# Synthesis of novel 2-methyl and 2-cyanomethyl-12-aryl-8,12-dihydro-9*H*-chromeno[3,2-*e*][1,2,4]triazolo[1,5-*c*]pyrimidin-11(10*H*)-one derivatives

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2-Methyl and 2-cyanomethyl-12-aryl-8,12-dihydro-9*H*-chromeno[3,2-*e*][1,2,4]triazolo[1,5-*c*]pyrimidin-11(10*H*)-one derivatives were synthesised by the cyclisations of acetic anhydride or ethyl cyanoacetate with chromeno[2,3-*d*]pyrimidine derivatives, which were obtained by the reactions of hydrazine monohydrate and formimidate derivatives. In addition, 2,9,9-trimethyl-12-(*p*-tolyl)-8,12-dihydro-9*H*-chromeno[3,2-*e*][1,2,4]triazolo[1,5-*c*]pyrimidin-11(10*H*)-one and 2-cyanomethyl-12-phenyl-8,12-dihydro-9*H*-chromeno[3,2-*e*][1,2,4]triazolo[1,5-*c*]pyrimidin-11(10*H*)-one were further determined by single-crystal X-ray diffraction analysis.

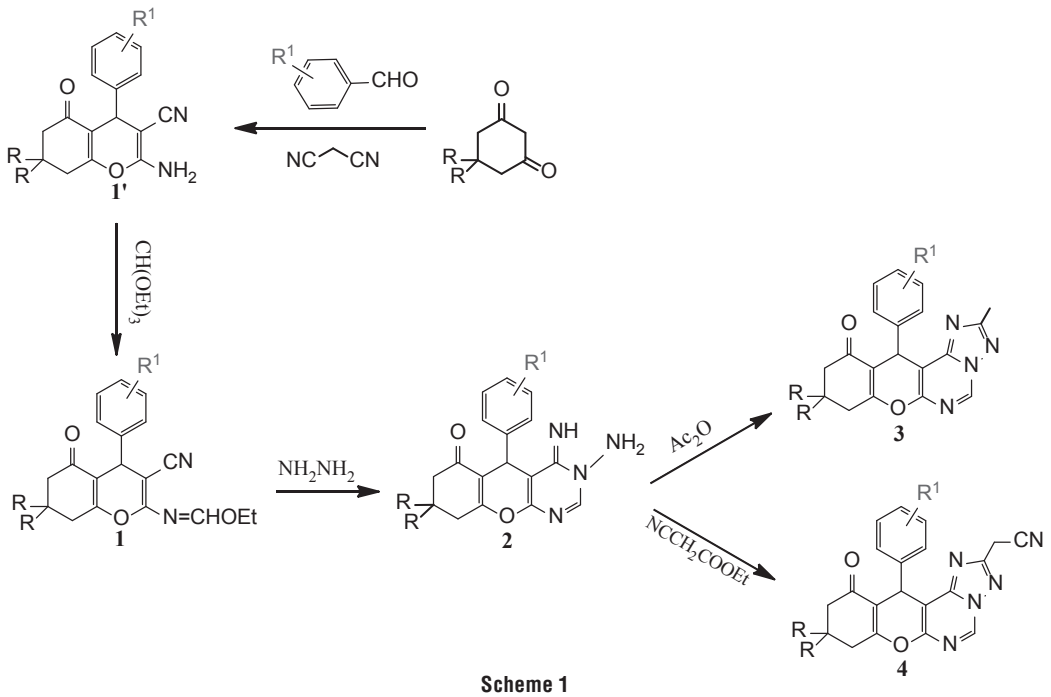
**Keywords:** chromeno[3,2-*e*][1,2,4]triazolo[1,5-*c*]pyrimidine-11(10*H*)-one, formimidate, synthesis of triazolopyrimidines

Much attention has been paid to the synthesis of various triazolopyrimidines[1–4] due to their pharmacological properties such as antibacterial, antioxidant and antimalarial activities.[5–7] The antioxidants that scavenge reactive oxygen species may be of great value in preventing the onset and propagation of oxidative diseases like autoimmune diseases, cardiovascular diseases, neurovascular diseases and neurodegenerative changes associated with ageing.[8] Chromene and its derivatives are also biologically interesting molecules which have antimicrobial, antifungal, antileishmanial, antitumour, hypotensive, local anaesthetic, antiallergenic, central nervous system activities, as well as being used in the treatment of Alzheimer's disease and bipolar disorder.[9,10]

In continuation of our previous works, we synthesised a series of novel analogues of 2-methyl and 2-cyanomethyl-12-aryl-8,12-dihydro-9*H*-chromeno[3,2-*e*][1,2,4]triazolo[1,5-*c*]pyrimidin-11(10*H*)-one derivatives.

## Results and discussion

The synthetic route of the title compounds are shown in Scheme 1. The ethyl *N*-(3-cyano-5-oxo-4-aryl-5,6,7,8-tetrahydro-4*H*-chromen-2-yl)formimidate derivatives **1** were prepared by the method reported in the literature.[11] Cyclisation of 3-amino-5-aryl-4-imino-3,4,8,9-tetrahydro-5*H*-chromeno[2,3-*d*]pyrimidin-6(7*H*)-one intermediates **2** with acetic anhydride or ethyl cyanoacetate afforded 2-methyl-12-aryl-8,12-dihydro-9*H*-chromeno[3,2-*e*][1,2,4]triazolo[1,5-*c*]pyrimidin-11(10*H*)-one derivatives **3** or 2-cyanomethyl-12-aryl-8,12-dihydro-9*H*-chromeno[3,2-*e*][1,2,4]triazolo[1,5-*c*]pyrimidin-11(10*H*)-one derivatives **4**, respectively. The key intermediates **2** were synthesised by the reaction of compounds **1** with 99% hydrazine monohydrate in ethanol at 0–5 °C. The melting points and yields of compounds **3** and **4** are shown in Tables 1 and 2, respectively.




