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Synthesis of dibenzo[*d*,*f*]diazepinones and alkenylindolinones through ring transformation of 2*H*-pyran-2-one-3-carbonitriles by indolin-2-ones

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ABSTRACT

First ever synthesis of functionalized 5,7-dihydro-6*H*-dibenzo[*d*,*f*][1,3]diazepin-6-ones (**6**, **9**) has been developed through base induced ring transformation of 2*H*-pyran-2-one-3-carbonitriles with indolin-2-ones. A protocol for alkenylating indolin-2-ones by 2*H*-pyran-2-one-3-carbonitriles has also been developed to obtain 3-alkenylindolin-2-ones (**11**). The nature and behaviour of intermolecular interactions of these compounds are studied by single crystal-X-ray analysis and quantum chemical calculations.

1. Introduction

Many seven membered cyclic compounds have been found to be biologically active.[1] In particular, diazepine analogues display diverse pharmacological activities, such as anxiolytic,[2] hypnotic,[2] HIV protease inhibitors[3] and as cardiovascular.[4] An extensive literature survey revealed that the chemistry and pharmacology of 5*H*-dibenzo[*d*,*f*][1,3]diazepine (**I**) is not explored extensively[5] except functionalized at position 6 by alkyl,[6–9] aryl,[10–12] and alkoxy[12] substituents. Besides these, compounds with keto[13] and thio functional groups (**IIa**, **b**) have also been synthesized and reported,[14] Fig. 1.

The majority of procedures reported for the synthesis of 5*H*-dibenzo[*d*,*f*][1,3]diazepine ring system involve the reaction of biphenyl-2,2′-diamine with 1,1′-dielectrophilic reagents, such as cyanogen bromide,[15a] benzamidine hydrochloride,[15b,c] benzonitrile[15d] or methyl arylcarbimidothioates.[15e] Recently, a new procedure for the construction of this ring system has been developed[16] from the reaction of 2-anilino-2-[oxido(phenyl)imino]-*N*-pyridin-2-ylacetamides with biphenyl-2,2′-diamine. However, this procedure is also not devoid of biphenyl-2,2′-diamine as a precursor.

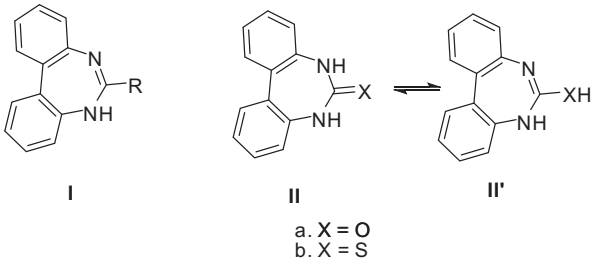

Fig. 1. Dibenzo[*d*,*f*][1,3]diazepines.

The limitation and dearth of synthetic procedures for the construction of 5,7-dihydro-6*H*-dibenzo[*d*,*f*][1,3]diazepin-6-ones and respective thiones, belie their importance as useful pharmaceuticals and intermediates for making more functionalized systems. Earlier, 5,7-dihydro-6*H*-dibenzo[*d*,*f*][1,3]diazepin-6-one (**II**) was prepared by heating biphenyl-2,2′-diamine with urea. Under the proper equilibrium conditions the exocyclic ketone may tautomerize to the endocyclic 5*H*-dibenzo[*d*,*f*][1,3]diazepin-6-ol (**II′**).[17] Recently, transition metal catalyzed biscarbonylation of

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2,2-dinitro-1,1-biphenyl with carbon monoxide, resulted in ring closure to form 5,7-dihydro-6*H*-dibenzo[*d*,*f*][1,3]diazepin-6-one in moderate yields.[18,19] Exocyclic [1,3]diazepin-6-thione (**IIb**) was first prepared in low yield by Le Fevre in 1929 by treating biphenyl-2,2′-diamine with carbon disulfide in refluxing ethanol.[14] However, a modification in the solvent system from ethanol to pyridine increased the yield up to 72%. Recently, use of thiophosgene as a reagent has also been reported[20] for the synthesis of [1,3]diazepin-6-thione.

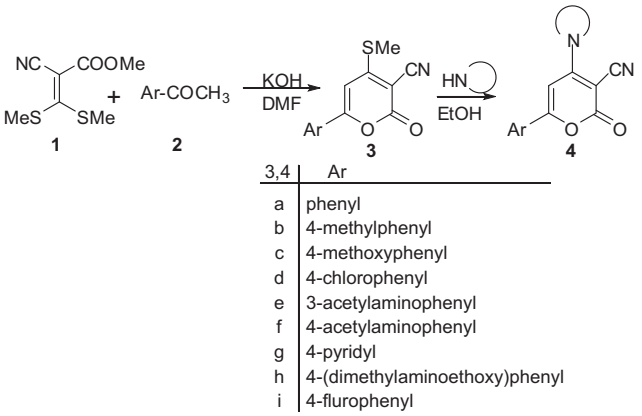
3-Alkenylindolin-2-ones are an important class of heterocycles, widely present in nature and known for their anticancer,[21] antibacterial,[22] antifungal,[23] antiviral,[23a] antipyretic,[24] anti-inflammatory[25] and analgesic[25] properties. Though there are numerous routes for the synthesis of this class of compounds in which condensation of indolin-2-one with aldehyde is prominent. Condensation of isatin with reactive methylene compounds, such as malononitrile, ethyl cyanoacetate etc. is another option to synthesize alkenylindolin-2-ones. Over the past 5–10 years, numerous metal catalyzed syntheses[26] of 3-alkenylindolin-2-ones have emerged.

2. Results and discussion

2.1. Chemistry

We have developed a new route, which does not require biphenyl-2,2′-diamine as a precursor but also provides an opportunity to functionalize not only the 1,3-diazapine ring but also other aromatic rings present in the molecular scaffold. The synthetic methodology for the construction of 5,7-dihydro-6*H*-dibenzo[*d*,*f*][1,3]diazepin-6-one is based on base induced ring transformation of suitably functionalized 2*H*-pyran-2-one-3-carbonitriles by indolin-2-ones. An intensive literature survey revealed that ring transformation of 2*H*-pyan-2-one-3-carbonitriles by indolin-2-one is the first report and has not been explored so far.

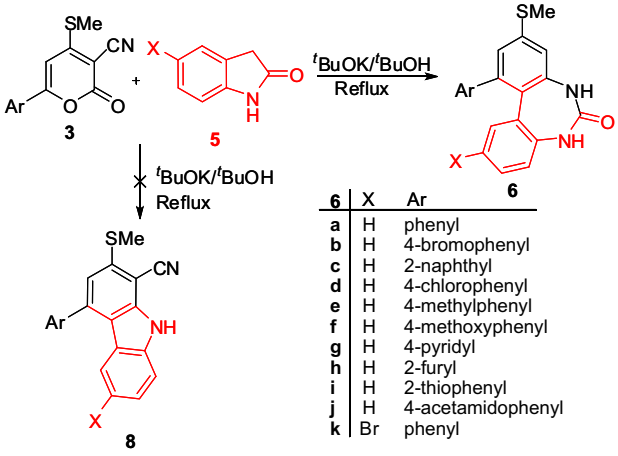
6-Aryl-4-methylthio-2*H*-pyran-2-one-3-carbonitriles (**3**) as the precursors for the synthesis of highly functionalized 3-methylthiodibenzo[*d*,*f*][1,3]diazepin-6-ones (**6**) were obtained[27] from the reaction of methyl 2-cyano-3,3-dimethylthioacrylate[28] (**1**) and aryl methyl ketone (**2**) using powdered KOH as a base in DMF at room temperature. 6-aryl-4-*sec*-amino-2*H*-pyran-2-one-3-carbonitriles (**4**), obtained from amination of **3** with *sec*-amine in boiling ethanol, were used further as precursors for the synthesis of 1-aryl-3-*sec*-aminodibenzo[*d*,*f*][1,3]diazepin-6-ones (**9**) (Scheme 1).[29]



3,4	Ar
a	phenyl
b	4-methylphenyl
c	4-methoxyphenyl
d	4-chlorophenyl
e	3-acetylaminophenyl
f	4-acetylaminophenyl
g	4-pyridyl
h	4-(dimethylaminoethoxy)phenyl
i	4-flurophenyl

Scheme 1. Synthesis of substituted-2*H*-pyran-2-ones.

Reaction of 6-aryl-4-methylthio-2*H*-pyran-2-one-3-carbonitiles (**3**) with indolin-2-one (**5**) was carried out in *tert*-butanol at reflux temperature using ^{t}BuOK as a base proceeded smoothly and was complete within 6 h. After column chromatography of the crude product on silica gel using hexane/chloroform (60:40) as eluent, 1-aryl-3-(methylthio)-5*H*-dibenzo[*d*,*f*][1,3]diazepin-6(7*H*)-ones (**6**) were obtained in 38–58% yields in lieu of an expected carbazole derivate (**8**) (Scheme 2). The structure of the isolated compound



6	X	Ar
a	H	phenyl
b	H	4-bromophenyl
c	H	2-naphthyl
d	H	4-chlorophenyl
e	H	4-methylphenyl
f	H	4-methoxyphenyl
g	H	4-pyridyl
h	H	2-furyl
i	H	2-thiophenyl
j	H	4-acetamidophenyl
k	Br	phenyl

Scheme 2. Synthesis of 1-aryl-3-methylthio-5,7-dihydro-6*H*-dibenzo[*d*,*f*][1,3]diazepin-6-one (**6**).

was corroborated by spectral analyses and single crystal X-ray diffraction, (Fig. 2). Optimization of the reaction condition, i.e., reduction in reflux period from 6 to 3 h, resulted poor yield (12%) of desired compound with recovery of reactants while an increase in reflux period from 6 to 10 h did not improve the yields. However, best yields of **6** were achieved when reaction was refluxed for 6 h.

