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MEDICINAL CHEMISTRY RESEARCH

ORIGINAL RESEARCH

Synthesis and antibacterial, antifungal activities of some 2*r*,4*c*-diaryl-3-azabicyclo[3.3.1]nonan-9-one-4-aminobenzoyl hydrazones

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Abstract A series of biologically active seven 2*r*, 4*c*-diaryl-3-azabicyclo[3.3.1]nonan-9-one-4-aminobenzoyl hydrazone derivatives have been synthesized in good yield. The structures of compounds have been established on the basis of IR, ^{1}H, ^{13}C NMR, and elemental analysis. The structure–activity relationships (SAR) have been studied by screening of antimicrobial activity over a representative panel of bacterial and fungal strains using two-fold serial dilution method. All these synthesized compounds exhibited significant activities against all bacterial and fungal strains.

Keywords 2*r*,4*c*-Diaryl-3-azabicyclo[3.3.1]nonan-9-one · 4-Aminobenzoic acid hydrazide · Antibacterial activity · Antifungal activity

Introduction

In the broad spectrum of biological activity, in recent years, there has been a growing interest in the synthesis of bioactive compounds in the field of heterocyclic chemistry. Among the family of heterocyclic compounds, the nitrogen-containing heterocycles especially 3-azabicyclononones have gained considerable importance presumably because of their varied biological properties, such as antiviral, antitumor (El-Subbagh *et al.*, 2000), analgesic (Jerom and Spencer, 1988), local anesthetic (Perumal *et al.*, 2001; Hagenbach and Gysin, 1952) antibactericidal, antifungicidal (Parthiban *et al.*, 2010), herbicidal, insecticidal, antihistaminic, anti-inflammatory, anticancer, and central nervous system (CNS) stimulant and depressant activities (Mobio *et al.*, 1989; Katritzky and Fan, 1968 and references cited therein; Ganellin and Spickett, 1965). Lijinsky and Taylor (1975) found that the blocking of α-positions to that of nitrogen in 3-azabicyclanone using alkyl groups provided advantages over unblocked ones in terms of biological activity. The 3-azabicyclonone pharmacopore is present in numerous naturally abundant diterpenoid/norditerpinoid alkaloids and is responsible for a wide variety of pharmacological actions.

Meanwhile, hydrazide-hydrazones have been claimed to exhibit appreciable antimicrobial (Eisa *et al.*, 1991; Gursoy *et al.*, 1997; Rollas *et al.*, 2002; Vicini *et al.*, 2002), antitubercular (Sankar and Pandiarajan, 2010), anticonvulsant (Sinha *et al.*, 2010), antiviral (El-Sabbagh and Rady, 2009), and anti-inflammatory (Kalsi *et al.*, 1990) activities. On the basis of these observations, the authors had the impetus to synthesize a number of hydrazones of the synthetically accessible 3-azabicyclo[3.3.1]nonanes and subsequently evaluate their in vitro antimicrobial activity.

Materials and methods

Measurements and instruments

Ethyl-4-amino benzoate was purchased from Sigma-Aldrich. All the other chemicals were used as analytic grade. Reactions were monitored by TLC. All the reported melting points were measured in open capillaries and are uncorrected. FT-IR spectra were recorded as potassium bromide pellets on AVATAR 330 FT-IR Thermo Nicolet Spectrometer. ^{1}H and ^{13}C NMR spectra were recorded at ambient temperature on a Bruker AMX 500 NMR

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spectrometer operating at 400.13 MHz for ^{1}H and 100.62 MHz for ^{13}C NMR spectra. Solutions for the measurement of spectra were prepared by dissolving 10 mg of the sample in 0.5 ml DMSO-d_6 and chemical shifts (δ) are expressed in parts per million (ppm). Elemental analyses were carried out in Heraeus Carlo Erba 1108 CHN analyzer. Splitting patterns are designated as follows: s—singlet; d—doublet; t—triplet; q—quartet; and m—multiplet.

