Synthesis of 1-Acyl-2-oxo-3-pyrrolidinecarbonitriles by the Reaction of 2-Acylamino-4,5-dihydro-3-furancarbonitriles with Sodium Iodide

Kenji Yamagata*, Fumi Okabe, Hiroshi Maruoka and Yoshinobu Tagawa

Faculty of Pharmaceutical Sciences, Fukuoka University, 8-19-1 Nanakuma, Jounan-ku,
Fukuoka 814-0180, Japan

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The reaction of 2-acylamino-4,5-dihydro-3-furancarbonitriles **1** with sodium iodide in *N*,*N*-dimethylformamide gave the corresponding 1-acyl-2-oxo-3-pyrrolidinecarbonitriles **2** in good yields. Successive treatment of **1** with titanium(IV) chloride and potassium carbonate resulted in the formation of *N*-acyl-1-cyanocyclopropanecarboxamides **4**. The same compounds **2** were also obtained by treatment of **4** with sodium iodide. The starting compounds **1** were synthesized by the reaction of 2-amino-4,5-dihydro-3-furancarbonitrile with acyl chlorides in pyridine.

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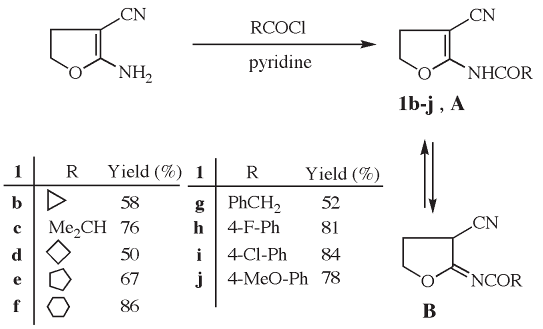
The 2-pyrrolidinone (γ-lactam) ring system is present in a large number of molecules possessing medicinal values such as psychotropic agents [1,2], muscarinic acid agonists [3], antihypertensive agents [4], peptide mimics [5,6]. γ-Lactams are also versatile synthetic intermediates, particularly of pyrrolidine alkaloids and γ-aminobutyric acid analogues [7-9]. Consequently, there has been an ongoing interest in the synthesis of substituted 2-pyrrolidinones [10].

We have previously reported a synthesis of 1-benzoyl-2-oxo-3-pyrrolidine carbonitrile or 3-ethyl-2-oxo-3-pyrrolidinecarbonitrile by the reaction of 2-benzamido-4,5-dihydro-3-furancarbonitrile or ethyl *N*-2-(3-cyano-4,5-dihydro-2-furyl)carbamate with sodium iodide [11]. Since this procedure provides an attractive one-pot synthesis from readily available dihydrofuran to pyrrolidine, we have now extended to other furan substrates.

The starting compounds, 2-acylamino-4,5-dihydro-3-furancarbonitriles **1b-j**, were prepared by reaction of 2-amino-4,5-dihydro-3-furancarbonitrile [12] with acyl chlorides in pyridine. The ^{1}H nmr spectra of **1d**, **f-i** in deuteriochloroform indicate that **1d**, **f-i** consist of approximately a 7:3 tautomeric mixture of the enamine **A** and the imine **B** forms. Compounds **1b**, **c**, **e**, **j** exist predominantly in the enamine **A** forms in deuteriochloroform (Scheme 1).