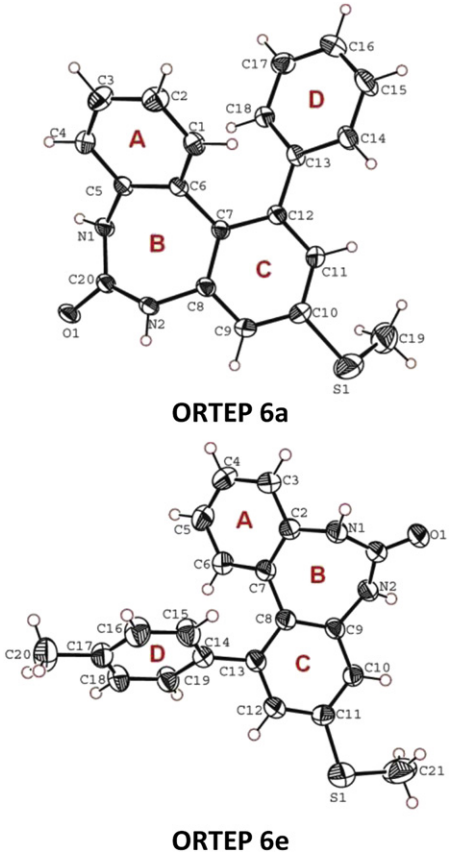
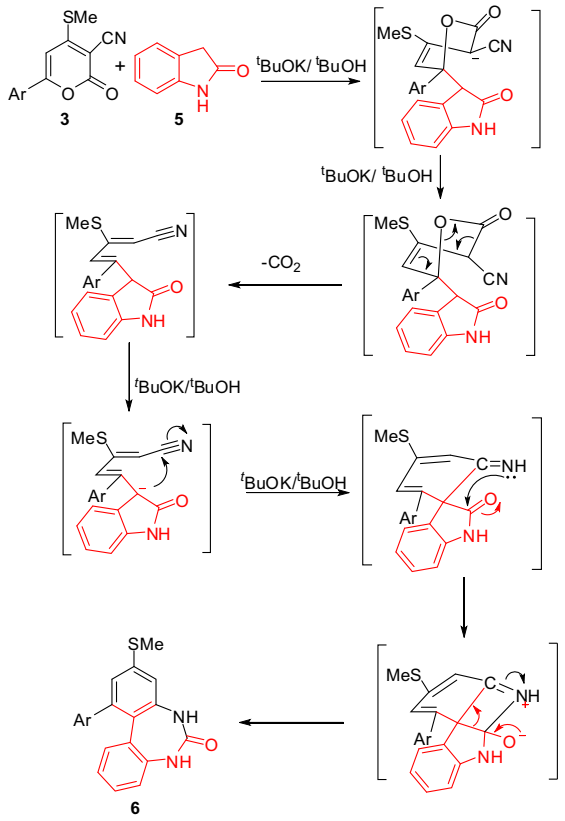


Fig. 2. ORTEP diagrams of **6a** and **6e** at 30% probability with atom numbering scheme. The solvent molecules are removed for clarity.

A plausible mechanism for the formation of 1-aryl-3-methylthio-5,7-dihydro-6*H*-dibenzo[*d*,*f*][1,3]diazepin-6-one is illustrated in Scheme 3. The position 6 of the 2-pyranone is highly vulnerable to nucleophilic attack due to extended conjugation to

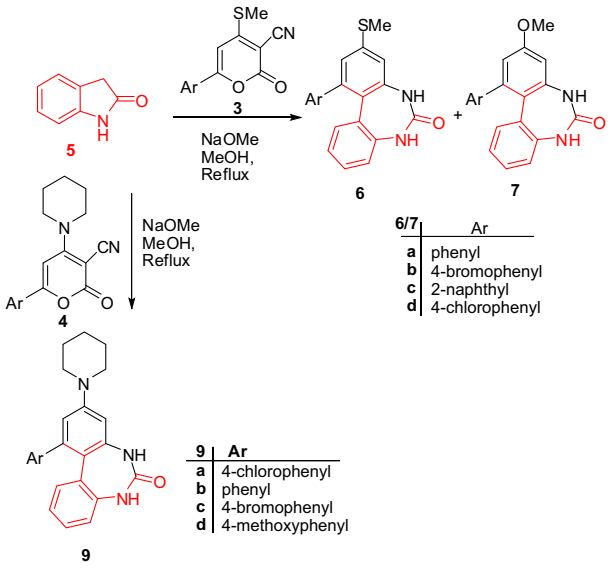


Scheme 3. A plausible mechanism for the formation of products 1-aryl-5,7-dihydro-6*H*-dibenzo[*d*,*f*][1,3]diazepin-6-ones (**6**).

C=O at position 2 and also to the CN, an electron withdrawing substituent present at position 3. Possibly, the reaction is initiated with formation of the Michael adduct by attack of carbanion, formed from indolin-2-one in the presence of base at position 6 of the pyran-2-one ring with liberation of carbon dioxide followed by ring closure and ring expansion to yield 1-aryl-3-(methylthio)-5*H*-dibenzo[*d*,*f*][1,3]diazepin-6(7*H*)-one (**6**), Scheme 3.

On the other hand, heating the mixture of **3** with **5** in methanol as a solvent and sodium methoxide as a base at reflux temperature over 10 h afforded a mixture of 1-aryl-3-methylthio-5,7-dihydro-6*H*-dibenzo[*d*,*f*][1,3]diazepin-6-one (**6**) and 1-aryl-3-methoxy-5,7-dihydro-6*H*-dibenzo[*d*,*f*][1,3]diazepin-6-one (**7**) in 46–66% yields after column chromatography of the crude product on silica gel using hexane/chloroform (60:40) as eluent (Scheme 4). The ratio of both the compounds in the mixture was ascertained by ^{1}H NMR. With the exception of few cases, the methoxy analogues (**7**) were mostly obtained in 5–11% yields. We also tried to convert **6** to **7** by increasing the amount of base and reflux period from 5 to 25 h but complete conversion did not occur. Reduction in reaction time led to isolation of unreacted starting material.

The formation of 1-phenyl-3-methoxy-5,7-dihydro-6*H*-dibenzo[*d*,*f*][1,3]diazepin-6-one (**7**) along with compound **6** is attributed to the exchange of –SMe by –OMe in **3** to form 6-aryl-4-methoxy-2*H*-pyran-2-one-3-carbonitriles under applied reaction conditions. The transformation of **3** to 6-aryl-4-methoxy-2*H*-pyran-2-one-3-carbonitriles is reported earlier by Tominaga et al.[27c] in the presence of sodium methoxide in methanol at reflux temperature. Thus, the ring transformation of 6-aryl-4-methylthio-2*H*-pyran-2-one-3-



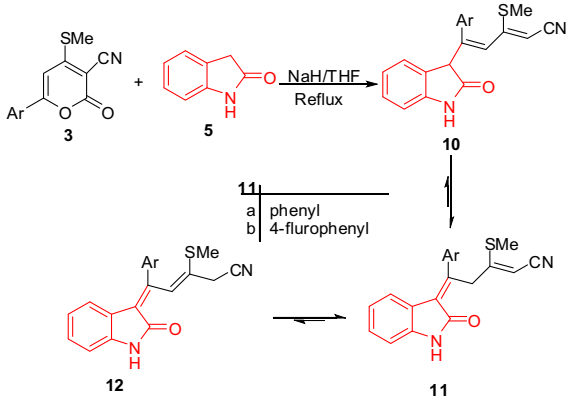
Scheme 4. Synthesis of mixture of 1-aryl-3-methylthio/*sec*-amino-5,7-dihydro-6*H*-dibenzo[*d*,*f*][1,3]diazepin-6-ones (**6**, **9**) and 1-aryl-3-methoxy-5,7-dihydro-6*H*-dibenzo[*d*,*f*][1,3]diazepin-6-ones (**7**).

carbonitriles (**3**) by indolin-2-one (**5**) in freshly prepared NaOMe at reflux temperature is obvious to deliver **7** along with **6**.

Interestingly, utilization of 6-aryl-4-*sec*-amino-2*H*-pyran-2-one-3-carbonitriles (**4**) containing the secondary amine group having poorer leaving group character under similar conditions afforded exclusively 1-aryl-3-*sec*-amino-5,7-dihydro-6*H*-dibenzo[*d*,*f*][1,3]diazapin-6-ones (**9**) (Scheme 4).

