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A FACILE ONE-POT SYNTHESIS OF NOVEL 1,1′-(ALKANEDIYL)BIS(5-OXO-3-ALKYL/ARALKYL/ARYL-1,2,3,4,5,6,7,8-OCTAHYDROQUINAZOLINES & THEIR ANTI-BACTERIAL ACTIVITIES

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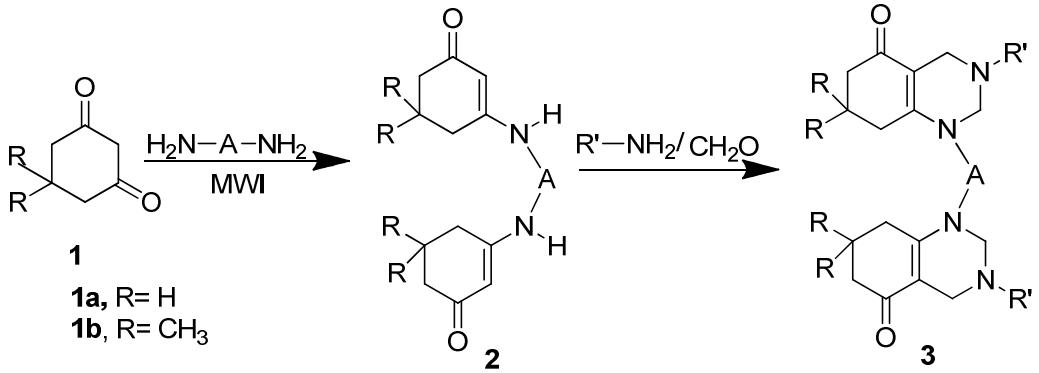
Abstract: A facile one-pot synthesis of novel 1,1′-(alkanediyl)bis(5-oxo-3-alkyl/aralkyl/aryl-1,2,3,4,5,6,7,8-octahydroquinazolines) **3a-r** has been devised by the cyclocondensation of bis-enaminones **2a-f** with primary amine and formaldehyde. The structures of the products have been established by spectral and analytical data as 1, 1′-(alkanediyl)bis(5-oxo-3-alkyl/ aralkyl/aryl-1,2,3,4,5,6,7,8-octahydroquinazolines). Some of the compounds have been found to possess promising anti-bacterial properties.

Keywords: octahydroquinazolines, bis-enaminones, cyclocondensation.

Introduction: Quinazolines have attracted considerable attention because of their great pharmacological importance and biological activities. Keeping in view the biological properties of octahydroquinazolines[1-3], we have recently reported[4-6] the synthesis of 5-oxo octahydroquinazolines bearing phenyl, benzyl and methyl groups in position 1 of the ring and bis(5-oxo-octahydroquinazolines) bearing phenyl, benzyl and methyl groups in position 1 of the ring. In the bis-quinazolines reported, we have connected the two quinazoline rings by both flexible aliphatic and rigid aromatic linkers at 3, 3′ positions. The biological properties of these molecules are under investigation. We now wish to report herein a facile one-pot synthesis of novel 1,1′-(alkanediyl)bis(5-oxo-3-alkyl/aralkyl/aryl-1,2,3,4,5,6,7,8-octahydroquinazolines) wherein the two quinazoline rings are connected at 1, 1′ positions to see the impact of this linkage on the biological properties of these molecules.



Scheme

Table: Synthesis of 1,1′-(alkanediyl)bis(5-oxo-3-alkyl/aralkyl/aryl-1,2,3,4,5,6,7,8-octahydroquinazolines)

