Antileishmanial, Antimicrobial and Antifungal Activities of Some New Aryl Azomethines

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Abstract: A series of eighteen azomethines has been synthesized by the reaction of appropriate primary aromatic amines with aryl and/or heteroaryl carboxaldehydes. The synthesized azomethines have been evaluated for their in vitro antileishmanial, antibacterial and antifungal activities. The results revealed some antifungal activity of most of the synthesized compounds, whereas the antileishmaniasis activity results highlighted that all synthesized azomethines inhibited parasite growth and most of them showed highly potent action towards Leishmania major promastigotes. No remarkable bactericidal activities were observed.

Keywords: azomethines; primary aromatic amines; hetaryl carboxyladehyes; antileishmanial activity; antifungal activity; antibacterial activity

Introduction

Although the last century has been characterized by a drastic lowering in the mortality caused by infectious diseases, some diseases still represent a dreadful menace to human health and therefore, for a more efficient control, require the steady development of new, more powerful and inexpensive drugs. Leischmaniasis, considered a serious public health concern in many countries, is one of these diseases. It is now endemic in many parts of Pakistan and Balochistan and the Upper Sindh are vulnerable to cutaneous leishmaniasis. The World Health Organization (WHO) has identified leishmaniasis as a
major and increasing public health problem [1]. In spite of the social and economic importance of leishmaniasis as a tropical infectious disease, efforts directed towards the discovery of new drugs against it remain undeveloped [2,3]. Moreover, the drugs currently in use are expensive, require long-term treatment [4], display high liver and heart toxicities, develop clinical resistance after few weeks of treatment and currently contribute to increase leishmaniasis-AIDS co-infections in some countries [5,6]. Azomethines are characterized by the –CH=N- (imino group) which has special importance in elucidating the mechanism of transmination and racemization in biological system [7–9]. Azomethines have high potential chemical permutation possibilities and show diuretic [10], anticancer [11–14], antibacterial [15–19], and antifungal activities [20–22]. This class of compounds has also exhibited activity against a wide range of organisms and is known to have medicinal importance and is used in drug design [23–25]. It has been also reported that when some aldehydes were functionalized by condensation with various amines, the resulting azomethines had antiparasitic activities [26].

Results and Discussion

The present work is a continuation of our ongoing programme devoted to the utilization of simple and readily obtainable materials in the synthesis of different biologically active compounds [27–33], aiming at the same time to seek a cure for the cutaneous antileishmaniasis facing our society in Pakistan by presenting some cheap azomethines that might be useful in antileishmanial and antifungal drug development.

Reaction of various substituted anilines with aromatic and/or heterocyclic aldehydes in hot methanol containing a catalytic amount of glacial acetic acid afforded the target azomethines 1-18 in good yields (55–87%). (cf. Scheme 1).

The structural features of the synthesized azomethines were determined from the corresponding IR, $^1$H-NMR, $^{13}$C-NMR and mass spectroscopy data, listed in Tables 1-4. All compounds showed in the IR spectra a strong absorption band at 1,592–1,637 cm$^{-1}$, typical of the stretching vibrations of the C=N functionality, as well as the bands corresponding to C-H stretching vibrations.

The $^1$H-NMR spectra of compounds 1-18 contained multiple signals in the $\delta$ 6.90 to 8.08 ppm regions due to aromatic protons and a singlet at 8.43–9.75 ppm from the C-H protons of the CH=N groups. In the spectra of compounds 5, 6, 11, 12, 13 and 14, signals between $\delta$ 3.50 and 4.0 ppm were attributed to –OCH$_3$ groups. The signals at $\delta$ 2.36 and 2.33 ppm which appeared as singlets in compounds 15 and 16 were assigned for methyl groups. In the DEPT spectra of compounds 1-18, there are no peaks at 189.0-196.0 ppm due to CHO group and the observed peaks were shifted to ~160.0-163.0 ppm which were attributable to HC=N group.