**Scheme 1**

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**Table 1** Synthesis of 2-methyl-12-aryl-8,12-dihydro-9*H*-chromeno[3,2-*e*][1,2,4]triazolo[1,5-*c*]pyrimidin-11(10*H*)-one derivatives **3a–i**[a]

| Entry | $R^1$ | R | M.p./°C | Yield/%[b] |
|---|---|---|---|---|
| **3a** | H | $CH_3$ | 210–212 | 70 |
| **3b** | 4-$OCH_3$ | $CH_3$ | 214–216 | 73 |
| **3c** | 3,4-$(OCH_3)_2$ | $CH_3$ | 158–160 | 80 |
| **3d** | 3-$NO_2$ | $CH_3$ | 206–208 | 65 |
| **3e** | 4-$CH_3$ | $CH_3$ | 230–232 | 81 |
| **3f** | 2,4-$Cl_2$ | $CH_3$ | 172–174 | 67 |
| **3g** | 2-Cl | $CH_3$ | 162–164 | 65 |
| **3h** | 2,4-$Cl_2$ | H | 246–248 | 60 |
| **3i** | H | H | 206–208 | 70 |

[a]Reaction conditions: 1 mmol compounds **2**, 10 mL acetic anhydride, reflux.
[b]Isolated yield.

**Table 2** Synthesis of 2-cyanomethyl-12-aryl-8,12-dihydro-9*H*-chromeno[3,2-*e*][1,2,4]triazolo[1,5-*c*]pyrimidin-11(10*H*)-one derivatives **4a–f**[a]

| Entry | $R^1$ | R | M.p./°C | Yield/%[b] |
|---|---|---|---|---|
| **4a** | H | $CH_3$ | 200–202 | 70 |
| **4b** | 4-$OCH_3$ | $CH_3$ | 180–182 | 68 |
| **4c** | 4-$CH_3$ | $CH_3$ | 196–198 | 76 |
| **4d** | 2,4-$Cl_2$ | $CH_3$ | 174–176 | 72 |
| **4e** | 2-Cl | $CH_3$ | 196–198 | 77 |
| **4f** | H | H | 198–200 | 65 |

[a]Reaction conditions: 10 mL ethanol, 1 mmol compounds **2**, 2 mmol ethyl cyanoacetate, reflux.
[b]Isolated yield.

Iminoethers are known to react with compounds containing $–NH_2$ moiety such as hydrazides.[12,13] Because there are mainly two reactive sites of iminoethers **1**, the cyano group and the imidic group, these make them susceptible to react with hydrazides in absolute ethanol to give the key intermediates. As shown in Scheme 2, three plausible pathways and different products are possible.

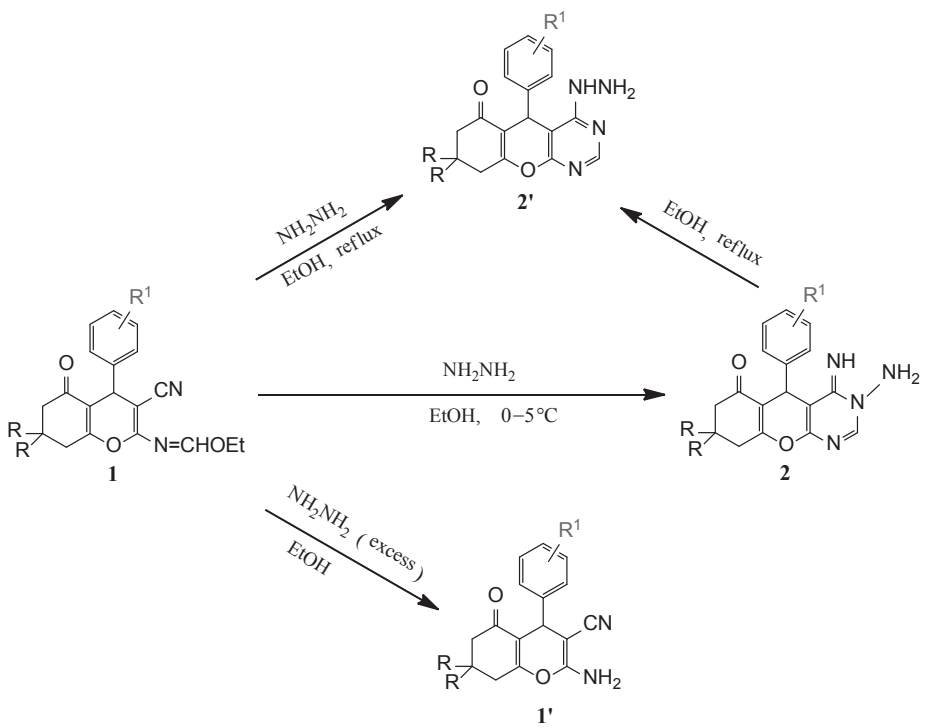
(1) Successive two nucleophilic additions of $–NH_2$ group on the imidic carbon and on the cyano function to yield compounds **2**.

(2) Compound **1** in absolute ethanol with 99% hydrazine monohydrate at reflux afforded 4-hydrazinyl-5-aryl-8,9-dihydro-5*H*-chromeno[2,3-*d*]pyrimidin-6(7*H*)-one derivatives **2′**. In addition, compound **2** may also undergo Dimroth rearrangement in absolute ethanol at reflux to give the more stable isomer **2′**. Because of the synthesis rate of compound **2** is higher than isomer **2′**, iminoethers **1** react with hydrazine monohydrate more easily to give intermediate **2** at a lower temperature.[14]

(3) Upon hydrazinolysis of compounds **1** using excess 99% hydrazine monohydrate instead of equimolar amounts, the raw material 2-amino-5-oxo-4-aryl-5,6,7,8-tetrahydro-4*H*-chromene-3-carbonitrile derivatives **1′** was recovered. This may be attributed to the reaction of one mole of hydrazine monohydrate with the iminoether **1**, followed by elimination of ethyl formate hydrazone rather than cyclisation to give the pyrimidine ring.[15]

For studying the optimal reaction for the synthesis of compounds **3**, we have selected 3-amino-5-phenyl-4-imino-3,4,8,9-tetrahydro-5*H*-chromeno[2,3-*d*]pyrimidin-6(7*H*)-one **2f** as the raw material. First we examined the reaction of the compound **2f** and acetic anhydride at low temperature in ethanol. However, no reaction was observed. When the reaction was at reflux, compound **2f** underwent Dimroth rearrangement to give 4-hydrazinyl-5-phenyl-8,9-dihydro-5*H*-chromeno[2,3-*d*]pyrimidin-6(7*H*)-one **2′f**. The structure of isomer **2′f** was characterised by IR, $^1$H NMR and elemental analysis. Finally we observed that by using acetic anhydride as a solvent at reflux, the reaction gave a good yield.

