Journal of Molecular Structure 1036 (2013) 257–266

Contents lists available at SciVerse ScienceDirect

Journal of Molecular Structure

journal homepage: www.elsevier.com/locate/molstruc

# Synthesis and spectral studies of some 4*H*-pyran derivatives: Crystal and molecular structure of isobutyl 6-amino-5-cyano-2-methyl-4-phenyl-4*H*-pyran -3-carboxylate

C. Udhaya Kumar, A. Sethukumar, B. Arul Prakasam *

*Department of Chemistry, Annamalai University, Annamalainagar, Chidambaram 608 002, India*

## HIGHLIGHTS

- $BF_3$:$OEt_2$ catalyzed synthesis of 4*H*-pyrans. MCR between isobutyl ethylacetoacetate, aryl aldehydes and malononitrile.
- Spectral characterization by IR, 1D and 2D NMR.
- Single crystal XRD analysis of isobutyl 6-amino-5-cyano-2-methyl-4-phenyl-4*H*-pyran-3-carboxylate.

## ARTICLE INFO

*Article history:*
Received 3 October 2012
Received in revised form 24 November 2012
Accepted 26 November 2012
Available online 5 December 2012

*Keywords:*
MCR
$BF_3$:$OEt_2$
HSQC
HMBC
XRD

## ABSTRACT

A series of isobutyl 6-amino-4-aryl-5-cyano-2-methyl-4*H*-pyran-3-carboxylates (**1**–**9**) have been synthesized by the multicomponent reaction (MCR) between isobutyl ethylacetoacetate, aryl aldehydes and malononitrile using $BF_3$:$OEt_2$ as catalyst. The derived compounds have been analyzed by IR and NMR (1D and 2D) spectra. Single crystal X-ray structural analysis of **1**, evidences the flattened-boat conformation of pyran ring.



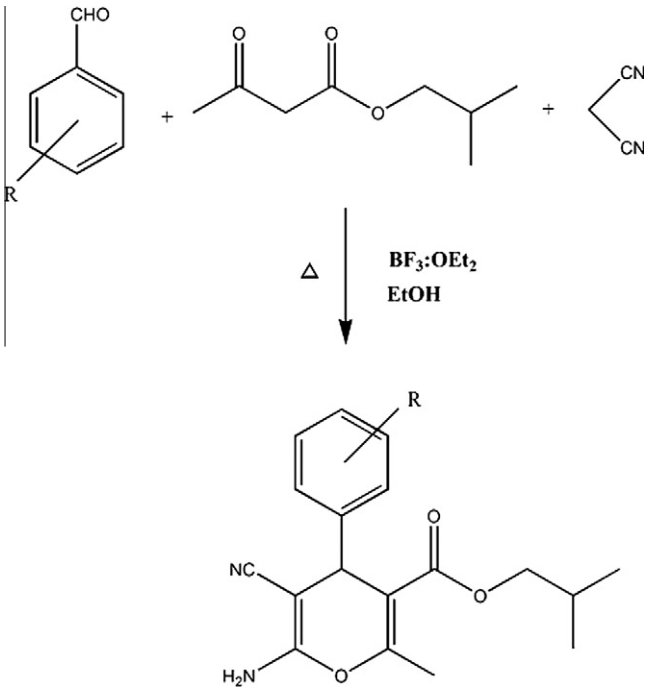
## 1. Introduction

Development of environmentally benign and clean synthetic procedures has become the goal of present day organic synthesis [1]. Multi-step reactions usually produce significant amount of waste, principally due to a series of complex isolation procedures which often involves hazardous and expensive solvents after each step. Multicomponent domino reactions (MDRs), have become an increasingly useful tool for the synthesis of chemically and biologically important compounds because of their convergence atom economy and other suitable characteristics form the point of view of green chemistry [2–6].

Heterocyclic compounds occur very widely in nature and are essential to life. Oxygen containing heterocyclic molecules constitutes the significant portion of chemical entities, which are part of many natural products and biologically active pharmaceuticals vital for enhancing quality of life [7]. The development of efficient chemical processes for the preparation of new biologically active and structurally captivating molecules constitutes a major challenge for chemists in organic synthesis. Significant advances have been made in the chemical processes to achieve the ultimate goal of hazard-free, waste-free and energy-efficient synthesis [8]. In this context, multicomponent reactions have played an important role in these processes [9,10]. MCR is the well-known concept [11,12] and has been used extensively in both liquid-phase and solid-phase [13] chemistry for the rapid assembly of complex heterocyclic structures of therapeutic importance [14]. Pyran based heterocyclic compounds are having an important place due to their distinct structures and great potential for further transformations. Some novel methods for the synthesis of pyrans via MCR's have been reported. Several catalysts like CTACl [15], Baker's yeast [16], L-proline [17], NaBr [18], phenylboronic acid [19], piperidine [20,21], KF-montmorillonite [22], Ru [23], imidazole [24], $NiCl_2$ [25], nano-ZnO [26,27], S-proline [28], $SiO_2$ NPs [29], DMAP [30] and $NEt_3$ [31] have been utilized for this transformations. However,

* Corresponding author. Tel.: +91 9443583619.
*E-mail address:* arul7777@yahoo.com (B. Arul Prakasam).

0022-2860/$ - see front matter © 2012 Elsevier B.V. All rights reserved.
http://dx.doi.org/10.1016/j.molstruc.2012.11.057




**Scheme 1.**

in this era, when green methods are warranted, many of these methods are not satisfactory as they involve the use of halogenated solvents, drastic reaction conditions, low yields and tedious work up procedure, which hampers their applications and leaves room for further upgradation.

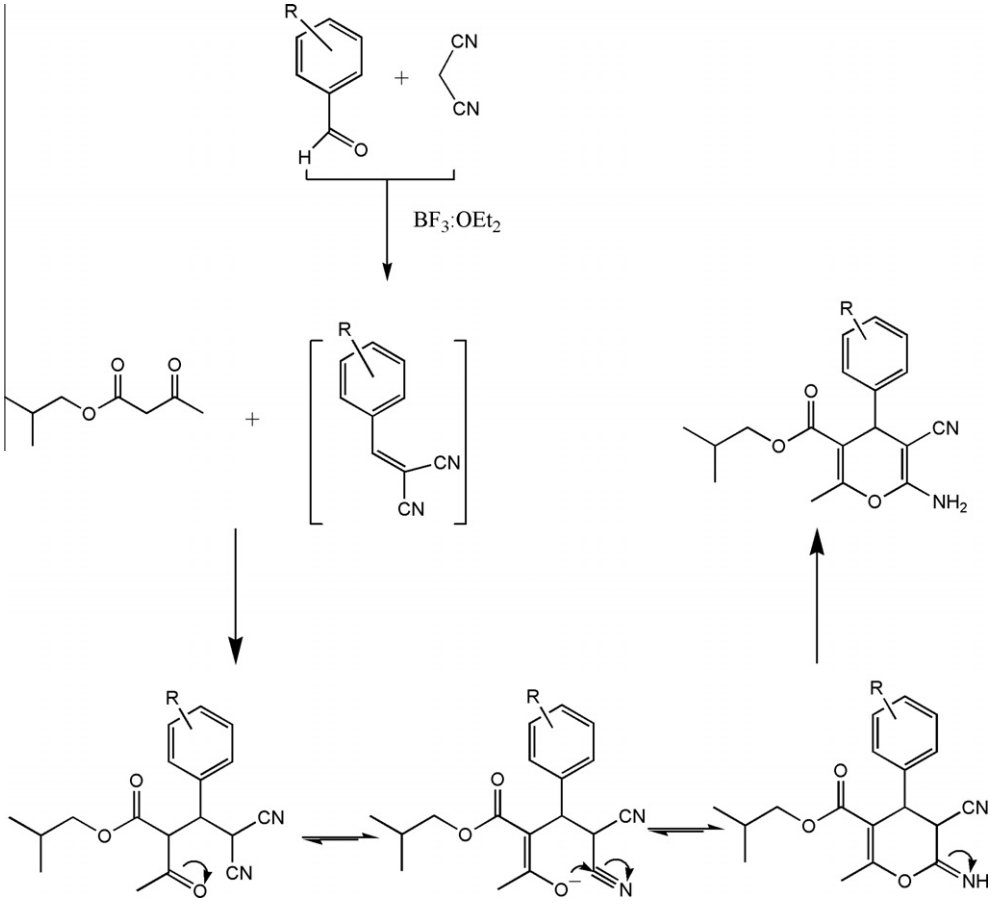
A careful survey of literature reveals that there is a need for general method of the synthesis of structurally diverse isobutyl 6-amino-4-aryl-5-cyano-2-methyl-4*H*-pyran-3-carboxylates. In this paper, we report the synthesis of a series of isobutyl 6-amino-4-aryl-5-cyano-2-methyl-4*H*-pyran-3-carboxylates using $BF_3$:$OEt_2$ as a catalyst.