Microbiology

All the bacterial strains, namely, *Salmonella typhimurium* (MTCC 98), *Escherichia coli* (MTCC 443), *Vibrio cholerae* (recultured), *Salmonella typhi* (MTCC 531), *Pseudomonas aeruginosa* (MTCC 741), *Klebsiella pneumoniae* (MTCC 2272), *Bacillus subtilis* (MTCC 121), and *Staphylococcus aureus* (MTCC 96), and the fungal strains, namely, *Candida albicans*, *Fusarium oxysporum*, *Aspergillus flavus*, *Aspergillus niger*, and *Cryptococcus neoformans* were obtained from the Faculty of Medicine, Annamalai University, Annamalainagar, Tamilnadu, India.

In vitro antibacterial and antifungal activity

In vitro antimicrobial activities of the compounds were tested in Sabouraud's dextrose broth (SDB, Hi-media, Mumbai) for fungi and in nutrient broth (NB, Hi-media, Mumbai) for bacteria by the two-fold serial dilution method (Dhar *et al.*, 1968). The test compounds were dissolved in dimethylsulfoxide (DMSO) to obtain 1 mg/ml stock solutions. Seeded broth (broth containing microbial spores) was prepared in nutrient broth from 24-h-old bacterial cultures on nutrient agar (Hi-media, Mumbai) at 37 ± 1°C, while fungal spores from 24 h to 7 days old Sabouraud's agar slant cultures were suspended in SDB. The colony-forming units (cfu) of the seeded broth were determined by plate count technique and adjusted with the help of McFarland standards in the range of 10^4–10^5 cfu/ml. The final inoculums size was 10^5 cfu/ml for antibacterial assay, and 1.1–1.5 × 10^2 cfu/ml for antifungal assay. Testing was performed at pH 6.5 ± 0.2 for bacteria, and pH 5.6 ± 0.2 for fungal studies. Exactly 0.2 ml of the solution of the test compound was added to 1.8 ml of the seeded broth to form the first dilution. One milliliter of this was diluted with a further 1 ml of the seeded broth to give the second dilution and so on, till six such dilutions were obtained. A set of assay tubes containing only the seeded broth was kept as control and, likewise, the solvent controls were also run simultaneously. The tubes were incubated in Biochemical Oxygen demand (BOD) incubators at 37 ± 1°C for bacteria, and 28 ± 1°C for fungal studies. The minimum inhibitory concentrations (MICs) were recorded by visual observations after 24 h (for bacteria) and 72–96 h (for fungi except *C. albicans*) of incubation. Streptomycin and Amphotericin B were used as standards for bacterial and fungal studies, respectively.