Encouraged by these results, we tried using ethyl cyanoacetate as the solvent to synthesise compound **4**, but its characteristics, such as its high boiling point, make it hard to evaporate from the reaction, so we used ethanol instead. By constantly experimenting with the mole ratio of ethyl cyanoacetate, compound **2f** and ethanol, we observed that 1 : 2 : 10 is the optimal mole ratio to yield compound **4f**.




**Scheme 2**

The structure of compound **2′f** was confirmed by IR spectra with characteristic absorption bands of 1665 $cm^{-1}$ for (C=O), 3323, 3394 for (–NH, $–NH_2$). The structure of this compound was further confirmed by $^1H$ NMR. In the $^1H$ NMR spectrum of compound **2′f**, a sharp single proton peak at δ 4.72 attributes to the characteristic absorption proton peak of 5-H.

The data of IR, $^1H$ NMR, elemental analysis shown in the experimental section are in accordance with the chemical structures of the target compounds. The structure of compound **3h** was confirmed by IR spectra with characteristic absorption bands of 1663 $cm^{-1}$ for C=O, 2873, 2957 $cm^{-1}$ for $–CH_3$, and 3073 $cm^{-1}$ for aromatic-H. The structure of this compound was further confirmed by $^1H$ NMR. In the $^1H$ NMR spectrum of compound **3h**, a sharp single proton peak at δ 5.67 is attributed to the characteristic absorption proton peak of 12-H.

The structure of compound **4d** was confirmed by IR spectra which showed characteristic absorption bands of 1663 $cm^{-1}$ for (C=O), 2255 $cm^{-1}$ for (C≡N), 2881, 2965 $cm^{-1}$ for ($–CH_3$), and 3065 $cm^{-1}$ for (aromatic-H), and the structure of this compound further determined by $^1H$ NMR. In the $^1H$ NMR spectrum of compound **4d**, a sharp single proton peak at δ 5.67 was the characteristic absorption proton peak of 12-H.

## Conclusion

The present study affords a series of novel 2-methyl-12-aryl-8,12-dihydro-9*H*-chromeno[3,2-*e*][1,2,4]triazolo[1,5-*c*]pyrimidin-11(10*H*)-one derivatives **3** and 2-cyanomethyl-12-aryl-8,12-dihydro-9*H*-chromeno[3,2-*e*][1,2,4]triazolo[1,5-*c*]pyrimidin-11(10*H*)-one derivatives **4** by the reaction of 3-amino-5-aryl-4-imino-3,4,8,9-tetrahydro-5*H*-chromeno[2,3-*d*]pyrimidin-6(7*H*)-one derivatives **2** with acetic anhydride and ethyl cyanoacetate respectively in good yields. This methodology is of interest due to the use of acetic anhydride as solvent without any other organic solvent nor toxic metals as catalyst, thus minimising the cost, the operational hazards and the environmental pollution.

## Experimental

Melting points were determined by an electrothermal apparatus and the temperature was uncorrected. Microanalysis was performed by the PerkinElmer 2400 Microanalytical Service. IR spectra were obtained on a PerkinElmer 1700 spectrophotometer. $^1H$ NMR spectra were recorded on a Bruker ARX-400 instrument. All reactions were monitored by TLC, which carried out on 0.2 mm silica GF254 (Merck) plates using UV light (254 and 365 nm) for detection.

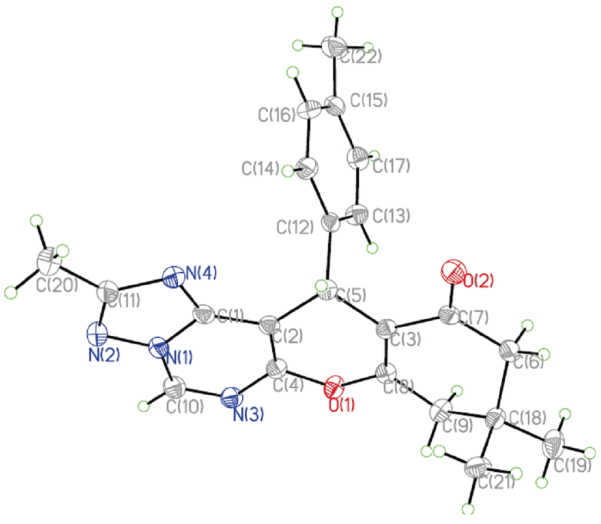



**Fig. 1** Molecular structure of compound **3e**.

*Synthesis of 2-methyl-12-aryl-8,12-dihydro-9*H*-chromeno [3,2-e][1,2,4]triazolo[1,5-c]pyrimidin-11(10*H*)-one derivatives* (**3a**–**i**)*; general procedure*

A mixture of compounds **2** (1 mmol) and acetic anhydride (10 mL) was heated to reflux for 6 h. After cooling, the precipitate were filtered off, washed with ethanol, and recrystallised from ethanol to afford compound **3**.

*Synthesis of 2-cyanomethyl-12-aryl-8,12-dihydro-9*H*-chromeno [3,2-e][1,2,4]triazolo[1,5-c]pyrimidin-11(10*H*)-one derivatives* (**4a**–**f**)*; general procedure*

A mixture of compounds **2** (1 mmol) and ethyl cyanoacetate (2 mmol) in absolute ethanol (10 mL) was heated to reflux for 4 h, the reaction progress was monitored by TLC. After cooling, the solid formed was collected, and then purified by silica gel flash chromatography using ethyl acetate/petroleum ether (2 : 1) as eluent to obtain pure 2-cyanomethyl-12-aryl-8,12-dihydro-9*H*-chromeno[3,2-*e*][1,2,4]triazolo[1,5-*c*]pyrimidin-11(10*H*)-one derivatives **4**.

