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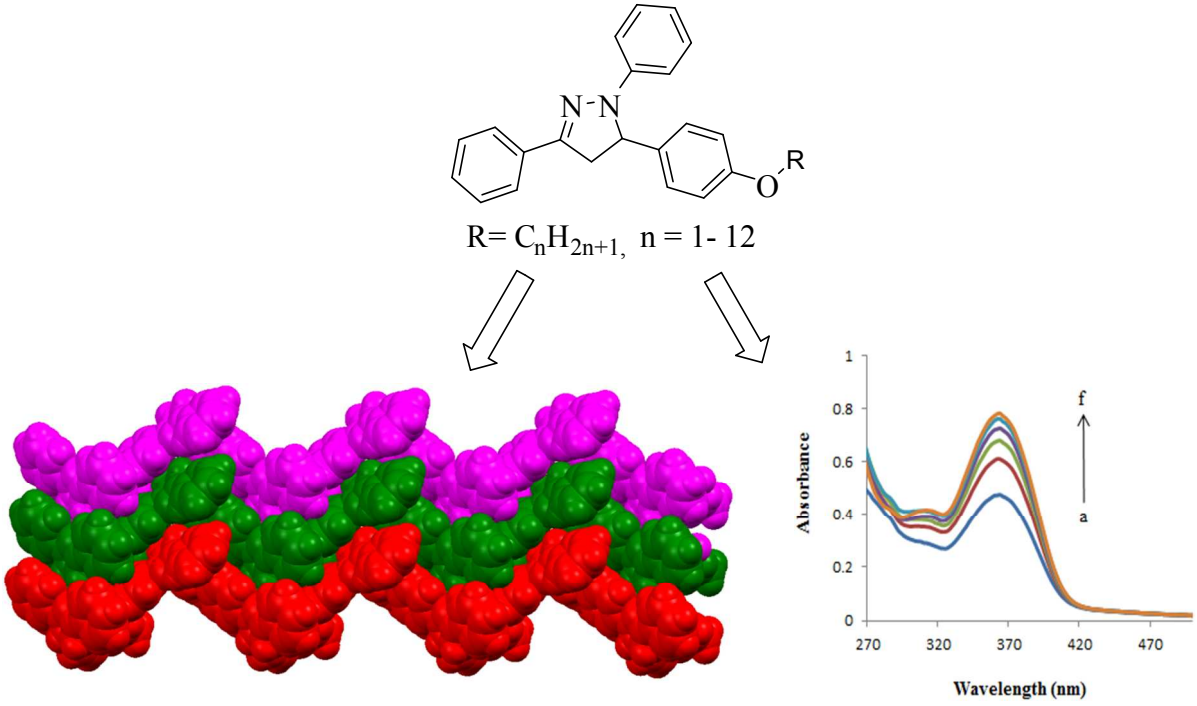
GRAPHICAL ABSTRACT

Homologous 1,3,5-triarylpyrazolines: Synthesis, CH···π interactions guided self-assembly and effect of alkyloxy chain length on DNA binding properties

F. Anum, A. Abbas, K. M. Lo, Z. Rehman, S. Hameed, M. M. Naseer

The synthesis, CH···π interactions-driven self-assembled structure and DNA binding properties (10^5-10^6 M^{-1} binding constants) of new homologous 1,3,5-triaryl-2-pyrazolines are being reported.



Homologous 1,3,5-triarylpyrazolines: Synthesis, CH···π interactions guided self-assembly and effect of alkyloxy chain length on DNA binding properties

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ABSTRACT

A series of new 2-pyrazoline derivatives (**1c-12c**) bearing one to twelve carbon homologous alkyloxy side chains have been synthesized in good to excellent yields *via* intramolecular cyclization reaction on treatment of chalcone intermediates (**1a-12a**) with phenyl hydrazine (**1b**) and characterized on the basis of their physical and spectral (IR, ^{1}H & ^{13}C NMR, GC-MS) data. The solid state structure of compound (**2c**) showed intriguing and unique 1D-supramolecular zig zag chains-like self-assembled structure, the driving force of which is only CH···π interactions. The DNA interaction studies have also been carried out on selected compounds **1c, 3c, 5c, 6c, 9c** and **12c** of the series by UV-visible spectroscopy to evaluate their anticancer potential and the effect of alkyloxy chain length on DNA binding property. All the tested compounds showed strong DNA binding (10^{5}-10^{6} M^{-1} binding constants) with hyperchromic effect. A slight increase in the DNA binding strength, observed on increasing the chain length of alkyloxy groups, was attributed to their conformational arrangements leading to the best fit conformation of 1,3,5-triaryl moiety in the minor groove of DNA structure.

Keywords: 1,3,5-Triarylpyrazolines, Synthesis, CH···π guided self-assembly, UV-Vis spectroscopy, DNA binding

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1. Introduction:

Amongst the weak non-covalent interactions, C-H···π interactions are considered to be the most important, in which C-H group and π ring acts as hydrogen donor and acceptor, respectively.[1-5] The energy associated with these important type of weak hydrogen bonds are much smaller (0.8 $kcalmol^{-1}$) as compared to that of typical strong hydrogen-bonds between O···H or N···H (7.8 to 3.5 $kcalmol^{-1}$).[6, 7] However, these interactions have been found strong enough to stabilize a particular conformation of molecules for their higher-order self-assembly.[6, 7] These are recognized as the main non-covalent forces in protein folding that stabilize their secondary and tertiary structures [8, 9] in addition to their role in orienting alkyl chains towards the phenyl group of amino acid residues, binding of proteins with cofactors and carbohydrates etc.[10] In spite of the tremendous progress, the study of these interactions is usually difficult due to their weak nature and their cooperative occurrence that complicate their individual study. Therefore, molecular self-assemblies driven solely by CH-π interactions are very important and the molecules displaying such properties may serve as the model for future studies.

Pyrazolines occupy unique place in the family of five membered heterocycles owing to their easy synthesis and versatile pharmacological applications.[11-13] Anti-tumor, antiproliferative or anticancer potential of pyrazoline derivatives have recently been explored.[14-18] Other applications of their derivatives include antiamoebic,[19] antimycobacterial,[20] antibacterial/antifungal,[21, 22] anti-inflammatory,[23] antidepressant,[24] neuroprotector,[25] antiviral[26] and anti-obesity activities.[27] The pyrazoline moiety is present in a number of pharmacologically active molecules such as azolid/ tandearil (anti-inflammatory), phenazone/ amidopyrene/ methampyrone (analgesic and antipyretic), anturane (uricosuric) and indoxacarb (insecticidal). Furthermore, their antidiabetic potential has also been reviewed.[28]

DNA having all the genetic information/coding for cellular functions, such as cell replications and transcriptions, is usually a primary target for most of the anticancer drugs.[29-39] The anticancer drug molecules interact with DNA through different non-covalent interactions, depending on the structure of a drug, and can modify/unwind the double stranded helical structure of DNA and thus destroy its normal functions leading ultimately to cell death. The interaction of anticancer drug molecules with DNA can be categorized into three types (i) electrostatic interaction with the anionic phosphate of DNA backbone, (ii) intercalation into the stacked base pairs of DNA and (iii) groove binding. The DNA binding studies thus provide

preliminary information and are of paramount importance in the discovery and development of novel anticancer agents.

Despite being proven bioactive moiety, very little attention has been paid to study the effect of lipophilicity on a specific bioactivity of pyrazoline derivatives. Since long, lipophilicity is recognized as a meaningful parameter in determining the overall effectiveness of candidate drug molecule. It is the most important and informative physiochemical property of a drug and plays a vital role in determining the preclinical processes of drug disposition such as absorption, distribution, metabolism, excretion and toxicity (ADMET).[40-44] The control of lipophilicity within a defined optimal range not only improves the efficacy of a test compound, it also increases the likelihood of its therapeutic success. We can say that lipophilicity determines the overall suitability of compound to become a drug. Therefore, the role of lipophilicity in drug discovery and drug design is important and a critical one.