Results and discussion

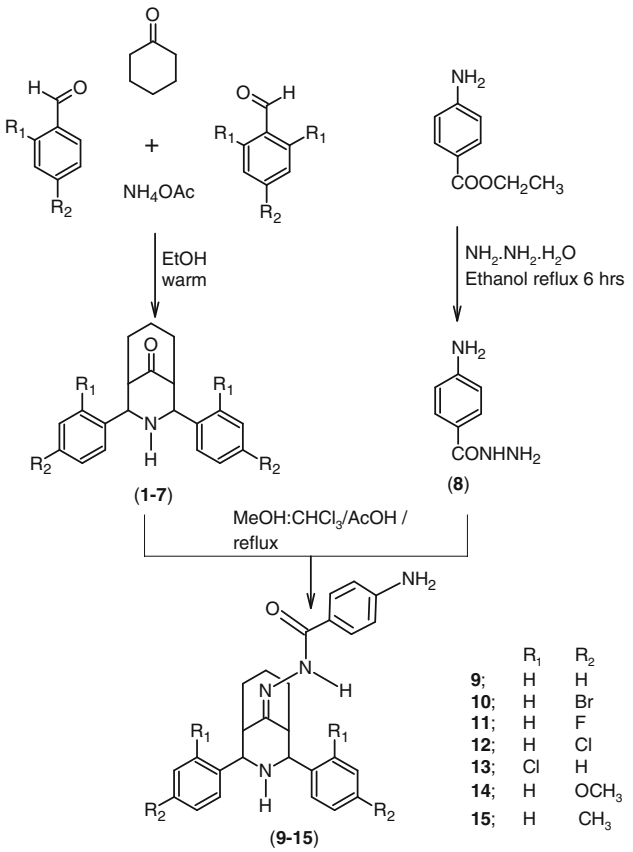
Chemistry

The authors have synthesized of seven 2*r*,4*c*-diaryl-3-azabicyclo[3.3.1]nonan-9-one-4-aminobenzoyl hydrazone derivatives as illustrated in Scheme 1. A three-step synthetic strategy yielded the compounds (**9**–**15**). According to the literature precedent (Baliah and Jeyaraman, 1971), 2,4-diaryl-3-azabicyclo[3.3.1]nonan-9-ones **1**–**7** were prepared by the condensation of cyclohexanone, substituted benzaldehyde, and ammonium acetate in 1:2:1.5 ratio in ethanol. These reaction mixtures were very gently warmed and stirred until the completion of the reaction. The crude products formed were filtered and washed with an ethanol–ether (1:5) mixture to yield the compounds **1**–**7** and recrystallized from ethanol–chloroform–acetone to obtain the pure compounds **1**–**7**. 4-Aminobenzoic acid hydrazide (**8**) was prepared from ethyl-4-aminobenzoate and hydrazine hydrate in ethanol medium. 2*r*,4*c*-Diaryl-3-azabicyclo[3.3.1]nonan-9-one-4-aminobenzoyl hydrazones (**9**–**14**) were synthesized from condensation reaction of 3-azabicyclo[3.3.1]nonan-9-ones and 4-aminobenzoic acid hydrazide.

Structures of all the synthesized compounds were established on the basis of IR, ^{1}H NMR and ^{13}C NMR spectral data. The purities of the compounds were checked by elemental analysis. The analytic data agreed well with their proposed molecular formulas.

The atoms of the bicyclo[3.3.1]nonane part are numbered as shown in Fig. 1. The *ipso* carbons of the aryl groups at C-2 and C-4 are designated as C-2′ and C-4′, respectively. The other carbons of the aryl group at C-2 are denoted as *o*, *m*, and *p*-carbons, and those of the aryl group at C-4 are denoted as *o*′, *m*′, and *p*′-carbons. The carbons of the 4-aminobenzoyl ring are designated using C-1″, C-2″, and C-3″. The protons are numbered accordingly. For example, the benzylic proton at C-2 is denoted as H-2, that at C-2″ is denoted as H-2″, and so on. The methylene protons in the cyclohexane ring are denoted as axial and equatorial protons assuming chair conformation for the cyclohexane ring. Thus, the methylene protons at C-7 are denoted as H-7a and H-7e.

In IR spectra, the presence of C=N stretching frequency around 1640 and 1648 cm^{-1} confirms the hydrazone formation. The piperidine NH stretching frequency was in the range 3330–3370 cm^{-1}, while the absorption bands in the



Scheme 1 Synthetic routes of compounds **9–15**

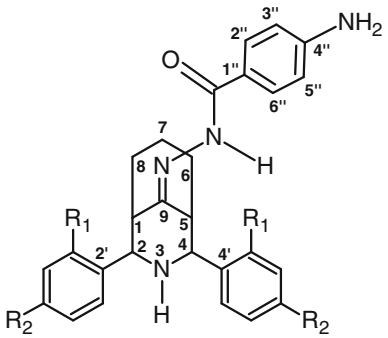


Fig. 1 Numbering the bicyclo[3.3.1]nonane

region of 3070–2800 cm^{-1} are ascribed to aromatic and aliphatic C–H stretching frequencies.

In the ^{1}H NMR spectra of the target hydrazones, a broad and more downfield D_2O exchangeable singlet at 10.50 ppm was characteristic of the NH amide group. The broad singlet signal appeared at 4.31 ppm, corresponding to two protons integrals. These two signals are attributed to benzylic protons H-2 and H-4, respectively. However, signals that appeared at 3.25 and 3.57 ppm should be due to the bridgehead protons H-1 and H-5, respectively. The bridgehead protons H-1 merged with the solvent signal. Two protons signals that were observed at 1.64 and 1.45 ppm should, respectively, be due to methylene protons C-6 and C-8.

