (4.67)	8.16 (8.01)
6f	p-$OCH_3C_6H_4$	p-$OCH_3C_6H_4$	94	$C_{45}H_{38}O_7$ N_4	76	72.39 (72.17)	5.09 (5.17)	7.51 (7.47)
6g	p-$OCH_3C_6H_4$	p-ClC_6H_4	93	$C_{43}H_{32}O_5N_4Cl_2$	58	68.34 (68.27)	4.24 (4.11)	7.42 (7.31)
6h	p-$OCH_3C_6H_4$	p-NO_2. C_6H_4	168	$C_{43}H_{32}O_9N_6$	72	66.49 (66.33)	4.12 (4.04)	10.82 (10.68)
6i	p-ClC_6H_4	C_6H_5	154	$C_{41}H_{28}O_3N_4Cl_2$	53	70.79 (70.69)	4.03 (4.17)	8.06 (7.91)
6j	p-ClC_6H_4	p-$OCH_3C_6H_4$	117	$C_{43}H_{32}O_5N_4Cl_2$	74	68.34 (68.23)	4.24 (4.39)	7.42 (7.19)
6k	p-ClC_6H_4	p-ClC_6H_4	135	$C_{41}H_{26}O_3N_4Cl_4$	63	64.40 (64.27)	3.40 (3.51)	7.33 (7.27)
6l	p-ClC_6H_4	p-NO_2. C_6H_4	253	$C_{41}H_{26}O_7N_6Cl_2$	58	62.68 (62.53)	3.31 (3.16)	10.70 (10.57)
7b	C_6H_5	p-$OCH_3C_6H_4$	118	$C_{37}H_{29}O_6N_3$	58	72.67 (72.53)	4.75 (4.81)	6.87 (6.71)
7c	C_6H_5	p-ClC_6H_4	136	$C_{35}H_{23}O_4N_3Cl_2$	65	67.74 (67.63)	3.71 (3.95)	6.77 (6.52)
7d	C_6H_5	p-NO_2. C_6H_4	269	$C_{35}H_{23}O_8N_5$	76	65.52 (65.49)	3.59 (3.47)	10.92 (10.83)
7e	p-OCH_3. C_6H_4	C_6H_5	120	$C_{37}H_{29}O_6N_3S$	59	72.67 (72.51)	4.75 (4.93)	6.87 (6.69)
7f	p-OCH_3. C_6H_4	p-$OCH_3C_6H_4$	108	$C_{39}H_{33}O_8N_3$	67	69.75 (69.58)	4.92(5.11)	6.26 (6.18)
7g	p-OCH_3. C_6H_4	p-ClC_6H_4	109	$C_{37}H_{27}O_6N_3Cl_2$	68	65.29 (65.17)	3.97 (4.08)	6.18 (6.04)
7h	p-OCH_3. C_6H_4	p-NO_2. C_6H_4	78	$C_{37}H_{27}O_{10}N_5$	73	63.34 (63.21)	3.85 (3.91)	9.99 (9.76)
7i	p-Cl. C_6H_4	C_6H_5	111	$C_{35}H_{23}O_4N_3Cl_2$	55	67.74 (67.62)	3.71 (3.78)	6.77 (6.52)
7j	p-Cl. C_6H_4	p-$OCH_3C_6H_4$	118	$C_{37}H_{27}O_6N_3Cl_2$	72	65.29 (65.13)	3.97 (4.07)	6.18 (6.05)
7k	p-Cl. C_6H_4	p-ClC_6H_4	137	$C_{35}H_{21}O_4N_3Cl_4$	66	60.96 (60.78)	3.05 (3.17)	6.10 (6.23)
7l	p-Cl. C_6H_4	p-NO_2. C_6H_4	267	$C_{35}H_{21}O_8N_5Cl_2$	49	59.15 (59.07)	2.96 (2.78)	9.86 (9.91)
8b	C_6H_5	p-$OCH_3C_6H_4$	92	$C_{38}H_{30}O_6N_4$	82	71.47 (71.32)	4.70 (4.81)	8.78 (8.69)
8c	C_6H_5	p-ClC_6H_4	125	$C_{36}H_{24}O_4N_4Cl_2$	71	66.77 (66.68)	3.71 (3.65)	8.66 (8.53)
8d	C_6H_5	p-NO_2. C_6H_4	206	$C_{36}H_{24}O_8N_6$	68	64.67 (64.38)	3.59 (3.62)	12.57 (12.61)
8e	p-OCH_3. C_6H_4	C_6H_5	98	$C_{38}H_{30}O_6N_4$	59	71.47 (71.31)	4.70 (4.62)	8.78 (8.59)
8f	p-OCH_3. C_6H_4	p-$OCH_3C_6H_4$	78	$C_{40}H_{34}O_8N_4$	73	68.77 (68.63)	4.87 (4.82)	8.02 (7.92)
8g	p-OCH_3. C_6H_4	p-ClC_6H_4	82	$C_{38}H_{28}O_6N_4Cl_2$	53	64.50 (64.37)	3.96 (3.73)	7.92 (7.87)

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TABLE II Physical and Analytical Data *(Continued)*