In this context and as continuation of our recent project on the synthesis and applications of pyrazolines,[45-47] herein, we report the synthesis of a series of new homologous 1,3,5-triarylpyrazolines, the sole CH-π interactions guided solid state self-assembly of compound **2c** and DNA binding properties to study the effect of increasing alkyloxy chain length on their DNA binding capabilities.

2. Experimental

2.1. General

All reagents and solvents were used as obtained from the supplier or recrystallized/redistilled as required. Thin layer chromatography (TLC) was performed using aluminium sheets coated with silica gel 60 F_{254} (Merck). Melting points of all the synthesized compounds have been determined in open capillary tubes by using Gallenkamp apparatus (MP-D) and were uncorrected. IR spectrum in the range of 4000-400 cm^{-1} was obtained on a Thermo Nicolet-6700 FT-IR Spectrophotometer. The ^{1}H and ^{13}C NMR spectra were recorded on Bruker spectrometer at 300 MHz and 75 MHz in $CDCl_3$, respectively using residual solvent signals as a reference. The GC-MS spectra were performed with Agilent 5973 inert mass selective detector in combination with Agilent 6890N gas chromatograph. The UV-Vis spectra were recorded on Shimadzu 1601 spectrophotometer.

*2.2. General procedure for the synthesis of 1,3,5-triaryl-2-pyrazolines (**1c-12c**)*

The synthesis of 1,3,5-triaryl-2-pyrazolines (**1c-12c**) were carried out by dissolving 4-alkyloxychalcones (0.01 mole) in 5 ml DMF-ethanol (8:2) mixture, containing 2-3 drops of concentrated hydrochloric acid. The reaction mixture was then heated at 60-65 ^{0}C for half an hour with constant stirring before the addition of second reactant i.e. phenylhydrazine (2.16 g, 0.02 mole) (**1b**). After the addition of compound **1b** to the reaction flask, the reaction mixture was heated to reflux for 5-6 hours. The reaction mixture was then cooled to room temperature and poured onto the crushed ice. The precipitates so obtained, were filtered, washed thoroughly with distilled water and dried. To get highly pure compounds (**1c-12c)** for spectral characterization and DNA interaction studies**,** the obtained crude products were subjected to silica gel column chromatography using n-hexane/ethylacetate (9:1) as eluent.

For better understanding of ^{1}H NMR chemical shift values described in the experimental data, the different protons of compounds **1c-12c** are labelled as shown in Fig. 1.

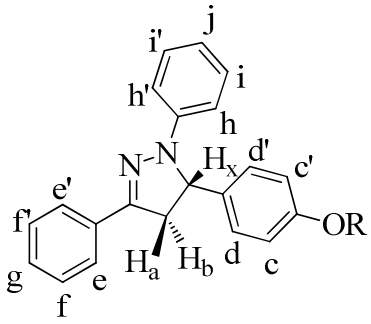


Fig. 1. Proton labeling scheme for compounds **1c–12c.**

*2.2.1. 1,3-Diphenyl-5-(4-methoxyphenyl)-2-pyrazoline (**1c**)*

Yield 80%; pale yellow solid; m. p. 133-136˚C; R_f = 0.52 (n-hexane:ethyl acetate, 9:1); UV-Vis (DMSO) λmax in nm (log ε) 362 (5.4); FT-IR: 1594 (C=N), 1175 (C-N), 1242, 1029 (Ar-O-R), ^{1}H NMR (300 MHz, $CDCl_3$) δ 3.14 (1H,dd, J_{ab} = 17.1 Hz, J_{ax} = 7.2 Hz, H_a), 3.80 (3H, s, -O-CH_3), 3.83 (1H, dd, J_{ab}= 16.8 Hz, J_{bx} =12 Hz, H_b), 5.26 (1H, dd, J_{bx}= 12.3 Hz , J_{ax}= 7.2 Hz, H_x), 6.78-6.83 (1H, m, N-ArH_j), 6.88 (2H, d, J = 8.7 Hz, N-Ar$H_{h=h'}$), 7.11 (2H, d, J =7.8 Hz , Ar$H_{c=c'}$), 7.18-7.28 (4H, m, Ar$H_{d=d'}$, N-Ar$H_{i=i'}$), 7.34-7.44 (3H, m, Ar$H_{f=f',g}$), 7.75 (2H, d, J = 6.9 Hz, Ar$H_{e=e'}$); ^{13}C NMR (75 MHz, $CDCl_3$) δ 43.63, 55.29, 64.00, 113.40, 114.48, 119.05, 125.73, 127.07, 128.56, 128.90, 132.82, 134.21, 134.66, 144.88, 146.72, 158.96 EIMS: *m/z* 328 ($M^{+\bullet}$, base peak); Anal. calcd. for $C_{22}H_{20}N_2O$: C, 80.46; H, 6.14; N, 8.53; Found: C, 80.51; H, 6.20; N, 8.39 %.

*2.2.2. 1,3-Diphenyl-5-(4-ethoxyphenyl)-2-pyrazoline (**2c**)*

Yield 84%; brown crystals; m. p. 114-116˚C; R_f = 0.55 (n-hexane:ethyl acetate, 9:1); UV-Vis (DMSO) λmax in nm (log ε) 364 (5.7); FT-IR: 1596 (C=N), 1171 (C-N), 1244,1048 (Ar-O-R), ^{1}H NMR (300 MHz, $CDCl_3$) δ 1.41 (3H, t, J = 6.9 Hz,-O-$CH_2C\boldsymbol{H}_3$), 3.15 (1H, dd, J_{ab} = 17.1 Hz, J_{ax} = 7.2 Hz, H_a), 3.83 (1H, dd, J_{ab} = 17.1 Hz, J_{bx} = 12.3Hz, H_b), 4.02 (2H, q, J = 6.9 Hz, -O$C\boldsymbol{H}_2$-), 5.25 (1H, dd, J_{bx} = 12.3 Hz , J_{ax} = 7.2 Hz , H_x), 6.78-6.83 (1H, m, N-ArH_j) ,6.87 (2H , d, J = 8.1 Hz, N-Ar$H_{h=h'}$) ,7.10 (2H, d, J = 7.8 Hz , Ar$H_{c=c'}$), 7.18-7.28 (4H, m, Ar$H_{d=d'}$, N-Ar$H_{i=i'}$), 7.32-7.44 (3H, m, Ar$H_{f=f',g}$), 7.75 (2H, d, J = 6.9 Hz, Ar$H_{e=e'}$); ^{13}C NMR (75 MHz, $CDCl_3$) δ 14.88, 43.63, 63.43, 64.00, 113.38, 114.97, 119.02, 125.72, 127.05, 128.57, 128.91, 132.81, 134.19, 134.48, 144.87, 146.73, 158.33 EIMS: *m/z* 342 ($M^{+\bullet}$, base peak); Anal. calcd. for $C_{23}H_{22}N_2O$: C, 80.67; H, 6.48; N, 8.18; Found: C, 80.79; H, 6.46; N, 8.25 %.