## Single-crystal X-ray crystallography

X-ray diffraction experiments were carried out using Bruker SMART APEX CCD with MoKα radiation (λ = 0.71073 Å) at 291(2) K. Data collection, cell refinement, and data reduction were performed by using the CrystalClear software package. Absorption corrections were applied using SADABS.[16] The structures were solved by direct methods using SHELXS-97[17–18] and refined by full-matrix least-squares methods anisotropically for non-hydrogen atoms using SHELXL-97. Calculations were performed on a personal computer with the Siemens SHELXTL program package. Crystallographic data (excluding structure factors) for the structures in this paper have been deposited with the Cambridge Crystallographic Data Centre as supplementary publication CCDC Nos. 1022159 for **3e**, 1022673 for **4f**.

The single crystal structure of **3e** was determined by single-crystal X-ray diffraction analysis (Figs 1 and 2) and the crystal data and structure refinement are summarised in Table 3. The dihedral angle between the least-squares pyrimidine ring and the least-squares plane of the triazole ring in complex **3e** is 2.972(78)°. Furthermore, the dihedral angle between the least-squares pyran ring and the least-squares plane of the cyclohexane ring is 14.086(87)°. The molecular packing of **3e** is further stabilised by intermolecular H-bond between O(2) atoms and C(10) atoms of the neighbouring molecule.

Crystal data for **3e**: $C_{22}H_{22}N_4O_2$, $M_w$ = 374.44, monoclinic $P2_1$, $a$ = 5.662(3) Å, $b$ = 16.271(10) Å, $c$ = 10.324(6) Å, V = 942.6(10)

**Table 3** Crystallographic data for compounds **3e** and **4f**

| | **3e** | **4f** |
|---|---|---|
| Empirical formula | $C_{22}H_{22}N_4O_2$ | $C_{20}H_{15}N_5O_2$ |
| Formula weight | 374.44 | 357.37 |
| Wavelength/nm | 0.71073 | 0.71073 |
| Crystal system | Monoclinic | Triclinic |
| Space group | $P2_1$ | $P1$ |
| $a$/Å | 5.662(3) | 7.143(2) |
| $b$/Å | 16.271(10) | 9.347(3) |
| $c$/Å | 10.324(6) | 13.445(5) |
| α/(°) | 90.00 | 98.246(4) |
| β/(°) | 97.696(7) | 104.990(4) |
| γ/(°) | 90.00 | 99.722(4) |
| Volume/Å$^3$ | 942.6(10) | 838.0(5) |
| Z | 2 | 2 |
| Calculated density/g·cm$^{-3}$ | 1.319 | 1.416 |
| Absorption coefficient/mm$^{-1}$ | 0.087 | 0.096 |
| F (000) | 396 | 372 |
| Final R indices [I > 2sigma(I)] | $R^1$ = 0.0372, $wR^2$ = 0.0798 | $R^1$ = 0.0442, $wR^2$ = 0.1290 |
| R indices (all data) | $R^1$ = 0.0500, $wR^2$ = 0.0873 | $R^1$ = 0.0647, $wR^2$ = 0.1481 |

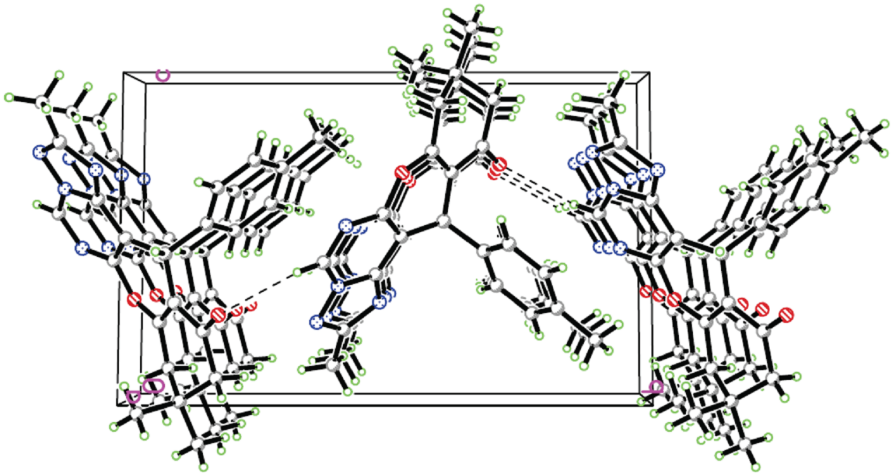


**Fig. 2** Packing diagram of compound **3e** in unit-cell along *a* axis.

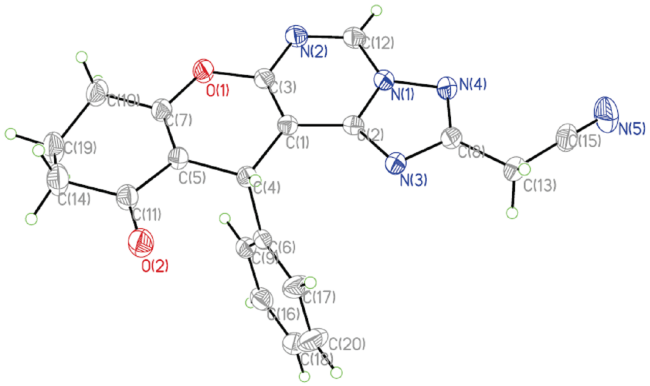



**Fig. 3** Molecular structure of compound **4f**.

Å$^3$, Z=2, $D_c$=1.319 g cm$^{-3}$, $R^1$ (I>2σ)=0.0372, $wR^2$=0.0873, μ=0.087 mm$^{-1}$, S=0.992.

The single crystal structure of **4f** was determined by single-crystal X-ray diffraction analysis (Figs 3 and 4) and the crystal data and structure refinement are summarised in Table 3. The dihedral angle between the least-squares pyrimidine ring and the least-squares plane of the triazole in complex **4f** is 1.085(59)°. Furthermore, the dihedral angle between the least-squares pyran ring and the least-squares plane of the cyclohexane ring is 5.273(61)°.