In search of an efficient and novel route to synthesize 3-alkenylindolin-2-ones, a reaction of 6-aryl-4-methylthio-2*H*-pyran-2-one-3-carbonitriles (**3**) and indolin-2-one (**5**) was performed in NaH/THF at reflux temperature, which gave an entirely different product, other than 1-aryl-5,7-dihydro-6*H*-dibenzo[*d*,*f*][1,3]diazepin-6-ones (**6**) and carbazole derivatives (**8**). Finally, the compounds isolated were characterized as 3-alkenylindolin-2-one (**11**) by spectroscopic and X-ray diffraction studies.

Based on the suggested mechanism depicted in Scheme 5, products **11** seem to have been formed from the initially generated



Scheme 5. Synthesis of 3-alkenyindolin-2-ones (**11**).

intermediate **10**. The structural ambiguity of tautomers **10**, **11** and **12** was resolved by single crystal X-ray diffraction analysis (vide infra) and ultimately the structure was assigned as **11** (Fig. 3).

The reaction is initiated by attack of carbanion generated from indolin-2-one (**5**) at C-6 of the pyran-2-one forming Michael

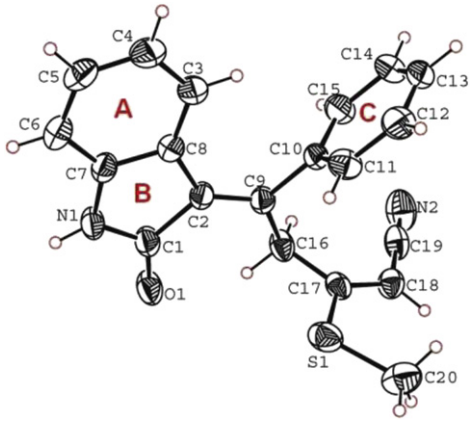


Fig. 3. ORTEP diagram of **11a** at 30% probability with atom numbering scheme.

adduct followed by elimination of carbon dioxide to form 3-alkenylindolin-2-one (**11**) without undergoing further cyclization to yield **6**. This discrepancy is possibly due to a large difference in polarity of both the solvents as dielectric constant of THF is 7.48 while for methanol is 32.7, Scheme 5.

2.2. Structural description

The molecular view (ORTEP) for the three compounds **6a**, **6e** and **11a** with atom numbering scheme is presented in Figs. 2 and 3. In the case of **6a**, the 1,3-diazepin-2-one ring B is puckered and has neither adopted the boat-chair nor crown conformation. This is due to the fusion of aromatic rings with the 1,3-diazepine ring, i.e., the phenyl ring A and methylthiophenyl ring C. The dihedral angle between the rings A and C is 43.80°; rings C and D is 47.42° while between A and D is 49.98°. In the case of **6e**, the 1,3-diazepin-2-one ring B is puckered and has adopted neither boat-chair nor crown conformation. The dihedral angle between rings A and C is 42.73°; C and D is 56.99° and A and D is 59.87°. In **11a**, rings A and B are almost coplanar with respect to each other displaying a dihedral angle 2.72°. However, the dihedral angle between the rings A and C is 74.18°. The bond lengths C2–C9, C9–C10, C9–C16, C16–C17 and C17–C18 have dimensions 1.339(3), 1.496(3), 1.506(3), 1.500(3) and 1.337(3) Å, respectively. The angles <C2–C9–C10, <C2–C9–C16, <C9–C16–C17 and <C16–C17–C18 have magnitudes of 122.6(2)°, 122.8(2)°, 112.79(18)° and 122.6(2), respectively.

The supramolecular aggregations in **6a**, **6e** and **11a** are stabilized by a pair of weak N–H···O interactions (Figs. 4–6) that led to the formation of centrosymmetric dimers. In the case of **6a** the H···O interaction distance is of 2.105 Å and the <N–H···O of magnitude 176.44° is almost linear. In the case of **6e**, H···O interaction is of distance 2.243 Å and the <N–H···O is 166.45°. For **11a**, the

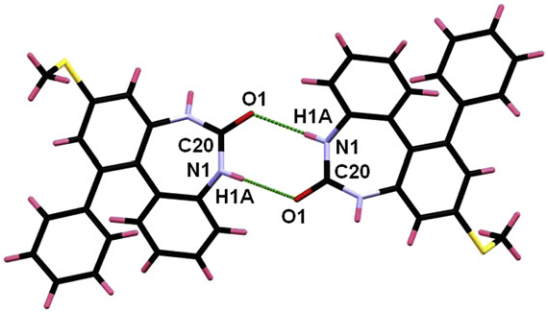


Fig. 4. Centrosymmetric dimer of **6a** bound by pair of weak N–H···O intermolecular interactions.

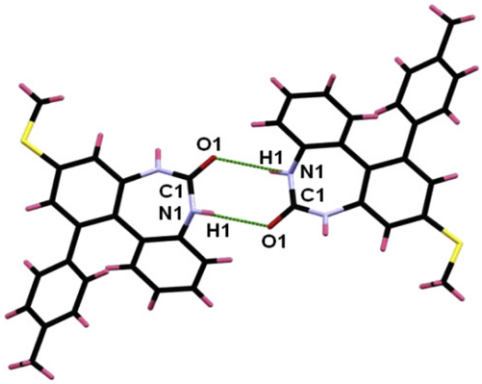


Fig. 5. Centrosymmetric dimer of **6e** bound by pair of weak N–H···O intermolecular interactions (symm. op. 1−*x*,−*y*,1−*z*).

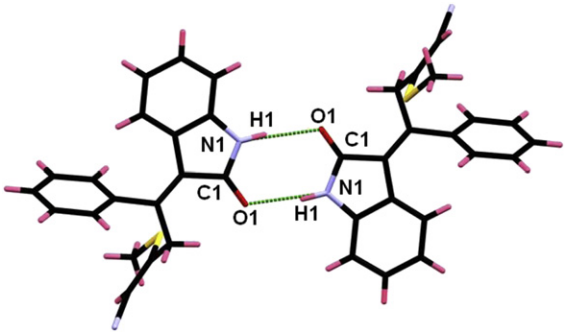


Fig. 6. Centrosymmetric dimer of **11a** bound by pair of weak N–H···O intermolecular interactions (symm. op. 1−*x*,−*y*,−*z*).

centrosymmetric dimer bound by N–H···O interactions have H···O interaction distance of 2.005 Å and the <N–H···O is 171.13°.

The crystal structures of the compounds **6a**, **6e** and **11a** as discussed above are good examples of the molecular interactions that lead to interesting supramolecular aggregates in the solid state. In order to analyze the various interactions that lead to the crystal structure, interaction energies and electrostatic potentials have been calculated for dimer fragments (Fig. 7). The analysis of the interaction energy in the crystal structures of **6a**, **6e** and **11a** by means of dimer

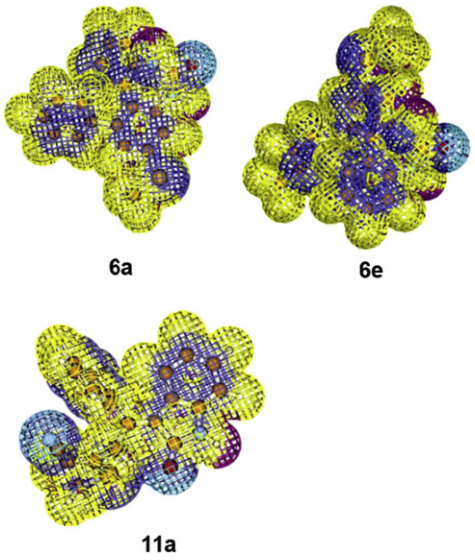


Fig. 7. Electrostatic potential surfaces for **6a**, **6e** and **11a**. The blue/yellow colours indicate the low and high charge density.

unit bound by N–H···O interactions at the DFT level of theory yields the interaction energies −14.51, −14.62 and −13.56 kcal/mol, respectively.

To confirm further the presence of N–H···O interaction, bond critical points (bcp) were calculated for all the three dimers by using the Atoms in Molecules Theory.[30] The bond critical points observed between the H and O atoms confirm the presence of N–H···O between two molecules of **6a**, **6e** and **11a** (Fig. 8). The value of electron density (ρ); Laplacian ($\nabla^2_{\rho_{bcp}}$); bond ellipticity (ε) and total energy density (H) at the bond critical point for N–H···O interactions in **6a**, **6e** and **11a** are presented in Table 1. From table it is evident that the electron density for all the three compounds at bond critical point (ρ_{bcp}) are less than +0.10 au, which indicates a closed shell hydrogen bonding interactions. Additionally, the Laplacian of the electron density $\nabla^2_{\rho_{bcp}}$ in all the three cases are greater than zero, which indicates the depletion of electron density in the region of contact between the H···O atoms. The bond ellipticity (ε) measures the extent to which the density is preferentially accumulated in a given plane containing the bond path. The ε values for all the three compounds indicate that these N–H···O interactions are not cylindrically symmetrical in nature.