Comp	R	A	R′	Reflux (hrs)	M.P.^{o}C	Yield %
3a	H	$-CH_2-CH_2-$	$-CH_3$	12	Gum	61
3b	H	$-CH_2-CH_2-$	$-C_6H_5$	14	106	57
3c	H	$-CH_2-CH_2-$	$-CH_2-C_6H_5$	11	115	52
3d	H	$-CH_2-CH_2-CH_2-$	$-CH_3$	15	Gum	56
3e	H	$-CH_2-CH_2-CH_2-$	$-C_6H_5$	17	Gum	58
3f	H	$-CH_2-CH_2-CH_2-$	$-CH_2-C_6H_5$	13	Gum	51
3g	H	$-CH_2-CH_2-CH_2-CH_2-$	$-CH_3$	11	Gum	73
3h	H	$-CH_2-CH_2-CH_2-CH_2-$	$-C_6H_5$	9	Gum	71
3i	H	$-CH_2-CH_2-CH_2-CH_2-$	$-CH_2-C_6H_5$	9	Gum	65
3j	$-CH_3$	$-CH_2-CH_2-$	$-CH_3$	7	Gum	53
3k	$-CH_3$	$-CH_2-CH_2-$	$-C_6H_5$	9	245	61
3l	$-CH_3$	$-CH_2-CH_2-$	$-CH_2-C_6H_5$	8	205	71
3m	$-CH_3$	$-CH_2-CH_2-CH_2-$	$-CH_3$	12	186	49
3n	$-CH_3$	$-CH_2-CH_2-CH_2-$	$-C_6H_5$	10	Gum	65
3o	$-CH_3$	$-CH_2-CH_2-CH_2-$	$-CH_2-C_6H_5$	11	Gum	58
3p	$-CH_3$	$-CH_2-CH_2-CH_2-CH_2-$	$-CH_3$	8	140	73
3q	$-CH_3$	$-CH_2-CH_2-CH_2-CH_2-$	$-C_6H_5$	8.5	Gum	57
3r	$-CH_3$	$-CH_2-CH_2-CH_2-CH_2-$	$-CH_2-C_6H_5$	7	125	73

Experimental

Melting points were recorded by open capillary method and are uncorrected. The IR spectra were recorded on a Perkin-Elmer-983 spectrometer. High-resolution ^{1}H NMR and ^{13}C NMR (300MHz) spectra were recorded on Bruker ACF-300 spectrometer. The chemical shift (δ ppm) and coupling constants (Hz) are reported in standard fashion with reference to TMS as internal reference. FAB-Mass spectra (MS) were measured on JEOL 3SX 102/DA-6000 using Argon as the FAB gas and m-nitrobenzyl alcohol as the matrix. Elemental analysis was performed on a Vario-EL-III instrument. Microwave irradiation was carried out in a CEM Discover Benchmate

microwave digester. Bis-enaminones **2a-f** were synthesized by the condensation of diketones **1a-b** with diamines in microwave digester.

General procedure

Synthesis of 3, 3′-(alkanediyl)bis(azanediyl)bis(cyclohex-2-enone) 2a-f:

A mixture of 1, 3-diketone (2 mmole) and diamine (1 mmole) in a 10 ml round bottom flask placed in a beaker was irradiated in a microwave digester at 180 watt for 2-4 minutes. After the completion of the reaction (monitored by TLC), water formed during the reaction was sucked out under reduced pressure to give a solid mass, which was triturated with methanol, filtered and then recrystallized from methanol to give the bis-enaminones **2a-f**. Physical and spectral data of the compounds are given below:

3, 3′-(ethane-1,2-diyl)bis(azanediyl)bis(cyclohex-2-enone) (2a)

This compound was obtained as pale yellow solid in 85% yield; mp 178 ^{0}C; IR (KBr): 1533, 1600, 3257, 3245 cm^{-1}; ^{1}H NMR ($CDCl_3$): δ 1.26-1.30 (m, 4H), 3.02-3.04 (m, 4H), 3.56-3.61 (m, 8H), 5.40 (s, 2H); 7.50 (br m, 2H); MS: m/z 249.4 (MH^+). Anal. Calcd. for $C_{14}H_{20}N_2O_2$ (248): C, 67.71; H, 8.12; N, 11.28. Found: C, 67.65; H, 8.15; N, 11.22%.

3,3′-(propane-1,3-diyl)bis(azanediyl)bis(cyclohex-2-enone) (2b)

This compound was obtained as pale yellow solid in 78% yield; mp 145 ^{0}C; IR (KBr): 1537, 1560, 3257, 32445 cm^{-1}; ^{1}H NMR ($CDCl_3$): δ 1.54-1.67 (m, 6H), 2.84-2.89 (m, 4H), 3.14-3.18 (m, 4H), 3.56-3.61 (m, 4H), 5.40 (s, 2H), 7.55 (br m, 2H); MS: m/z 263.5(MH^+). Anal. Calcd. for $C_{15}H_{22}N_2O_2$ (262.35): C, 68.67; H, 8.45; N, 10.68. Found: C, 68.55; H, 8.51; N, 10.65%.