*2.2.3. 1,3-Diphenyl-5-(4-propoxyphenyl)-2-pyrazoline (**3c**)*

Yield 82%; pale yellow solid; m. p. 108-109˚C; R_f = 0.56 (n-hexane:ethyl acetate, 9:1); UV-Vis (DMSO) λmax in nm (log ε) 364 (5.2); FT-IR: 1595 (C=N), 1172 (C-N), 1243,1046 (Ar-O-R), ^{1}H NMR (300 MHz, $CDCl_3$) δ 1.04 (3H, t, J = 7.5 Hz,-O-$CH_2CH_2C\boldsymbol{H}_3$) ,1.81 (2H, sextet, J = 7.2 Hz,-O-$CH_2C\boldsymbol{H}_2CH_3$), 3.14 (1H, dd, J_{ab} = 17.1 Hz, J_{ax} = 7.2 Hz, H_a), 3.81 (1H, dd, J_{ab} = 17.1 Hz, J_{bx} = 12.3 Hz, H_b), 3.90 (2H, t, J = 6.6 Hz,-O$C\boldsymbol{H}_2$-), 5.25 (1H, dd, J_{bx} =12 Hz, J_{ax} = 7.2 Hz ,H_x), 6.78-6.83 (1H, m, N-ArH_j) , 6.87 (2H, d, J = 8.7Hz, N-Ar$H_{h=h'}$) ,7.11 (2H, d, J = 7.5 Hz , Ar$H_{c=c'}$), 7.18-7.28 (4H, m, Ar$H_{d=d'}$,N-Ar$H_{i=i'}$), 7.32-7.46 (3H, m, Ar$H_{f=f',g}$), 7.75 (2H, d, J = 6.9

Hz, $ArH_{e=e'}$);^{13}C NMR (75 MHz, $CDCl_3$) δ 10.58, 22.60, 43.64, 64.03, 69.49, 113.40, 115.01, 119.02, 125.72, 127.03, 128.56, 128.90, 132.84, 134.16, 134.44, 144.90, 146.72, 158.54; EIMS: *m/z* 356 ($M^{+\bullet}$, base peak); Anal. calcd. for $C_{24}H_{24}N_2O$: C, 80.87; H, 6.79; N, 7.86; Found: C, 80.75; H, 6.70; N, 7.98 %.

*2.2.4. 1,3-Diphenyl-5-(4-butoxyphenyl)-2-pyrazoline (**4c**)*

Yield 85%; Brown solid; m. p. 89-91˚C; R_f = 0.59 (n-hexane:ethyl acetate, 9:1); UV-Vis (DMSO) λmax in nm (log ε) 363 (5.2); FT-IR: 1592 (C=N), 1177 (C-N), 1242,1067 (Ar-O-R), ^{1}H NMR (300 MHz,$CDCl_3$) δ 0.98 (3H, t, *J* =7.2 Hz, -O-$(CH_2)_3C\boldsymbol{H}_3$) , 1.49 (2H, sextet, *J* =7.8 Hz, -O-$CH_2CH_2C\boldsymbol{H}_2CH_3$), 1.76 (2H, qn, *J* = 6.9 Hz, −O−CH_2−$C\boldsymbol{H}_2$−C_2H_5) , 3.13 (1H, dd, J_{ab} = 17.1 Hz, J_{ax} = 7.2 Hz, H_a), 3.83 (1H, dd, J_{ab} =17.1 Hz, J_{bx} =12.3 Hz, H_b), 3.94 (2H, t, *J* = 6.6 Hz,-O$C\boldsymbol{H}_2$-), 5.24 (1H, dd, J_{bx} =12 Hz, J_{ax} = 7.2 Hz, H_x), 6.77-6.82 (1H, m, N-ArH_j) ,6.87 (2H, d, *J* = 8.7 Hz, N-$ArH_{h=h'}$) ,7.10 (2H, d, *J* = 7.8 Hz , $ArH_{c=c'}$), 7.16-7.28 (4H, m, $ArH_{d=d'}$, N-$ArH_{i=i'}$), 7.29-7.42 (3H, m, $ArH_{f=f',g}$), 7.73 (2H, d, *J* = 6.9 Hz,$ArH_{e=e'}$); ^{13}C NMR (75 MHz, $CDCl_3$) δ 13.88, 19.26, 31.33, 43.62, 64.03, 67.68, 113.40, 115.00, 119.02, 125.72, 127.02, 128.55, 128.89, 132.83, 134.15, 134.41, 144.90, 146.73, 158.56, EIMS: *m/z* 370 ($M^{+\bullet}$, base peak); Anal. calcd. for $C_{25}H_{26}N_2O$: C, 81.05; H, 7.07; N, 7.56; Found: C, 80.90; H, 7.09; N, 7.47 %.

*2.2.5. 1,3-Diphenyl-5-(4-pentyloxyphenyl)-2-pyrazoline (**5c**)*

Yield 84%; pale yellow solid; m. p. 86-89˚C; R_f = 0.62 (n-hexane:ethyl acetate, 9:1); UV-Vis (DMSO) λmax in nm (log ε) 364 (5.2); FT-IR: 1593 (C=N), 1173 (C-N), 1242, 1027 (Ar-O-R); ^{1}H NMR (300 MHz, $CDCl_3$) δ 0 .94 (3H, t, *J* = 7.2 Hz, -O-$(CH_2)_4C\boldsymbol{H}_3$) , 1.35-1.47 (4H, m, −O−CH_2− CH_2 − $(C\boldsymbol{H}_2)_2$ −CH_3), 1.77 (2H, qn, *J* = 6.6 Hz, −O−CH_2−$C\boldsymbol{H}_2$−C_3H_7), 3.14 (1H, dd, J_{ab} = 17.1 Hz, J_{ax} = 7.2 Hz, H_a), 3.83 (1H, dd, J_{ab} = 17.1 Hz, J_{bx} = 12.3 Hz, H_b), 3.93 (2H, t, *J* = 6.6 Hz, -O$C\boldsymbol{H}_2$-), 5.25 (1H, dd, J_{bx} =12.3 Hz, J_{ax} = 7.2 Hz , H_x), 6.77-6.83 (1H, m, N-ArH_j), 6.87 (2H, d, *J* = 8.7 Hz, N-$ArH_{h=h'}$), 7.10 (2H, d, *J* = 7.5 Hz , $ArH_{c=c'}$), 7.17-7.28 (4H, m, $ArH_{d=d}$, N-$ArH_{i=i'}$), 7.35-7.44 (3H, m, $ArH_{f=f',g}$), 7.75 (2H, d, *J* = 6.9 Hz, $ArH_{e=e'}$); ^{13}C NMR (75MHz, $CDCl_3$) δ 14.06, 22.48, 28.22, 28.99, 43.64, 64.04, 67.62, 113.40, 115.00, 119.02, 125.72, 127.02, 128.55, 128.89, 132.84, 134.15, 134.42, 144.90, 146.71, 158.56; EIMS: *m/z* 384 ($M^{+\bullet}$, base peak); Anal. calcd. for $C_{26}H_{28}N_2O$: C, 81.21; H, 7.34; N, 7.29; Found: C, 81.36; H, 7.39; N, 7.33 %.

*2.2.6. 1,3-Diphenyl-5-(4-hexyloxyphenyl)-2-pyrazoline (**6c**)*

Yield 86%; brown solid; m. p. 87-89˚C; R_f = 0.62 (n-hexane:ethyl acetate, 9:1); UV-Vis (DMSO) λmax in nm (log ε) 364 (5.2); FT-IR: 1595 (C=N), 1172 (C-N), 1243, 1068 (Ar-O-R), ^{1}H NMR (300 MHz, $CDCl_3$) δ 0.92 (3H, t, J = 6.6 Hz, -O-$(CH_2)_5$C***H***$_3$), 1.32-1.48 (6H, m, −O−CH_2−CH_2−(C***H*** $_2)_3$−CH_3), 1.77 (2H, qn, J = 6.6 Hz, −O−CH_2−C***H***$_2$–C_4H_9) , 3.14 (1H, dd, J_{ab} = 17.1 Hz, J_{ax} = 7.2 Hz, H_a), 3.82 (1H, dd, J_{ab} = 17.1 Hz, J_{bx} = 12.3 Hz, H_b), 3.93 (2H, t, J = 6.6 Hz, -OC***H***$_2$-), 5.24 (1H, dd, J_{bx} = 12.3 Hz , J_{ax} = 7.2 Hz, H_x), 6.78-6.82 (1H, m, N-ArH_j), 6.87 (2H, d , J = 8.7 Hz, N-Ar$H_{h=h'}$) , 7.11 (2H, d, J =7.5Hz , Ar$H_{c=c'}$), 7.18-7.28 (4H, m, Ar$H_{d=d'}$, N-Ar$H_{i=i'}$), 7.34-7.44 (3H, m, Ar$H_{f=f',g}$), 7.75 (2H, d, J = 6.9 Hz, Ar$H_{e=e'}$); ^{13}C NMR (75 MHz, $CDCl_3$) δ 14.08, 22.63, 25.75, 29.26, 31.61, 34.76, 43.64, 64.04, 68.01, 113.40, 115.01, 119.02, 125.33, 125.72, 127.02, 128.56, 128.89, 132.84, 134.14, 134.32, 144.90, 146.72, 158.56; EIMS: *m/z* 398 ($M^{+\bullet}$, base peak); Anal. calcd. for $C_{27}H_{30}N_2O$: C, 81.37; H, 7.59; N, 7.03; Found: C, 81.33; H, 7.54; N, 7.21 %.