Scheme 1. General synthetic route.
Scheme 1. Cont.

| Compd. No. | Ar                           | R₁ | R₂ | R₃ |
|------------|------------------------------|----|----|----|
| 1          | C₆H₄(Cl)-4                   | H  | H  | H  |
| 2          | C₆H₄(Cl)-4                   | H  | H  | NO₂|
| 3          |                              | H  | H  | H  |
| 4          |                              | H  | H  | NO₂|
| 5          | C₆H₅(OH)(OCH₃)-3,4          | H  | H  | NO₂|
| 6          | C₆H₅(OH)(OCH₃)-3,4          | H  | H  | H  |
| 7          | C₆H₅CH=CH-                  | H  | H  | NO₂|
| 8          | C₆H₅CH=CH-                  | H  | H  | H  |
| 9          | C₆H₄(OH)-2                  | H  | H  | NO₂|
| 10         | C₆H₅(Cl)-4 -CH=CH-CH=CH-     | H  | H  | OCH₃|
| 11         | C₆H₅(OH)(OCH₃)-3,4 -CH=CH-CH=CH- | H |
| 12         | C₆H₅(Cl)-4                  | H  | H  | CH₃|
| 13         | C₆H₅(OH)(OCH₃)-3,4          | H  | H  | OCH₃|
| 14         | C₆H₅(OH)-2                  | H  | H  | CH₃|
| 15         | C₆H₅(Cl)-4                  | H  | H  | CH₃|
| 16         | C₆H₅(OH)-2                  | H  | H  | CH₃|
| 17         | C₆H₅CH=CH-                  | H  | H  | NO₂|
| 18         |                              | H  | H  | NO₂|

Table 1. Physical and select IR data of the synthesized azomethines 1-18.

| Compd. | Color          | Molecularized formula (Mol. Mass) | Mp (°C) (recryst. solvent) | Yield (%) | N=C | Azomethine C-H | Substituent          |
|--------|----------------|----------------------------------|---------------------------|-----------|-----|----------------|----------------------|
| 1      | Pale yellow    | C₁₃H₁₀ClN [34] (215.05)          | 72-4 (L.P)                | 82        | 1621| 2874, 1352     | -                    |
| 2      | Yellow         | C₁₃H₁₁ClN₂O₂ [35] (260.04)       | 140-42 (L.P)              | 74        | 1625| 1333           | 1505, 1376(NO₂)      |
| 3      | Brown          | C₁₁H₉NO [36] (171.07)            | 106 d (B)                 | 79        | 1605| 2850, 1328     | 3360(OH)             |
| 4      | Brown          | C₁₁H₁₀N₂O₃ [37] (216.05)         | 196-98 (EtOH)             | 68        | 1592| 1285           | 1535, 1339(NO₂)      |
| 5      | Pale orange    | C₁₄H₁₂N₂O₂OH (272.08)           | 148-50 (L.P)              | 64        | 1628| 1325           | 3354–3480(OH) 1544, 1342 (NO₂) |
| 6      | Pale yellow    | C₁₄H₁₁NO₂ (227.09)              | 155-57 (L.P)              | 72        | 1621| 1388           | 3088 broad(OH)       |
| 7      | Orange         | C₁₄H₁₁N₂O₂ (252.09)             | 133d (MeOH)               | 65        | 1592| 1300           | 1512, 1335(NO₂)      |
Table 1. Cont.