In ^{13}C NMR spectra in compound **9**, two signals were observed around 163 and 161 ppm because of fluorine-attached *ipso* carbons. The observed two signals were due to C–F coupling between carbon and the attached fluorine atom. Similarly, another pair of signals observed for all the hydrazones in the region 135–145 ppm is assigned to C-2′ and C-4′ *ipso* carbons. C=O and C=N carbon signals appeared at 165 and 167 ppm. However, there are two signals around 65 and 62 ppm, which are conveniently assigned to C-2 and C-4 carbons, respectively, whereas, the bridgehead carbons C-1 and C-5 appeared at 46 and 40 ppm, respectively. In the ^{1}H–^{1}H-COSY spectrum of the benzylic protons showed correlation with that of N(3)–H. Also H-2 showed correlation with H-1, and H-4 showed correlation with H-5. However, in all these cases H-1, H-2, N(3)–H, H-4, and H-5 gave unresolved signals. The unresolved nature of the signals for H-1, H-2, H-4, and H-5 suggests that the *vicinal* couplings for these protons are very small. However, H-7a showed three large couplings (one *geminal* coupling with H-7e and two diaxial *vicinal* coupling with H-6a and H-8a) and two small couplings (one with H-6e and another with H-8e). All these observations are consistent with twin-chair (CC) (Fig. 2) conformation for these compounds (Table 1).

Antibacterial activity

The newly synthesized compounds were screened for their in vitro antibacterial activity by disc diffusion method. MIC values were determined by twofold serial dilution method (Dhar *et al.*, 1968). Streptomycin was used as a

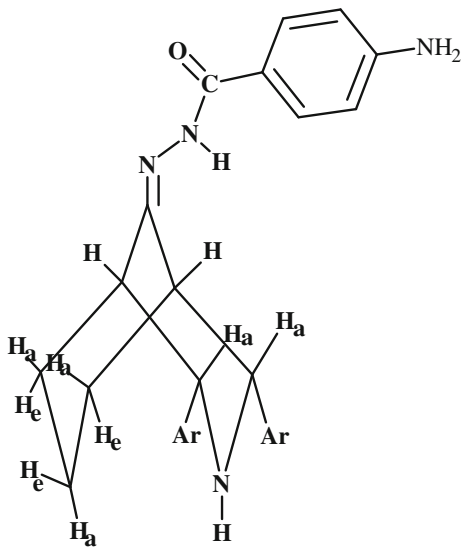


Fig. 2 Conformation of the molecule

Table 1 Physical constant of the synthesized compounds **9–15**

Compound	R_1	R_2	Yield (%)	m.p. (°C)	M.F	M.W
9	H	H	62	210	$C_{27}H_{28}N_4O$	424.30
10	H	Br	61	208	$C_{27}H_{26}N_4OBr$	502.20
11	H	F	64	200	$C_{27}H_{26}N_4OF$	441.30
12	H	Cl	64	190	$C_{27}H_{26}N_4OCl$	457.75
13	Cl	H	58	202	$C_{27}H_{26}N_4OCl$	457.75
14	H	OCH_3	62	212	$C_{30}H_{33}N_3O_3$	483.60
15	H	CH_3	60	195	$C_{30}H_{33}N_3O$	451.60

standard for the comparison of antibacterial activity, and the MIC results are summarized in Table 2. Streptomycin was used as an antibiotic against mycobacterium tuberculosis and dermatological diseases (Ruiz *et al.*, 2002 and references cited therein).

Ortho choloro-substituted compound **13** demonstrated good activities against *S. typhimurium*, *V. cholerae*, and *K. pneumoniae*, whereas *para* chloro-substituted compound **12** demonstrated strong activity against *E. coli*, *B. subtilis*, and *S. aureus*. Bromo- and fluoro-substituted compounds **10** and **11** demonstrated good activity against *S. aureus*. Compound **11** demonstrated strong activity against *B. subtilis* at 25 μg/ml. However, unsubstituted compound **9** showed a noticeable activity against *K. pneumoniae*.

The results obtained revealed that the nature of substituents and substitution pattern on the aryl ring may have a considerable impact on the antibacterial activities of the target hydrazone. In this context, *para*-substituted compounds appear to be more beneficial for antibacterial activity than the *ortho*-substituted pattern.