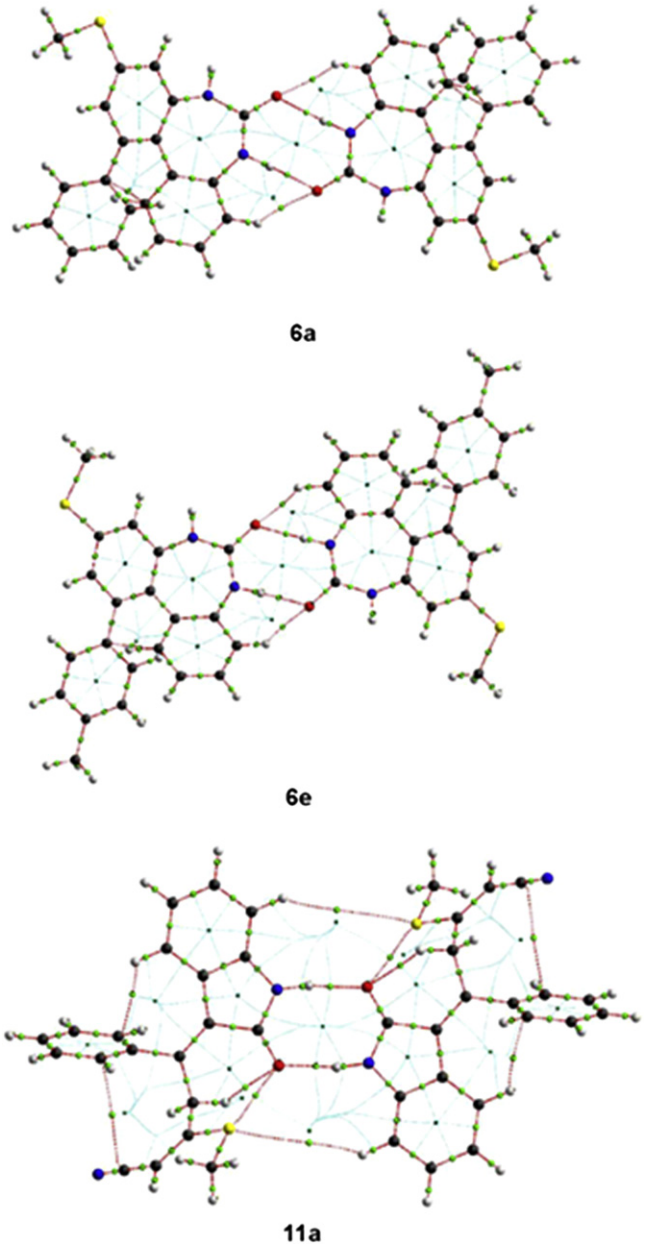


Fig. 8. Molecular graphs for the centrosymmetric dimers of **6a**, **6e** and **11a** by AIM calculations using B3LYP/6-31G** level of theory.

Table 1
Selected topographical features of N–H···O interactions computed at B3LYP/6-31G** level of theory

Compound	ρ_{bcp}	$\nabla^2_{\rho_{bcp}}$	E	H (au)
6a	+0.048570	+0.110629	+0.002298	+0.014785
6e	+0.048226	+0.110666	+0.002526	+0.014606
11a	+0.048751	+0.106262	+0.005152	+0.015339

3. Conclusions

In conclusion, we have developed a simple, efficient and economical procedure for the construction of highly functionalized 5,7-dihydro-6*H*-dibenzo[*d*,*f*][1,3]diazepin-6-ones (**6**, **9**) through unusual ring transformation of 2*H*-pyran-2-one-3-carbonitriles by indolin-2-ones without using biphenyl-2,2′-diamine as a precursor. This methodology provides an opportunity to make 5,7-dihydro-6*H*-dibenzo[*d*,*f*][1,3]diazepin-6-ones with substitution not only in 1,3-diazepine ring but also in all aromatic rings. The most important feature of this protocol is that it replaces the use of biphenyl-2,2′-diamine as a key precursor for the construction of 5,7-dihydro-6*H*-dibenzo[*d*,*f*][1,3]diazepin-6-ones.The versatility of pyran-2-one as precursor is not limited to the synthesis of functionalized 1,3-diazepines but also useful as a reagent for the alkenylation of indolin-2-ones. Thus, it opens a new avenue for an efficient synthesis of 3-alkenyindolin-2-ones. The single crystal-X-ray analysis revealed that these molecules form centrosymmetric dimers bound by N–H···O interactions. Additionally, the interaction angles were close to 180°, indicating strong interactions and this is established by quantum chemical calculations.

4. Experimental section

4.1. General

6-Aryl-2*H*-pyran-2-one-3-carbonitriles (**3** and **4**) are prepared as reported in literature.[27–29] Indolin-2-one was purchased from Sigma Aldrich. Commercially available reagents were used without further purification. ^{1}H and ^{13}C NMR spectra were recorded on a Bruker 400 MHz and 300 MHz NMR spectrophotometer. $CDCl_3$ and DMSO-d_6 were used as solvents. Chemical shifts are reported in parts per million (δ-value) from Me_4Si (δ=0 ppm for ^{1}H) or based on the middle peak of the solvent ($CDCl_3$) (δ=77.00 ppm for ^{13}C NMR) as an internal standard. Signal patterns are indicated as s, singlet; d, doublet; dd, double doublet; t, triplet; m, multiplet; bs, broad singlet; bm, broad multiplet. Coupling constant (J) is given in Hertz (Hz). Infrared (IR) spectra were recorded on a Perkin–Elmer AX-1 spectrophotometer in KBr disc and reported in wave number (cm^{-1}). 6520 Q-TOF (HRMS) Agilent spectrometer was used for mass spectral analysis from Sophisticated Analytical Instrumental Facility Lab in CDRI, Lucknow, India.

4.2. General procedure for the synthesis of 1-aryl-3-(methylthio)-5*H*-dibenzo[*d*,*f*][1,3]diazepin-6(7*H*)-ones (6)

A mixture of indolin-2-one **5** (0.146 g, 1.1 mmol), 2*H*-pyran-3-carbonitriles **3** (1.0 mmol) and potassium *tert*-butoxide (0.24 g, 2.1 mmol), in dry *tert*-butanol (10 mL) was refluxed for 6 h. Excess of solvent was removed and the viscous mass obtained was poured onto the crushed ice with vigorous stirring and thereafter neutralized with dil aq HCl. The precipitate obtained was filtered, dried

and the crude thus obtained was purified on silica gel column using hexane/chloroform (60:40) as eluent, to yield **6**.

*4.2.1. 3-(Methylthio)-1-phenyl-5H-dibenzo[d,f][1,3]diazepin-6(7H)-one (**6a**).* A mixture of indolin-2-one **5** (0.146 g, 1.1 mmol), 4-(methylthio)-2-oxo-6-phenyl-2*H*-pyran-3-carbonitrile **3a** (0.243 g, 1.0 mmol) and potassium *tert*-butoxide (0.24 g, 2.1 mmol), in dry *tert*-butanol (10 mL) was refluxed for 6 h. Excess of solvent was removed and the viscous mass obtained was poured onto the crushed ice with vigorous stirring and thereafter neutralized with dil aq HCl. The precipitate obtained was filtered, dried and the crude thus obtained was purified on silica gel column using hexane/chloroform (60:40) as eluent, to yield **6a** as a white powder, yield, 137 mg, (41%). Mp 235–236 °C. R_f (30% EtOAc/Hexane) 0.54. ν_{max} (KBr) 3246, 1695, 1560, 1360, 1219 cm^{-1}. ^1H NMR (400 MHz, DMSO-d_6): δ=2.49 (s, 3H, SCH_3), 6.45–6.55 (m, 2H, ArH), 6.90–7.16 (m, 9H, ArH), 8.70 (d, *J*=2.2 Hz, 1H, NHCO), 8.85 (d, *J*=2.2 Hz, 1H, CONH) ppm. ^{13}C NMR (100 MHz, DMSO-d_6): δ=14.4, 116.4, 121.1, 122.5, 123.2, 124.1, 126.9, 127.6, 128.2, 128.6, 129.5, 132.5, 138.7, 140.8, 141.1, 142.1, 142.6, 164.8 ppm. HRMS (ESI): calcd for $C_{20}H_{17}N_2OS$ $[MH]^+$ 333.1061; found 333.1058.

*4.2.2. 1-(4-Bromophenyl)-3-(methylthio)-5H-dibenzo[d,f][1,3]diazepin-6(7H)-one (**6b**).* It was obtained as a white solid from the reaction of indolin-2-one **5** (0.146 g, 1.1 mmol), 6-(4-bromophenyl)-4-(methylthio)-2-oxo-2*H*-pyran-3-carbonitrile **3b** (0.322 g, 1 mmol) and potassium *tert*-butoxide (0.24 g, 2.1 mmol) in dry *tert*-butanol. Yield, 180 mg, (44%). Mp >300 °C. R_f (30% EtOAc/Hexane) 0.52. ν_{max} (KBr) 3238, 3136, 1702, 1518, 1388, 1252, 1112 cm^{-1}. ^1H NMR (400 MHz, DMSO-d_6): δ=2.49 (s, 3H, SCH_3), 6.50 (d, *J*=8.0 Hz, 1H, ArH), 6.65 (t, *J*=6.8 Hz, 1H, ArH), 6.95–7.11 (m, 6H, ArH), 7.40 (d, *J*=8.0 Hz, 2H, ArH), 8.77 (s, 1H, NHCO), 8.92 (s, 1H, CONH) ppm. ^{13}C NMR (100 MHz, DMSO-d_6): δ=14.4, 116.6, 120.2, 121.2, 122.7, 123.0, 124.1, 127.8, 128.2, 131.2, 131.7, 132.6, 138.9, 140.4, 140.8, 140.9, 143.2, 164.7 ppm. HRMS (ESI): calcd for $C_{20}H_{16}BrN_2OS$ $[MH]^+$ 411.0167; found 411.0165.