| Compd. | Colour | Molecular Formula | Molar Mass (g/mol) | Melting Point | UV (λ max, nm) | IR (ν max, cm⁻¹) |
|--------|--------|-------------------|-------------------|--------------|----------------|------------------|
| 8      | Pale brown | C₁₅H₁₃N (207.10) | 100-02 (MeOH) | 66 | 1623 | 1375 | - |
| 9      | Orange | C₁₃H₁₀N₂O₃ (242.07) | 162-64 (L.P) | 59 | 1632 | 1338 | 1562, 1347 (NO₂), 3150 (OH) |
| 10     | Pale brown | C₁₅H₁₅N (265.07) | 107-09 (MeOH) | 78 | 1637 | 1391 | - |
| 11     | Brown | C₁₃H₁₃N₂O₂ (277.11) | 114-16 (B) | 76 | 1621 | 1381 | 3048(OH) |
| 12     | Pale Brown | C₁₄H₁₃CINO (245.06) | 136-37 (MeOH) | 87 | 1629 | 2838, 1364 | 2838, 2895 (CH₃) |
| 13     | Pale Brown | C₁₅H₁₅N₂O₃ (257.11) | 257-59 (MeOH) | 70 | 1621 | 2954, 1378 | 3000 (broad OH), 2954, 2982 (CH₃) |
| 14     | Greenish White | C₁₅H₁₅N₂O₂ (227.09) | 85-87 (MeOH) | 67 | 1637 | 2964, 1362 | 3610(OH), 2964, 2996 (CH₃) |
| 15     | White | C₁₃H₁₁CIN (229.07) | 127-29 (MeOH) | 79 | 1622 | 2929, 1354 | 2854, 2925 (CH₃) |
| 16     | White | C₁₃H₁₃NO (211.10) | 96-98 (MeOH) | 67 | 1615 | 2920, 1366 | 3100 (OH), 2920 (CH₃) |
| 17     | Pale Orange | C₁₆H₁₅N [38] (221.12) | 76-77 (MeOH) | 71 | 1627 | 2912, 1379 | 2912 (CH₃) |
| 18     | Pale Yellow | C₁₁H₉N₂O₂S [39] (232.03) | 135-37 (MeOH) | 55 | 1612 | 1323 | 1543, 1341 (NO₂) |

References: a references are given for known products, the others are new; b L.P = Light Petroleum b.p. 60–80°C, B = benzene, EtOH = ethanol, MeOH = methanol.

Table 2. ¹H-NMR of azomethines 5-16 (DMSO-d₆) (δ, ppm).

| Compd. | ¹H-NMR |
|--------|--------|
| 5      | 9.45 (s, 1H, -OH, exchangeable), 8.36 (s, 1H, benzylidenimine H), 8.08-6.90 (m, 7H, Ar-H), 3.80 (s, 3H, -OCH₃). |
| 6      | 9.75 (s, 1H, -OH, exchangeable), 8.43 (s, 1H, -CH=N), 7.52-6.88 (m, 8H, Ar-H), 3.84 (s, 3H, -OCH₃). |
| 7      | 8.10 (m, 1H, -CH=N), 7.60-6.95 (m, 11H, Ar-H and olefinic H). |
| 8      | 8.25 (d, 1H, benzyldeimin H, J = 5.36 Hz), 7.54-7.07 (m, 12H, Ar-H and olefinic H). |
| 9      | 12.27 (s, 1H, OH, exchangeable), 8.99 (s, 1H, -CH=N), 8.32-6.98 (m, 7H, Ar-H). |
| 10     | 8.73 (s, 1H, benzylidenimine H), 8.09-7.23 (m, 11H, Ar-H). |
| 11     | 9.76 (s, 1H, OH, exchangeable), 8.53 (s, 1H, benzylidenimine H), 8.29-6.92 (m, 10H, Ar-H), 3.89 (s, 3H, -OCH₃). |
| 12     | 8.64 (s, 1H, -CH=N), 7.93-6.97 (m, 8H, Ar-H), 3.77 (s, 3H, -OCH₃). |
| 13     | 9.60 (s, 1H, OH, exchangeable), 8.44 (s, 1H, -CH=N), 7.49-6.86 (m, 7H, Ar-H), 3.83 and 3.76 (2s, 6H, 2-OCH₃). |
Table 2. Cont.