Scheme 1



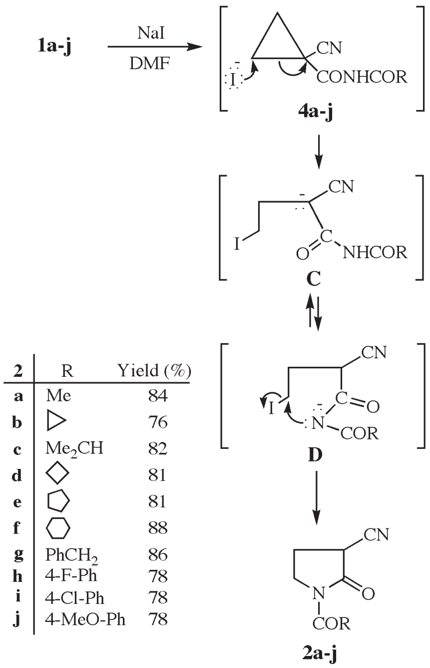
1b-j , **A**

B

1	R	Yield (%)	1	R	Yield (%)
b	▷	58	g	PhCH$_2$	52
c	Me$_2$CH	76	h	4-F-Ph	81
d	◇	50	i	4-Cl-Ph	84
e	⬠	67	j	4-MeO-Ph	78
f	⬡	86			

When a solution of 2-acetamido-4,5-dihydro-3-furancarbonitrile (**1a**) [13] and sodium iodide in *N*,*N*-dimethylformamide (DMF) was stirred at 150° for 1 hour, the ring transforming product, 1-acetyl-2-oxo-3-pyrrolidinecarbonitrile (**2a**), was obtained in 84% yield. The ir spectrum of **2a** reveals a band at 2255 cm^{-1} due to a nonconjugated cyano group and two carbonyl bands at 1746 and 1698 cm^{-1} attributable to the acetyl and the 2-pyrrolidinone groups, whereas that of **1a** appears two N-H bands at 3220 and 3140 cm^{-1} for an amide group, and a band at 2210 cm^{-1} due to a conjugated cyano group. Elemental analysis, ^{1}H nmr and ^{13}C nmr spectra of **2a** are consistent with the assigned structure. Compounds **1b-j** reacted with sodium iodide under the same conditions to give the corresponding 1-acyl-2-oxo-3-pyrrolidinecarbonitriles **2b-j** in good

Scheme 2



4a-j

C

D

2a-j

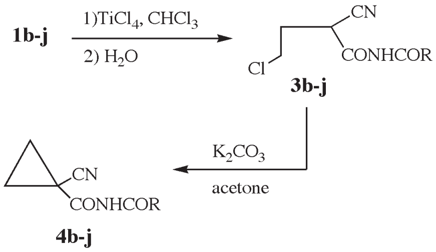
2	R	Yield (%)
a	Me	84
b	▷	76
c	Me$_2$CH	82
d	◇	81
e	⬠	81
f	⬡	88
g	PhCH$_2$	86
h	4-F-Ph	78
i	4-Cl-Ph	78
j	4-MeO-Ph	78

yields.

In a previous communication [11], we suggested the following mechanism for the formation of **2** from **1**. The reaction proceeds by initial ring contraction to form the cyclopropane **4**, which is converted into the carbanion **C** by iodide ion, and then the carbanion rearranges into the imide ion **D**, which undergoes intramolecular cyclization to form **2** (Scheme 2).

Subsequently, we examine the reaction of the compounds **4** with sodium iodide in DMF in order to prove whether or not compounds **2** are formed. The required cyclopropanes **4b-j** were prepared from 4-chlorobutanamides **3b-j** and potassium carbonate according to the method of ref. [13]. The ^{1}H nmr spectra of **4b-j** showed a pair of two-proton multiplets at near δ 1.80 assignable to the ring protons of the cyclopropane moiety. The cyclopropane ring proton signals in **4b-j** appeared at higher magnetic field than the proton signals at 3-H and 4-H in **3b-j**. The ring-opening compounds **3b-j** were synthesized by reaction of **1b-j** and titanium (IV) chloride (Scheme 3).