## 2. Experimental

Starting materials obtained from commercially available analytical grade materials were used as supplied, without further purification. IR spectra were recorded on Avatar Nicolet FT-IR spectrophotometer (range 4000–400 $cm^{-1}$) as KBr pellets. Proton NMR spectra were recorded at room temperature (298 K) on Bruker AMX-400 spectrometer operating at 400.23 MHz using TMS as internal reference. $^{13}C$ NMR spectra were recorded in proton decoupled mode on Bruker AMX-400 spectrometer operating at 100.63 MHz. $CDCl_3$ was used as solvent for NMR spectral studies.

### 2.1. General procedure for the synthesis of compounds **1–9**

A mixture of aromatic aldehyde (1.0 mmol), malononitrile (1.0 mmol), isobutyl ethylacetoacetate (1.0 mmol), and $BF_3$:$OEt_2$ (0.04 mmol) was stirred magnetically in 25 ml of absolute ethanol at 80 °C (Scheme 1) for required period of time (~80 min). The progress of the reaction was monitored by TLC. After completion of the reaction, the reaction mixture was allowed to cool to room temperature and the solvent was evaporated. The solid thus appeared was




**Scheme 2.**

collected and washed with cold water and finally recrystallized from ethanol to get the pure product. The proposed mechanism of the reaction is given in Scheme 2.

*2.1.1. Isobutyl 6-amino-5-cyano-2-methyl-4-phenyl-4H-pyran-3-carboxylate* ***1***

Yellow solid, yield: 92%. m.p. 158–160 °C; IR (KBr, $cm^{-1}$) 3408, 3332, 2963, 2191, 1696, 1380, 1263, 1061; $^1H$ NMR (δ): 7.31–7.18 (m, 5H, Ar—H), 4.47 (s, 2H, $NH_2$), 4.44 (s, 1H, H-4), 3.76 (m, 2H, H-8), 2.4 (s, 3H, H-12), 1.74 (m, 1H, H-9), 0.76 (d, *J* = 8 Hz, 3H, H-10), 0.73 (d, *J* = 6.8 Hz, 3H, H-11); $^{13}C$ NMR (δ): 166.0, 157.4, 157.2, 143.7, 128.6, 127.3, 127.2, 119.0, 107.7, 70.9, 62.5, 38.7, 27.5, 19.0, 19.0, 18.5; Anal. Calcd. (%) for $C_{18}H_{20}N_2O_3$: C, 69.21; H, 6.45; N, 8.97. Found (%): C, 69.01; H, 6.34; N, 8.25; HRMS (ESI): *m*/*z* 312.8.

*2.1.2. Isobutyl 6-amino-4-(2-chlorophenyl)-5-cyano-2-methyl-4H-pyran-3-carboxylate* ***2***

Yellow solid, yield: 87%. m.p. 145–147 °C; IR (KBr, $cm^{-1}$) 3423, 3329, 2962, 2195, 1691, 1377, 1264, 1060; $^1H$ NMR (δ): 7.34–7.12 (m, 4*H*, Ar—H), 5.06 (s, 1H, H-4), 4.49 (s, 2H, $NH_2$), 3.75 (m, 2H, H-8), 2.43 (s, 3H, H-12), 1.77 (m, 1H, H-9), 0.75 (d, *J* = 6.8 Hz, 3H, H-10), 0.67 (d, *J* = 6.8 Hz, 3H, H-11); $^{13}C$ NMR (δ): 166.7, 158.2, 157.6, 141.1, 133.0, 129.9, 129.5, 128.3, 127.3, 118.5, 106.8, 71.1, 61.3, 35.2, 27.5, 18.9, 18.9, 18.5; Anal. Calcd. (%) for $C_{18}H_{19}ClN_2O_3$: C, 62.34; H, 5.52; N, 8.08. Found (%): C, 62.02; H, 5.32; N, 7.92; HRMS (ESI): *m*/*z* 346.7.

*2.1.3. Isobutyl 6-amino-4-(4-chlorophenyl)-5-cyano-2-methyl-4H-pyran-3-carboxylate* ***3***

Yellow solid, yield: 89%. m.p. 139–140 °C; IR (KBr, $cm^{-1}$) 3403, 3330, 2963, 2196, 1694, 1339, 1268, 1062; $^1H$ NMR (δ): 7.28–7.08 (m, 4*H*, Ar—H), 4.52 (s, 2H, $NH_2$), 4.46 (s, 1H, H-4), 3.76 (m, 2H, H-8), 2.39 (s, 3H, H-12), 1.77 (m, 1H, H-9), 0.79 (d, *J* = 6.4 Hz, 3H, H-10), 0.76 (d, *J* = 6.8 Hz, 3H, H-11); $^{13}C$ NMR (δ): 166.0, 157.4, 157.3, 132.9, 129.6, 129.6, 129.1, 119.0, 107.9, 70.9, 66.2, 38.3, 27.5, 19.0, 19.0, 18.6; Anal. Calcd. (%) for $C_{18}H_{19}ClN_2O_3$: C, 62.34; H, 5.52; N, 8.08. Found (%): C, 62.10; H, 5.38; N, 7.84; HRMS (ESI): *m*/*z* 346.4.

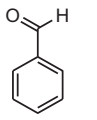
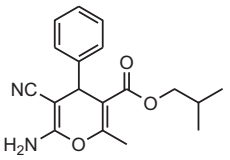
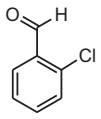
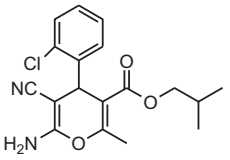
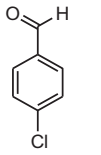
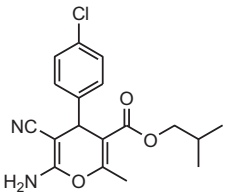
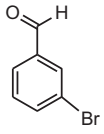
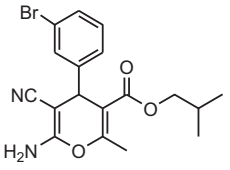
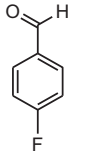
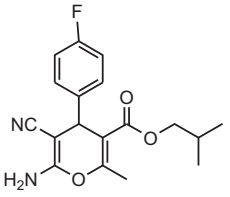
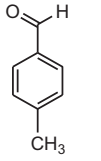
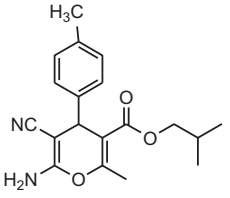
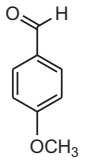
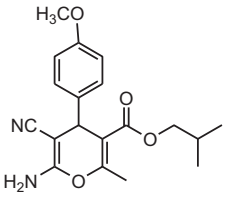
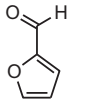
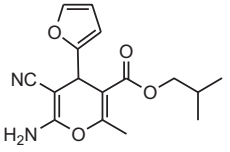
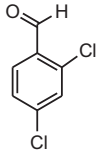
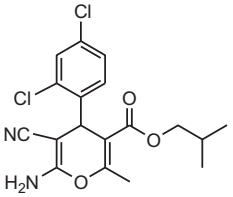
*2.1.4. Isobutyl 6-amino-4-(3-bromophenyl)-5-cyano-2-methyl-4H-pyran-3-carboxylate* ***4***

Yellow solid, yield: 90%. m.p. 142–144 °C; IR (KBr, $cm^{-1}$) 3405, 3326, 2958, 2190, 1695, 1379, 1263, 1060; $^1H$ NMR (δ): 7.34–7.14 (m, 4*H*, Ar—H), 4.54 (s, 2H, $NH_2$), 4.40 (s, 1H, H-4), 3.78 (m, 2H, H-8), 2.41 (s, 3H, H-12), 1.78 (m, 1H, H-9), 0.79 (d, *J* = 6.8 Hz, 3H, H-10), 0.76 (d, *J* = 6.8 Hz, 3H, H-11); $^{13}C$ NMR (δ): 165.6, 157.7, 157.5, 146.1, 130.4, 130.3, 130.2, 126.2, 122.8, 118.6, 107.2, 71.1, 61.9, 38.5, 27.5, 19.0, 19.0, 18.6; Anal. Calcd. (%) for $C_{18}H_{19}BrN_2O_3$: C, 55.26; H, 4.89; N, 7.16. Found (%): C, 55.12; H, 4.52; N, 7.02; HRMS (ESI): *m*/*z* 390.9.