3,3′-(butane-1,4-diyl)bis(azanediyl)bis(cyclohex-2-enone) (2c)

This compound was obtained as pale yellow solid in 75% yield; mp 202 ^{0}C; IR (KBr): 1531, 1566, 3247, 3243 cm^{-1}; ^{1}H NMR ($CDCl_3$): δ 1.26-1.28 (m, 4H), 1.30-1.32 (m, 4H), 3.02-3.08 (m, 4H), 3.56-3.61 (m, 8H), 5.40 (s, 2H), 7.46 (br m, 2H); MS: m/z 277.5 (MH^+). Anal. Calcd. for $C_{16}H_{24}N_2O_2$ (276.37): C, 69.53; H, 8.75; N, 10.14. Found: C, 69.64; H, 8.82; N, 10.09%.

3, 3′-(ethane-1, 2-diyl)bis(azanediyl)bis(5,5-dimethylcyclohex-2-enone) (2d)

This compound was obtained as pale yellow solid in 91% yield; mp 153^{0}C; IR (KBr): 1541, 1593, 3257, 3445 cm^{-1}; ^{1}H NMR ($CDCl_3$): δ 1.01-1.08 (m, 12H), 2.24 (s, 4H), 2.50-2.55 (m, 4H), 3.56 (s, 4H), 5.46 (s, 2H), 7.45 (br m, 2H); MS: m/z 305.9 (MH^+). Anal. Calcd. for $C_{18}H_{28}N_2O_2$ (304.22): C, 71.02; H, 9.27; N, 9.20. Found: C, 71.11; H, 9.23; N, 9.25%.

3, 3′-(propane-1,3-diyl)bis(azanediyl)bis(5,5-dimethylcyclohex-2-enone) (2e)

This compound was obtained as pale yellow solid in 82% yield; mp 173 ^{0}C; IR (KBr): 1545, 1600, 3276, 3456, cm^{-1}; ^{1}H NMR ($CDCl_3$): δ 1.04-1.06 (m, 12H), 1.26 (m, 2H), 2.24 (s, 4H), 2.50 (s, 4H), 3.56-3.60 (m, 4H), 5.45 (s, 2H), 7.50 (br m, 2H); MS: m/z 319.3 (MH^+). Anal. Calcd. for $C_{19}H_{30}N_2O_2$ (318.23): C, 71.66; H, 9.50; N, 8.80. Found: C, 71.77; H, 9.55; N, 8.83%.

3,3′-(butane-1,4-diyl)bis(azanediyl)bis(5,5-dimethylcyclohex-2-enone) (2f)

This compound was obtained as pale yellow solid in 85% yield; mp 168 ^{0}C; IR (KBr): 1537, 1560, 3331, 3343 cm^{-1}; ^{1}H NMR ($CDCl_3$): δ 1.01-1.04 (m, 12H), 1.26-1.28 (m, 4H), 3.02-3.04 (m, 8H), 3.52-3.58 (m, 4H), 5.40 (s, 2H), 7.51 (br m, 2H); MS: m/z 333.6 (MH^+). Anal. Calcd. for $C_{20}H_{32}N_2O_2$ (332.25): C, 72.25; H, 9.70; N, 8.43. Found: C, 72.15; H, 9.77; N, 8.45%.

Synthesis of 1,1′-(alkanediyl)bis(5-oxo-3-alkyl/aryl/aralkyl-1,2,3,4,5,6,7,8-octahydro-quinazolines) (3a-r). General procedure. A mixture of primary amine (2 mmol) and formaldehyde (4 mmol, 40% aqueous solution) in 1 mL of methanol was stirred for 5 minutes and to this was added a solution of bis-enaminone **2** (1 mmol) in 4 mL methanol in one portion. The resulting reaction mixture was refluxed at 65^0C for 7-15 hours. At the end of the reaction (tlc), methanol was distilled off under reduced pressure to give a gum which was purified by using chromatographic column (silica gel, EtOAc) to isolate **3a-r** in 51-73% yields.

1,1′-(ethane-1,2-diyl)bis(5-oxo-3-methyl-1,2,3,4,5,6,7,8-octahydroquinazoline) (3a)
This compound was obtained as light brown gum in 61% yield. IR (KBr): 1552, 1609 cm^{-1}; ^{1}H NMR ($CDCl_3$): δ 1.96-2.02 (m, 4H), 2.31-2.45 (m, 14H), 3.38-3.42 (m, 8H), 3.83 (s, 4H); ^{13}C NMR ($CDCl_3$): δ 21.46, 25.57, 35.63, 41.47, 41.70, 47.99, 50.28, 105.90, 157.10, 193.89; MS: m/z 359.2 (MH^+). Anal. Calcd. for $C_{20}H_{30}N_4O_2$ (358.24): C, 67.01; H, 8.44; N, 15.63, Found C, 67.00; H, 8.37; N, 15.63%.