Comp. No.	21Ar	Ar′	Mp (°C)	Mol. Formula	Yield in %	C % Cal. (Found)	H %Cal. (Found)	N % Cal. (Found)
8h	*p*-OCH_3. C_6H_4	*p*-NO_2. C_6H_4	143	$C_{38}H_{28}O_{10}N_6$	77	62.64 (62.58)	3.85 (3.73)	11.54 (11.47)
8i	*p*-Cl. C_6H_4	C_6H_5	85	$C_{36}H_{24}O_4N_4Cl_2$	59	66.77 (66.59)	3.71 (3.58)	8.66 (8.49)
8j	*p*-Cl. C_6H_4	*p*-$OCH_3C_6H_4$	101	$C_{38}H_{28}O_6N_4Cl_2$	67	64.50 (64.39)	3.96 (4.08)	7.92 (8.02)
8k	*p*-Cl. C_6H_4	*p*-ClC_6H_4	128	$C_{36}H_{22}O_4N_4Cl_4$	63	60.34 (60.21)	3.07 (3.19)	7.82 (7.67)
8l	*p*-Cl. C_6H_4	*p*-NO_2. C_6H_4	256	$C_{36}H_{22}ON_6Cl_2$	59	58.62 (58.57)	2.99 (2.81)	11.40 (11.49)
9b	C_6H_5	*p*-$OCH_3C_6H_4$	147	$C_{38}H_{31}O_5N_5$	59	71.59 (71.43)	4.87 (5.03)	10.99 (10.83)
9c	C_6H_5	*p*-ClC_6H_4	155	$C_{36}H_{25}O_3N_5Cl_2$	68	66.87 (66.73)	3.87 (3.76)	10.84 (10.69)
9d	C_6H_5	*p*-NO_2. C_6H_4	232	$C_{36}H_{25}O_7N_7$	67	64.77 (64.68)	3.75 (3.89)	14.69 (14.56)
9e	*p*-OCH_3. C_6H_4	C_6H_5	147	$C_{38}H_{31}O_5N_5$	63	71.59 (71.65)	4.87 (4.67)	10.99 (10.85)
9f	*p*-OCH_3. C_6H_4	*p*-$OCH_3C_6H_4$	86	$C_{40}H_{35}O_7N_5$	71	68.87 (68.76)	5.02 (5.12)	10.04 (9.89)
9g	*p*-OCH_3. C_6H_4	*p*-ClC_6H_4	170	$C_{38}H_{29}O_5N_5Cl_2$	65	64.59 (64.48)	4.11 (4.03)	9.92 (9.79)
9h	*p*-OCH_3. C_6H_4	*p*-NO_2. C_6H_4	273	$C_{38}H_{29}O_9N_7$	59	62.72 (62.59)	3.99 (3.81)	13.48 (13.37)
9i	*p*-Cl. C_6H_4	C_6H_5	188	$C_{36}H_{25}O_3N_5Cl_2$	51	66.87 (66.79)	3.87 (3.69)	10.84 (10.79)
9j	*p*-Cl. C_6H_4	*p*-$OCH_3C_6H_4$	182	$C_{38}H_{29}O_5N_5Cl_2$	63	64.59 (64.71)	4.11 (4.19)	9.92 (9.87)
9k	*p*-Cl. C_6H_4	*p*-ClC_6H_4	162	$C_{36}H_{23}O_3N_5Cl_4$	68	60.42 (60.29)	3.22 (3.17)	9.79 (9.65)
9l	*p*-Cl. C_6H_4	*p*-NO_2. C_6H_4	271	$C_{36}H_{23}O_7N_7Cl_2$	56	58.70 (58.59)	3.13 (3.01)	13.32 (13.11)
10b	C_6H_5	*p*-$OCH_3C_6H_4$	135	$C_{39}H_{32}O_5N_4S$	50	71.78 (71.67)	4.91 (4.83)	8.59 (8.43)
10c	C_6H_5	*p*-ClC_6H_4	156	$C_{37}H_{26}O_3N_4SCl_2$	65	67.17 (67.03)	3.93 (3.83)	8.47 (8.35)
10d	C_6H_5	*p*-NO_2. C_6H_4	183	$C_{37}H_{26}O_7N_6S$	68	65.10 (65.02)	3.81 (3.77)	12.32 (12.24)
10e	*p*-OCH_3. C_6H_4	C_6H_5	144	$C_{39}H_{32}O_5N_4S$	58	71.78 (71.68)	4.91 (4.81)	8.59 (8.45)
10f	*p*-OCH_3. C_6H_4	*p*-$OCH_3C_6H_4$	112	$C_{41}H_{36}O_7N_4S$	59	69.10 (68.93)	5.06 (4.85)	7.87 (7.67)
10g	*p*-OCH_3. C_6H_4	*p*-ClC_6H_4	97	$C_{39}H_{30}O_5N_4SCl_2$	67	64.91 (64.82)	4.16 (4.03)	7.77 (7.63)
10h	*p*-OCH_3. C_6H_4	*p*-NO_2. C_6H_4	152	$C_{39}H_{30}O_9N_6S$	72	63.07 (62.83)	4.04 (3.87)	11.32 (11.13)
10i	*p*-Cl. C_6H_4	C_6H_5	143	$C_{37}H_{26}O_3N_4SCl_2$	67	67.17 (67.01)	3.93 (3.81)	8.47 (8.29)
10j	*p*-Cl. C_6H_4	*p*-$OCH_3C_6H_4$	126	$C_{39}H_{30}O_5N_4SCl_2$	59	64.91 (64.78)	4.16 (4.32)	7.77 (7.56)
10k	*p*-Cl. C_6H_4	*p*-ClC_6H_4	140	$C_{37}H_{24}O_3N_4SCl_4$	49	60.82 (60.69)	3.29 (3.31)	7.67 (7.51)
10l	*p*-Cl. C_6H_4	*p*-NO_2. C_6H_4	255	$C_{37}H_{24}O_7N_6SCl_2$	63	59.12 (59.03)	3.20 (3.03)	11.19 (11.03)

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