*4.2.3. 3-(Methylthio)-1-(naphthalen-2-yl)-5H-dibenzo[d,f][1,3]diazepin-6(7H)-one (**6c**).* It was prepared from the reaction of indolin-2-one **5** (0.146 g, 1.1 mmol), 4-(methylthio)-6-(naphthalen-2-yl)-2-oxo-2*H*-pyran-3-carbonitrile **3c** (0.293 g, 1 mmol) and potassium *tert*-butoxide (0.24 g, 2.1 mmol) in *tert*-butanol as a white amorphous solid. Yield, 183 mg, (48%). Mp 246–248 °C. R_f (30% EtOAc/Hexane) 0.42. ν_{max} (KBr) 3235, 3130, 1701, 1557, 1390, 1236, 1129 cm^{-1}. ^1H NMR (400 MHz, DMSO-d_6): δ=2.45 (s, 3H, SCH_3), 6.45–6.52 (m, 2H, ArH), 7.00–7.07 (m, 5H, ArH), 7.43 (t, *J*=4.0 Hz, 2H, ArH), 7.61 (m, 1H, ArH), 7.77 (d, *J*=6.0 Hz, 3H, ArH), 8.76 (s, 1H, NHCO), 8.92 (s, 1H, CONH) ppm. ^{13}C NMR (100 MHz, DMSO-d_6): δ=14.5, 116.6, 121.08, 122.6, 123.6, 124.1, 126.2, 127.0, 127.4, 127.7, 128.0, 128.1, 131.7, 132.5, 132.8, 138.8, 141.0, 142.1, 143.2, 164.8; HRMS (ESI): calcd for $C_{24}H_{19}N_2OS$ $[MH]^+$ 383.1218; found 383.1223.

*4.2.4. 1-(4-Chlorophenyl)-3-(methylthio)-5H-dibenzo[d,f][1,3]diazepin-6(7H)-one (**6d**).* It was isolated from the reaction of indolin-2-one **5** (0.146 g, 1.1 mmol), 6-(4-chlorophenyl)-4-(methylthio)-2-oxo-2*H*-pyran-3-carbonitrile **3d** (0.278 g, 1 mmol) and potassium *tert*-butoxide (0.24 g, 2.1 mmol) in dry *tert*-butanol as an amorphous powder. Yield, 154 mg, (42%). Mp 288–290 °C. R_f (30% EtOAc/Hexane) 0.51. ν_{max} (KBr) 3229, 3127, 1701, 1560, 1390, 1238, 1091 cm^{-1}. ^1H NMR (400 MHz, DMSO-d_6): δ=2.49 (s, 3H, CH_3), 6.49 (d, *J*=8.0 Hz, 1H, ArH), 6.65 (t, *J*=6.8 Hz, 1H, ArH), 6.95 (s, 1H, ArH), 7.07 (m, 5H, ArH), 7.26 (d, *J*=8.0 Hz, 2H, ArH), 8.77 (s, 1H, NHCO), 8.92 (s, 1H, CONH) ppm. ^{13}C NMR (100 MHz, DMSO-d_6): δ=14.4, 116.6, 121.1, 122.7, 123.0, 124.1, 127.8, 128.3, 131.3, 131.6, 132.5, 138.9, 140.0, 140.7, 140.9, 143.2, 164.7 ppm. HRMS (ESI): calcd for $C_{20}H_{16}ClN_2OS$ $[MH]^+$ 367.0671; found 367.0675.

*4.2.5. 1-(4-Methyphenyl)-3-(methylthio)-5H-dibenzo[d,f][1,3]diazepin-6(7H)-one (**6e**).* It was obtained as a white powder from the reaction of indolin-2-one **5** (0.146 g, 1.1 mmol), 4-(methylthio)-2-oxo-6-*p*-tolyl-2*H*-pyran-3-carbonitrile **3e** (0.257 g, 1 mmol) and potassium *tert*-butoxide (0.24 g, 2.1 mmol) in *tert*-butanol. Yield, 131 mg, (38%). Mp 271–273 °C. R_f (30% EtOAc/Hexane) 0.75. ν_{max} (KBr) 3231, 3125, 1701, 1557, 1390, 1236, 1113 cm^{-1}. ^1H NMR (400 MHz, DMSO-d_6): δ=2.24 (s, 3H, $ArCH_3$), 2.48 (s, 3H, SCH_3), 6.51–6.62 (m, 2H, ArH), 6.94–7.06 (m, 8H, ArH), 8.72 (s, 1H, NHCO), 8.88 (s, 1H, CONH) ppm. ^{13}C NMR (100 MHz, DMSO-d_6): δ=14.4, 20.6, 116.2, 121.0, 122.6, 123.1, 123.8, 127.5, 128.7, 128.9, 129.4, 132.5, 136.1, 138.1, 138.6, 140.7, 142.1, 143.1, 164.8 ppm. HRMS (ESI): calcd for $C_{21}H_{19}N_2OS$ $[MH]^+$ 347.1218; found 347.1214.

*4.2.6. 1-(4-Methoxyphenyl)-3-(methylthio)-5H-dibenzo[d,f][1,3]diazepin-6(7H)-one (**6f**).* It was obtained from the reaction of indolin-2-one **5** (0.146 g, 1.1 mmol), 6-(4-methoxyphenyl)-4-(methylthio)-2-oxo-2*H*-pyran-3-carbonitrile **3f** (0.273 g, 1 mmol) and potassium *tert*-butoxide (0.24 g, 2.1 mmol) in *tert*-butanol as a white powder, yield, 170 mg, (47%). Mp 236–238 °C. R_f (30% EtOAc/Hexane) 0.52. ν_{max} (KBr) 3234, 3132, 1700, 1512, 1388, 1244, 1171 cm^{-1}. ^1H NMR (400 MHz, DMSO-d_6): δ=2.49 (s, 3H, $ArOCH_3$), 3.69 (s, 3H, SCH_3), 6.54 (m, 1H, ArH), 6.63 (m, 1H, ArH), 6.77 (d, *J*=8.8 Hz, 2H, ArH), 6.91–7.05 (m, 6H, ArH), 8.70 (s, 1H, NHCO), 8.86 (s, 1H, CONH) ppm. ^{13}C NMR (100 MHz, DMSO-d_6): δ=14.4, 55.1, 113.7, 116.0, 121.1, 122.6, 123.0, 123.7, 127.5, 130.7, 132.5, 132.6, 133.3, 138.5, 140.5, 141.7, 143.1, 158.2, 164.7 ppm. HRMS (ESI): calcd for $C_{21}H_{19}N_2O_2S$ $[MH]^+$ 363.1167; found 363.1164.

*4.2.7. 3-(Methylthio)-1-(pyridin-4-yl)-5H-dibenzo[d,f][1,3]diazepin-6(7H)-one (**6g**).* It was obtained from the reaction of indolin-2-one **5** (0.146 g, 1.1 mmol), 4-(methylthio)-2-oxo-6-(pyridin-4-yl)-2*H*-pyran-3-carbonitrile **3g** (0.244 g, 1 mmol) and potassium *tert*-butoxide (0.24 g, 2.1 mmol) in *tert*-butanol, as a white powder, yield, 143 mg, (43%). Mp >300 °C. R_f (60% EtOAc/Hexane) 0.68. ν_{max} (KBr) 3213, 3140, 1695, 1591, 1497, 1377, 1228, 1120 cm^{-1}. ^1H NMR (400 MHz, DMSO-d_6): δ=2.49 (s, 3H, SCH_3), 6.45 (m, 1H, ArH), 6.61 (m, 1H, ArH), 6.97–7.07 (m, 6H, ArH), 8.36 (d, *J*=6.0 Hz, 2H, ArH), 8.78 (s, 1H, NHCO), 8.92 (s, 1H, CONH) ppm. ^{13}C NMR (100 MHz, DMSO-d_6): δ=14.4, 117.3, 121.2, 122.7, 123.0, 123.9, 124.5, 127.9, 128.1, 132.6, 139.3, 139.4, 140.9, 143.2, 148.8, 149.5, 164.6 ppm. HRMS (ESI): calcd for $C_{19}H_{16}N_3OS$ $[MH]^+$ 334.1014; found 334.1013.