Scheme 3



3	R	Yield (%)
b	▷	54
c	Me$_2$CH	36
d	◇	47
e	⬠	61
f	⬡	66
g	PhCH$_2$	48
h	4-F-Ph	44
i	4-Cl-Ph	53
j	4-MeO-Ph	49

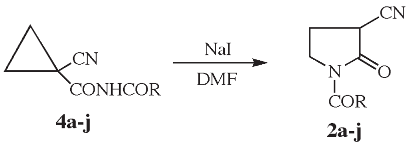
4	R	Yield (%)
b	▷	75
c	Me$_2$CH	69
d	◇	69
e	⬠	83
f	⬡	94
g	PhCH$_2$	80
h	4-F-Ph	88
i	4-Cl-Ph	95
j	4-MeO-Ph	92

The reaction of **4a-j** with sodium iodide resulted in the formation of the expected compounds **2a-j** in high yields (Scheme 4).

On the basis of the above observation, the reaction pathway for the formation of **2a-j** can be illustrated as shown in Scheme 2.

In conclusion, we have presented a useful method for the synthesis of 1-acyl-2-oxo-3-pyrrolidinecarbonitriles in good yields starting from easily accessible 2-acylamino-4,5-dihydro-3-furancarbonitriles.

Scheme 4



2	R	Yield (%)	2	R	Yield (%)
a	Me	87	f	⬡	89
b	▷	84	g	PhCH$_2$	89
c	Me$_2$CH	87	h	4-F-Ph	86
d	◇	83	i	4-Cl-Ph	84
e	⬠	87	j	4-MeO-Ph	88

EXPERIMENTAL

All melting points are uncorrected. Ir spectra were recorded on a JASCO FT/IR-230 spectrometer. ^{1}H nmr and ^{13}C nmr spectra were measured with a JEOL JNM-A500 instrument (500.00 MHz for ^{1}H, 125.65 MHz for ^{13}C) in $CDCl_3$ with TMS as internal standard. ^{13}C signal assignments were confirmed by the DEPT and ^{13}C-^{1}H COSY technique. FAB mass spectra were taken with a JEOL JMS-HX100 instrument at 70 eV. Elemental analyses were performed using a YANACO MT-6 elemental analyzer.

General Procedure for the Preparation of 2-Acylamino-4,5-dihydro-3-furancarbonitriles **1**.

A mixture of 2-amino-4,5-dihydro-3-furancarbonitrile [12] (5.50 g, 50 mmoles) and acyl chloride (55 mmoles) in pyridine (25 ml) was stirred at room temperature for 3 hours. After removal of the solvent *in vacuo*, 5% sodium bicarbonate solution (100 ml) was added to the residue. The resulting precipitate was collected by filtration, washed with water and dried to give **1**.

2-Cyclopropanecarboxamido-4,5-dihydro-3-furancarbonitrile (**1b**).

This compound was obtained as pale yellow columns (5.16 g, 58%), mp 166-167° (acetone-petroleum ether); ir (potassium bromide): ν 3210, 3140 (NH), 2205 (CN), 1687 cm^{-1} (C=O); ^{1}H nmr (deuteriochloroform): δ, ppm 0.90-0.92 (m, 2H, CH_2), 1.11-1.13 (m, 2H, CH_2), 1.66-1.70 (m, 1H, CH), 2.97 (t, J = 9.5 Hz, 2H, 4-H), 4.54 (t, J = 9.5 Hz, 2H, 5-H); ^{13}C nmr (deuteriochloroform):δ, ppm 9.4 (CH_2), 14.9 (CH), 29.5 (C-4), 65.2 (C-3), 70.9 (C-5), 116.4 (CN), 159.1 (C-2), 171.2 (C=O); ms: m/z 179 $[M+H]^+$.

Anal. Calcd. for $C_9H_{10}N_2O_2$ (MW 178.2): C, 60.66; H, 5.66; N, 15.72. Found: C, 60.61; H, 5.71; N, 15.63.

2-(2-Propanecarboxamido)-4,5-dihydro-3-furancarbonitrile (**1c**).