*2.2.7. 1,3-Diphenyl-5-(4-heptyloxyphenyl)-2-pyrazoline (**7c**)*

Yield 83%; pale yellow solid; m. p. 78-80˚C; R_f = 0.62 (n-hexane:ethyl acetate, 9:1); UV-Vis (DMSO) λmax in nm (log ε) 365 (5.3); FT-IR: 1589 (C=N), 1169 (C-N), 1241, 1066 (Ar-O-R), ^{1}H NMR (300 MHz, $CDCl_3$) δ 0.91(3H, t, J=6.6Hz, -O-$(CH_2)_6$C***H***$_3$) , 1.32-1.58 (8H, m,−O−CH_2−CH_2−(C***H***$_2)_4$−CH_3) 1.78 (2H, qn, J = 6.9 Hz, −O−CH_2−C***H***$_2$ –C_5H_{11}) , 3.14 (1H, dd, J_{ab} = 17.1 Hz, J_{ax} = 7.2 Hz, H_a), 3.83 (1H, dd, J_{ab} = 17.1 Hz, J_{bx} = 12.3 Hz, H_b), 3.93 (2H, t, J = 6.6 Hz,-OC***H***$_2$-), 5.25 (1H, dd, J_{bx} = 12.3Hz, J_{ax} = 7.2 Hz, H_x), 6.77-6.83 (1H, m, N-ArH_j), 6.87 (2H, d, J = 8.7 Hz, N-Ar$H_{h=h'}$) , 7.12 (2H, d, J = 7.5Hz , Ar$H_{c=c'}$), 7.17-7.28 (4H, m, Ar$H_{d=d'}$, N-Ar$H_{i=i'}$), 7.34-7.43 (3H, m, Ar$H_{f=f',g}$), 7.75 (2H, d, J = 6.9Hz, Ar$H_{e=e'}$); ^{13}C NMR (75 MHz, $CDCl_3$) δ 14.51, 22.65, 29.04, 29.10, 29.30, 31.81, 43.63, 64.03, 68.00, 113.39, 115.00, 119.02, 125.7, 127.02, 128.56, 128.90, 132.84, 134.14, 134.41, 144.89, 146.71, 158.56; EIMS: *m/z* 412 ($M^{+\bullet}$, base peak); Anal. calcd. for $C_{28}H_{32}N_2O$: C, 81.51; H, 7.82; N, 6.79; Found: C, 81.43; H, 7.94; N, 6.81 %.

*2.2.8. 1,3-Diphenyl-5-(4-octyloxyphenyl)-2-pyrazoline (**8c**)*

Yield 87%; pale yellow solid; m. p. 88-89˚C; R_f = 0.63 (n-hexane:ethyl acetate, 9:1); UV-Vis (DMSO) λmax in nm (log ε) 365 (5.0); FT-IR: 1592 (C=N), 1169 (C-N), 1230,1027 (Ar-O-R); ^{1}H NMR (300 MHz, $CDCl_3$) δ 0.90 (3H, t, J = 6.9Hz, -O-$(CH_2)_7$C***H***$_3$), 1.31-1.47 (10H, m,

−O−CH_2−CH_2−(C***H***$_2$)$_5$− CH_3), 1.79 (2H, qn, *J* = 6.6 Hz, −O−CH_2−C***H***$_2$–C_6H_{13}) , 3.13 (1H, dd, J_{ab} = 16.2 Hz, J_{ax} = 7.2 Hz, H_a), 3.82 (1H, dd, J_{ab} = 17.1 Hz, J_{bx} = 12.3 Hz, H_b), 3.95 (2H, t, *J* = 6.6 Hz, -OC***H***$_2$-), 5.24 (1H, dd, J_{bx} = 12.3 Hz , J_{ax} = 7.2, H_x), 6.85-6.92 (3H, m, N-ArH_j , N-Ar$H_{h=h'}$), 7.10 (2H, d, *J* = 7.8Hz , Ar$H_{c=c'}$), 7.17-7.28 (4H, m, Ar$H_{d=d'}$, N-Ar$H_{i=i'}$), 7.32-7.49 (3H, m, Ar$H_{f=f',g}$), 7.74 (2H, d, *J* = 6.9Hz, Ar$H_{e=e'}$); ^{13}C NMR (75 MHz, $CDCl_3$) δ 14.14, 22.68, 26.06, 29.26, 29.37, 31.83, 43.64, 64.04, 68.01, 68.07, 113.40, 115.00, 119.02, 125.49, 125.72, 127.01, 128.54, 128.97, 132.83, 134.41, 144.90, 146.73, 158.56; EIMS : *m/z* 426 ($M^{+\bullet}$, base peak); Anal. calcd. for $C_{29}H_{34}N_2O$: C, 81.65; H, 8.03; N, 6.57; Found: C, 81.54; H, 7.91; N, 6.63 %.

*2.2.9. 1,3-Diphenyl-5-(4-nonyloxyphenyl)-2-pyrazoline (**9c**)*

Yield 85%; pale yellow solid; m. p. 90-92˚C; R_f = 0.64 (n-hexane:ethyl acetate, 9:1); UV-Vis (DMSO) λmax in nm (log ε) 363 (5.3); FT-IR: 1592 (C=N), 1170 (C-N), 1241, 1014 (Ar-O-R), ^{1}H NMR (300 MHz, $CDCl_3$) δ 0.90 (3H,t, *J* =6.9 Hz, -O-$(CH_2)_8$C***H***$_3$), 1.30-1.46(12H,m,−O−CH_2−CH_2−(C***H***$_2$)$_6$−CH_3) ,1.78 (2H, qn, *J* = 6.6 Hz, −O−CH_2−C***H***$_2$ –C_7H_{15}) , 3.14 (1H, dd, J_{ab} = 17.1 Hz, J_{ax} = 7.2 Hz, H_a), 3.83 (1H, dd, J_{ab} 16.8 Hz, J_{bx} = 12.3 Hz, H_b), 3.93 (2H, t, *J* = 6.6 Hz,-OC***H***$_2$-), 5.25 (1H, dd, J_{bx} = 12.3 Hz , J_{ax} = 7.2 Hz, H_x), 6.78-6.88 (3H, m, N-ArH_j , N-Ar$H_{h=h'}$), 7.11 (2H, d, *J* =7.8Hz , Ar$H_{c=c'}$), 7.18-7.28 (4H, m, Ar$H_{d=d'}$, N-Ar$H_{i=i'}$), 7.32-7.45 (3H, m, Ar$H_{f=f',g}$), 7.75 (2H, d, *J* = 6.9Hz, Ar$H_{e=e'}$);^{13}C NMR (75MHz, $CDCl_3$) δ 14.17, 22.71, 26.08, 29.30, 29.43, 29.56, 31.91, 34.76, 43.64, 64.05, 68.01, 113.40, 115.00, 119.02, 125.73, 127.03, 128.54, 128.89, 132.84, 134.14, 134.41, 144.90, 146.71, 158.56; EIMS: *m/z* 440 ($M^{+\bullet}$, base peak); Anal. calcd. for $C_{30}H_{36}N_2O$: C, 81.78; H, 8.24; N, 6.36; Found: C, 81.83; H, 8.23; N, 6.32 %.