*2.1.5. Isobutyl 6-amino-5-cyano-4-(4-fluorophenyl)-2-methyl-4H-pyran-3-carboxylate* ***5***

Yellow solid, yield: 88%. m.p. 147–149 °C; IR (KBr, $cm^{-1}$) 3410, 3335, 2963, 2197, 1688, 1378, 1266, 1063; $^1H$ NMR (δ): 7.18–6.96 (m, 4*H*, Ar—H), 4.55 (s, 2H, $NH_2$), 4.43 (s, 1H, H-4), 3.77 (m, 2H, H-8), 2.39 (s, 3H, H-12), 1.77 (m, 1H, H-9), 0.78 (d, *J* = 6.8 Hz, 3H, H-10), 0.75 (d, *J* = 6.8 Hz, 3H, H-11); $^{13}C$ NMR (δ): 165.9, 157.4, 157.2, 139.6, 128.9, 128.8, 118.9, 116.4, 115.6, 115.4, 107.6, 71.3, 62.2, 38.1, 27.5, 19.2, 18.8, 18.5; Anal. Calcd. (%) for $C_{18}H_{19}FN_2O_3$: C, 65.44; H, 5.80; N, 8.48. Found (%): C, 65.02; H, 5.49; N, 8.20; HRMS (ESI): *m*/*z* 330.8.

**Table 1**
Structure and yield for compounds **1**–**9**.

| Compound nos. | Aldehyde | Product | Yield (%) |
|---|---|---|---|
| **1** |  |  | 92 |
| **2** |  |  | 87 |
| **3** |  |  | 89 |
| **4** |  |  | 90 |
| **5** |  |  | 88 |
| **6** |  |  | 91 |
| **7** |  |  | 92 |
| **8** |  |  | 86 |
| **9** |  |  | 86 |

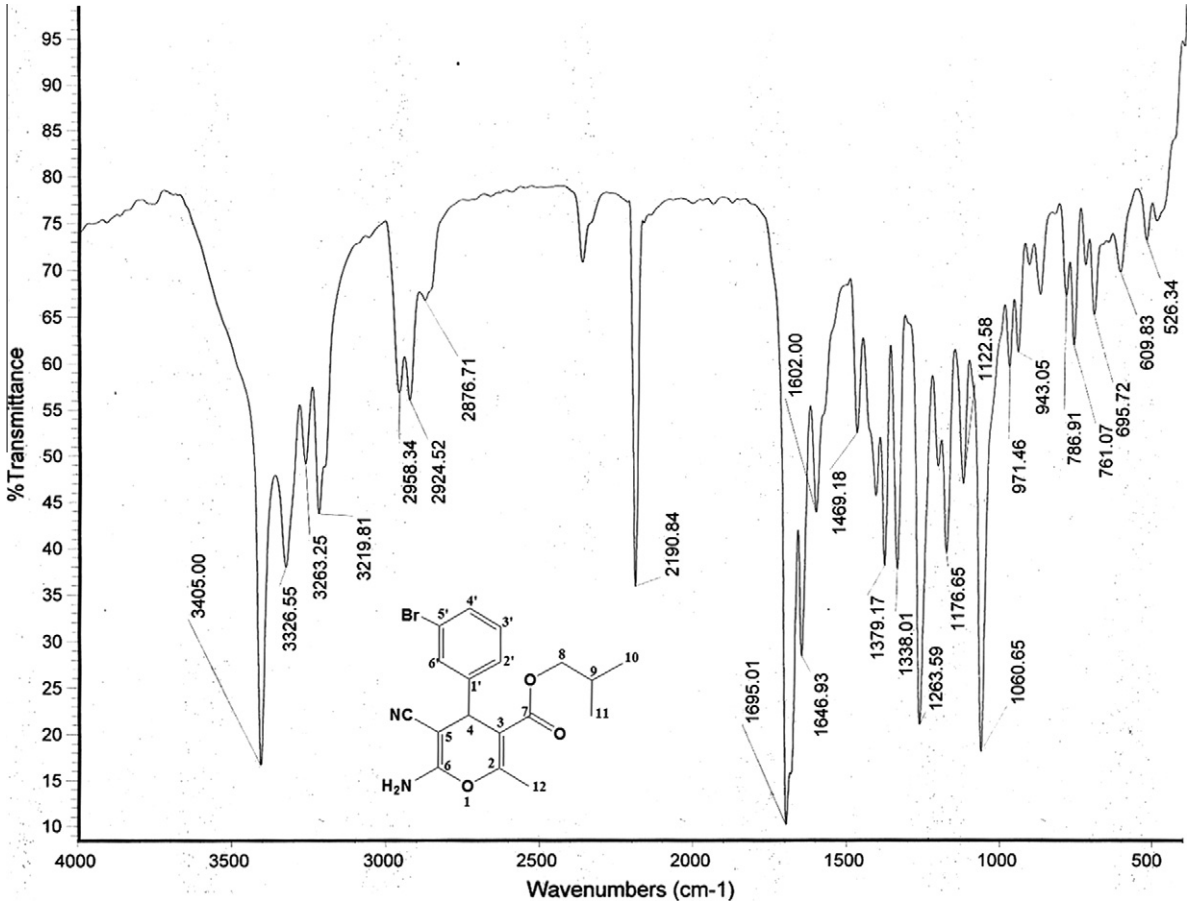



**Fig. 1.** IR spectrum of compound **4**.

*2.1.6. Isobutyl 6-amino-5-cyano-2-methyl-4-(4-methylphenyl)-4H-pyran-3-carboxylate **6***

Yellow solid, yield: 91%. m.p. 137–139 °C; IR (KBr, $cm^{-1}$) 3407, 3330, 2962, 2198, 1690, 1379, 1266, 1060; $^1H$ NMR (δ): 7.20–7.08 (m, 4*H*, Ar—H), 4.47 (s, 2H, $NH_2$), 4.40 (s, 1H, H-4), 3.76 (m, *J* = 6.4 Hz, 2H, H-8), 2.38 (s, 3H, H-12), 1.78 (m, 1H, H-9), 0.79 (d, *J* = 6.8 Hz, 3H, H-10), 0.76 (d, *J* = 6.8 Hz, 3H, H-11); $^{13}C$ NMR (δ): 166.0, 157.3, 156.9, 140.8, 136.7, 129.3, 127.1, 119.0, 107.9, 70.9, 62.8, 38.3, 27.5, 21.0, 19.0, 19.0, 18.5; Anal. Calcd. (%) for $C_{19}H_{22}N_2O_3$: C, 69.92; H, 6.79; N, 8.58. Found (%): C, 69.52; H, 6.38; N, 8.02; HRMS (ESI): *m*/*z* 326.4.

*2.1.7. Isobutyl 6-amino-5-cyano-4-(4-methoxyphenyl)-2-methyl-4H-pyran-3-carboxylate **7***

Yellow solid, yield: 92%. m.p. 135–137 °C; IR (KBr, $cm^{-1}$) 3404, 3330, 2962, 2192, 1691, 1378, 1260, 1062; $^1H$ NMR (δ): 7.26–6.81 (m, 4*H*, Ar—H), 4.41 (s, 2H, $NH_2$), 4.40 (s, 1H, H-4), 3.77 (m, 2H, H-8), 2.38 (s, 3H, H-12), 1.78 (m, 1H, H-9), 0.80 (d, *J* = 6.8 Hz, 3H, H-10), 0.77 (d, *J* = 6.8 Hz, 3H, H-11); $^{13}C$ NMR (δ): 166.1, 158.7, 157.2, 156.7, 136.0, 128.4, 119.0, 114.0, 108.0, 70.9, 62.9, 55.3, 37.9, 27.5, 19.0, 19.0, 18.5; Anal. Calcd. (%) for $C_{19}H_{22}N_2O_4$: C, 66.65; H, 6.48; N, 8.18. Found (%): C, 66.25; H, 6.39; N, 7.92; HRMS (ESI): *m*/*z* 342.7.