Crystal data for **4f**: $C_{20}H_{15}N_5O_2$, $M_w$=357.37, Triclinic *P*1, *a*=7.143(2) Å, *b*=9.347(3) Å, *c*=13.445(5) Å, V=838.0(5) Å$^3$, Z=2, $D_c$=1.416 g cm$^{-3}$, $R^1$ (I>2σ)=0.0442, $wR^2$=0.1481, μ=0.096 mm$^{-1}$, S=0.990;

*4-Hydrazinyl-5-phenyl-8,9-dihydro-5*H*-chromeno[2,3-*d*]pyrimidin-6(7*H*)-one* (**2′f**): Yield 55%; m.p. 162–164 °C. IR (KBr, ν, cm$^{-1}$): 3394, 3323, 1665; $^1$H NMR ($CDCl_3$, 400 MHz) δ 1.93–2.03 (m, 2H, $C^8$-H), 2.32–2.36 (m, 2H, $C^9$-H), 2.64–2.70 (m, 2H, $C^7$-H), 4.72 (s, 1H, $C^5$-H),4.76 (s, 2H, –$NH_2$), 7.16–7.35 (m, 5H, PhH), 8.00 (s, 1H,

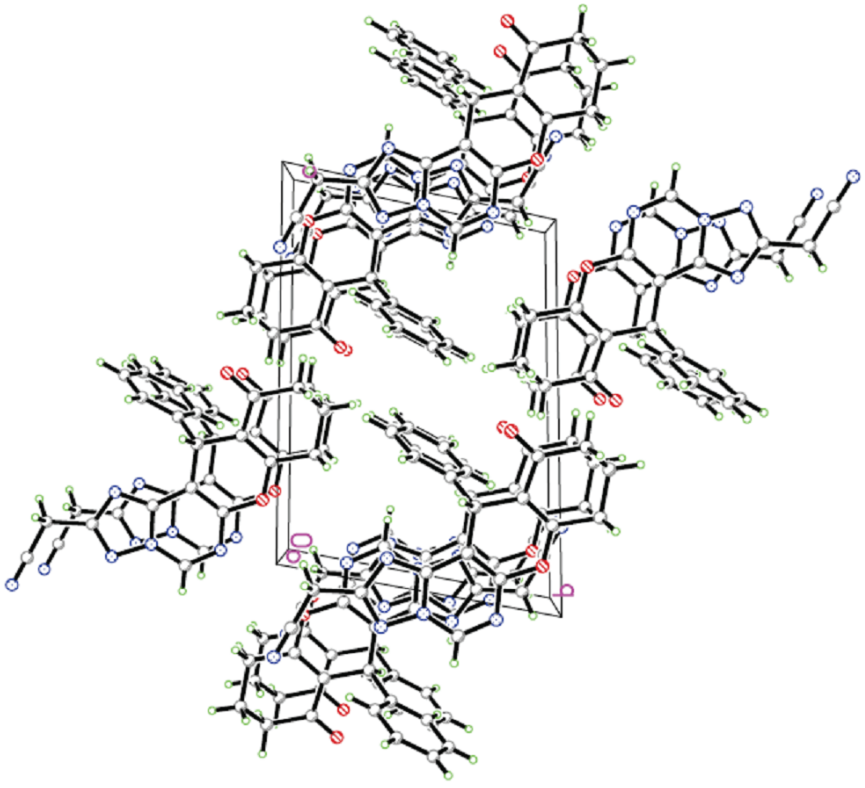


**Fig. 4** Packing diagram of compound **4f** in unit-cell along *b* axis.

$C^2$-H). Anal. calcd for $C_{17}H_{16}N_4O_2$: C, 66.22; H, 5.23; N, 18.17; found: C, 66.35; H, 5.14; N, 18.08%.

*2,9,9-Trimethyl-12-phenyl-8,12-dihydro-9*H-*chromeno[3,2-*e*][1,2,4]triazolo[1,5-*c*]pyrimidin-11(10*H*)-one* (**3a**): Yield 70%; m.p. 210–212 °C. IR (KBr, ν, $cm^{-1}$): 3073, 2965, 2890, 1646; $^1$H NMR($CDCl_3$, 400 MHz) δ 1.09 (s, 3H, $-CH_3$), 1.15 (s, 3H, $-CH_3$), 2.24–2.35 (dd, $J_1$ = 16.2 Hz, $J_2$ = 24.3 Hz, 2H, $C^8$-H), 2.53 (s, 3H, $-CH_3$), 2.62–2.72 (dd, $J_1$ = 18.6 Hz, $J_2$ = 23.0 Hz, 2H, $C^{10}$-H), 5.47 (s, 1H, $C^{12}$-H), 7.14–7.18 (t, $J$ = 7.3 Hz, 1H, 12-4′-H), 7.24–7.27 (m, 2H, 12-(2′+6′)-H), 7.42–7.44 (d, $J$ = 7.3 Hz, 2H, 12-(3′+5′)-H), 8.97 (s, 1H, $C^5$-H). Anal. calcd for $C_{21}H_{20}N_4O_2$: C, 69.98; H, 5.59; N, 15.55; found: C, 69.75; H, 5.68; N, 15.66%.

*12-(4-Methoxyphenyl)-2,9,9-trimethyl-8,12-dihydro-9*H-*chromeno[3,2-*e*][1,2,4]triazolo[1,5-*c*]pyrimidin-11(10*H*)-one* (**3b**): Yield 73%; m.p. 214–216 °C. IR (KBr, ν, $cm^{-1}$): 3082, 2973, 2890, 1696; $^1$H NMR($CDCl_3$, 400 MHz) δ 1.09 (s, 3H, $-CH_3$), 1.15 (s, 3H, $-CH_3$), 2.24–2.34 (dd, $J_1$ = 16.4 Hz, $J_2$ = 24.0 Hz, 2H, $C^8$-H), 2.54 (s, 3H, $-CH_3$), 2.61–2.71 (dd, $J_1$ = 18.5 Hz, $J_2$ = 21.7 Hz, 2H, $C^{10}$-H), 3.73 (s, 3H, 12-$OCH_3$), 5.42 (s, 1H, $C^{12}$-H), 6.77–6.79 (d, $J$ = 8.7 Hz, 2H, 12-(3′+5′)-H), 7.33–7.35 (d, $J$ = 8.7 Hz, 2H, 12-(2′+6′)-H), 8.98 (s, 1H, $C^5$-H). Anal. calcd for $C_{22}H_{22}N_4O_3$: C, 67.68; H, 5.68; N, 14.35; found: C, 67.79; H, 5.59; N, 14.21%.