*2.2.10. 1,3-Diphenyl-5-(4-decyloxyphenyl)-2-pyrazoline (**10c**)*

Yield 81%; pale yellow solid; m. p. 90-91˚C; R_f = 0.64 (n-hexane:ethyl acetate, 9:1); UV-Vis (DMSO) λmax in nm (log ε) 364 (5.2); FT-IR: 1594 (C=N), 1175 (C-N), 1242, 1025 (Ar-O-R); ^{1}H NMR (300 MHz, $CDCl_3$) δ 0.90 (3H, t, *J* = 6.9Hz, -O-$(CH_2)_9$C***H***$_3$), 1.28-1.47 (14H, m, −O−CH_2−CH_2−(C***H***$_2$)$_7$− CH_3), 1.77 (2H, qn, *J* = 6.6 Hz, −O−CH_2−C***H***$_2$–C_8H_{17}) , 3.13 (1H, dd, J_{ab} = 17.1 Hz, J_{ax} = 7.5 Hz, H_a), 3.83 (1H, dd, J_{ab} = 17.1 Hz, J_{bx} = 12.3 Hz, H_b), 3.93 (2H, t, *J* = 6.6 Hz, -OC***H***$_2$-), 5.24 (1H, dd, J_{bx} = 12 Hz , J_{ax} = 7.2, H_x), 6.79-6.89 (3H, m, N-ArH_j , N-Ar$H_{h=h'}$), 7.11 (2H, d, *J* = 7.8 Hz , Ar$H_{c=c'}$), 7.18-7.28 (4H, m, Ar$H_{d=d'}$, N-Ar$H_{i=i'}$), 7.31-7.47(3H,

m, $ArH_{f=f',g}$), 7.74 (2H, d, J = 6.9 Hz, $ArH_{e=e'}$); ^{13}C NMR (75 MHz, $CDCl_3$) δ 14.15, 22.70, 26.06, 29.28, 29.34, 29.41, 29.57, 31.91, 43.64, 64.04, 68.00, 113.39, 114.42, 115.00, 119.01, 125.71, 127.01, 128.54, 128.88, 130.01, 132.83, 134.41, 144, 90, 146.71, 158.55; EIMS: *m/z* 454 ($M^{+\bullet}$, base peak); Anal. calcd. for $C_{31}H_{38}N_2O$: C, 81.89; H, 8.42; N, 6.16; Found: C, 81.77; H, 8.50; N, 6.25 %.

*2.2.11. 1,3-Diphenyl-5-(4-undecyloxyphenyl)-2-pyrazoline (**11c**)*

Yield 86%; pale yellow solid; m. p. 90-92˚C; R_f = 0.67 (n-hexane:ethyl acetate, 9:1); UV-Vis (DMSO) λmax in nm (log ε) 363 (5.3); FT-IR: 1594 (C=N), 1171 (C-N), 1232, 1014 (Ar-O-R), ^1H NMR (300 MHz, $CDCl_3$) δ 0.90 (3H, t, J = 6.9Hz, -O-$(CH_2)_{10}C\boldsymbol{H}_3$), 1.28-1.47 (16H, m, −O−CH_2−CH_2−$(C\boldsymbol{H}_2)_8$− CH_3), 1.77 (2H, qn, J = 6.6 Hz, −O−CH_2−$C\boldsymbol{H}_2$–C_9H_{19}) , 3.14 (1H, dd, J_{ab} = 17.1 Hz, J_{ax} = 7.2 Hz, H_a), 3.83 (1H, dd, J_{ab} = 17.1 Hz, J_{bx} = 12.3 Hz, H_b), 3.93 (2H, t, J = 6.6 Hz, -O$C\boldsymbol{H}_2$-), 5.25 (1H, dd, J_{bx} = 12.3 Hz , J_{ax} = 7.2, H_x), 6.77-6.88 (3H, m, N-ArH_j , N-$ArH_{h=h'}$), 7.10 (2H, d, J = 7.8Hz , $ArH_{c=c'}$), 7.18-7.28 (4H, m, $ArH_{d=d'}$, N-$ArH_{i=i'}$), 7.32-7.48 (3H, m, $ArH_{f=f',g}$), 7.75 (2H, d, J = 6.9Hz, $ArH_{e=e'}$); ^{13}C NMR (75 MHz, $CDCl_3$) δ 14.18, 22.73, 26.07, 29.29, 29.37, 29.43, 29.61, 29.64, 31.94, 34.43, 43.64, 64.03, 68.00, 113.39, 115.00, 119.02, 125.32, 125.72, 127.02, 128.56, 128.89, 132.84, 134.41, 144.70, 146.71, 158.56; EIMS: *m/z* 468 ($M^{+\bullet}$, base peak); Anal. calcd. for $C_{32}H_{40}N_2O$: C, 82.01; H, 8.60; N, 5.98; Found: C, 81.96; H, 8.70; N, 5.99 %.

*2.2.12. 1,3-Diphenyl-5-(4-dodecyloxyphenyl)-2-pyrazoline (**12c**)*

Yield 83%; pale yellow solid; m. p. 91-93˚C; R_f = 0.67 (n-hexane:ethyl acetate, 9:1); UV-Vis (DMSO) λmax in nm (log ε) 363 (5.4); FT-IR: 1593 (C=N), 1171 (C-N), 1239, 1000 (Ar-O-R); ^1H NMR (300 MHz, $CDCl_3$) δ 0.90 (3H, t, J = 6.9Hz, -O-$(CH_2)_{11}C\boldsymbol{H}_3$), 1.28-1.47 (18H, m, −O−CH_2−CH_2−$(C\boldsymbol{H}_2)_9$− CH_3), 1.78 (2H, qn, J = 6.6 Hz, −O−CH_2−$C\boldsymbol{H}_2$–$C_{10}H_{21}$) , 3.13 (1H, dd, J_{ab} = 17.1 Hz, J_{ax} = 7.2 Hz, H_a), 3.82 (1H, dd, J_{ab} = 17.1 Hz, J_{bx} = 12.3 Hz, H_b), 3.94 (2H, t, J = 6.6 Hz, -O$C\boldsymbol{H}_2$-), 5.24 (1H, dd, J_{bx} = 12 Hz , J_{ax} = 7.2, H_x), 6.77-6.88 (3H, m, N-ArH_j , N-$ArH_{h=h'}$), 7.11 (2H, d, J = 7.5 Hz , $ArH_{c=c'}$), 7.17-7.28 (4H, m, $ArH_{d=d'}$, N-$ArH_{i=i'}$), 7.30-7.47 (3H, m, $ArH_{f=f',g}$), 7.74 (2H, d, J = 6.9 Hz, $ArH_{e=e'}$); ^{13}C NMR (75 MHz, $CDCl_3$) δ 14.16, 22.72, 26.06, 29.29, 29.37, 29.42, 29.57, 29.62, 29.66, 31.94, 43.64, 64.04, 68.01, 113.40, 115.00, 119.02, 125.39, 125.71, 125.88, 127.01, 128.54, 128.88, 132.83, 134.41, 144.70, 146.71, 158.56;

EIMS: *m/z* 482 ($M^{+\bullet}$, base peak); Anal. calcd. for $C_{33}H_{42}N_2O$: C, 82.11; H, 8.77; N, 5.80; Found: C, 82.01; H, 8.84; N, 6.02 %.

2.3. Crystallographic data collection and structure refinements

The single crystal X-Ray diffraction measurements for the compound **2c** were carried out using Bruker APEX-II CCD area-detector equipped with graphite monochromator at 296(2) K with MoK\α radiations (λ = 0.71073 Å). The structure is solved by direct methods[48] full-matrix least-squares refinement on F² and 236 parameters for 4323 unique intensities (R_{int} = 0.011). The crystal data and refinement details of compound **2c** are summarized in Table 1.