1,1′-(ethane-1,2-diyl)bis(5-oxo-3-phenyl-1,2,3,4,5,6,7,8-octahydroquinazoline) (3b)
This compound was obtained as yellow solid in 57% yield, m.p 106^0C. IR (KBr): 1557, 1603 cm^{-1}; ^{1}H NMR ($CDCl_3$): δ 1.86-1.89 (m, 4H), 2.29-2.32 (t, 4H, J=6.4Hz), 3.20-3.24 (m, 4H), 4.04-4.08 (m, 4H), 4.45-4.54 (m, 4H), 4.84-4.89 (m, 4H), 6.84-7.02 (m, 6H), 7.19-7.28 (m,4H); MS: m/z 483.4 (MH^+). Anal. Calcd. for $C_{30}H_{34}N_4O_2$ (482.27): C, 74.66; H, 7.10; N, 11.61. Found: C, 74.51; H, 7.06; N, 11.63%.

1,1′-(ethane-1,2-diyl)bis(5-oxo-3-benzyl-1,2,3,4,5,6,7,8-octahydroquinazoline) (3c)
This compound was obtained as yellow solid in 52% yield, m.p 115^0C: IR (KBr): 1554, 1653 cm^{-1}; ^{1}H NMR ($CDCl_3$): δ 1.89-1.92 (m, 4H), 2.24-2.32 (m, 8H), 3.11 (s, 4H), 3.50 (s, 4H), 3.60 (s, 4H), 3.70 (s, 4H), 7.26-7.34 (m, 10H); MS: m/z 511.8 (MH^+). Anal. Calcd. for $C_{32}H_{38}N_4O_2$ (510.30): C, 75.26; H, 7.50; N, 10.97. Found: C, 75.35; H, 7.54; N, 10.90%.

1,1′-(propane-1,3-diyl)bis(5-oxo-3-methyl-1,2,3,4,5,6,7,8-octahydroquinazoline) (3d)
This compound was obtained as pale yellow gum in 56 % yield. IR (KBr): 1553, 1600 cm^{-1}; ^{1}H NMR ($CDCl_3$): δ 1.84-1.86 (m, 6H), 1.93-1.98 (m, 4H), 2.26-2.29 (m, 4H), 2.40 (s, 6H), 2.45-2.48 (m, 4H), 2.59 (s, 4H), 3.86 (m, 4H); ^{13}C NMR ($CDCl_3$): δ 21.17, 25.14, 35.38, 39.08, 40.13, 40.34, 41.27, 45.91, 49.87, 157.86, 193.06; MS: m/z 373.1 (MH^+). Anal. Calcd. for $C_{21}H_{32}N_4O_2$ (372.25): C, 67.71; H, 8.66; N, 15.01, Found: C, 67.60; H, 8.66; N, 15.14%.

1,1′-(propane-1,3-diyl)bis(5-oxo-3-phenyl-1,2,3,4,5,6,7,8-octahydroquinazoline) (3e)
This compound was obtained as brown gum in 58% yield. IR (KBr): 1573, 1653 cm^{-1}; ^{1}H NMR ($CDCl_3$): δ 1.03-1.09 (m, 4H), 1.14-1.25 (m, 2H), 2.12-2.20 (m, 8H) 3.15-3.18 (m, 4H), 4.11 (s, 4H), 4.47 (s, 4H), 6.89-6.93 (m, 6H), 7.23-7.26 (m, 4H); ^{13}C NMR ($CDCl_3$): δ 28.14, 29.19, 31.75, 38.82, 44.73, 45.63, 48.78, 67.53, 120.70, 128.70, 128.85, 147.96, 156.83, 192.64; MS: m/z 497.5 (MH^+). Anal. Calcd. for $C_{31}H_{36}N_4O_2$ (496.28): C, 74.97; H, 7.31; N, 11.28, Found: C, 74.91; H, 7.28; N, 11.21%.