*12-(3,4-Dimethoxyphenyl)-2,9,9-trimethyl-8,12-dihydro-9*H-*chromeno[3,2-*e*][1,2,4]triazolo[1,5-*c*]pyrimidin-11(10*H*)-one* (**3c**): Yield 80%; m.p. 158–160 °C. IR (KBr, ν, $cm^{-1}$): 3073, 2965, 2840, 1688; $^1$H NMR($CDCl_3$, 400 MHz) δ 1.12 (s, 3H, $-CH_3$), 1.16 (s, 3H, $-CH_3$), 2.27–2.36 (dd, $J_1$ = 16.3 Hz, $J_2$ = 21.2 Hz, 2H, $C^8$-H), 2.55 (s, 3H, $-CH_3$), 2.63–2.72 (t, $J$ = 18.5 Hz, 2H, $C^{10}$-H), 3.79 (s, 3H, 12-$OCH_3$), 3.89 (s, 3H, 12-$OCH_3$), 5.43 (s, 1H, $C^{12}$-H), 6.71–6.74 (d, $J$ = 8.3 Hz, 1H, 12-6′-H), 6.82–6.84 (m, 1H, 12-5′-H), 7.14–7.15 (d, $J$ = 2.0 Hz, 1H, 12-2′-H), 8.97 (s, 1H, $C^5$-H). Anal. calcd for $C_{23}H_{24}N_4O_4$: C, 65.70; H, 5.75; N, 13.33; found: C, 65.95; H, 5.68; N, 13.19%.

*2,9,9-Trimethyl-12-(3-nitrophenyl)-8,12-dihydro-9*H-*chromeno[3,2-*e*][1,2,4]triazolo[1,5-*c*]pyrimidin-11(10*H*)-one* (**3d**): Yield 65%; m.p. 206–208 °C. IR (KBr, ν, $cm^{-1}$): 3082, 2948, 2823, 1688; $^1$H NMR($CDCl_3$, 400 MHz) δ 1.11 (s, 3H, $-CH_3$), 1.17 (s, 3H, $-CH_3$), 2.26–2.37 (dd, $J_1$ = 16.3 Hz, $J_2$ = 27.7 Hz, 2H, $C^8$-H), 2.53 (s, 3H, $-CH_3$), 2.66–2.78 (dd, $J_1$ = 17.8 Hz, $J_2$ = 28.9 Hz, 2H, $C^{10}$-H), 5.57 (s, 1H, $C^{12}$-H), 7.44–7.48 (t, $J$ = 7.9 Hz, 1H, 12-5′-H), 7.93–7.95 (d, $J$ = 7.7 Hz, 1H, 12-6′-H), 8.03–8.05 (d, $J$ = 8.2 Hz, 1H, 12-4′-H), 8.17 (s, 1H, 12-2′-H), 9.02 (s, 1H, $C^5$-H). Anal. calcd for $C_{21}H_{19}N_5O_4$: C, 62.22; H, 4.72; N, 17.27; found: C, 62.48; H, 4.81; N, 17.05%.

*2,9,9-Trimethyl-12-(*p*-tolyl)-8,12-dihydro-9*H-*chromeno[3,2-*e*][1,2,4]triazolo[1,5-*c*]pyrimidin-11(10*H*)-one* (**3e**): Yield 81%; m.p. 230–232 °C. IR (KBr, ν, $cm^{-1}$): 3056, 2957, 2840, 1688; $^1$H NMR($CDCl_3$, 400 MHz) δ 1.09 (s, 3H, $-CH_3$), 1.15 (s, 3H, $-CH_3$), 2.24 (s, 3H, 12-$CH_3$), 2.24–2.34 (dd, $J_1$ = 14.5 Hz, $J_2$ = 22.9 Hz, 2H, $C^8$-H), 2.53 (s, 3H, $-CH_3$), 2.62–2.72 (dd, $J_1$ = 18.4 Hz, $J_2$ = 22.3 Hz, 2H, $C^{10}$-H), 5.44 (s, 1H, $C^{12}$-H), 7.05–7.07 (d, $J$ = 7.9 Hz, 2H, 12-(3′+5′)-H), 7.31–7.33 (d, $J$ = 8.1 Hz, 2H, 12-(2′+6′)-H), 8.97 (s, 1H, $C^5$-H). Anal. calcd for $C_{22}H_{22}N_4O_2$: C, 70.57; H, 5.92; N, 14.96; found: C, 70.43; H, 5.87; N, 15.13%.

*12-(2,4-Dichlorophenyl)-2,9,9-trimethyl-8,12-dihydro-9*H-*chromeno[3,2-*e*][1,2,4]triazolo[1,5-*c*]pyrimidin-11(10*H*)-one* (**3f**): Yield 67%; m.p. 172–174 °C. IR (KBr, ν, $cm^{-1}$): 3073, 2981, 2890, 1646; $^1$H NMR($CDCl_3$, 400 MHz) δ 1.10 (s, 3H, $-CH_3$), 1.15 (s, 3H, $-CH_3$), 2.23–2.33 (dd, $J_1$ = 16.4 Hz, $J_2$ = 26.7 Hz, 2H, $C^8$-H), 2.50 (s, 3H, $-CH_3$), 2.64 (s, 2H, $C^{10}$-H), 5.66 (s, 1H, $C^{12}$-H), 7.20–7.22 (m, 1H, 12-6′-H), 7.25–7.27 (m, 1H, 12-5′-H), 7.55–7.58 (d, $J$ = 8.2 Hz, 1H, 12-3′-H), 9.01 (s, 1H, $C^5$-H). Anal. calcd for $C_{21}H_{18}Cl_2N_4O_2$: C, 58.75; H, 4.23; N, 13.05; found: C, 58.45; H, 4.28; N, 13.40%.