*2.1.8. Isobutyl 6-amino-5-cyano- 4-(furan-2-yl)-2-methyl-4H-pyran-3-carboxylate **8***

Yellow solid, yield: 86%. m.p. 132–134 °C; IR (KBr, $cm^{-1}$) 3409, 3331, 3267, 2969, 2192, 1697, 1332, 1263, 1061; $^1H$ NMR (δ): 7.29–6.08 (m, 3H, Ar—H), 4.62 (s, 2H, $NH_2$), 4.57 (s, 1H, H-4), 3.87 (m, 2H, H-8), 2.37 (s, 3H, H-12), 1.87 (m, 1H, H-9), 0.86 (d, *J* = 2.8 Hz, 3H, H-10), 0.85 (d, *J* = 2.8 Hz, 3H, H-11); $^{13}C$ NMR (δ): 165.7, 158.5, 158.1, 155.2, 141.9, 118.8, 110.4, 105.7, 105.6, 71.1, 59.4, 32.3, 30.9, 27.6, 19.0, 18.5; Anal. Calcd. (%) for $C_{16}H_{18}N_2O_4$: C, 63.56; H, 6.00; N, 9.27. Found (%): C, 63.21; H, 5.89; N, 9.14; HRMS (ESI): *m*/*z* 302.9.

*2.1.9. Isobutyl 6-amino-5-cyano-4-(2,4-dichlorophenyl)-2-methyl-4H-pyran-3-carboxylate **9***

Yellow solid, yield: 86%. m.p. 144–146 °C; IR (KBr, $cm^{-1}$) 3414, 3329, 3260, 2961, 2195, 1709, 1315, 1260, 1065; $^1H$ NMR (δ): 7.36–7.08 (m, 3H, Ar—H), 5.01 (s, 1H, H-4), 4.57 (s, 2H, $NH_2$), 3.76 (m, 2H, H-8), 2.42 (s, 3H, H-12), 1.78 (m, 1H, H-9), 0.93 (d, *J* = 6.8 Hz, 3H, H-10), 0.78 (d, *J* = 6.8 Hz, 3H, H-11); $^{13}C$ NMR (δ): 165.5, 158.5, 157.7, 139.9, 133.7, 133.4, 129.6, 127.7, 118.3, 106.4, 71.2, 60.7, 35.0, 27.5, 19.1, 18.9, 18.9, 18.6 Anal. Calcd. (%) for $C_{18}H_{18}Cl_2N_2O_3$: C, 56.71; H, 4.76; N, 7.35. Found (%): C, 56.54; H, 4.52; N, 7.21; HRMS (ESI): *m*/*z* 380.8.

*2.2. X-ray crystallography*

Crystal was grown by slow evaporation technique using ethanol as solvent. Diffraction data were collected on a Bruker, 2004 APEX 2 diffractometer using graphite-monochromated Mo Kα radiation (λ = 0.71073 Å) at 293 K with crystal size of 0.30 × 0.30 × 0.30 mm. The structure was solved by direct methods and successive Fourier difference syntheses (SHELXS-97) [32] and refined by full matrix least square procedure on $F^2$ with anisotropic thermal parameters. All non-hydrogen atoms were refined (SHELXL-97) [33] and placed at chemically acceptable positions. A total of 269 parameters were refined with 3023 unique reflections which