*4.2.8. 1-(Furan-2-yl)-3-(methylthio)-5H-dibenzo[d,f][1,3]diazepin-6(7H)-one (**6h**).* It was isolated from the reaction of indolin-2-one **5** (0.146 g, 1.1 mmol), 6-(furan-2-yl)-4-(methylthio)-2-oxo-2*H*-pyran-3-carbonitrile **3h** (0.233 g, 1 mmol) and potassium *tert*-butoxide (0.24 g, 2.1 mmol) as white amorphous powder, yield, 187 mg, (58%). Mp 230–232 °C. R_f (30% EtOAc/Hexane) 0.49. ν_{max} (KBr) 3347, 3241, 3130, 1698, 1562, 1390, 1237, 1161 cm^{-1}. ^1H NMR (400 MHz, DMSO-d_6): δ=2.49 (s, 3H, SCH_3), 6.35 (d, *J*=2.4 Hz, 2H, ArH), 6.34–6.45 (m, 2H, ArH), 6.70–6.82 (m, 2H, ArH), 7.03–7.17 (m, 4H, ArH), 7.47 (s, 1H, ArH), 8.74 (s, 1H, NHCO), 8.89 (s, 1H, CONH) ppm. ^{13}C NMR (100 MHz, DMSO-d_6): δ=14.4, 109.5, 111.6, 116.9, 121.3, 123.0, 127.9, 128.8, 130.5, 130.7, 138.9, 140.3, 142.8, 143.2, 152.8, 164.5 ppm. HRMS (ESI): calcd for $C_{18}H_{15}N_2O_2S$ $[MH]^+$ 323.0854; found 323.0847.

*4.2.9. 3-(Methylthio)-1-(thiophen-2-yl)-5H-dibenzo[d,f][1,3]diazepin-6(7H)-one (**6i**).* It was obtained from the reaction of indolin-2-one **5** (0.146 g, 1.1 mmol), 4-(methylthio)-2-oxo-6-(thiophen-2-yl)-2*H*-pyran-3-carbonitrile **3i** (0.249 g, 1 mmol) and potassium *tert*-butoxide (0.24 g, 2.1 mmol) as a white amorphous powder,

yield, 176 mg, (52%). Mp 265–270 °C. R_f (30% EtOAc/Hexane) 0.45. ν_{max} (KBr) 3234, 3102, 1694, 1553, 1397, 1235, 1123 cm^{-1}. ^1H NMR (400 MHz, DMSO-d_6): δ=2.49 (s, 3H, SCH_3), 6.74–7.16 (m, 8H, ArH), 7.45 (m, 1H, ArH), 8.75 (s, 1H, NHCO), 8.90 (s, 1H, CONH) ppm. ^{13}C NMR (100 MHz, DMSO-d_6): δ=14.4, 105.5, 116.7, 121.1, 122.8, 123.2, 123.9, 127.2, 127.3, 128.0, 128.2, 131.8, 134.5, 138.9, 140.9, 142.8, 143.2, 164.6 ppm. HRMS (ESI): calcd for $C_{18}H_{15}N_2OS_2$ $[MH]^+$ 339.0625; found 339.0622.

*4.2.10. N-(4-(3-(Methylthio)-6-oxo-6,7-dihydro-5H-dibenzo[d,f][1,3]diazepin-1-yl)phenyl)acetamide (**6j**).* It was prepared from the reaction of indolin-2-one **5** (0.146 g, 1.1 mmol), *N*-(4-(3-cyano-4-(methylthio)-2-oxo-2*H*-pyran-6-yl)phenyl)acetamide **3j** (0.3 g, 1 mmol) and potassium *tert*-butoxide (0.24 g, 2.1 mmol) as a white amorphous solid, yield, 206 mg, (53%). Mp 287–290 °C. R_f (50% EtOAc/Hexane) 0.37. ν_{max} (KBr) 3508, 3394, 3319, 3246, 1689, 1594, 1534, 1375, 1232, 1164 cm^{-1}. ^1H NMR (400 MHz, DMSO-d_6): δ=1.96 (s, 3H, $COCH_3$), 2.46 (s, 3H, SCH_3), 6.47–6.65 (m, 3H, ArH), 6.90–7.02 (m, 5H, ArH), 7.38 (d, *J*=7.0 Hz, 2H, ArH), 8.67 (s, 1H, NHCO), 8.84 (s, 1H, CONH) ppm. HRMS (ESI): calcd for $C_{22}H_{20}N_3O_2S$ $[MH]^+$ 390.1276; found 390.1275.

*4.2.11. 11-Bromo-3-(methylthio)-1-phenyl-5H-dibenzo[d,f][1,3]diazepin-6(7H)-one (**6k**).* It was isolated from the reaction of 5-bromoindolin-2-one (0.212 g, 1 mmol), 4-(methylthio)-2-oxo-6-phenyl-2*H*-pyran-3-carbonitrile **3a** (0.243 g, 1 mmol) and potassium *tert*-butoxide (0.24 g, 2.1 mmol) as a white amorphous powder, yield,160 mg, (39%). Mp 265–270 °C. R_f (30% EtOAc/Hexane) 0.32. ν_{max} (KBr) 3399, 3238, 3125, 2923, 2850, 1705, 1591, 1556, 1373, 1231 cm^{-1}. ^1H NMR (400 MHz, DMSO-d_6): δ=2.47 (s, 3H, SCH_3), 6.56 (m, 1H, ArH), 6.96–7.03 (m, 5H, ArH), 7.22–7.25 (m, 4H, ArH), 8.83 (s, 1H, NHCO), 9.01 (s, 1H, CONH) ppm. ^{13}C NMR (100 MHz, DMSO-d_6): δ=14.3, 114.5, 116.4, 122.4, 122.8, 123.0, 127.2, 128.4, 129.6, 130.2, 130.6, 134.8, 139.7, 140.1, 140.6, 142.2, 142.9, 164.3 ppm. HRMS (ESI): calcd for $C_{20}H_{16}BrN_2OS$ $[MH]^+$ 411.0166; found 411.0165.

*4.2.12. 3-(Methylthio)-1-phenyl-5H-dibenzo[d,f][1,3]diazepin-6(7H)-one (**6a**) and 3-methoxy-1-phenyl-5H-dibenzo[d,f][1,3]diazepin-6(7H)-one (**7a**).* A mixture of indolin-2-one **5** (0.146 g, 1.1 mmol) and 4-(methylthio)-2-oxo-6-phenyl-2*H*-pyran-3-carbonitrile **3a** (0.243 g, 1 mmol) in freshly prepared solution of sodium methoxide by dissolving sodium (48 mg, 2.1 mmol) in methanol (10 mL) was refluxed for 10 h. The excess of solvent was removed and viscous mass was poured onto the crushed ice with vigorous stirring and neutralized with 10% aq HCl. The precipitate obtained was filtered, washed with water and dried. The dried crude product was purified on silica gel column using hexane/chloroform (60:40) as eluent, yield 173 mg (52%). The product isolated was distinguished by ^1H NMR as a mixture of **6a** and **7a** in ratio of 69:31. **6a**: ^1H NMR (400 MHz, DMSO-d_6): δ=2.48 (s, 3H, SCH_3), 6.49–6.70 (m, 2H, ArH), 6.95–7.07 (m, 5H, ArH), 7.20 (s, 3H, ArH), 8.74 (s, 1H, NHCO), 8.89 (s, 1H, CONH) ppm. HRMS (ESI): calcd for $C_{20}H_{17}N_2OS$ $[MH]^+$ 333.1061; found 333.1055. **7a**: ^1H NMR (400 MHz, DMSO-d_6): δ=3.78 (s, 3H, OCH_3), 6.49–6.70 (m, 2H, ArH), 6.95–7.07 (m, 5H, ArH), 7.20 (s, 3H, ArH), 8.71 (s, 1H, NHCO), 8.59 (s, 1H, CONH) ppm. HRMS (ESI): calcd for $C_{20}H_{17}N_2O_2$ $[MH]^+$ 317.1290; found 317.1282.

*4.2.13. 1-(4-Bromophenyl)-3-(methylthio)-5H-dibenzo[d,f][1,3]diazepin-6(7H)-one (**6b**) and 1-(4-bromophenyl)-3-methoxy-5H-dibenzo[d,f][1,3]diazepin-6(7H)-one (**7b**).* It was prepared from the reaction of indolin-2-one **5** (0.146 g, 1.1 mmol) and 6-(4-bromophenyl)-4-(methylthio)-2-oxo-2*H*-pyran-3-carbonitrile **3b** (0.322 g, 1 mmol) and isolated as described earlier, yield, 197 mg, (48%) as a mixture of **6b** and **7b** in ratio 9:1. **6b**: ^1H NMR (400 MHz, DMSO-d_6): δ=2.48 (s, 3H, SCH_3), 6.50–6.52 (m, 1H, ArH), 6.67–6.77 (m, 2H, ArH), 6.94–7.11 (m, 6H, ArH), 7.40–7.42 (d, *J*=8.4 Hz, 2H, ArH), 8.78 (s, 1H, NHCO), 8.93 (s, 1H, CONH) ppm. HRMS (ESI): calcd for $C_{20}H_{16}BrN_2OS$ $[MH]^+$ 411.0167 found 411.0165. **7b**: ^1H NMR (400 MHz, DMSO-d_6): δ=3.79 (s, 3H, OCH_3), 6.49–6.70 (m, 2H, ArH), 6.95–7.07 (m, 5H, ArH), 7.20 (s, 3H, ArH), 8.75 (s, 1H, NHCO), 8.89 (s, 1H, CONH) ppm. HRMS (ESI): calcd for $C_{20}H_{16}BrN_2O_2$ $[MH]^+$ 395.0395; found 395.0397.