This compound was obtained as colorless needles (6.84 g, 76%), mp 131-132° (acetone-petroleum ether); ir (potassium bromide): ν 3220, 3150 (NH), 2204 (CN), 1696 cm^{-1} (C=O); ^{1}H nmr (deuteriochloroform): δ, ppm 1.21 (d, J = 7.0 Hz, 6H, $2CH_3$), 2.55-2.61 (m, 1H, CH), 2.98 (t, J = 9.2 Hz, 2H, 4-H), 4.53 (t, J = 9.2 Hz, 2H, 5-H), 7.76 (br.s, 1H, NH); ^{13}C nmr (deuteriochloroform): δ, ppm 19.1, 19.4 (CH_3) 29.8 (C-4), 35.8 (CH), 66.2 (C-3), 70.7 (C-5), 116.2 (CN), 158.6 (C-2), 173.8 (C=O); ms: m/z 181 $[M+H]^+$.

Anal. Calcd. for $C_9H_{12}N_2O_2$ (MW 180.2): C, 59.99; H, 6.71;

N, 15.55. Found: C, 59.96; H, 6.72; N, 15.50.

2-Cyclobutanecarboxamido-4,5-dihydro-3-furancarbonitrile (**1d**).

This compound was obtained as colorless needles (4.82 g, 50%), mp 134-135° (acetone-petroleum ether); ir (potassium bromide): ν 3218, 3139 (NH), 2203 (CN), 1694 cm^{-1} (C=O); ^{1}H nmr (deuteriochloroform): δ, ppm 1.80-2.40 (m, 6H, 3CH$_3$), 2.60-2.80 (m, 1H, CH), 2.97 (t, J = 9.5 Hz, 1.4H, 4-H), 3.15-3.25 (m, 0.6H, 4-H), 3.70 (dd, J = 9.2, 10.1 Hz, 0.3H, 3-H), 4.53 (t, J = 9.5 Hz, 2H, 5-H), 7.49 (br. s, 0.7H, NH); ^{13}C nmr (deuteriochloroform): δ, ppm 17.9, 18.1, 24.9, 25.4, 26.5 (CH$_2$), 27.8 (C-4), 29.7 (C-4), 31.4 (C-3), 39.3 (CH), 39.9 (CH), 65.9 (C-3), 67.1 (C-5), 70.8 (C-5), 114.6 (CN), 116.1 (CN), 158.6 (C-2), 168.2 (C-2), 171.8, 175.2 (C=O); ms: m/z 193 [M+H]$^+$.

Anal. Calcd. for $C_{10}H_{12}N_2O_2$ (MW 192.2): C, 62.49; H, 6.29; N, 14.57. Found: C, 62.46; H, 6.32; N, 14.43.

2-Cyclopentanecarboxamido-4,5-dihydro-3-furancarbonitrile (**1e**).

This compound was obtained as colorless columns (6.92 g, 67%), mp 122-123° (acetone-petroleum ether); ir (potassium bromide): ν 3270, 3165 (NH), 2213 (CN), 1696 cm^{-1} (C=O); ^{1}H nmr (deuteriochloroform): δ, ppm 1.55-2.00 (m, 8H, 4CH$_2$), 2.60-2.80 (m, 1H, CH), 2.97 (t, J = 9.5 Hz, 2H, 4-H), 4.52 (t, J = 9.5 Hz, 2H, 5-H), 7.69 (br. s, 1H, NH); ^{13}C nmr (deuteriochloroform): δ, ppm 25.8, 25.9 (CH$_2$), 29.8 (C-4), 30.1, 30.4 (CH$_2$), 45.8 (CH), 65.9 (C-3), 116.2 (CN), 158.6 (C-2), 173.2 (C=O); ms: m/z 207 [M+H]$^+$.

Anal. Calcd. for $C_{11}H_{14}N_2O_2$ (MW 206.2): C, 64.06; H, 6.84; N, 13.58. Found: C, 64.16; H 6.77; N, 13.58.

2-Cyclohexanecarboxamido-4,5-dihydro-3-furancarbonitrile (**1f**).