| Compd | 13.38 (s, 1H, OH, exchangeable), 8.59 (s, 1H, benzyldenimine H), 7.36-6.89 (m, 7H, Ar-H), 3.82 (s, 3H, -OCH3) |
|-------|---------------------------------------------------------------------------------------------------------------|
| 15    | 8.41 (s, 1H, -CH=N), 7.83-7.11 (m, 8H, Ar-H), 2.36 (s, 3H, -CH3)                                             |
| 16    | 13.19 (s, 1H, OH, exchangeable), 8.94 (s, 1H, -CH=N), 7.63-6.93 (m, 7H, Ar-H), 2.33 (s, 3H, -CH3) |

Table 3. $^{13}$C-NMR (DMSO-d$_6$) (δ, ppm) of azomethines 5-16.

| Compd | $^{13}$C-NMR                                                                                     |
|-------|-------------------------------------------------------------------------------------------------|
| 5     | 160.0, 154.2, 152.4, 147.3, 146.3, 131.0, 125.5, 125.2, 123.2, 115.9, 112.3, 56.1.          |
| 6     | 160.2, 152.4, 152.0, 147.3, 131.1, 129.9, 127.2, 125.5, 122.3, 115.9, 112.3, 56.1.          |
| 7     | 163.7, 158.6, 146.4, 135.2, 133.3, 128.5, 128.5, 127.9, 125.2, 123.2, 119.8.               |
| 8     | 163.7, 152.4, 135.2, 133.3, 130.0, 128.6, 128.5, 127.9, 127.2, 122.3, 119.9.              |
| 9     | 161.1, 160.0, 154.2, 146.4, 132.4, 132.1, 125.2, 123.2, 121.4, 120.5, 117.8.              |
| 10    | 160.0, 151.9, 136.6, 135.0, 134.5, 130.5, 128.9, 128.6, 127.8, 126.8, 126.3, 115.2.      |
| 11    | 160.0, 152.2, 151.9, 147.9, 147.3, 135.0, 131.1, 128.5, 128.3, 127.8, 126.7, 126.3, 125.5, 115.9, 115.1, 112.3, 56.1. |
| 12    | 160.0, 159.1, 144.3, 136.5, 134.5, 130.6, 128.8, 122.1, 115.6, 55.8.                     |
| 13    | 159.9, 159.1, 152.4, 147.3, 144.3, 131.1, 125.5, 115.9, 115.6, 122.1, 112.3, 56.1, 55.8.  |
| 14    | 161.1, 160.1, 159.1, 144.3, 132.4, 132.1, 122.1, 121.4, 120.4, 117.8, 115.5, 55.8.      |
| 15    | 160.1, 149.1, 136.9, 136.5, 134.5, 130.6, 128.9, 122.2, 21.3.                             |
| 16    | 161.1, 159.9, 149.1, 136.8, 132.4, 132.1, 130.3, 122.2, 121.4, 120.5, 117.7, 21.3.      |

Table 4. Mass spectra of azomethines 5-16.