1,1′-(propane-1,3-diyl)bis(5-oxo-3-benzyl-1,2,3,4,5,6,7,8-octahydroquinazoline) (3f)
This compound was obtained as yellow gum in 56% yield. IR (KBr): 1560, 1603 cm^{-1}; ^{1}H NMR ($CDCl_3$): δ 0.92-1.01 (m, 6H), 1.18 (br s, 4H), 2.08-2.15 (m, 4H), 3.03-3.07 (m, 4H), 3.57 (s,

4H), 3.63 (s, 4H), 3.83 (s, 4H), 7.24 (s, 10H); ^{13}C NMR ($CDCl_3$): δ 21.42, 25.47, 28.93, 35.62, 46.15, 48.93, 57.90, 67.97, 104.97, 128.49, 128.94, 129.18, 137.52, 158.08, 193.75; MS: m/z 525.6 (MH^+). Anal. Calcd. for $C_{33}H_{40}N_4O_2$ (524.32): C, 75.54; H, 7.68; N, 10.68, Found: C, 75.42; H, 7.57; N, 10.61%

1,1′-(butane-1,4-diyl)bis(5-oxo-3-methyl-1,2,3,4,5,6,7,8-octahydroquinazoline) (3g)
This compound was obtained as yellow gum in 73 % yield. IR (KBr): 1560, 1602 cm^{-1}; ^{1}H NMR ($CDCl_3$): δ 1.89-1.96 (m, 8H), 2.43 (s, 6H) 2.80-2.85 (m, 4H), 2.87-2.99 (m, 4H), 3.79-3.83 (m, 4H), 4.31 (s, 4H), 4.84 (s, 4H); MS: m/z 387.1 (MH^+). Anal. Calcd. for $C_{22}H_{34}N_4O_2$ (386.53): C, 68.36; H, 8.87; N, 14.49, Found: C, 68.27; H, 8.81; N, 14.42%

1,1′-(butane-1,4-diyl)bis(5-oxo-3-phenyl-1,2,3,4,5,6,7,8-octahydroquinazoline) (3h)
This compound was obtained as yellow gum in 65 % yield. IR (KBr): 1545, 1613 cm^{-1}; ^{1}H NMR ($CDCl_3$): δ 1.32-1.36 (m, 4H), 1.62-1.68 (m, 4H), 2.23-2.40 (m, 4H) 2.73-2.75 (m, 4H), 3.03 (s, 4H), 3.79 (s, 4H), 4.31 (s, 4H), 6.94-7.27 (m, 10H); MS: m/z 511.6 (MH^+). Anal. Calcd. for $C_{32}H_{38}N_4O_2$ (510.32): C, 75.26; H, 7.50; N, 10.97, Found: C, 75.25; H, 7.50; N, 10.95%

1,1′-(butane-1,4-diyl) bis(5-oxo-3-benzyl-1,2,3,4,5,6,7,8-octahydroquinazoline) (3i)
This compound was obtained as yellow gum in 71 % yield. IR (KBr): 1527, 1606 cm^{-1}; ^{1}H NMR ($CDCl_3$): δ 1.26-1.30 (m, 4H), 1.88-1.99 (m, 4H) 2.23-2.42 (m, 8H), 3.03 (s, 4H), 3.50 (s, 4H), 3.57 (s,4H), 3.74 (s,4H), 7.19-7.24 (m,10H); MS: m/z 539.1 (MH^+). Anal. Calcd. for $C_{34}H_{42}N_4O_2$ (538.33): C, 75.80; H, 7.86; N, 10.40, Found: C, 75.56; H, 7.82; N, 10.32%

1,1′-(ethane-1,2-diyl)bis(5-oxo-3,7,7-trimethyl-1,2,3,4,5,6,7,8-octahydroquinazoline) (3j)
This compound was obtained as yellow gum in 53 % yield. IR (KBr): 1557, 1608 cm^{-1}; ^{1}H NMR ($CDCl_3$): δ 1.07(s, 12H), 2.28(s, 4H), 2.39(s, 4H), 3.36-3.42(m, 10H), 3.84(s, 4H), 5.30(s, 4H); ^{13}C NMR ($CDCl_3$): δ 28.79, 32.23, 39.50, 41.42, 41.69, 48.04, 49.26, 53.43, 53.43, 71.46, 104.53, 155.44, 193.47; MS: m/z 415.4 (MH^+). Anal. Calcd. for $C_{24}H_{38}N_4O_2$ (414.3): C, 69.53; H, 9.24; N, 13.51, Found: C, 69.42; H, 9.16; N, 13.52%