Antifungal activity

All the synthesized compounds were screened for in vitro antifungal activity. The antifungal activities were evaluated against different fungal strains, such as *Candida albicans*, *Fusarium oxysporum*, *Aspergillus flavus*, *Aspergillus niger*, and *Cryptococcus neoformans*. MIC values were determined by twofold serial dilution method (Dhar *et al.*, 1968). Amphotericin B was used as a standard for the comparison of antifungal activity. DMSO was used as solvent control. MIC values of the tested compounds are presented in Table 3. From the antifungal activity data

Table 2 In vitro antibacterial activities of compounds **9–15**

Compd.	Entry		*S. typhimurium*	*E. coli*	*V. cholerae*	*S. typhi*	*P. aeruginosa*	*K. pneumoniae*	*B. subtilis*	*S. aureus*
	R_1	R_2								
9	H	H	200	200	100	200	200	50	100	200
10	H	*p*-Br	200	100	200	50	50	200	200	50
11	H	*p*-F	100	100	50	100	200	50	25	50
12	H	*p*-Cl	200	50	100	200	100	200	50	50
13	*o*-Cl	H	50	100	50	100	100	50	200	200
14	*H*	*p*-OCH_3	200	100	50	100	200	200	100	100
15	*H*	*p*-CH_3	200	100	200	100	200	200	100	200
Strept.			25	50	50	25	50	20	12.5	25

Strept. Streptomycin

Table 3 In vitro antifungal activities of compounds **9–15**

Compd.	Entry		*C. albicans*	*F. oxysporum*	*A. flavus*	*A. niger*	*C. neoformans*
	R_1	R_2					
9	H	H		200	200		
10	H	*p*-Br	200	100	100	50	100
11	H	*p*-F	100	50	200	100	200
12	H	*p*-Cl	100	200	100	50	200
13	*o*-Cl	H	200	100	200	100	100
14	*H*	*p*-OCH_3	200	100	50	100	200
15	*H*	*p*-CH_3	200	100	200	100	100
Amp. B			25	25	50	50	25

Amp. B Amphotericin B

(Table 3), it can be observed that the compounds **10** and **11** are the most active among all the synthesized compounds compared with all the tested organisms except *Cryptococcus neoformans*. It is seen that **9** shows no activity compared with *A. niger* and *C. neoformans* even at a concentration of 200 μg/ml. However, it shows antifungal activity compared to all the other tested fungi in the range 50–200 μg/ml. Compounds **9–15** which have substituents in the C-2 and C-4 aryl groups are more active than the unsubstituent compound **9** compared with all the tested fungi. The *o*-chloro compound **13** is less active than the *p*-chloro compound **12** compared with *C. albicans*, *A. flavus*, and *A. niger*. The results suggest that the antibacterial and antifungal activities are markedly influenced by the aromatic substituents. Thus, **9–15** with electron-withdrawing substituents in the aromatic ring show greater antibacterial activity.

Experimental section

General procedure for synthesis of 2*r*,4*c*-diaryl-3-azabicyclo[3.3.1]nonan-9-one-4-aminobenzoyl hydrazones (**9–15**)

A mixture of 2,4-diaryl-3-azabicyclo[3.3.1]nonan-9-one (**1–7**) (1 mmol), 4-aminobenzoic acid hydrazide (1.5 mmol) in methanol and chloroform (1:1 v/v), and a few drops of acetic acid was added and refluxed for 2–4 h. On completion of the reaction time, a solid mass was formed, which was then cooled to room temperature. The precipitate was filtered off and washed with ice-cooled water–ethanol mixture. The crude product was recrystallized from ethanol.