Table 1. Crystallographic data for compound **2c**

Crystal data	**2c**
CCDC	983902
Chemical formula	$C_{23}H_{22}N_2O$
M_r	342.43
Crystal system, space group	Monoclinic, $P2_1/c$
Temperature (K)	296
a, *b*, *c* (Å)	22.0227 (5), 5.5302 (2), 15.8613 (4)
β (°)	102.984 (2)
V (Å^3)	1882.36 (9)
Z	4
Radiation type	Mo *K*α
μ (mm^{-1})	0.07
Crystal size (mm)	0.10 × 0.08 × 0.04
Data collection	
Diffractometer	Bruker *APEX*-II CCD area-detector diffractometer
Absorption correction	Multi-scan (*SADABS*; Sheldrick, 1996)
T_{min}, T_{max}	0.660, 0.746
No. of measured, independent and observed [$I > 2\sigma(I)$] reflections	17282, 4323, 2108
R_{int}	0.110
$(\sin\theta/\lambda)_{max}$ (Å^{-1})	0.650
Refinement	
$R[F^2 > 2\sigma(F^2)]$, $wR(F^2)$, S	0.062, 0.174, 1.02
No. of reflections	4323

No. of parameters	236
H-atom treatment	H-atom parameters constrained
$\Delta\rangle_{max}$, $\Delta\rangle_{min}$ (e Å^{-3})	0.21, -0.23

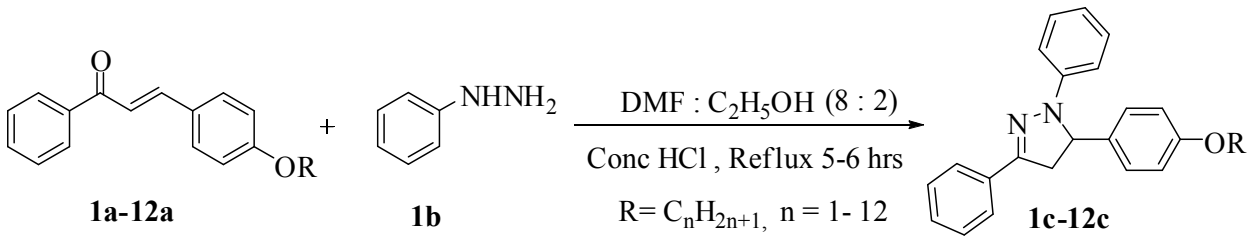
2.4. DNA binding studies

The Salmon sperm DNA was solubilized in double-distilled water to prepare a stock DNA solution having 5x10^{-4} M concentration, which was stored at 4^{0}C. Solutions of varying DNA concentrations, for measuring binding interactions, were prepared from this stock DNA solution by dilution method. The concentration of stock solution was measured by UV absorbance at 260 nm using molar extinction coefficient of 6600 M^{-1}cm^{-1}. The ratio factor value (A_{260}/A_{280} > 1.8) suggested that the DNA was free of protein moieties. All the spectroscopic titrations were carried out by keeping the concentration of test compound constant in the sample cell while varying the concentration of DNA from 5 μM to 25 μM. All the samples were equilibrated at room temperature for 5 minutes prior to measurements.

3. Results and discussion

3.1. Chemistry

The compounds (**1c-12c**) were synthesized by reacting 4-alkyloxychalcones (**1a**−**12a**) with two equivalents of phenyl hydrazine in DMF-ethanol solvent mixture (8:2) containing 2-3 drops of conc. HCl under reflux conditions for 5-6 hours and purified by silica gel column chromatography using n-hexane/ethyl acetate as the mobile phase (Scheme 1). All the products were obtained as solids in 80-87% yield. The structures of all the compounds were confirmed on the basis of their FT-IR, ^{1}H NMR, ^{13}C NMR and EIMS data. In addition, single-crystal X-Ray analysis was used to unambiguously prove the three dimensional structure of compound **2c**.



1a-12a **1b** **1c-12c**

Scheme 1. Synthesis of homologous 1,3,5-triaryl 2-pyrazolines, **1c–12c**.

*3.2. Spectral characterization of **1c–12c***

In FT-IR spectroscopy of compounds (**1c-12c**), two absorption bands in the range of 1596-1589 cm^{-1} and 1177-1169 cm^{-1} were assigned to carbon-nitrogen (C=N) double bonds and carbon-nitrogen single bonds (C-N), respectively[49-51] that indicates the formation of pyrazoline skeleton. In addition, two strong bands at stretching frequencies in the range of 1244-1230 cm^{-1} and 1068-1000 cm^{-1} were also observed, which indicates the presence of Ar-O-R groups in the synthesized compounds.

The formation of the five membered pyrazoline ring was further confirmed by the presence of three doublet of doublets corresponding to two methylene protons (H_a and H_b) and one methine proton (H_x) in the ^{1}H NMR spectra. The chemical shifts of H_a protons of the compounds (**1c−12c**) were observed in the range of 3.13-3.15 ppm, with coupling constants J_{ax} = 7.2 Hz and J_{ab} = 17.1 Hz, whereas chemical shifts of methylenic protons (H_b) of the compounds (**1c−12c**) were observed at 3.81-3.83 ppm with coupling constants in the range of J_{bx} = 12.0–12.3 Hz and J_{ab} = 16.8–17.1 Hz. However, shifts for H_x protons were observed slightly in the down field region, ranging from 5.20-5.26 ppm and having coupling constants J_{ax} = 7.2 and J_{bx} = 12.0–12.3 Hz. Furthermore, the methyl and methylene protons of alkyloxy groups adjacent to oxygen atom were observed in the range of 3.80-4.02 ppm as singlet for compound (**1c**), quartet for (**2c**) and triplets for all other compounds of the series (**3c−12c**) showing the presence of alkyloxy side chain in target compounds. The aromatic protons appeared downfield between 6.77 and 7.75 ppm with expected multiplicity. In ^{13}C-NMR, the methylenic carbons of alkyloxy side chain directly attached to oxygen atom (ArO−CH_2-) were observed in the range of 64-69 ppm. The characteristic signals for methylene (−CH_2−) and methine carbon (−CH−) of the five membered pyrazoline rings were observed in the range of 43.62-43.64 ppm and 55-64 ppm, respectively which further support the conclusions drawn from FT-IR and ^{1}H NMR spectroscopy. All the aromatic carbons of compounds (**1c−12c**) were found at their respective places in the aromatic region, ranging from 113-158 ppm.

The formation of proposed structures of compounds (**1c-12c**) discussed in IR, ^{1}H & ^{13}C NMR spectroscopy were further confirmed by their EIMS analysis. The molecular ion peaks ($M^{+\bullet}$) for all the compounds were observed at their respective molecular masses. Furthermore, fragmentation pattern was also in good agreement with already reported 2-pyrazoline

derivatives.[52] The most stable fragment or base peak in compounds (**1c-12c**) was the molecular ion peak. The molecular mass data of all the synthesized 1,3,5-triarylpyrazolines (**1c-12c**) are provided in the experimental part. However, a representative compound (1**2c**) with proposed mass fragmentation pattern, where molecular ion peak and most stable fragment, $[C_{33}H_{42}N_2O]^{\cdot+}$, appeared at m/z 482 (Calcd. 482.33) is shown in Fig. S1 (Supporting Information).

3.3. Solid state self-assembly

To study the packing properties of 1,3,5-triarylpyrazolines (**1c-12c**), good quality single crystals of compound **2c** suitable for X-ray analysis were grown in ethanol solvent by slow evaporation at ambient conditions and were found to have a monoclinic crystal lattice with the $P2_1/c$ space group. The ORTEP representation and atom labeling of the compound **2c** is shown in Fig. 2. The two phenyl rings present on 1 and 3 position of central pyrazoline moiety are nearly in the same plane as that of pyrazoline, making a dihedral angle of 2.97° (N_1-N_2-C_{18}-C_{19}) and 0.88° (N_1-C_{11}-C_{12}-C_{13}), respectively. The aryl ring with alkyloxy side chain substituted on asymmetric carbon of pyrazoline moiety is oriented in such a way that one of its hydrogen is located on almost top of the pyrazoline moiety with 2.803 Å distance from the centre of pyrazoline ring. The angles around asymmetric carbon are 112.76° (C_1-C_9-C_{10}), 113.76° (C_1-C_9-N_2), 109.51° (C_1-C_9-H_9), 109.53° (N_2-C_9-H_9). In the pyrazoline moiety, the C-N, C=N and N-N bond lengths are 1.472 Å, 1.285 Å and 1.385 Å, respectively.