1,1′-(ethane-1,2-diyl)bis(5-oxo-7,7-dimethyl-3-phenyl-1,2,3,4,5,6,7,8-octahydroquinazoline) (3k)
This compound was obtained as yellow solid in 61 % yield, m.p 245^{0}C; IR (KBr): 1578, 1597 cm^{-1}; ^{1}H NMR ($CDCl_3$): δ 1.05 (s, 12H), 1.87 (s, 4H), 2.12-2.24 (m, 4H), 2.59 (s, 4H), 5.06 (s, 4H), 5.42 (s, 4H), 7.05 (s, 4H), 7.73 (s, 6H); MS: m/z 539.1 (MH^+). Anal. Calc. for $C_{34}H_{42}N_4O_2$ (538.33): C, 75.80; H, 7.86; N, 10.40. Found: C, 75.93; H, 7.80; N, 10.46%

1,1′-(ethane-1,2-diyl)bis(5-oxo-3-benzyl-7,7-dimethyl-1,2,3,4,5,6,7,8-octahydroquinazoline) (3l)
This compound was obtained as yellow solid in 71 % yield, m.p 205^{0}C; IR (KBr): 1557, 1606 cm^{-1}; ^{1}H NMR ($CDCl_3$): δ 1.07 (s, 12H), 2.17 (s, 4H), 2.59-2.88 (m, 8H), 3.16 (s, 4H), 3.51 s, 4H), 3.82 (s, 4H), 5.33 (s, 4H), 7.02-7.30 (m, 10H); ^{13}C NMR ($CDCl_3$): δ 28.27, 31.61, 38.75, 39.12, 39.74, 39.95, 47.49, 47.77, 47.84, 57.15, 68.14, 127.06, 127.96, 128.32, 136.91, 192.72;

MS: m/z 567.5 (MH^+). Anal. Calcd. for $C_{36}H_{46}N_4O_2$ (566.36): C, 76.29; H, 8.18; N, 9.89. Found: C, 76.15; H, 8.13; N, 9.86%.

1,1′-(propane-1,3-diyl)bis(5-oxo-3,7,7-trimethyl-1,2,3,4,5,6,7,8-octahydro-quinazoline) (3m)
This compound was obtained as yellow solid in 73 % yield, m.p 186^{0}C; IR (KBr): 1533, 1578 cm^{-1}; ^{1}H NMR ($CDCl_3$): δ 1.07-1.61 (s, 18H), 1.88-1.91 (s, 4H), 2.20-2.21 (m, 4H), 3.21 (s, 6H), 3.49-3.52 (m, 4H), 5.15 (s, 4H); MS: m/z 529.9 (MH^+). Anal. Calcd. for $C_{25}H_{40}N_4O_2$ (428.32): C, 70.06; H, 9.41; N, 13.07, Found C, 70.21; H, 9.43; N, 13.02%.

1,1′-(propane-1,3-diyl)bis(5-oxo-7,7-dimethyl-3-phenyl-1,2,3,4,5,6,7,8-octahydro-quinazoline) (3n)
This compound was obtained as light brown gum in 58 % yield; IR (KBr): 1560, 1599 cm^{-1}; ^{1}H NMR ($CDCl_3$): δ 1.07 (s, 12H), 1.18(s, 4H), 2.06-2.21 (m, 6H), 3.09-3.13 (m, 4H), 4.04 (s, 4H), 4.57 (s, 4H), 6.84-6.86 (m, 6H), 7.16-7.20 (m, 4H); ^{13}C NMR ($CDCl_3$): δ 28.59, 29.36, 31.93, 32.27, 39.33, 45.13, 46.19, 48.71, 68.18, 104.19, 117.72, 121.40, 129.40, 148.29, 158.38, 192.89; MS: m/z 553.6 (MH^+). Anal. Calcd. for $C_{35}H_{44}N_4O_2$ (552.35): C, 76.05; H, 8.02; N, 10.14, Found: C, 76.23; H, 8.13; N, 10.14%.