2*r*,4*c*-Diphenyl-3-azabicyclo[3.3.1]nonane-9-one-4-aminobenzoyl hydrazone (**9**)

White solid: m.p. 210°C, and yield 62%. IR (KBr) (cm^{-1}): 3032, 2922, and 2859 (C–H stretching); 1636 (C=N stretching); 1603 (C=C ring stretching); and 3335 (N–H stretching). ^{1}H NMR (400 MHz—DMSO-d_6 ppm). δ: 10.50 (s, 1H, amide NH); 7.60 (d, 2H, Ph-α); 6.62 (d, 2H, Ph-β); 7.66 (q, 4H, *ortho*); 7.41 (q, 4H, *meta*); 7.29 (q, 2H, *para*); 4.31 (d, 2H, H-2a, H-4a); 3.25 (s, 1H, H-5e); 2.76 (m, 1H, H-7a); 1.64 (m, H, H-8e); 1.45 (m, 3H, H-6a, H-6e); 1.51 (m, 3H, H-8a); 1.26 (m, 1H, H-7e); 2.84 (s, 1H, ring NH); and 5.69 (s, 2H, *p*-NH_2). ^{13}C NMR (400 MHz): 65.0 (C-2); 62.7 (C-4); 46.4 (C-1); 28.6 (C-8); 27.3 (C-6); 21.4 (C-7); 167.7 (C-9); 152.4(C-4″); 130.1 (C-3″); 113.0 (C-2″); 121.4 (C-1″); 143.5 (C-2′, C-4′); and 165.6 (NH–*C*O). Anal found (cal.) for $C_{27}H_{28}N_4O$ (%): C, 76.33 (76.36); H, 5.56 (6.59); and N, 13.17 (13.20).

2*r*,4*c*-Bis(*p*-bromophenyl)-3-azabicyclo[3.3.1]nonan-9-one-4-aminobenzoyl hydrazone (**10**)

White solid: m.p. 208°C, and yield 61%. IR (KBr) (cm^{-1}): 3060, 2924, and 2854 (C–H stretching); 1632, 1605 (C=C ring stretching); and 3334 (N–H stretching). ^{1}H NMR (400 MHz—DMSO-d_6 ppm). δ: 10.40 (s, 1H, amide NH); 8.81 (d, 2H, H-3″); 6.60 (d, 2H, H-2″); 7.71 (q, 4H, *ortho*); 7.42 (q, 4H, *meta*); 4.62 (d, 2H, H-2a); 4.48 (d, 2H, H-4a); 2.99 (s, 1H, H-5e); 2.78 (m, 1H, H-7a); 1.68 (m, H, H-8e); 1.53 (m, 1H, H-6a); 1.44 (m, 2H, H-6e, H-8a); 1.25 (m, 1H, H-7e); 2.77 (s, 1H, ring NH); and 5.81 (s, 2H, *p*-NH_2). ^{13}C NMR (400 MHz): 62.3 (C-2); 60.6 (C-4); 42.3 (C-1); 28.1 (C-6); 21.0 (C-7); 165.7 (C-9); 164.0 (NH*C*O); 152.9 (C-4″); 113.1 (C-2″); 119.7 (C-1″); and 139.9, and 139.8 (C-2′, and C-4′). Anal found (Cal.) for $C_{27}H_{26}N_4Obr$ (%): C, 64.50 (64.51); H, 5.16 (5.18); and N, 11.14 (11.15).

2*r*,4*c*-Bis(*p*-fluorophenyl)-3-azabicyclo[3.3.1]nonan-9-one-4-aminobenzoyl hydrazone (**11**)

White solid: m.p. 200°C, and yield 64%. IR (KBr) (cm^{-1}): 3335 (N–H stretching); 3061, 2925, and 2855 (C–H stretching); 1627 (C=N stretching); and 1605 (C=O stretching). ^{1}H NMR (400 MHz—DMSO-d_6 ppm). δ: 10.47 (s, 1H, amide NH); 7.7 (d, 2H, H-3″); 6.6 (d, 2H, H-2″); 7.63 (q, 4H, *ortho*); 7.23 (q, 4H, *meta*); 4.29 (d, 2H, H-2a, H-4a); 3.2 (s, 1H, H-5e); 2.7 (m, 1H, H-7a); 1.60 (m, 1H, H-8e); 1.45 (m, 3H, H-6a, H-6e, H-8a); 1.26 (m, 1H, H-7e); and 2.94 (m, 1H, ring NH); 5.67 (s, 2H, *p*-NH_2). ^{13}C NMR (400 MHz): 64.2 (C-2); 61.9 (C-4); 46.2 (C-1); 28.5 (C-8); 27.2 (C-6); 21.3 (C-7); 170.0 (C-9); 162.0 (NH*C*O); 152.4 (C-4″); 130.1 (C-3″); 112.9 (C-2″); 121.0 (C-1″); 139.5, and 139.4 (C-2′, and C-4′). Anal found (Cal.) for $C_{27}H_{26}N_4OF$ (%): C, 73.39 (73.42); H, 5.87 (5.89); and N, 12.65 (12.69).