This compound was obtained as colorless needles (9.43 g, 86%), mp 157-158°(acetone-petroleum ether); ir (potassium bromide): ν 3278, 3163 (NH), 2212 (CN), 1697 cm^{-1} (C=O); ^{1}H nmr (deuteriochloroform): δ, ppm 1.20-2.80 (m, 11.3H, 5CH$_2$, CH, 4-H), 2.98 (t, J = 8.9 Hz, 1.4H, 4-H), 3.96 (dd, J = 9.5 Hz, 10.1H, 0.3H, 3-H), 4.34-4.39 (m, 0.6H, 5-H), 4.52 (t, J = 8.9 Hz, 1.4H, 5-H), 7.50 (br. s, 0.7H, NH); ^{13}C nmr (deuteriochloroform): δ, ppm 25.1, 25.2, 25.4, 25.5, 25.67, 25.73 (CH$_2$), 27.8 (C-4), 29.2 (C-4), 29.7, 29.8 (CH$_2$), 31.4 (C-3), 44.8 (CH), 45.5 (CH), 66.3 (C-3), 67.1 (C-5), 70.7 (C-5), 114.6 (CN), 116.1 (CN), 158.4 (C-2), 168.2 (C-2), 172.6, 176.5 (C=O); ms: m/z 221 [M+H]$^+$.

Anal. Calcd. for $C_{12}H_{16}N_2O_2$ (MW 220.3): C, 65.43; H, 7.32; N, 12.72. Found: C, 65.26; H, 7.35; N, 12.69.

2-Phenylacetamido-4,5-dihydro-3-furancarbonitrile (**1g**).

This compound was obtained as colorless needles (5.89 g, 52%,) mp 193-194° (acetone); ir (potassium bromide): ν 3212, 3152 (NH), 2203 (CN), 1697 cm^{-1} (C=O); ^{1}H nmr (deuteriochloroform): δ, ppm 2.60-2.75 (m, 0.6H, 4-H), 2.95 (t, J = 9.2 Hz, 1.4H, 4-H), 3.59 (s, 0.6H, CH$_2$CO), 3.67 (dd, J = 9.2, 10.1 Hz, 0.3H, 3-H), 3.73 (s, 1.4H, CH$_2$CO), 4.47 (t, J = 9.2 Hz, 1.4H, 5-H), 4.50-4.55 (m, 0.6H, 5-H), 7.27-7.40 (m, 5H, aryl H), 7.48 (br. s, 0.7H, NH); ^{13}C nmr (deuteriochloroform): δ, ppm 27.8 (C-4), 29.9 (C-4), 31.4 (C-3), 43.3, 43.9 (CH$_2$), 67.1 (C-5), 67.3 (C-3), 70.6 (C-5), 114.6 (CN), 115.7 (CN), 127.5, 128.0, 129.1, 129.3, 129.4, 129.5, 133.0, 134.8 (C aryl), 157.8 (C-2), 167.6 (C-2), 168.1, 173.2 (C=O); ms: m/z 229 [M+H]$^+$.

Anal. Calcd. for $C_{13}H_{12}N_2O_2$ (MW 228.3): C, 68.41; H, 5.30; N, 12.27. Found: C, 68.33; H, 5.38; N, 12.15.

2-(4-Fluorobenzamido)-4,5-dihydro-3-furancarbonitrile (**1h**).

This compound was obtained as pale yellow needles (9.45 g, 81%), mp 156-157° (acetone-petroleum ether); ir (potassium bromide): ν 3282 (NH), 2212 (CN), 1692 cm^{-1} (C=O); ^{1}H nmr (deuteriochloroform): δ, ppm 2.60-2.80 (m, 0.6H, 4-H), 3.04 (t, J = 9.2 Hz, 1.4H, 4-H), 3.72 (t, J = 9.4 Hz, 0.3H, 3-H), 4.35-4.50 (m, 0.6H, 5-H), 4.55 (t, J = 9.2 Hz, 1.4H, 5-H), 7.05-7.20 (m, 2H, aryl H), 7.85-7.95 (m, 2H, aryl H), 8.22 (br. s, 0.7H, NH); ^{13}C nmr (deuteriochloroform): δ, ppm 27.8 (C-4), 30.3 (C-4), 31.4 (C-3), 68.0 (C-3), 70.3 (C-5), 70.5 (C-5), 115.6 (CN), 116.0 (CN), 116.0, 128.4, 128.5, 129.8, 130.4, 132.4, (C aryl), 158.0 (C-2), 162.6 (C-2), 164.6, 166.7 (C=O); ms: m/z 233 [M+H]$^+$.