1,1′-(propane-1,3-diyl)bis(5-oxo-3-benzyl-7,7-dimethyl-1,2,3,4,5,6,7,8-octahydro-quinazoline) (3o)
This compound was obtained as light brown gum in 65 % yield; IR (KBr): 1560, 1599 cm^{-1}; ^{1}H NMR ($CDCl_3$): δ 1.07 (s, 12H), 1.24 (s, 4H), 1.56-1.59 (t, 2H J=6.8Hz), 2.15 (s, 4H), 3.05-3.09 (m, 4H), 3.50-3.63 (m, 8H), 3.79 (s, 4H), 7.29 (s,10H); ^{13}C NMR ($CDCl_3$): δ 28.33, 29.19, 31.75, 38.66, 38.83, 45.65, 47.91, 48.83, 57.21, 67.79, 102.94, 127.10, 127.99, 128.48, 137.09, 155.70, 192.70; MS: m/z 581.6 (MH^+). Anal. Calcd. for $C_{37}H_{48}N_4O_2$ (580.38): C, 76.51; H, 8.33; N, 9.65, Found: C, 76.23; H, 8.13; N, 10.14%.

1,1′-(butane-1,4-diyl)bis(5-oxo-3,7,7-trimethyl-1,2,3,4,5,6,7,8-octahydroquinazoline) (3p)
This compound was obtained as light brown solid in 70 % yield, m.p 140^{0}C; IR (KBr): 1557, 1603 cm^{-1}; ^{1}H NMR ($CDCl_3$): δ 1.08 (s, 12H), 1.57 (s, 4H), 1.91 (s, 4H), 2.21 (s, 4H), 2.40 (s, 6H), 3.24 (s, 4H), 3.44 (s, 4H), 3.87 (s, 4H); ^{13}C NMR ($CDCl_3$): δ 26.92, 28.79, 30.94,32.23, 39.30, 41.50, 48.49, 49.26, 49.83, 70.83, 102.82, 155.97; MS: m/z 443.6 (MH^+). Anal. Calcd. for $C_{26}H_{42}N_4O_2$ (442.3): C, 70.55; H, 9.56; N, 12.66. Found: C, 70.41; H, 9.51; N, 12.70%.

1,1′-(butane-1,4-diyl)bis(5-oxo-7,7-dimethyl-3-phenyl-1,2,3,4,5,6,7,8-octahydroquinazoline) (3q)
This compound was obtained as light brown gum in 57 % yield; IR (KBr): 1559, 1600 cm^{-1}; ^{1}H NMR ($CDCl_3$): δ 1.01 (s, 12H), 1.95-2.29 (m, 8H), 3.01-3.18 (m, 8H), 4.08 (s, 4H), 4.45 (s, 4H), 6.81-6.96 (m, 6H), 7.15-7.29 (m, 4H); ^{13}C NMR ($CDCl_3$): δ 27.92, 28.35, 29.16, 39.21, 45.15, 48.15, 48.67, 49.23, 49.31, 67.80,117.69, 120.75, 129.44, 148.60, 157.59, 192.91; MS: m/z 566.8 (M^+). Anal. Calcd. for $C_{36}H_{46}N_4O_2$ (566.78): C, 76.29; H, 8.18; N, 9.89, Found: C, 76.23; H, 8.13; N, 10.14%

1,1′-(butane-1,4-diyl)bis(5-oxo-3-benzyl-7,7-dimethyl-1,2,3,4,5,6,7,8-octahydro-quinazoline) (3r)

This compound was obtained as light yellow solid in 73 % yield, m.p 125^{0}C; IR (KBr): 1559, 1603 cm^{-1}; ^{1}H NMR ($CDCl_3$): δ 1.06 (s, 12H), 1.77 (s, 4H), 2.14-2.25 (m, 8H), 3.10 (s, 4H), 3.59-3.63 (m, 8H), 3.86 (s, 4H), 7.27-7.32 (m, 10H); ^{13}C NMR ($CDCl_3$): δ 26.88, 28.82, 30.94, 32.24, 39.39, 48.33, 48.48, 49.30, 57.57, 68.07, 102.75, 127.51, 128.45, 128.96, 137.77, 156.50,193.14; MS: m/z 595.6 (MH^+). Anal. Calcd. for $C_{38}H_{50}N_4O_2$ (594.39): C, 76.73; H, 8.47; N, 9.42. Found: C, 76.60; H, 8.51; N, 9.39%.