2*r*,4*c*-Bis(*p*-chlorophenyl)-3-azabicyclo[3.3.1]nonan-9-one-4-aminobenzoyl hydrazone (**12**)

White solid: m.p. 190°C, and yield 65%. IR (KBr) (cm^{-1}): 3332 (N–H stretching); 3034, 2923, and 2855 (C–H stretching); 1634 (C=N stretching); and 1598 (C=O stretching). ^{1}H NMR (400 MHz—DMSO-d_6 ppm), δ: 10.44 (s, 1H, amide NH); 7.67 (d, 2H, H-3″); 6.6 (d, 2H, H-2″); 7.60 (q, 4H, *ortho*); 7.45 (q, 4H, *meta*); 4.28 (d, 2H, H-2a, H-4a); 3.2 (s, 1H, H-5e); 2.6 (m, 1H, H-7a); 1.60 (m, 1H, H-8e); 1.44 (m, 3H, H-6a, H-6e, H-8a); 1.25 (m, 1H, H-7e); 3.01 (m, 1H, ring NH); and 5.66 (s, 2H, *p*-NH_2). ^{13}C NMR (400 MHz): 63.6 (C-2); 61.4 (C-4); 45.6 (C-1); 28.5 (C-8); 26.7 (C-6); 20.8 (C-7); 170.2 (C-9); 162.1 (NH*C*O);151.9 (C-4″); 129.6 (C-3″); 112.5 (C-2″); 120.5 (C-1″); and 141.8 (C-2′, C-4′). Anal found (Cal.) for

$C_{27}H_{26}N_4Ocl$ (%): C, 70.76 (70.78); H, 5.65 (5.68); and N, 12.21 (12.23).

2*r*,4*c*-Bis(*o*-chlorophenyl)-3-azabicyclo[3.3.1]nonan-9-one-4-aminobenzoyl hydrazone (**13**)

White solid: m.p. 202°C, and yield 58%. IR (KBr) (cm^{-1}): 3331 (N–H stretching); 3035, 2926, and 2855 (C–H stretching); and 1630 (C=N stretching). ^1H NMR (400 MHz—DMSO-d_6 ppm), δ: 10.46 (s, 1H, amide NH); 7.66 (d, 2H, H-3″); 6.6 (d, 2H, H-2″); 7.59 (q, 4H, *ortho*); 7.46 (q, 4H, *meta*); 4.27 (d, 2H, H-2a, H-4a); 3.20 (s, 1H, H-5e); 2.65 (m, 1H, H-7a); 1.59 (m, 1H, H-8e); 1.45 (m, 3H, H-6a); 1.45 (m, 2H, H-6e, H-8a); 1.25 (m, 1H, H-7e); 3.04 (s, 1H, ring NH); and 5.68 (s, 2H, *p*-NH_2). ^{13}C NMR (400 MHz): 64.2 (C-2); 61.9 (C-4); 46.0 (C-1); 28.5 (C-8); 27.2 (C-6); 21.3 (C-7); 171.0 (C-9); 169.9 (NH*C*O); 152 (C-4″); 113 (C–2″); 121.0(C-1″); and 142.8 (C-2′, C-4′). Anal found (cal.) for $C_{27}H_{26}N_4Ocl$ (%): C, 70.74 (70.78); H, 5.66 (5.68); and N, 12.20 (12.23).

Conclusion

2*r*,4*c*-Diaryl-3-azabicyclo[3.3.1]-nonan-9-one-4-aminobenzoyl hydrazones **9**–**15** adopt twin-chair conformation with equatorial orientations of the aryl groups. All the newly synthesized compounds were screened for their preliminary antibacterial and antifungal activities. Most of the compounds show good antibacterial and antifungal activities. However, the antibacterial and antifungal activities are significantly influenced by the aromatic substituents.

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