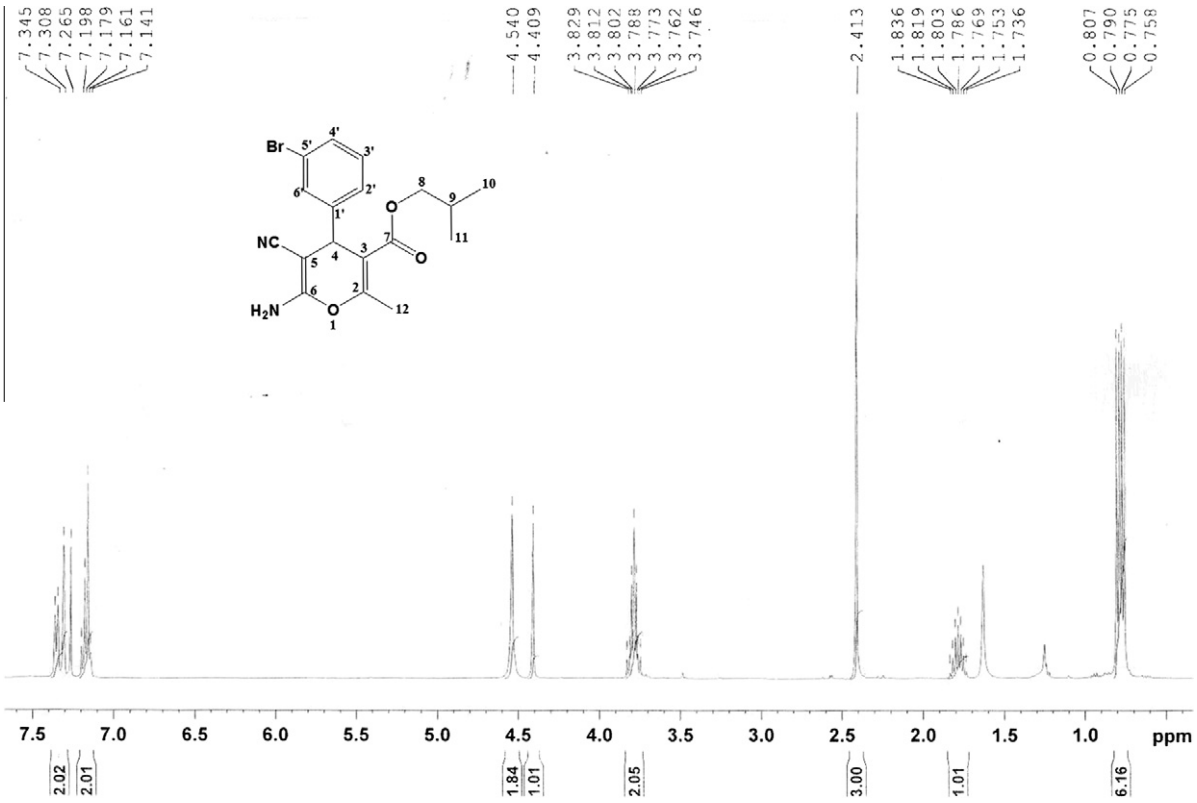



**Fig. 2.** $^{1}$H NMR spectrum of compound **4**.

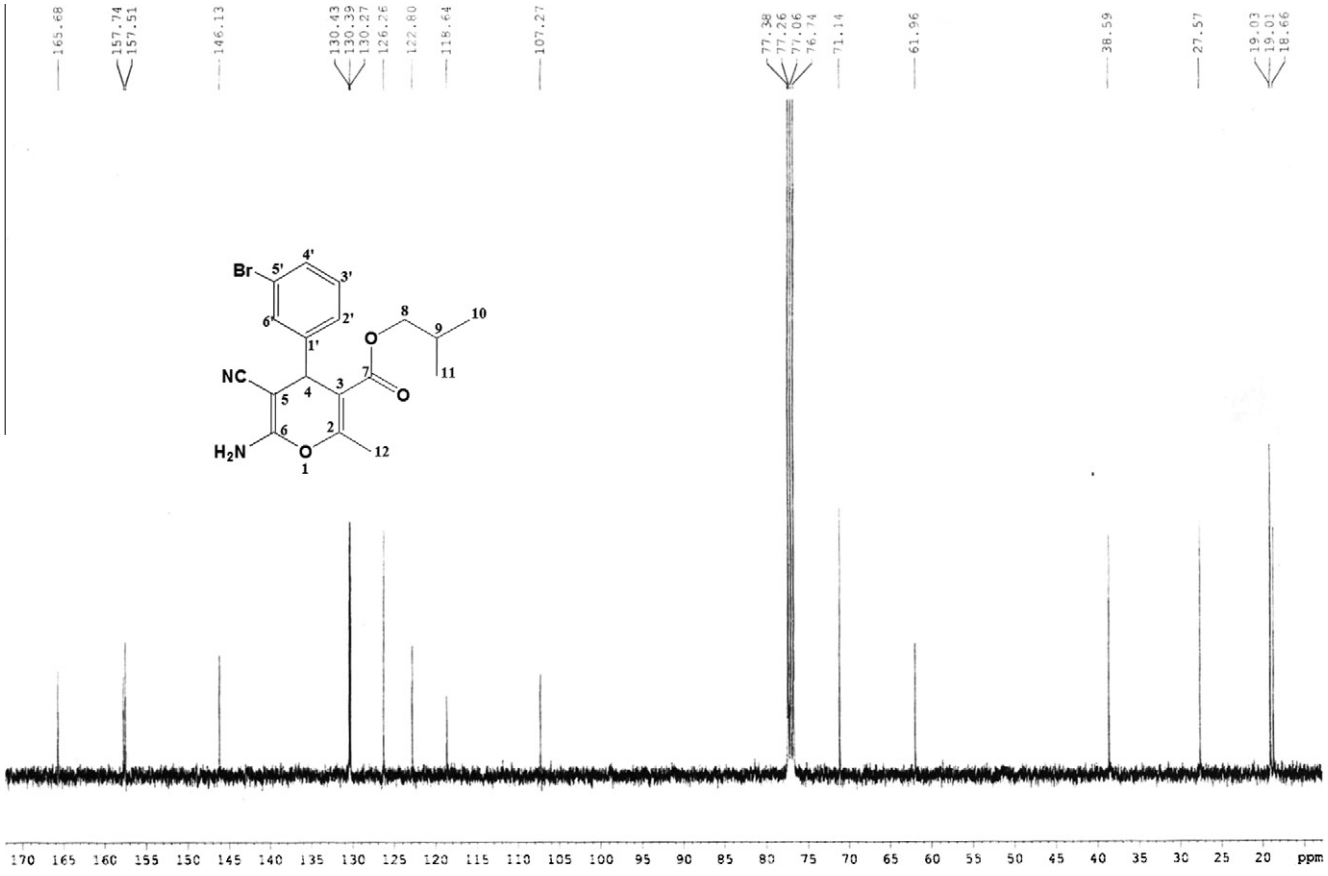



**Fig. 3.** $^{13}$C NMR spectrum of compound **4**.

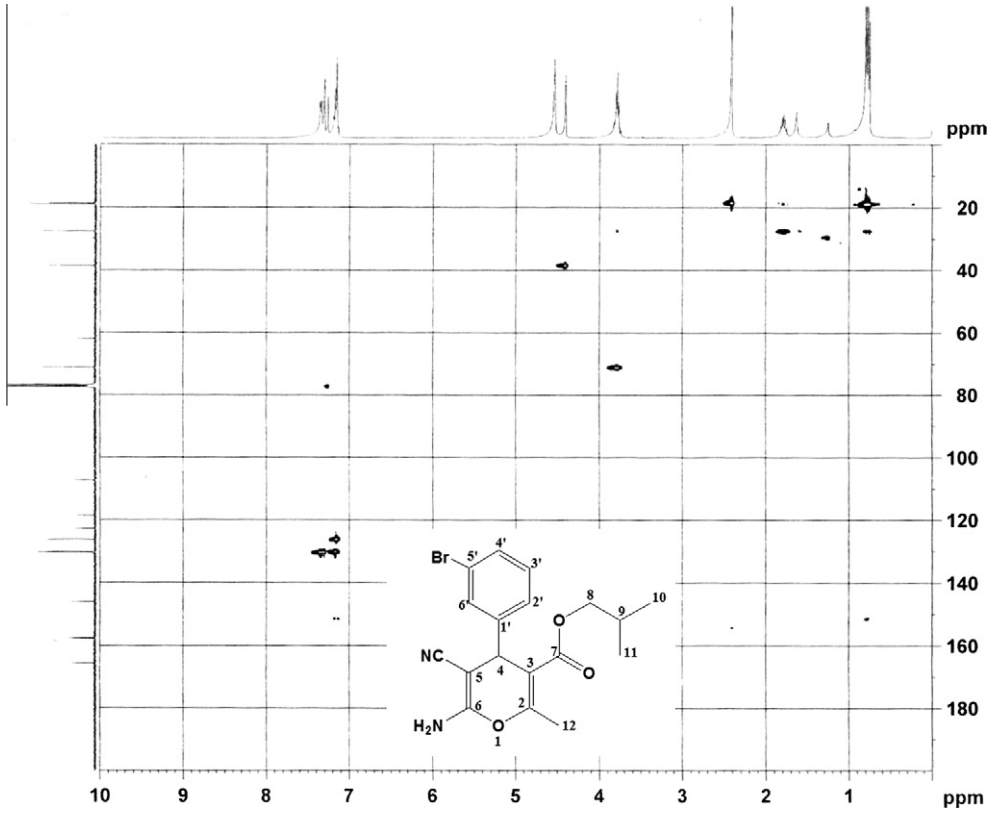



**Fig. 4.** HSQC spectrum of compound **4**.

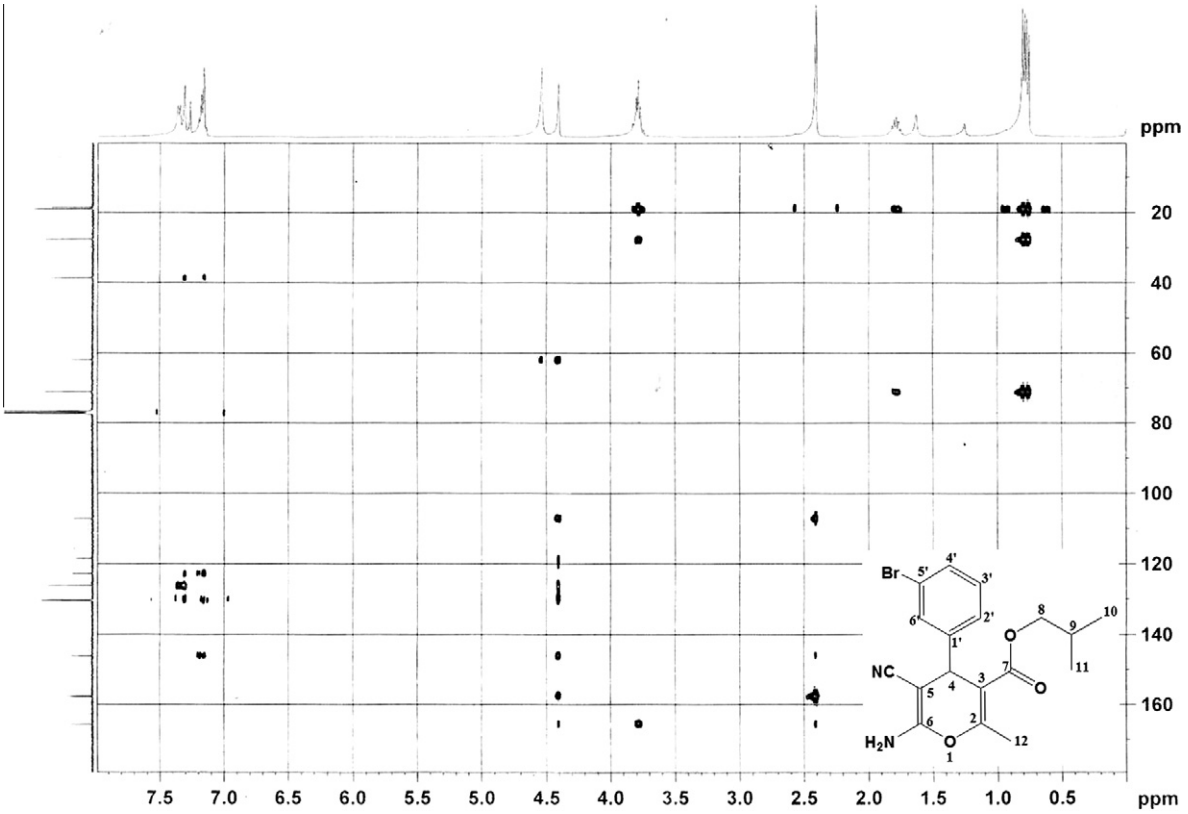



**Fig. 5.** HMBC spectrum of compound **4**.

**Table 2**
Correlations in the HSQC and HMBC spectra of compound **4.**

| Signals | Correlations in HSQC | Correlations in HMBC |
|---|---|---|
| 7.36–7.14 (Ar—H) | 146.1–122.8 | H2′: 130.2 (α), 130.4 (β), 146.1 (α), 122.8 (β), 38.5 (β)<br>H3′: 130.3 (α), 146.1 (β), 122.8 (γ), 130.4 (α), 126.2 (β), 38.5 (γ)<br>H4′: 130.2 (α), 130.3 (β), 146.1 (γ)<br>H6′: 146.1 (α), 130.3 (β), 130.2 (γ), 126.2 (α), 130.4 (β), 38.5 (β) |
| 4.40 (Benzylic proton) | 38.5 | 146.1 (α), 130.3 (β), 130.2 (γ), 122.8 (β), 126.2 (γ), 61.9 (α), 157.5 (β), 107.2 (α), 157.7 (β), 165.6 (β) |
| 2.4 ($CH_3$) | 18.6 | 157.7 (α), 107.2 (β), 165.6 (γ), 157.5 (γ) |
| 3.82–3.74 (O—$CH_2$) | 71.1 | 27.5 (α), 19.03 (β), 19.01 (β), 165.6 (β) |
| 1.83–1.73 (Isobutyl CH) | 27.5 | 19.01 (α), 19.03 (α), 71.1 (α) |
| 0.80–0.79 (Isobutyl $CH_3$) | 19.03 | 27.5 (α), 19.01 (α), 71.1 (β) |
| 0.77–0.75 (Isobutyl $CH_3$) | 19.01 | 27.5 (α), 19.03 (β), 71.1 (β) |