| Compd. | m/z (% Relative abundance)                                                                 |
|--------|-------------------------------------------------------------------------------------------|
| 5      | 272 (M+, 4.25), 227 (2.34), 139 (4.85), 138 (70.25), 107 (76.60), 92 (48.80), 91 (6.91), 65 (100.00). |
| 6      | 227 (M+, 98.26), 211 (21.66), 166 (14.45), 154 (7.12), 139 (5.12), 104 (22.42), 77 (100.00) |
| 7      | 252 (M+, 27.28), 251 (M-1+, 83.41), 205 (56.73), 178 (4.88), 149 (4.88), 138 (54.55), 115 (70.16), 92 (48.50), 91 (47.95), 65 (100.00) |
| 8      | 207 (M+, 33.52), 206 (M-1+, 100.00), 178 (3.25), 128 (13.57), 115 (18.72), 77 (90.33).    |
| 9      | 242 (M+, 96.65), 212 (13.38), 195 (37.11), 167 (29.72), 151 (5.91), 120 (44.48), 76 (100.00) |
| 10     | 267 (M+2+, 20.42), 266 (M+1+, 20.79), 265 (M+, 60.68), 230 (2.89), 202 (3.48), 154 (23.00), 127 (100.00), 77 (29.47), 51 (9.14). |
| 11     | 277 (M+, 100.00), 261 (7.13), 216 (6.07), 204 (5.90), 178 (3.99), 154 (19.97), 127 (80.53), 101 (11.97), 85 (44.01), 83 (69.57), 77 (27.60). |
| 12     | 247 (M+2+, 26.19), 246 (M+1+, 25.13), 245 (M+, 77.99), 230 (100.00), 201 (10.17), 167 (27.80), 149 (5.64), 139 (10.67), 114 (4.26), 77 (35.29), 63 (45.11). |
| 13     | 257 (M+, 100.00), 242 (85.72), 227 (3.73), 198 (5.24), 170 (15.75), 154 (7.33), 134 (6.16), 115 (7.02), 77 (4.02), 64 (19.33). |
| 14     | 228 (M+1+, 16.62), 227 (M+, 100.00), 212 (71.79), 183 (4.33), 154 (3.40), 128 (5.33), 105 (3.08), 77 (55.04), 65 (38.15). |
| 15     | 231 (M+2+, 30.49), 230 (M+1+, 33.41), 229 (M+, 90.60), 193 (2.89), 165 (4.57), 150 (2.05), 118 (22.99), 91 (100.00), 77 (9.79), 65 (61.60). |
| 16     | 211 (M+, 100.00), 210 (M-1+, 76.87), 167 (6.29), 120 (12.86), 118 (8.68), 91 (80.65), 65 (74.49). |
Antileishmaniasis activity

Antileishmanial activity of the compounds (1-18) was assayed by Zhai’s method [40] using a pre-established culture of _L. major_ (Table 5) Parasites were cultured in medium M199 with 10% foetal bovine serum; 25 mM of HEPES, and 0.22 µg of penicillin and streptomycin, respectively, at 24 °C in a shaking incubator. Compounds 1, 6 and 16 have moderate activity against _L major_. Azomethines 4, 10, 14, 15, and 17 show good activity against _L major_ and azomethines 9 and 12 show significant activity. The high _in vitro_ antileishmaniasis activity of these compounds makes them promising leads for development of effective therapeutic agents.

Table 5. % Inhibition of azomethines against _L. major_ leishmania.

| Compound | _L. major*_a |
|----------|-------------|
| 1        | 0.77 ± 0.09 |
| 2        | -           |
| 3        | -           |
| 4        | 0.65 ± 0.01 |
| 5        | -           |
| 6        | 0.73 ± 0.16 |
| 7        | -           |
| 8        | -           |
| 9        | 0.59 ± 0.07 |
| 10       | 0.61 ± 0.27 |
| 11       | -           |
| 12       | 0.57 ± 0.11 |
| 13       | 0.63 ± 0.04 |
| 14       | 0.68 ± 0.12 |
| 15       | 0.66 ± 0.18 |
| 16       | 0.81 ± 0.03 |
| 17       | 0.62 ± 0.08 |
| 18       | -           |

*Standard Drug IC50 (µg/mL ± S.D)*

|           | 0.56 ± 0.20 |

*a* percentage inhibition activity: 100 = (non-significant; 0.95–0.80 = low; 0.79–0.70 = Moderate; 0.69–0.60 = Good; below 0.59–0.56 = Significant activity).

Antifungal activity

The antifungal bioassay is screened by the Agar Tube Dilution Method [41–42], in which the test compounds were screened for activity against the following organisms: _Candida albicans, Aspergillus flavus, Microsporum canis, Fusarium solani_ and _Candida glabrata_. Table 6 shows % inhibition of the synthesized azomethines. In all tests the linear growth in control was 100 mm. It is evident from the antifungal screening that:

(i) None of the compounds are inactive against _C. albicans_ or _C. glabrata_.