*4.2.14. 3-(Methylthio)-1-(naphthalen-2-yl)-5H-dibenzo[d,f][1,3]diazepin-6(7H)-one (**6c**) and 3-methoxy-1-(naphthalen-2-yl)-5H-dibenzo[d,f][1,3]diazepin-6(7H)-one (**7c**).* It was prepared from the reaction of indolin-2-one **5** (0.146 g, 1.1 mmol) and 4-(methylthio)-6-(naphthalen-2-yl)-2-oxo-2*H*-pyran-3-carbonitrile **3c** (0.293 g, 1 mmol) and isolated as described earlier, yield 252 mg, (66%) as a mixture of **6c** and **7c** in ratio of 86:14. **6c**: ^1H NMR (300 MHz, DMSO-d_6): δ=2.49 (s, 3H, SCH_3), 6.49–6.53 (m, 2H, ArH), 7.07–7.10 (m, 5H, ArH), 7.45–7.48 (t, *J*=4.0 Hz, 2H, ArH), 7.65 (m, 1H, ArH), 7.77 (d, *J*=6.0 Hz, 3H, ArH), 8.79 (s, 1H, NHCO), 8.94 (s, 1H, CONH), HRMS (ESI): calcd for $C_{24}H_{19}N_2OS$ $[MH]^+$ 383.1218; found 383.1214. **7c**: ^1H NMR (300 MHz, DMSO-d_6): δ=3.81 (s, 3H, OCH_3), 6.49–6.53 (m, 2H, ArH), 7.07–7.10 (m, 5H, ArH), 7.45–7.48 (t, *J*=4.0 Hz, 2H, ArH), 7.65 (m, 1H, ArH), 7.77 (d, *J*=6.0 Hz, 3H, ArH), 8.75 (s, 1H, NHCO), 8.89 (s, 1H, CONH) ppm. HRMS (ESI): calcd for $C_{24}H_{19}N_2O_2$ $[MH]^+$ 367.1446; found 367.1436.

*4.2.15. 1-(4-Chlorophenyl)-3-(methylthio)-5H-dibenzo[d,f][1,3]diazepin-6(7H)-one (**6d**) and 1-(4-chlorophenyl)-3-methoxy-5H-dibenzo[d,f][1,3]diazepin-6(7H)-one (**7d**).* It was isolated from the reaction of indolin-2-one **5** (0.146 g, 1.1 mmol) and 6-(4-chlorophenyl)-4-(methylthio)-2-oxo-2*H*-pyran-3-carbonitrile **3d** (0.278 g, 1 mmol) as described earlier, yield 169 mg, (46%) as a mixture of **6d** and **7d** in ratio 65:35. **6d**: ^1H NMR (400 MHz, DMSO-d_6): δ=2.52 (s, 3H, SCH_3), 6.51–6.78 (m, 2H, ArH), 6.98–7.11 (m, 6H, ArH), 7.30 (d, *J*=8.0 Hz, 2H, ArH), 8.76 (s, 1H, NHCO), 8.91 (s, 1H, CONH) ppm. HRMS (ESI): calcd for $C_{20}H_{16}ClN_2OS$ $[MH]^+$ 367.0671; found 367.0671. **7d**: ^1H NMR (400 MHz, DMSO-d_6): δ=3.80 (s, 3H, SCH_3), 6.51–6.78 (m, 2H, ArH), 6.98–7.11 (m, 6H, ArH), 7.30 (d, *J*=8.0 Hz, 2H, ArH), 8.72 (s, 1H, NHCO), 8.86 (s, 1H, CONH) ppm. HRMS (ESI): calcd for $C_{20}H_{16}ClN_2O_2$ $[MH]^+$ 351.0900; found 351.0905.

*4.2.16. 1-(4-Chlorophenyl)-3-(piperidin-1-yl)-5H-dibenzo[d,f][1,3]diazepin-6(7H)-one (**9a**).* A mixture of **5** (0.146 g, 1.1 mmol) and 6-(4-chlorophenyl)-4-(piperidin-1-yl)-2*H*-pyran-2-one-3-carbonitriles **4d** (0.316 g, 1.0 mmol) in a freshly prepared solution of Na (48 mg, 2.1 mmol) in dry methanol (10 mL) was refluxed for 4 h. The excess methanol was removed under reduced pressure and thereafter, poured onto the crushed ice with vigorous stirring. The reaction mixture was neutralized with aq HCl and the precipitate obtained was filtered, dried and purified on silica gel column using hexane/chloroform (60:40) as eluent to get a white powder yield, 222 mg (55%). Mp 280–282 °C. R_f (30% EtOAc/Hexane) 0.65. ν_{max} (KBr) 3457, 3420, 3243, 3022, 2934, 1696, 1607, 1216; cm^{-1}. ^1H NMR (400 MHz, DMSO-d_6): δ=1.54–1.55 (m, 6H, piperidinyl–CH_2), 3.18 (bs, 4H, piperidinyl–CH_2), 6.40–6.41 (m, 1H, ArH), 6.61–6.91 (m, 2H, ArH), 6.67 (m, 1H, ArH), 6.99–7.00 (m, 4H, ArH), 7.21–7.23 (m, 2H, ArH), 8.47 (s, 1H, NHCO), 8.76 (s, 1H, CONH) ppm. ^{13}C NMR (100 MHz, DMSO-d_6): δ=24.1, 25.0, 48.7, 106.0, 106.2, 113.6, 116.7, 120.9, 122.5, 126.8, 128.1, 128.9, 131.4, 132.4, 140.4, 140.8, 141.2, 143.7, 150.7, 164.6. HRMS (ESI): calcd for $C_{24}H_{23}ClN_3O$ $[MH]^+$ 404.1529; found 404.1528.

*4.2.17. 1-Phenyl-3-(piperidin-1-yl)-5H-dibenzo[d,f][1,3]diazepin-6(7H)-one (**9b**).* It was obtained by refluxing indolin-2-one **5** (0.146 g, 1.1 mmol) and 2-oxo-6-phenyl-4-(piperidin-1-yl)-2*H*-pyran-3-carbonitrile **4a** (0.28 g, 1 mmol) in a freshly prepared solution

of sodium (48 mg, 2.1 mmol) in methanol (10 mL) for 6 h and worked up as described earlier, yield 215 mg, (58%) as a colourless powder. Mp 272–275 °C. R_f (30% EtOAc/Hexane) 0.69. ν_{max} (KBr) 3452, 3240, 2931, 1687, 1222 cm^{-1}. ^1H NMR (400 MHz, DMSO-d_6): δ=1.58 (bs, 6H, piperidinyl–CH_2), 3.20 (bs, 4H, piperidinyl–CH_2), 6.43–6.56 (m, 3H, ArH), 6.64–6.70 (m, 4H, ArH), 6.99–7.07 (m, 3H, ArH), 7.19 (d, J=6.0 Hz, 2H, ArH), 8.48 (s, 1H, NHCO), 8.77 (s, 1H, CONH) ppm. ^{13}C NMR (100 MHz, DMSO-d_6) δ=24.0, 25.0, 48.8, 105.8, 113.8, 116.9, 120.8, 122.3, 126.5, 126.6, 128.1, 129.2, 129.6, 132.4, 140.4, 142.2, 142.3, 143.6, 150.8, 164.9 ppm. HRMS (ESI): calcd for $C_{24}H_{24}N_3O$ $[MH]^+$ 370.1919; found 370.1917.

*4.2.18. 1-(4-Bromophenyl)-3-(piperidin-1-yl)-5H-dibenzo[d,f][1,3]diazepin-6(7H)-one (**9c**).* It was obtained from the reaction of indolin-2-one **5** (0.146 g, 1.1 mmol) and 6-(4-bromophenyl)-2-oxo-4-(piperidin-1-yl)-2*H*-pyran-3-carbonitrile **4b** (0.36 g, 1 mmol) in a freshly prepared solution of sodium (48 mg, 2.1 mmol) in methanol (10 mL) and worked up as described earlier, yield (228 mg, 51%) as a white amorphous powder. Mp >300 °C. R_f (30% EtOAc/Hexane) 0.51. ν_{max} (KBr) 3475, 2930, 1639, 1220 cm^{-1}. ^1H NMR (400 MHz, DMSO-d_6) δ=1.57–1.58 (bs 6H, piperidinyl–CH_2), 3.21 (bs, 4H, piperidinyl–CH_2), 6.43 (d, J=8.04 Hz, 1H, ArH), 6.63–6.70 (m, 3H, ArH), 7.01–7.02 (m, 4H, ArH), 7.38–7.42 (m, 2H, ArH), 8.49 (s, 1H, NHCO), 8.78 (s, 1H, CONH). HRMS (ESI): calcd for $C_{24}H_{23}BrN_3O$ $[MH]^+$ 448.1024; found 448.1025.