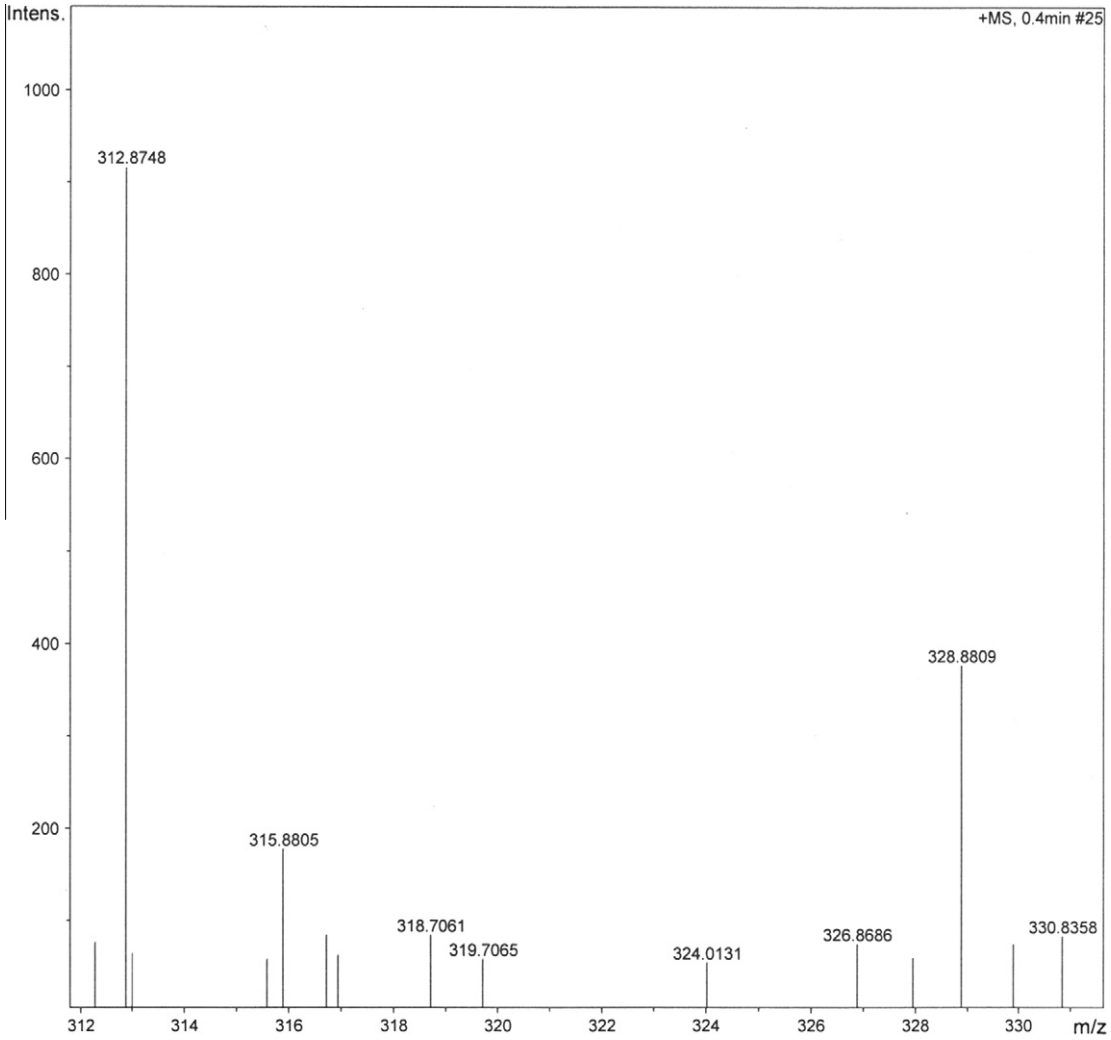



**Fig. 6.** Mass spectrum of **1**.

covered the residuals to $R_1 = 0.0566$. Crystallographic data have been deposited with the Cambridge Crystallographic Data Centre as supplementary publications number CCDC 901850 for **1**. Copies of the data can be obtained free of charge via http://www.ccdc.cam.ac.uk/conts/retrieving.html, or from the Cambridge Crystallographic Data Centre, 12 Union Road, Cambridge CB2 1EZ, UK; fax: +44 1223 336 033: or e-mail: deposit@ccdc.cam.ac.uk.

## 3. Results and discussion

Initially, the reaction between benzaldehyde, malononitrile and isobutyl ethylacetoacetate was selected as a model reaction. The same reaction was carried out with substituted aryl aldehydes in ethanol using $BF_3$:$OEt_2$ as catalyst and the corresponding isobutyl 6-amino-4-aryl-5-cyano-2-methyl-4*H*-pyran-3-carboxylates were obtained in high yield (86–92%). The results are summarized in Table 1.

### 3.1. IR spectral analysis of compounds *1*–*9*

Characteristic absorption of the 4*H*-pyran derivatives **(1–9)** are due to $\nu_{C=O}$, $\nu_{C\equiv N}$, $\nu_{N-H}$ stretching modes. The observed maxima in the region of 1714–1688 $cm^{-1}$ are characteristic of carbonyl (C=O) stretching frequency of ester function. The observed bands around