*12-(2-Chlorophenyl)-2,9,9-trimethyl-8,12-dihydro-9*H-*chromeno[3,2-*e*][1,2,4]triazolo[1,5-*c*]pyrimidin-11(10*H*)-one* (**3g**): Yield 65%; m.p. 162–164 °C. IR (KBr, ν, $cm^{-1}$): 3067, 2953, 2873, 1665; $^1$H NMR($CDCl_3$, 400 MHz) δ 1.10 (s, 3H, $-CH_3$), 1.15 (s, 3H, $-CH_3$), 2.22–2.33 (dd, $J_1$ = 16.3 Hz, $J_2$ = 26.2 Hz, 2H, $C^8$-H), 2.49 (s, 3H, $-CH_3$), 2.60–2.69 (t, $J$ = 19.1 Hz, 2H, $C^{10}$-H), 5.71 (s, 1H, $C^{12}$-H), 7.10–7.14 (m, 1H, 12-6′-H), 7.21–7.24 (m, 2H, 12-(4′+5′)-H), 7.61–7.63 (d, $J$ = 7.6 Hz, 1H, 12-3′-H), 8.99 (s, 1H, $C^5$-H). Anal. calcd for $C_{21}H_{19}ClN_4O_2$: C, 63.88; H, 4.85; N, 14.19; found: C, 63.75; H, 4.81; N, 14.35%.

*12-(2,4-Dichlorophenyl)-2-methyl-8,12-dihydro-9*H-*chromeno[3,2-*e*][1,2,4]triazolo[1,5-*c*]pyrimidin-11(10*H*)-one* (**3h**): Yield 60%; m.p. 246–248 °C. IR (KBr, ν, $cm^{-1}$): 3073, 2957, 2873, 1663; $^1$H NMR($CDCl_3$, 400 MHz) δ 2.08–2.12 (m, 2H, $C^9$-H)), 2.40–2.44 (m, 2H, $C^8$-H)), 2.51 (s, 3H, $-CH_3$), 2.75–2.85 (m, 2H, $C^{10}$-H), 5.67 (s, 1H, $C^{12}$-H), 7.20–7.23 (m, 1H, 12-6′-H), 7.25 (m, 1H, 12-5′-H), 7.57–7.59 (d, $J$ = 8.3 Hz, 1H, 12-3′-H), 9.00 (s, 1H, $C^5$-H). Anal. calcd for $C_{19}H_{14}Cl_2N_4O_2$: C, 56.87; H, 3.52; N, 13.96; found: C, 56.98; H, 3.61; N, 13.81%.

*2-Methyl-12-phenyl-8,12-dihydro-9*H-*chromeno[3,2-*e*][1,2,4]triazolo[1,5-*c*]pyrimidin-11(10*H*)-one* (**3i**): Yield 70%; m.p. 206–208 °C. IR (KBr, ν, $cm^{-1}$): 3081, 2961, 2884, 1648; $^1$H NMR($CDCl_3$, 400 MHz) δ 2.10–2.13 (m, 2H, $C^9$-H)), 2.40–2.46 (m, 2H, $C^8$-H)), 2.53 (s, 3H, $-CH_3$), 2.77–2.89 (m, 2H, $C^{10}$-H), 5.51 (s, 1H, $C^{12}$-H), 7.14–7.18 (t, $J$ = 7.3 Hz, 1H, 12-4′-H), 7.23–7.27 (m, 2H, 12-(2′+6′)-H), 7.42–7.44 (d, $J$ = 7.2 Hz, 2H, 12-(3′+5′)-H), 8.98 (s, 1H, $C^5$-H). Anal. calcd for $C_{19}H_{16}N_4O_2$: C, 68.66; H, 4.85; N, 16.86; found: C, 68.88; H, 4.79; N, 16.61%.

*2-Cyanomethyl-9,9-dimethyl-12-phenyl-8,12-dihydro-9*H-*chromeno[3,2-*e*][1,2,4]triazolo [1,5-*c*]pyrimidin-11(10*H*)-one* (**4a**): Yield 70%; m.p. 200–202 °C. IR (KBr, ν, $cm^{-1}$): 2954, 2907, 2859, 2249, 1658; $^1$H NMR($CDCl_3$, 400 MHz) δ 1.11 (s, 3H, $-CH_3$), 1.16 (s, 3H, $-CH_3$), 2.26–2.36 (dd, $J_1$ = 16.4 Hz, $J_2$ = 22.8 Hz, 2H, $C^8$-H), 2.64–2.74 (dd, $J_1$ = 17.9 Hz, $J_2$ = 24.8 Hz, 2H, $C^{10}$-H), 3.99 (s, 2H, $-CH_2CN$), 5.46 (s, 1H, $C^{12}$-H), 7.14–7.18 (t, $J$ = 7.3 Hz, 1H, 12-4′-H), 7.24–7.28 (m, 2H, 12-(2′+6′)-H), 7.40–7.42 (d, $J$ = 7.3 Hz, 2H, 12-(3′+5′)-H), 9.06 (s, 1H, $C^5$-H). Anal. calcd for $C_{22}H_{19}N_5O_2$: C, 68.56; H, 4.97; N, 18.17; found: C, 68.78; H, 4.87; N, 18.01%.

*12-(4-Methoxyphenyl)-2-cyanomethyl-9,9-dimethyl-8,12-dihydro-9*H-*chromeno[3,2-*e*][1,2,4]triazolo [1,5-*c*]pyrimidin-11(10*H*)-one* (**4b**): Yield 68%; m.p. 180–182 °C. IR (KBr, ν, $cm^{-1}$): 3077, 2920, 2827, 2262, 1647; $^1$H NMR($CDCl_3$, 400 MHz) δ 1.11 (s, 3H, $-CH_3$), 1.16 (s, 3H, $-CH_3$), 2.25–2.35 (dd, $J_1$ = 16.3 Hz, $J_2$ = 22.1 Hz, 2H, $C^8$-H), 2.63–2.73 (dd, $J_1$ = 17.8 Hz, $J_2$ = 23.6 Hz, 2H, $C^{10}$-H), 3.73 (s, 3H, 12-$OCH_3$), 3.99 (s, 2H, $-CH_2CN$), 5.41 (s, 1H, $C^{12}$-H), 6.77–6.80 (d, $J$ = 8.7 Hz, 2H, 12-(3′+5′)-H), 7.31–7.33 (d, $J$ = 8.8 Hz, 2H, 12-(2′+6′)-H), 9.05 (s, 1H, $C^5$-H). Anal. calcd for $C_{23}H_{21}N_5O_3$: C, 66.49; H, 5.09; N, 16.86; found: C, 66.63; H, 5.01; N, 16.58%.