*4.2.19. 1-(4-Methoxyphenyl)-3-(piperidin-1-yl)-5H-dibenzo[d,f][1,3]diazepin-6(7H)-one (**9d**).* It was prepared by refluxing a mixture of indolin-2-one **5** (0.146 g, 1.1 mmol) and 6-(4-methoxyphenyl)-2-oxo-4-(piperidin-1-yl)-2*H*-pyran-3-carbonitrile **4f** (0.31 g, 1 mmol) in a freshly prepared solution of sodium (48 mg, 2.1 mmol) in methanol (10 mL) and worked up as described earlier, yield (188 mg, 47%) as a colourless powder. Mp >300 °C. R_f (30% EtOAc/Hexane) 0.48. ν_{max} (KBr) 3440, 3249, 2925, 1691, 1607, 1243 cm^{-1}. ^1H NMR (400 MHz, DMSO-d_6): δ=1.59 (bs, 6H, piperidinyl–CH_2), 3.18 (bs, 4H, piperidinyl–CH_2), 3.69 (s, 3H, ArH), 6.49–6.77 (m, 6H, ArH), 7.00–7.01 (m, 4H, ArH), 8.43 (s, 1H, NHCO), 8.73 (s, 1H, CONH); HRMS (ESI): calcd for $C_{25}H_{26}N_3O_2$ $[MH]^+$ 400.20.25; found 400.2024.

*4.2.20. (3Z,5Z)-3-(Methylthio)-5-(2-oxoindolin-3-ylidene)-5-phenylpent-3-enenitrile (**11a**).* A mixture of indolin-2-one **5** (0.146 g, 1.1 mmol), 4-(methylthio)-2-oxo-6-phenyl-2*H*-pyran-3-carbonitrile **3a** (0.243 g, 1.0 mmol) and sodium hydride (2.1 mmol, 60%) in dry THF (10 mL) was refluxed for 5 h. Excess of THF was removed under reduced pressure and thereafter poured onto the crushed ice with vigorous stirring. The aqueous solution was neutralized with dil aq HCl. The precipitate obtained was filtered, dried and purified as pale-yellow crystalline solid from silica gel column chromatography using hexane/chloroform (70:30) as eluent. Yield, 193 mg, (58%). Mp 192–193 °C. R_f (30% EtOAc/Hexane) 0.54. ν_{max} (KBr) 3174, 2962, 2205, 1689, 1613, 1561, 1220 cm^{-1}. ^1H NMR (400 MHz, DMSO-d_6): δ=2.23 (s, 3H, SCH_3), 4.77 (s, 2H, CH_2), 5.18 (s, 1H, CH), 5.92 (m, 1H, ArH), 6.53 (m, 1H, ArH), 6.79 (m, 1H, ArH), 7.08 (m, 1H, ArH), 7.29 (m, 2H, ArH), 7.48 (m, 3H, ArH), 10.70 (s, 1H, NHCO) ppm. ^{13}C NMR (100 MHz, DMSO-d_6): δ=14.6, 39.0, 89.8, 109.5, 116.8, 120.7, 122.2, 122.8, 126.2, 127.0, 128.8, 129.0, 129.3, 138.3, 141.1, 149.5, 163.6, 168.5 ppm. HRMS (ESI): calcd for $C_{20}H_{16}N_2OS$ $[MH]^+$ 333.1061; found 333.1061.

*4.2.21. (3Z,5Z)-5-(4-Fluorophenyl)-3-(methylthio)-5-(2-oxoindolin-3-ylidene)pent-3-enenitrile (**11b**).* It was obtained by refluxing a mixture of indolin-2-one **5** (0.146 g, 1.1 mmol), 6-(4-fluorophenyl)-4-(methylthio)-2-oxo-2*H*-pyran-3-carbonitrile **3k** (0.261 g, 1 mmol) and sodium hydride (2.1 mmol, 60%) in THF (10 mL) for 5 h as a yellow powder, yield, 194 mg, (55%). Mp 180–181 °C. R_f (30% EtOAc/Hexane) 0.46. ν_{max} (KBr) 3129, 2228, 1678, 1217 cm^{-1}. ^1H NMR (400 MHz, DMSO-d_6): δ=2.23 (s, 3H, SCH_3), 4.75 (s, 2H, CH_2), 5.19 (s, 1H, ArH), 5.89 (d, J=8.0 Hz, 1H, ArH), 6.59 (t, J=8.8 Hz, 1H, ArH), 6.78 (d, J=7.2 Hz, 1H, ArH), 7.08 (t, J=8.8 Hz, 1H, ArH), 7.33 (m, 4H, ArH), 10.7 (s, 1H, NHCO) ppm. ^{13}C NMR (100 MHz, DMSO-d_6): δ=14.7, 39.0, 89.9, 109.6, 116.0, 116.2, 116.8, 120.9, 122.1, 122.7, 126.6, 129.4, 129.5, 129.6, 141.1, 148.5, 163.5, 168.4; HRMS (ESI): calcd for $C_{20}H_{16}FN_2OS$ $[MH]^+$ 351.0967; found 351.0966.

4.3. X-ray crystallography

Intensity data for all the three compounds were collected at 298(2) K on a Sapphire2-CCD, OXFORD diffractometer system equipped with graphite monochromated Mo Kα radiation λ=0.71073 Å. The final unit cell determination, scaling of the data, and corrections for Lorentz and polarization effects were performed with CrysAlis RED.[31] The structures were solved by direct methods (SHELXS-97)[32] and refined by a full-matrix least-squares procedure based on F^2.[33] All the calculations were carried out using WinGX system Ver-1.64.[34] All non-hydrogen atoms were refined anisotropically; hydrogen atoms were located at calculated positions and refined using a riding model with isotropic thermal parameters fixed at 1.2 times the U_{eq} value of the appropriate carrier atom.

*4.3.1. Crystal data for **6a**.* $C_{42}H_{38}N_4O_3S_3$, formula mass 742.94, monoclinic space group P_12_1/C_1, a=19.5001(9), b=8.4923(3), c=22.8927(8) Å, β=92.088(3)°, V=3788.5(3) $Å^3$, Z=4, d_{calcd}=1.303 mg m^{-3}, linear absorption coefficient 0.241 mm^{-1}, F(000)=1560, crystal size 0.29×0.20×0.18 mm, reflections collected 37,984, independent reflections 9203 [R_{int}=0.0258], Final indices [$I>2\sigma(I)$] R_1=0.0797 wR_2=0.1919, R indices (all data) R_1=0.1048, wR_2=0.2065, gof 1.107, Largest difference peak and hole 0.564 and −0.706 e $Å^{-3}$.

*4.3.2. Crystal data for **6e**.* $C_{24}H_{25}N_3O_2S$, formula mass 419.53, triclinic space group P-1, a=8.704(5), b=11.427(5), c=12.210(5) Å, α=92.425(5), β=103.656(5), γ=109.446(5)°, V=1103.0(9) $Å^3$, Z=2, d_{calcd}=1.263 mg m^{-3}, linear absorption coefficient 0.172 mm^{-1}, F(000)=444, crystal size 0.40×0.25×0.15 mm, reflections collected 12,648, independent reflections 7268 [R_{int}=0.0652], Final indices [$I>2\sigma(I)$] R_1=0.0994 wR_2=0.2473, R indices (all data) R_1=0.1361, wR_2=0.2908, gof 1.053, Largest difference peak and hole 0.454 and −0.912 e $Å^{-3}$.

*4.3.3. Crystal data for **11a**.* $C_{20}H_{16}N_2OS$, formula mass 332.42, triclinic space group P-1, a=8.356(2), b=8.672(3), c=13.307(4) Å, α=93.81(3), β=92.30(2), γ=114.36(3)°, V=874.1(5) $Å^3$, Z=2, d_{calcd}=1.263 mg m^{-3}, linear absorption coefficient 0.193 mm^{-1}, F(000)=348, crystal size 0.30×0.20×0.15 mm, reflections collected 7120, independent reflections 3916 [R_{int}=0.0632], Final indices [$I>2\sigma(I)$] R_1=0.0586 wR_2=0.1590, R indices (all data) R_1=0.0989, wR_2=0.1928, gof 1.112, Largest difference peak and hole 0.209 and −0.273 e $Å^{-3}$.

CCDC 897838 (for **6a**), 897839 (for **6e**) and 897837 (for **11a**) contains supplementary crystallographic data. These data can be obtained free of charge from the Cambridge Crystallographic Data Centre via www.ccdc.cam.ac.uk/data_request/cif.

4.4. Computational methods

In order to understand the stability of various non-covalent interactions some quantum chemical calculations were carried out. All the calculations were performed using the Gaussian 03 package.[35] Initial geometries of the non-covalently bonded dimers were taken from the respective crystal structures. All calculations

were performed at the density functional theory (DFT) level using B3LYP[36] functional and 6-31G** basis set for all the atoms. The stabilization energies for dimeric motifs involving the two molecules were calculated from the formula $\Delta E_{dimer}=E_{dimer}-(2\times E_{monomer})$. $E_{monomer}$ was calculated by optimizing a single molecule at the same level of theory. The intermolecular interaction strengths are significantly weaker than either ionic or covalent bonding, therefore it was essential to do basis set superposition error (BSSE) corrections. The BSSE corrections in the interaction energies were done using Boys–Bernardi scheme. In this paper all interaction energies have been reported after BSSE correction.[37]

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Supplementary data

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