Results and Discussion

Thus, when 3,3′-(ethane-1,2-diyl)bis(azanediyl)bis(cyclohex-2-enone) **2a** was treated with methylamine and formaldehyde refluxed in methanol, a product was obtained in 61 % yields which was characterized as 1,1′-(ethane-1,2-diyl)bis(5-oxo-3-methyl-1,2,3,4,5,6,7,8-octahydroquinazoline) **3a** on the basis of analytical and spectral data. The reaction of **2** with other primary amines and formaldehyde behaved in a similar manner and bis-octahydroquinazolines **3b-r** were isolated in 52-73% yields. The infrared spectra of **3a-r** showed strong peaks in the region of 1553 to 1653 cm^{-1} due to extensively delocalized double bonds and carbonyl groups.[7] In the ^{1}H NMR spectra of **3a-i**, the methylene protons at C-7 appeared as multiplets near 1.89-1.96 ppm except in **3e** and **3f** where they appeared in the vicinity of 1.01-1.18 ppm . The methyl protons at C-7 for **3j-r** gave sharp singlets around 1.05 ppm. Methylene protons at C-2 for **3j-r** resonated at higher δ value than the corresponding **3a-i** which may be due to the presence of electron donating methyl groups at C-7 in **3j-r**. The CH_2 protons at C-8 resonate close to 2.3 ppm except in **3f** and **3h** where they were found to resonate near 1.88 and 1.95 ppm respectively. The rest of the methylene protons in the quinazoline ring resonated in the region of 3-4 ppm and the aromatic protons appeared in the usual region. The ^{13}C spectra of the molecules showed sharp signals near 193 ppm due to the carbonyl carbon and the sp^2 hybridised carbon of quinazoline ring along with those of benzene gave signals in the region of 102-156 ppm. The aliphatic carbons appeared in their usual range in the ^{13}C spectrum. Further, the structures of all the compounds were supported by their mass specta.

Anti-bacterial assay of selected bis(5-oxo-octahydroquinazolines) 3a, 3b, 3d, 3i and 3r:

Antibacterial activity was carried out by cup-plate agar diffusion[8] method by measuring zone of inhibition in mm in comparison with antibiotic control rifampicin (1mg/ml). All the compounds were screened in vitro for their antibacterial activity against a variety of gram-positive and gram-negative bacterial strains such as *S. aureus* (MTCC902), *B. subtilis* (MTCC2389), *S. pyogenes* (MTCC1927), *S. epidermidis* (MTCC435), *E. coli* (MTCC302), *P. aeruginosa* (MTCC425). The strains used for the activity were procured from the Institute of Microbial Technology, Chandigarh. The sample solutions were made at different dilutions i.e. 10mg/ml, 5mg/ml, 2.5mg/ml, 1.25mg/ml. In this method a layer of hard agar medium was made on the Petri plates then a layer of soft agar media was poured into it. The medium was allowed to solidify and punched to make wells, the solvent (DMSO), antibiotic control and the test sample (synthesized chemical) at different concentrations (10 mg/ml, 5 mg/ml, 2.5 mg/ml, 1.25 mg/ml respectively) were loaded in separate wells (20µl in each well). The plates were incubated at 37^{0}C for 24 hours. Rifampicin (1mg/ml) was loaded in one well as the antibiotic standard. The zone of inhibition was measured in mm.

Zone of inhibition of synthesized 1,1′-(alkanediyl)bis(5-oxo-3-alkyl/aryl/aralkyl-1,2,3,4,5,6,7,8-octahydroquinazolines) against different bacteria.

Compound (10 mg/ml)	Zone of inhibition (mm)					
	Gram-positive bacteria				**Gram-negative bacteria**	
	S. aureus	*B. subtilis*	*S. pyogenes*	*S. epidermidis.*	*E. coli*	*P. aeruginosa*
3a	0.56	0.76	-	0.85	1.34	0.96
3b	-	0.75	-	-	-	1.25
3d	-	-	-	1.28	-	-
3i	1.35	1.10	-	-	1.13	-
3r	-	0.99	-	-	0.78	-
Anti-biotic	2.25	1.82	1.98	2.32	1.76	2.20

It has been observed that the test compounds (**3a**, **3b**, **3d**, **3i**, **3r**) exhibited interesting antibacterial activity at a concentration of 10 mg/ml, however with a degree of variation. However, the mean zone of inhibition at other concentrations was not significantly different from the values obtained at higher concentrations. Compound **3a** showed largest zone of inhibition against gram negative bacteria *E.coli* and comparatively less activity against other bacterial strains. The minimum antibacterial activity was shown by the compound **3r** at all concentrations.

Conclusion

The present paper describes an efficient and simple strategy for the synthesis of hitherto unknown bis(5-oxo-octahydroquinazolines) from easily accessible starting materials in good yields with promising pharmacological and biological properties. The methodology reported herein is an example of multi-component reactions (MCRs).

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