*2-Cyanomethyl-9,9-dimethyl-12-(*p*-tolyl)-8,12-dihydro-9*H-*chromeno[3,2-*e*][1,2,4]triazolo[1,5-*c*]pyrimidin-11(10*H*)-one* (**4c**): Yield 76%; m.p. 196–198 °C. IR (KBr, ν, $cm^{-1}$): 3056, 2920, 2877, 2262, 1654; $^1$H NMR($CDCl_3$, 400 MHz) δ 1.11 (s, 3H, $-CH_3$), 1.16 (s, 3H, $-CH_3$), 2.25 (s, 3H, 12-$CH_3$), 2.25–2.35 (dd, $J_1$ = 18.0 Hz, $J_2$ = 24.7 Hz, 2H, $C^8$-H), 2.63–2.74 (dd, $J_1$ = 17.8 Hz, $J_2$ = 24.3 Hz, 2H, $C^{10}$-H), 3.99 (s, 2H, $-CH_2CN$), 5.42 (s, 1H, $C^{12}$-H), 7.05–7.07 (d, $J$ = 7.9 Hz, 2H, 12-(3′+5′)-H), 7.29–7.31 (d, $J$ = 8.1 Hz, 2H, 12-(2′+6′)-H), 9.05 (s, 1H, $C^5$-H). Anal. calcd for $C_{23}H_{21}N_5O_2$: C, 69.16; H, 5.30; N, 17.53; found: C, 69.43; H, 5.15; N, 17.32.

*12-(2,4-Dichlorophenyl)-2-cyanomethyl-9,9-dimethyl-8,12-dihydro-9*H-*chromeno[3,2-*e*][1,2,4]triazolo [1,5-*c*]pyrimidin-11(10*H*)-one* (**4d**): Yield 72%; m.p. 174–176 °C. IR (KBr, ν, $cm^{-1}$): 3065, 2965, 2881, 2255, 1663; $^1$H NMR($CDCl_3$, 400 MHz) δ 1.10 (s, 3H, $-CH_3$), 1.16 (s, 3H, $-CH_3$), 2.24–2.34 (dd, $J_1$ = 16.4 Hz, $J_2$ = 25.2 Hz, 2H, $C^8$-H), 2.65 (s, 2H, $C^{10}$-H), 3.96 (s, 2H, $-CH_2CN$), 5.67 (s, 1H, $C^{12}$-H), 7.19–7.22 (m, 1H, 12-6′-H), 7.26–7.27 (m, 1H, 12-5′-H), 7.50–7.52 (d, $J$ = 8.2 Hz, 1H, 12-3′-H), 9.10 (s, 1H, $C^5$-H). Anal. calcd for $C_{22}H_{17}Cl_2N_5O_2$: C, 58.16; H, 3.77; N, 15.42; found: C, 58.42; H, 3.68; N, 15.18%.

*12-(2-Chlorophenyl)-2-cyanomethyl-9,9-dimethyl-8,12-dihydro-9*H-*chromeno[3,2-*e*][1,2,4]triazolo [1,5-*c*]pyrimidin-11(10*H*)-one* (**4e**): Yield 77%; m.p. 196–198 °C. IR (KBr, ν, $cm^{-1}$): 3332, 2994, 2838, 2010, 1665; $^1$H NMR($CDCl_3$, 400 MHz) δ 1.10 (s, 3H, $-CH_3$), 1.16 (s, 3H, $-CH_3$), 2.23–2.33 (dd, $J_1$ = 16.3 Hz, $J_2$ = 24.0 Hz, 2H, $C^8$-H), 2.61–2.70 (dd, $J_1$ = 18.7 Hz, $J_2$ = 20.6 Hz, 2H, $C^{10}$-H), 3.95 (m, 2H, $-CH_2CN$), 5.72 (s, 1H, $C^{12}$-H), 7.12–7.16 (m, 1H, 12-6′-H), 7.23–7.26 (m, 2H, 12-(4′+5′)-H), 7.56–7.58 (d, $J$ = 7.4 Hz, 1H, 12-3′-H),

9.08 (s, 1H, $C^5$-H). Anal. calcd for $C_{22}H_{18}ClN_5O_2$: C, 62.93; H, 4.32; N, 16.68; found: C, 62.68; H, 4.39; N, 16.91%.

*2-Cyanomethyl-12-phenyl-8,12-dihydro-9*H-*chromeno[3,2*-e*][1,2,4] triazolo[1,5*-c*]pyrimidin-11(10*H*)-one* (**4f**): Yield 65%; m.p. 198–200 °C. IR (KBr, ν, $cm^{-1}$): 2965, 2923, 2823, 2255, 1645; $^1$H NMR($CDCl_3$, 400 MHz) δ 2.12–2.15 (m, 2H, $C^9$-H)), 2.42–2.48 (m, 2H, $C^8$-H)), 2.78–2.91 (m, 2H, $C^{10}$-H), 3.99 (s, 2H, $-CH_2CN$), 5.49 (s, 1H, $C^{12}$-H), 7.14–7.18 (m, 1H, 12-4′-H), 7.24–7.27 (m, 2H, 12-(2′+6′)-H), 7.40–7.42 (d, $J$=7.1 Hz, 2H, 12-(3′+5′)-H), 9.06 (s, 1H, $C^5$-H). Anal. calcd for $C_{20}H_{15}N_5O_2$: C, 67.22; H, 4.23; N, 19.60; found: C, 67.48; H, 4.15; N, 19.31%.

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