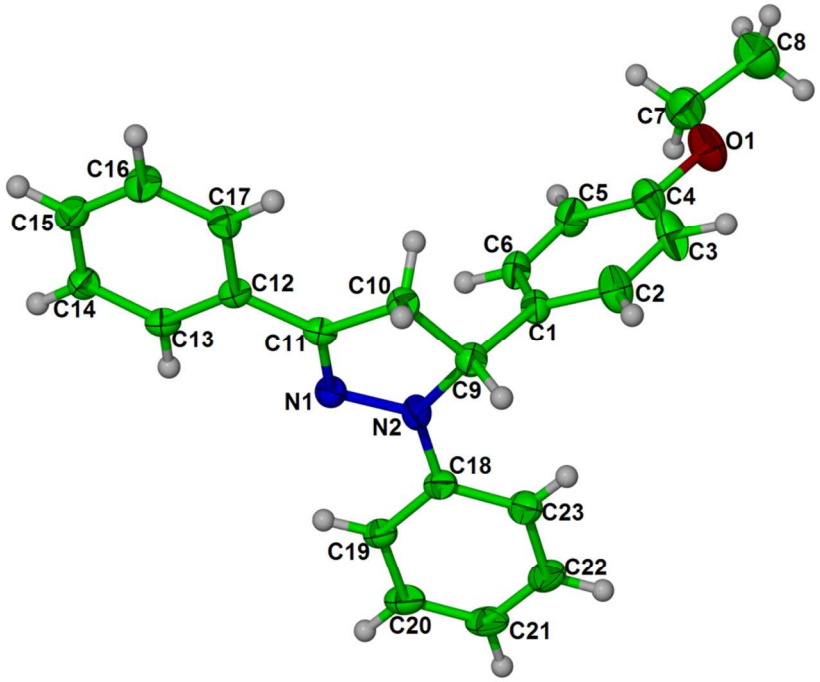


Fig. 2. ORTEP diagram and atom labeling of **2c**

The most important feature of this compound is the formation of 1D-supramolecular zigzag chains in the solid state packing, stabilized merely by CH-π interactions[53] (Fig. 3). It is worth mentioning here that compounds having only one type of non-covalent interactions in their packing are either very rare or not reported at all in the literature. As shown in Fig. 3, the molecules of **2c** are connected with each other by means of CH-π interactions [C(20)-H(20)…C(17) 2.789 Å, C(20)-H(20)…C(12) 2.883 Å] where C-H of aryl substituted at N_2 of pyrazoline moiety of one molecule is interacting with π-system of aryl ring present at 3-position of pyrazoline moiety of the other molecule, forming 1D-supramolecular zigzag chains-like structure. Individual chains of this assembly are also connected with each other with the help of CH-π interactions [C(9)-H(9)…C(19) 2.630 Å, C(9)-H(9)…C(20) 2.739 Å], but at this time hydrogen at asymmetric carbon of pyrazoline moiety is interacting as donor with the π-system of aryl ring substituted at N_2 of pyrazoline moiety of neighboring chain. The solid state assembly of this molecule presents a perfect example of CH-π interactions-driven self-assemblies. Therefore, compound **2c** can be used as a model to explore molecular self-assemblies and materials containing exceptional properties driven only by CH-π interactions. Various computational methods can be of great help to study the detailed nature of this type of weak interactions prior to any design, using compound **2c** as a model.

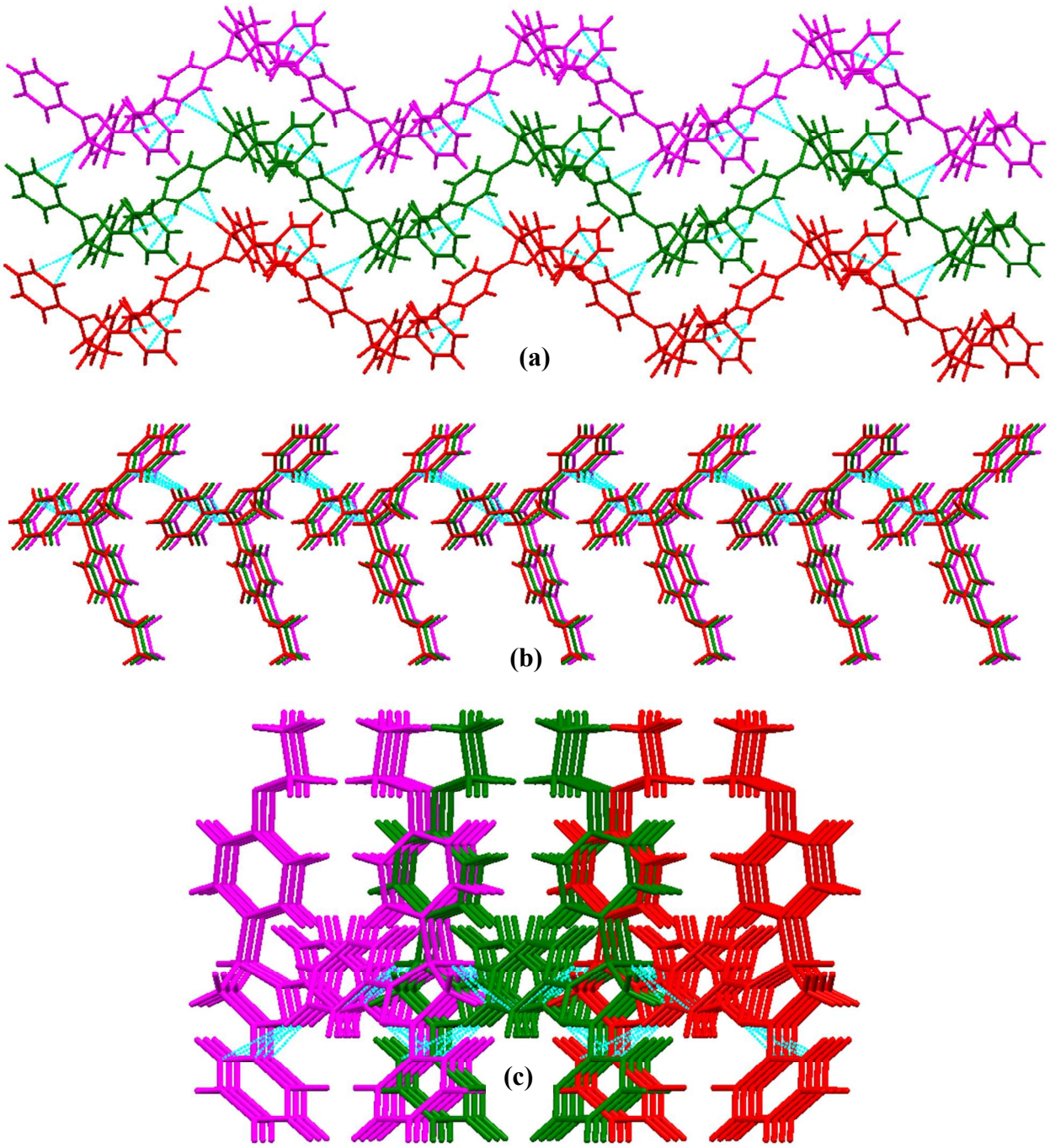


Fig. 3. 1D-supramolecular zigzag chains of **2c**, solely mediated by CH-π interactions [C(20)-H(20)…C(17) 2.789 Å, C(20)-H(20)…C(12) 2.883 Å, C(9)-H(9)…C(19) 2.630 Å, C(9)-H(9)…C(20) 2.739 Å] viewed along (a) a-axis (b) b-axis (c) c-axis

3.4. DNA binding studies

The UV-Visible absorption spectroscopy was used to study the interactions of synthesized compounds (**1c-12c**) with DNA which is a valuable technique for the determination of strength

and binding mode of drug-DNA interactions. In this technique, the variations in absorption intensity and wavelength are measured for the evaluation of binding parameters that reflect the corresponding changes in DNA conformation and structures after the drug binds to the DNA. In compounds (**1c-12c**), aryl groups at 1- and 3-position of pyrazoline ring form the conjugated backbone and are mainly responsible for absorption of photons, whereas the aryl group present at 5-position of the pyrazoline is not a part of that conjugated system. Therefore, the substitution of alkyloxy group at aryl group (not part of the conjugated backbone) can be expected to have some impact on the physico-chemical properties.