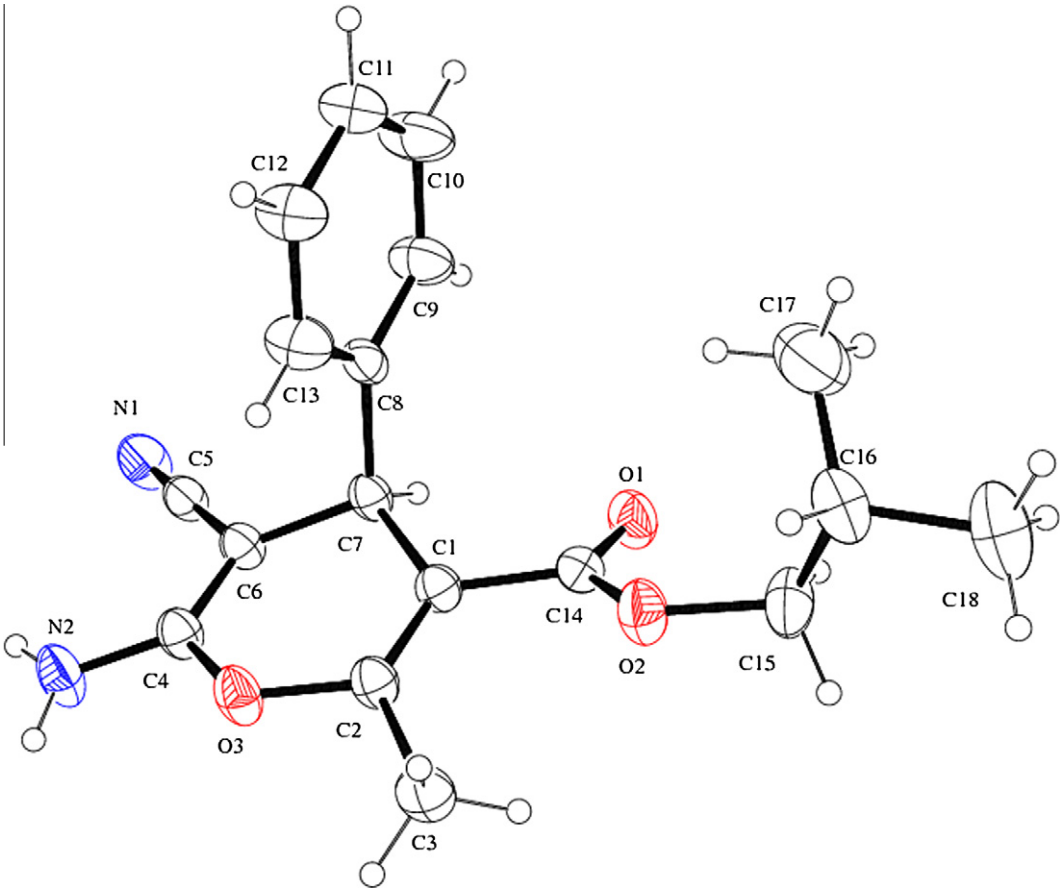



**Fig. 7.** ORTEP diagram of **1**.

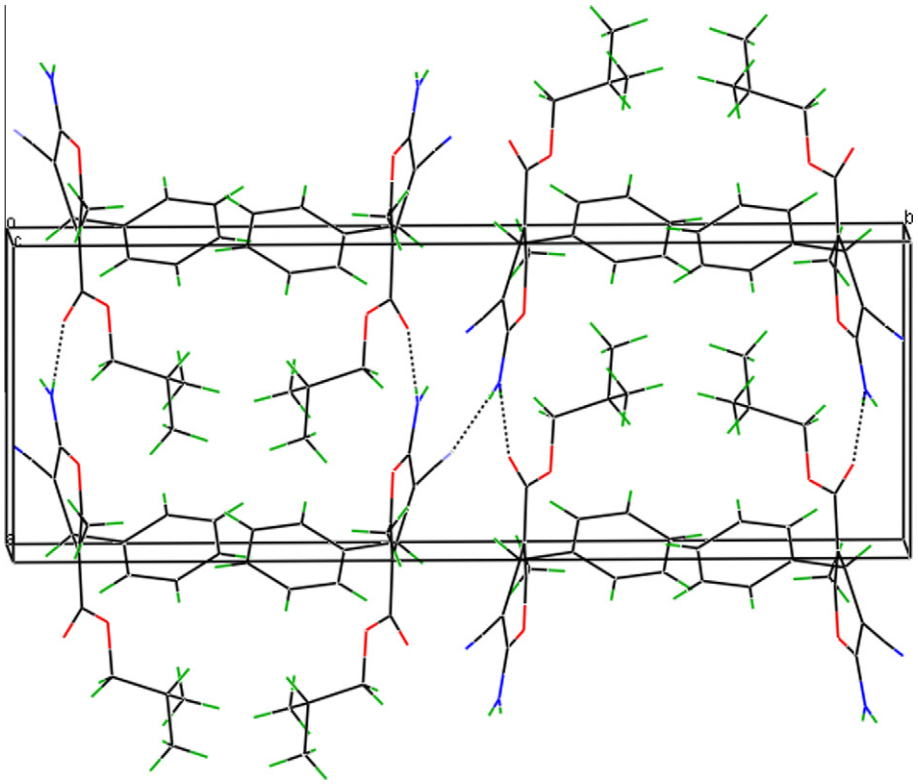



**Fig. 8.** Packing diagram of **1**.

**Table 3**
Crystal data and structure refinement details for **1**.

| | |
|---|---|
| Empirical formula | $C_{18}H_{20}N_2O_3$ |
| Formula weight | 312.3 |
| Temperature | 293(2) K |
| Wavelength | 0.71073 Å |
| Crystal system, space group | Monoclinic, P21/c |
| Unit cell dimension | $a$ = 8.526(5) Å |
| | $\alpha$ = 90.0(5)° |
| | $b$ = 23.138(5) Å |
| | $\beta$ = 103.719(5)° |
| | $c$ = 8.949(5) Å |
| | $\gamma$ = 90.0(5)° |
| Volume | 1715.0(14) Å$^3$ |
| $Z$, calculated density | 4, 1.210 mg/m$^3$ |
| Absorption coefficient | 0.083 mm$^{-1}$ |
| F(000) | 664 |
| Crystal size | 0.30 × 0.30 × 0.30 mm |
| Theta range for data collection | 2.46–25.0° |
| Limiting indices | $-6 \leqslant h \leqslant 10$, $-26 \leqslant k \leqslant 27$, $-10 \leqslant l \leqslant 10$ |
| Reflections collected/unique | 15,186/3023 |
| Completeness to theta | 100.0% |
| Absorption correction | Semi-empirical from equivalents |
| Max. and min. transmission | 0.970 and 0.942 |
| Refinement method | Full-matrix least squares on $F^2$ |
| Data/restraints/parameters | 3023/233/269 |
| Goodness-of-fit on $F^2$ | 1.034 |
| Final $R$, $R_W$ (obs, data) | 0.0566, 0.1218 |

**Table 4**
Selected bond distances (Å) and angles (°) for **1.**

| | |
|---|---|
| *Bond length* | |
| C(1)–C(2) | 1.336(2) |
| C(1)–C(7) | 1.508(2) |
| C(2)–O(3) | 1.391(2) |
| C(2)–C(3) | 1.484(2) |
| C(4)–N(2) | 1.330(2) |
| C(4)–C(6) | 1.352(2) |
| C(4)–O(3) | 1.361(2) |
| C(5)–N(1) | 1.146(2) |
| C(5)–C(6) | 1.409(2) |
| C(6)–C(7) | 1.506(2) |
| C(14)–O(1) | 1.203(2) |
| C(14)–O(2) | 1.327(2) |
| C(15)–O(2) | 1.450(2) |
| N(2)–H(2A) | 0.841(15) |
| N(2)–H(2B) | 0.866(16) |
| H(2A)···O(1)#1 | 2.150(17) |
| H(2B)···N(1)#2 | 2.187(17) |
| *Bond angles* | |
| C(1)–C(2)–O(3) | 120.95(15) |
| C(6)–C(4)–O(3) | 121.01(15) |
| N(1)–C(5)–C(6) | 178.4(2) |
| C(4)–C(6)–C(7) | 121.92(14) |
| C(6)–C(7)–C(1) | 109.57(11) |
| C(6)–C(7)–C(8) | 111.67(8) |
| C(1)–C(7)–C(8) | 109.91(8) |
| O(1)–C(14)–O(2) | 124.13(16) |
| O(1)–C(14)–C(1) | 122.00(16) |
| O(2)–C(14)–C(1) | 113.83(14) |
| C(14)–O(2)–C(15) | 119.47(15) |
| C(4)–O(3)–C(2) | 119.96(12) |
| N(2)–H(2A)···O(1)#1 | 160.9(19) |
| N(2)–H(2B)···N(1)#2 | 165(2) |

3423–3403 cm$^{-1}$ and 2190–2198 cm$^{-1}$ are due to amino and cyano groups respectively. The strong absorption band for C—O bond appeared around 1260–1268 cm$^{-1}$ and also the C—H stretching frequencies were observed in the region of 2962–2969 cm$^{-1}$. IR spectrum of compound **4** is shown in Fig. 1.

### 3.2. NMR spectra

#### 3.2.1. $^1$H NMR spectral analysis of compound *4*

For NMR spectral analysis, compound **4** was chosen as a representative. For **4**, the HSQC and HMBC NMR spectra were also recorded for the unambiguous assignment of signals. Proton NMR spectrum of this compound (Fig. 2) shows the presence of a sharp singlet at 4.40 ppm due to benzylic proton and another sharp singlet appeared at 2.41 ppm is due to the presence of three methyl protons. One sharp singlet appeared at 4.50 ppm is assigned to two amino ($NH_2$) protons. Two multiplets appeared around 1.83–1.73 ppm and 3.82–3.74 ppm is assigned to C9 and C8 protons. Methyl protons associated with C10 and C11 are appeared as two doublets (0.79–0.76 ppm) with the small difference in chemical shifts. Aromatic protons occur in the range of 7.36–7.14 ppm. Three sets of signals are observed for the aromatic protons and among the three; the multiplet in the range of 7.19–7.14 ppm is assigned to C3′ proton. In the remaining two signals, a singlet at 7.30 ppm is assigned to C6′ proton and another doublet at 7.34 ppm is due to C4′ and C2′ protons in the phenyl ring.