Anal. Calcd. for $C_{12}H_9FN_2O_2$ (MW 232.3): C, 62.07; H, 3.91; N, 12.06. Found: C, 62.11; H, 3.97; N, 11.99.

2-(4-Chlorobenzamido)-4,5-dihydro-3-furancarbonitrile (**1i**).

This compound was obtained as pale yellow prisms (10.41 g, 84%), mp 172-173° (acetone); ir (potassium bromide): ν 3210, 3155 (NH), 2206 (CN), 1707 cm^{-1} (C=O); ^{1}H nmr (deuteriochloroform): δ, ppm 2.60-2.75 (m, 0.6H, 4-H), 3.05 (t, J = 9.2 Hz, 1.4H, 4-H), 3.68 (t, J = 9.5 Hz, 0.3H, 3-H), 4.30-4.50 (m, 0.6H, 5-H), 4.56 (t, J = 9.2 Hz, 1.4H, 5-H), 7.35-7.50 (m, 2H, aryl H), 7.70-7.80 (m, 2H, aryl H), 8.11 (br. s, 0.7H, NH); ^{13}C nmr (deuteriochloroform): δ, ppm 27.8 (C-4), 30.3 (C-4), 31.4 (C-3), 67.1 (C-5), 68.2 (C-3), 70.6 (C-5), 115.0 (CN), 115.9 (CN), 128.8, 128.9, 129.2, 129.3, 130.5, 131.2, 138.0, 139.7 (C aryl), 157.8 (C-2), 162.6 (C-2), 168.0, 175.2 (C=O); ms: m/z 249 [M+H]$^+$.

Anal. Calcd. for $C_{12}H_9ClN_2O_2$ (MW 248.7): C, 57.96; H, 3.65; N, 11.27. Found: C, 57.95; H, 3.72; N, 11.26.

2-(4-Methoxybenzamido)-4,5-dihydro-3-furancarbonitrile (**1j**).

This compound was obtained as pale yellow needles (9.48 g, 78%), mp 145-146° (acetone-petroleum ether); ir (potassium bromide): ν 3296 (NH), 2205 (CN), 1685 cm^{-1} (C=O); ^{1}H nmr (deuteriochloroform): δ, ppm 3.03 (t, J = 9.2 Hz, 2H, 4-H), 3.86 (s, 3H, OCH$_3$), 4.53 (t, J = 9.2 Hz, 2H, 5-H), 6.90-7.00 (m, 2H, aryl H), 7.80-7.85 (m, 2H, aryl H), 8.12 (br. s, 1H, NH); ^{13}C nmr (deuteriochloroform): δ, ppm 30.3 (C-4), 55.5 (OCH$_3$), 67.2 (C-3), 70.5 (C-5), 113.8, 114.1 (C aryl), 116.3 (CN), 124.4, 129.8 (C aryl) 158.2 (C-2), 163.5 (C=O); ms: m/z 245 [M+H]$^+$.

Anal. Calcd. for $C_{13}H_{12}N_2O_3$ (MW 244.3): C, 63.93; H, 4.95; N, 11.47. Found: C, 63.89; H, 5.12; N, 11.37.

General Procedure for the Preparation of 1-Acyl-2-oxo-3-pyrrolidinecarbonitriles **2**.