(ii) Only compound 17 has moderate activity against _A. flavus_.

Table 6. % Inhibition of synthesized azomethines against the following organisms.
Azomethines 4, 5, 12 and 14 have low activity against M. canis, whereas compound 9 has good antifungal activity against the same fungus.

(iv) Azomethine 9 shows moderate activity against F. solani, whereas azomethines 4, 11, 17 and 18 have low activity against the same fungus.

**Table 6.** % inhibition of azomethines against different types of fungi.

| Compound | C. albicans | A. flavus | M. canis | F. solani | C. glabrata |
|----------|-------------|-----------|----------|-----------|-------------|
| 1        | 0           | 0         | 0        | 0         | 0           |
| 2        | 0           | 0         | 0        | 0         | 0           |
| 3        | 0           | 0         | 0        | 0         | 0           |
| 4        | 0           | 0         | 20<sup>a</sup> | 35 | 0           |
| 5        | 0           | 0         | 30       | 0         | 0           |
| 6        | 0           | 0         | 0        | 0         | 0           |
| 7        | 0           | 0         | 0        | 0         | 0           |
| 8        | 0           | 0         | 0        | 0         | 0           |
| 9        | 0           | 0         | 60       | 40        | 0           |
| 10       | 0           | 0         | 0        | 0         | 0           |
| 11       | 0           | 0         | 0        | 35       | 0           |
| 12       | 0           | 0         | 35       | 0         | 0           |
| 13       | 0           | 0         | 0        | 0         | 0           |
| 14       | 0           | 0         | 20       | 0         | 0           |
| 15       | 0           | 0         | 0        | 0         | 0           |
| 16       | 0           | 0         | 0        | 0         | 0           |
| 17       | 0           | 40        | 0        | 15       | 0           |
| 18       | 0           | 0         | 0        | 20       | 0           |

**Std. Drug MIC (mg/mL)**

|            | Miconazole | Amphotericin B |
|------------|------------|----------------|
|            | 110.8      | -              |
|            | 98.4       | 20.0           |
|            | 73.25      | -              |
|            | 110.28     | -              |

<sup>a</sup> percentage inhibition activity: 0-39 = low (non-significant); 40-59 = Moderate; 60-69 = Good; Above 70 = Significant activity.

**Antibacterial activity**

The antibacterial activity of the synthesized azomethines was screened by the agar well diffusion method [43–44] against Gram-negative and Gram-positive bacteria, namely Escherchia coli, Bacillus subtilis, Shigella flexen ari, Staphylococcus aureus, Pseudomonas aeruginosa and Salmonella typhi. Only compound 4 showed significant activity (25 mm inhibition zone) against E. coli and moderate activity (14 mm zone) against B. subtilis.

**Experimental**

**General**

All aromatic and heterocyclic aldehydes as well as primary aromatic amines were obtained commercially from the Aldrich Chemical Company. Solvents used were of analytical grade. M.p. were measured using a Stuart (UK) electric melting point apparatus. IR spectra were recorded with a Thermo 330 FTIR spectrometer. Mass spectra were measured on a MAT 312 Finnigan instrument.
operating at 70 eV. $^1$H- and $^{13}$C-NMR spectra were recorded on an Avance 400 Bruker instrument using TMS as internal standard and DMSO-d$_6$ as solvent.

**Chemistry: General procedure for synthesis of azomethines**

An equimolar mixture of aryl and/or hetaryl carboxaldehyde with selected primary aryl amine in methyl alcohol (30 mL) containing few drops of glacial acetic acid was heated to reflux temperature for 3-4 hours then left overnight until the product precipitated. The product was filtered off, washed with light petroleum and recrystallized from the suitable solvent [cf. Table 1]. It is worthy to mention that anhydrous dry solvents for recrystallization were essential to avoid decomposition by hydrolysis. The crystalline solid that separated out was filtered by suction using water pump and washed with light petrol to afford the desired azomethines 1-18 in pure state.