#### 3.2.2. $^{13}$C NMR and 2D NMR spectral analysis of compound *4*

In the $^{13}$C NMR spectrum of compound **4** (Fig. 3), the most upfiled resonances at 18.6, 19.01 and 19.03 ppm are assigned to the methyl carbons at C10, C11 and C12 respectively. In addition, there are three signals observed in the aliphatic region of 71.1, 38.5 and 27.5 ppm respectively. In its HSQC spectrum (Fig. 4), the carbon signal at 71.1 ppm has a cross peak with the proton resonance at 3.80 ppm. Hence, the signal is conveniently assigned to C8 carbon. Similarly, the carbon resonance at 38.5 ppm has a cross peak with the singlet at 4.40 ppm, in the $^1$H NMR spectrum and hence it is assigned to the benzylic carbon (C4). The remaining signal at 27.5 ppm shows correlation with a multiplet at 1.78 ppm and hence it is conveniently assigned to C9 carbon. A peak at 165.6 ppm without correlation is owed to carbonyl carbon of the ester moiety. Further the assignment of signals was irrefutably confirmed from its HMBC spectrum (Fig. 5). In the HMBC spectrum the signals from 146.1 to 122.8 ppm have correlations with phenyl protons multiplet. However, the lower frequency resonance at 146.1 ppm has good correlation with the benzylic proton signal at 4.40 ppm ($\alpha$-correlation); this clearly indicates that the signal is ascribed to the phenyl *ipso* carbon. All the HSQC and HMBC correlations are listed in Table 2. HRMS of compound **1** is given in Fig. 6.

### 3.3. Single crystal X-ray structural analysis of isobutyl 6-amino-5-cyano-2-methyl-4-phenyl-4H-pyran-3-carboxylate *1*

The structure and geometry of **1** in the solid state is established by single crystal X-ray structural analysis. Compound **1** crystallizes in a monoclinic system with P21/c space group. Four molecules are present in the unit cell. ORTEP of **1** is shown in Fig. 7 and the packing diagram is given in Fig. 8. Crystal data, data collection and structure refinement parameters are given in Table 3. Selected bond distances and angles are given in Table 4.

In the pyran ring C(1)—C(2) and C(4)—C(6) bonds are double bonded in nature [C(1)—C(2) = 1.336(2) and C(4)—C(6) = 1.352(2) Å] as indicated by the bond distances [34]. The conformation of the pyran ring can be described as flattened boat, which is evidenced from the small puckering parameters associated with the O(3) and C(7) atoms present at 1st and 4th positions, respectively, of the pyran ring. The atoms O(3) and C(7) are displaced by 0.141 and 0.231 Å, respectively, from the plane defined by C(6)/C(4)/C(2)/C(1). The phenyl group is almost perpendicular to the pyran ring with the angle of 88.35(2)° [35].

The bond parameters associated with the ester function [C(14)—O(1) = 1.203(2) and C(14)—O(2) = 1.327(2) Å] clearly indicate the partial delocalization of π electron density over $COO^-$ moiety. Similarly, the cyano group is just about linear [C(6)—C(5)—N(1) = 178.4(2)°] and also triple bonded in nature [C(5)—N(1) = 1.146(2) Å]. It is also observed from the packing diagram that there are two intermolecular hydrogen bonds [homonuclear [N—H···N] and heteronuclear [N—H···O] type] which stabilize the packing. However, the observed H···A distances and the corresponding hydrogen bond angles shows that the hydrogen bonds are significantly weak and they are not perfectly linear. The bond parameters associated with the phenyl ring and isopropyl groups are normal.

## 4. Conclusions

A series of isobutyl 6-amino-4-aryl-5-cyano-2-methyl-4*H*-pyran-3-carboxylates (**1**–**9**) have been synthesized by the multicomponent reaction (MCR) between isobutyl ethylacetoacetate, aryl aldehydes and malononitrile using $BF_3$:$OEt_2$ as catalyst. In the IR spectra bands due to $\nu_{C=O}$, $\nu_{C\equiv N}$, $\nu_{N\cdot H}$ stretching modes are observed clearly. $^1H$ and $^{13}C$ NMR spectral results are in line with the proposed structure of compounds. Subsequently, the assignment of signals is unambiguously confirmed from the HMBC and HSQC spectra of the representative compound (**4**). Single crystal X-ray structural analysis of **1**, has also been performed and the results evidence the mean plane deviations of atoms present at 1st and 4th positions of the pyran ring due to the "flattened-boat conformation". The packing of molecules is stabilized by homonuclear [N—H···N] and heteronuclear [N—H···O] intermolecular hydrogen bonds.

## References

[1] P.A. Grieco, Organic Synthesis in Water, Thomson Science, London, 1998. p. 1.
[2] A. Domling, I. Ugi, Angew. Chem. Int. Ed. Engl. 39 (2000) 3168.
[3] I. Ugi, A. Domling, Endeavour 18 (1994) 115.
[4] B. Ganem, Acc. Chem. Res. 42 (2009) 463.
[5] D.M. D'souza, T.J. Muller, Chem. Soc. Rev. 36 (2007) 1095.
[6] C.J. Li, L. Chen, Chem. Soc. Rev. 35 (2006) 68.
[7] M.C. Bagley, T. Davis, M.C. Dix, M.J. Rokicki, D. Kipling, Bioorg. Med. Chem. Lett. 17 (2007) 5107.
[8] D.J. Adams, P.J. Dyson, S.J. Tavener, Chemistry in Alternative Reaction Media, Wiley-VCH, Weinheim, 2004.
[9] L. Weber, M. Illgen, M. Almstetter, Synlett (1999) 366.
[10] P.A. Wender, S.T. Handy, D.L. Wright, Chem. Ind. (1997) 765.
[11] A. Strecker, Liebigs Ann. Chem. 75 (1850) 27.
[12] G.H. Posner, Chem. Rev. 86 (1986) 831.
[13] S.L. Dax, J.J. McNally, M.A. Youngman, Curr. Med. Chem. 6 (1999) 255.
[14] A. Nefzi, J.M. Ostresh, R.A. Houghten, Chem. Rev. 97 (1997) 449.
[15] R. Ballini, G. Bosica, M.L. Conforti, R. Maggi, A. Mazzacani, P. Righi, G. Sartori, Tetrahedron 57 (2001) 1395.
[16] U.R. Pratap, D.V. Jawale, P.D. Netankar, R.A. Mane, Tetrahedron. Let. 52 (2011) 5817.
[17] Y. Li, H. Chen, C. Shi, D. Shi, S. Ji, J. Comb. Chem. 12 (2010) 231.
[18] I. Devi, P.J. Bhuyan, Tetrahedron. Let. 45 (2004) 8625.
[19] S. Nemouchi, R. Boulicna, B. Carbon, A. Debache, C.R. Chimie 15 (2012) 394.
[20] T. Akbarzadeh, A. Rafinejad, J.M. Mollaghasem, M. Safari, A.F. Tafti, M. Pordeli, S.K. Ardestani, A. Shafiee, Arch. Pharm. Chem. Life Sci. 345 (2012) 386.
[21] A. Mahmoodi, A. Aliabadi, S. Emami, M. Safavi, S. Rajabalian, N. Lamei, A. Shafiee, A. Foroumadi, Arch. Pharm. Chem. Life Sci. 343 (2010) 411.
[22] Daqing Shi, Nan Wu, Qiya Zhuang, Chin. J. Chem. 27 (2009) 167.
[23] K. Tabatabaeian, H. Heidari, M. Mamaghani, N.O. Mahmoodi, Appl. Organomet. Chem. 26 (2012) 56.
[24] X. Guihuang, J. Liu, J. Den, T. Wang, W. Chen, B. Zeng, Tetrahedron 67 (2011) 6202.
[25] X.N. Zhang, Y.X. Li, Z.H. Zhang, Tetrahedron Let. 67 (2011) 7426.
[26] S. Paul, P. Bhattacharyya, A.R. Das, Tetrahedron Let. 52 (2011) 4636.
[27] P. Bhattacharyya, K. Prodhan, S. Paul, A.R. Das, Tetrahedron Let. 53 (2012) 4687.
[28] S. Abdolmohammadi, S. Balalaie, Tetrahedron Let. 48 (2007) 3299.
[29] S. Banerjee, A. Horn, H. Khatri, G. Sereda, Tetrahedron Let. 52 (2011) 1878.
[30] A.T. Khan, M. Lal, S. Ali, M. Khan, Tetrahedron Let. 52 (2011) 5327.
[31] M. Saeedi, Tetrahedron 66 (2010) 5345.
[32] G.M. Sheldrick, Acta Cryst. 46 (1990) 467.
[33] G.M. Sheldrick, SHELXL-97, University of Gottingen, Gottingen, Germany, 1997.
[34] W.H. Haynes, CRC Handbook of Chemistry and Physics, 92nd ed., (2011–2012).
[35] Mercury; Crystallographic Software from CCDC, <http://www.ccdc.cam.ac.uk>.