Compounds **1c**, **3c**, **5c**, **6c**, **9c** and **12c** were selected for DNA binding studies. In the electronic spectrum of all the tested compounds, an intense band at 362-365 nm was observed which is attributed to transitions between π-π* energy levels. An increase in absorption intensity i-e hyperchromism (29% after 5 μM, 43% after 10 μM, 53% after 15 μM, 63% after 20 μM and 65% after 25 μM addition of DNA) with no shift in λ_{max} was noticed by incremental addition of DNA for all the tested compounds (Fig. 4). Such a spectral characteristic is indicative of groove binding, which ultimately leads to intercalation, as the dominant mode of interaction. Hyperchromism results from denaturing (unwinding) of DNA double helix structure whereas the contraction of DNA in the helix axis, as well as from the change in conformation in DNA leads to hypochromism (decrease in absorption intensity). The DNA binding affinity of 1,3,5-triaryl 2-pyrazolines was quantified according to the Benesi–Hildebrand equation.[54]

$$\frac{\boldsymbol{A_\circ}}{\boldsymbol{A - A_\circ}} = \frac{\boldsymbol{\varepsilon_G}}{\boldsymbol{\varepsilon_{H-G} - \varepsilon_G}} + \frac{\boldsymbol{\varepsilon_G}}{\boldsymbol{\varepsilon_{H-G} - \varepsilon_G}} \cdot \frac{\mathbf{1}}{\boldsymbol{K\,[DNA]}}$$

where K is the association/binding constant, where A_0 and A are the absorbances of the free and DNA bound compound. ε_G and ε_{H-G} are the molar extinction coefficients of compound and its DNA adduct respectively. The association constants were obtained from the intercept-to-slope ratios of $A_0/(A - A_0)$ vs 1/[DNA] plots. The Gibb's free energy (G) was determined from the equation $\Delta G = -RT \ln K$ where R is general gas constant (8.314 $JK^{-1}mol^{-1}$) and T is the temperature (298 K).

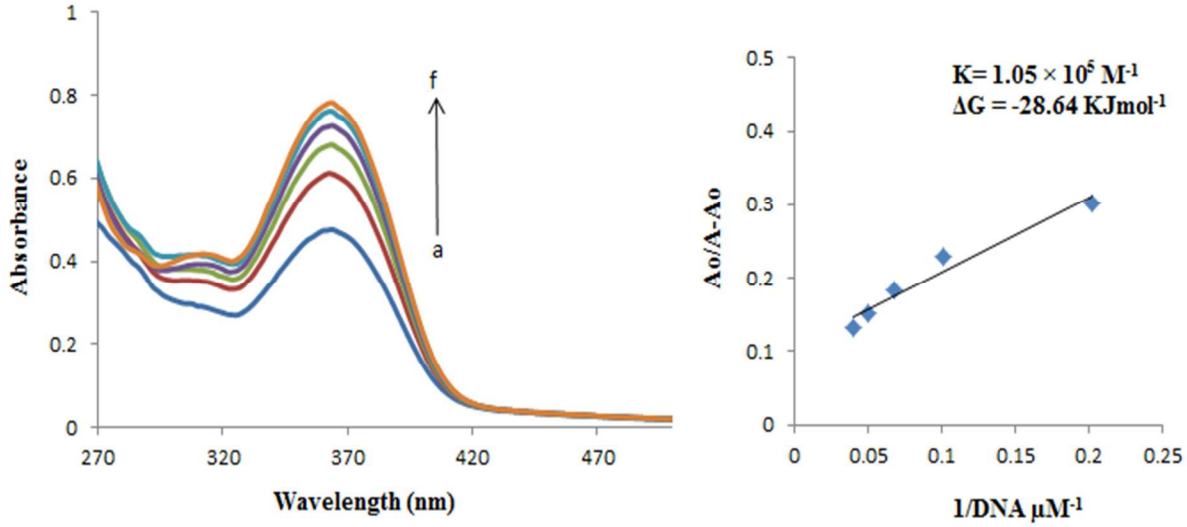


Fig. 4. Absorption spectrum of **5c** (15 µM) in absence (a) and in presence 5 µM (b) 10 µM (c) 15 µM (d) 20 µM (e) 25 µM, of DNA (f). The arrow direction indicates the increasing DNA concentration.

The binding constants and Gibb's free energies for compounds **1c**, **3c**, **5c**, **6c**, **9c** and **12c** are shown in Table 2. As it is clear from the binding constant values, all the tested compounds showed strong binding with the DNA. An increase in binding strength was observed with the increase in the alkyloxy chain length, which may be attributed to its different conformational arrangements leading to the best fit conformation of 1,3,5-triaryl moiety in the minor groove of DNA. Among the tested compounds, **12c** was found to be most active compound of the series with binding constant value of 1.17×10^6 M^{-1}. Furthermore, the interaction of the compounds with DNA is a spontaneous process as indicated by the negative values of ΔG. From the results of the present study, it is quite clear that the increase in the length of alkyloxy group greatly affect the DNA binding despite having the same skeleton. Apart from this strong binding, the compounds of the present series having good lipophilic character are ideal candidates for *in vitro* anticancer studies against different cell lines.

Table 2. The binding constants and Gibbs free energies of 1,3,5-triarylpyrazolines-DNA complexes

Compd. No.	R	Binding constant K (M^{-1})	Binding energy ΔG ($KJmol^{-1}$)
1c	CH_3	3.08×10^5	-31.31
3c	C_3H_7	2.63×10^5	-30.91
5c	C_5H_{11}	1.05×10^5	-28.64
6c	C_6H_{13}	7.70×10^5	-33.58
9c	C_9H_{19}	1.15×10^6	-34.57
12c	$C_{12}H_{25}$	1.17×10^6	-35.00

4. Conclusions

In summary, we have synthesized a series of new homologous 1,3,5-triaryl-2-pyrazolines (**1c-12c**) by the reaction of chalcones (**1a-12a**) with phenyl hydrazine (**1b**) in 80-87% yields and characterized by their physical and spectral (IR, ^{1}H & ^{13}C NMR, GC-MS) data. Single crystal X-ray diffraction analysis of compound **2c** showed 1D-supramolecular zigzag chains-like molecular self-assembly in the solid state. The specialty of this self-assembled structure is the presence of only CH-π interactions, which not only involved in the formation of chains but also in the connection of different chains. As molecular self-assemblies stabilized solely by one type of weak interactions are rare, therefore, the compound **2c** may serve as the model to get complete understanding of this non-covalent interaction. Furthermore, the interaction of six selected compounds with DNA was studied by UV-visible spectroscopy to get preliminary information of their anticancer potential and to see the role of alkyloxy chain length on DNA binding property. All the tested compounds showed strong binding, with compound **12c** was found to be the most active compound of the series. The difference in binding of compounds having same skeleton but

different alkyloxy chains is attributed to their different conformational arrangements resulting in the best fit conformation of 1,3,5-triaryl moiety in the minor groove of DNA.

Acknowledgements

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