**Biological Screening: Antileishmaniasis Activity - Preparation of Samples**

Each compound (1 mg) was dissolved in DMSO (1 mL) and Amphotericin B (1 mg) was also dissolved in DMSO (1 mL) as positive control. Parasites at log phase were centrifuged at 3,000 rpm for 3 minutes. Parasites were diluted in fresh culture medium to a final density of $2 \times 10^6$ cells/mL. In 96-well plates, 180 µL of medium was added in different wells. Twenty µL of the compound was added in medium and serially diluted. Parasite culture (100 µL) was added in all wells. Three rows were left for negative and positive controls. In the negative controls, DMSO was serially diluted in medium while the positive control contained varying concentrations of the standard antileishmanial compound Amphotericin B. The plates were incubated for 72 hours at 24 °C. The culture was examined microscopically on an improved Neubaur counting chamber and $IC_{50}$ values of compounds possessing antileishmanial activity were calculated. All assays were run in duplicate. $IC_{50}$ of samples was determined by using the Prism software.

**Antifungal activity**

The concentration of the tested compounds was 200 µg/mL of DMSO. A reference antifungal and DMSO were used as positive and negative control, respectively. Incubation temperature was 27 °C and time 7 days. The incubation of fungus was carried out with a 4 mm diameter piece of fungus removed from a seven-day-old culture. The growth in the compound-amended media was determined by measuring linear growth (mm) and growth inhibition calculated with reference to the negative control and calculating the % inhibition of fungal growth:

$$\% \text{ Inhibition} = 100 - \frac{\text{linear growth in test (mm)}}{\text{linear growth in control (mm)}} \times 100$$

**Antibacterial Activity**

The concentration of tested compound was 1 mg/mL of DMSO, whereas the concentration of the reference antibacterial drug imipenem was 10 µg/disc. Blank test showed that DMSO in the preparations of the test solutions does not affect the test organisms.
Conclusion

Eighteen azomethines were prepared by reacting an aromatic or heterocyclic aldehyde and an aromatic primary amine compound in a protic solvent like ethanol or methanol heated to reflux temperature in presence of few drops of acetic acid as a catalyst. The acidic catalyst leads to the increase of the electrophilicity of the caronyl function of the carboxaldehyde containing reactant. The results revealed some order of fungicidal activities of most of the synthesized compounds whereas the results of leishmanicidal activity highlighted that all synthesized azomethines inhibited the growth of parasite and most of them showed high potent action towards leishmania major promastigotes. No remarkable bactericidal activities have been recorded. Azomethines are characterized by the –CH=N- (imino group) which has special importance in elucidating the mechanism of transmination and racemization in biological system. Azomethines have high potential chemical permutation and show diuretic, anticancer, antibacterial, and antifungal activities. This class of compounds also exhibited activity against a wide range of organisms and are known to have medicinal importance and used in drugs design. It has been also reported that some aldehydes when were functionalized by condensation with various amines, the produced azomethines had antiparasitic activities. It is evident that Azomethine compounds 1, 6 and 16 have moderate activity against L major. Azomethines 4, 10, 14, 15, and 17 show good activity against L major and azomethine 9 and 12, shows significant activity against L.major. The high in vitro Anti leishmaniasis activity of these compounds makes them a promising lead for development of effective therapeutic agents. It is clear that the synthesize of Azomethines showed only compound 17 has moderated activity against A flavus. Azomethine 4,5,12 and 14 have low activity against M. Canis whereas compound 9 has good anti fungal activity against same fungus. Azomethine 9 shows a moderate activity against F. Solani whereas azomehtines 4,11,17 and 18 have low activity against the same fungus. In bacteria among the 18 synthesize of azomethines tested only compound 4 showed significant activity against E.coli and low activity against B. subtilis.

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Sample Availability: Samples of the compounds 1-18 are available from the authors.

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