A solution of **1a-j** (10 mmoles) and sodium iodide (3.00 g, 20 mmoles) in DMF (10 ml) was stirred at 150° for 1 hour. The solvent was removed *in vacuo* and cold water was added to the residue. The mixture was extracted with ethyl acetate. The extract was washed with water, dried over anhydrous sodium sulfate and concentrated *in vacuo*. The residue was purified by column chromatography on silica gel with dichloromethane as the eluent to give **2**.

1-Acetyl-2-oxo-3-pyrrolidinecarbonitrile (**2a**).

This compound was obtained as colorless prisms (1.27 g, 84%), mp 68-69° (acetone-petroleum ether); ir (potassium bromide): ν 2255 (CN), 1746, 1698 cm^{-1} (C=O); ^{1}H nmr (deuteriochloroform):

δ, ppm 2.30-2.40 (m, 1H, 4-H), 2.50-2.60 (m, 1H, 4-H), 2.53 (s, 3H, CH_3), 3.70 (ddd. J = 7.3, 9.2, 11.9 Hz, 1H, 5-H), 3.76 (dd, J = 8.9, 10.1 Hz, 1H, 3-H), 4.03 (ddd, J = 3.4, 8.6, 11.9 Hz, 1H, 5-H); ^{13}C nmr (deuteriochloroform): δ, ppm 22.8 (C-4), 24.7 (CH_3), 36.1 (C-3), 43.4 (C-5), 115.4 (CN), 166.5, 170.4 (C=O); ms: m/z 153 [M+H]$^+$.

Anal. Calcd. for $C_7H_8N_2O_2$ (MW 152.2): C, 55.26; H, 5.30; N, 18.41. Found: C, 55.28; H, 5.30; N, 18.36.

1-Cyclopropanecarbonyl-2-oxo-3-pyrrolidinecarbonitrile (**2b**).

This compound was obtained as colorless plates (1.35 g, 76%), mp 107-108° (acetone-petroleum ether); ir (potassium bromide): ν 2252 (CN), 1730, 1685 cm^{-1} (C=O); ^{1}H nmr (deuteriochloroform): δ, ppm 1.00-1.18 (m, 4H, $2CH_2$), 2.30-2.40 (m, 1H, 4-H), 2.50-2.60 (m, 1H, 4-H), 3.06-3.10 (m, 1H, CH), 3.71 (ddd. J = 7.1, 8.9, 11.9 Hz, 1H, 5-H), 3.78 (dd, J = 8.9, 10.4 Hz, 1H, 3-H), 4.02 (ddd, J = 3.1, 8.6, 11.9 Hz, 1H, 5-H); ^{13}C nmr (deuteriochloroform): δ, ppm 11.23, 11.25 (CH_2), 13.6 (CH), 22.8 (C-4), 36.5 (C-3), 44.0 (C-5), 115.5 (CN), 166.7, 174.8 (C=O); ms: m/z 179 [M+H]$^+$.

Anal. Calcd. for $C_9H_{10}N_2O_2$ (MW 178.2): C, 60.66; H, 5.66; N, 15.72. Found: C, 60.58; H, 5.71; N, 15.60.

1-(2-Propanecarbonyl)-2-oxo-3-pyrrolidinecarbonitrile (**2c**).

This compound was obtained as colorless plates (1.47 g, 82%), mp 92-93° (acetone-petroleum ether); ir (potassium bromide): ν 2259 (CN), 1755, 1679 cm^{-1} (C=O); ^{1}H nmr (deuteriochloroform): δ, ppm 1.16 (d, J = 7.0 Hz, 3H, CH_3), 1.19 (d, J = 7.0 Hz, 3H, CH_3), 2.30-2.40 (m, 1H, 4-H), 2.50-2.56 (m, 1H, 4-H), 3.58-3.67 (m, 1H, CH), 3.71 (ddd. J = 7.4, 9.2, 12.9 Hz, 1H, 5-H), 3.75 (dd, J = 8.9, 10.4 Hz, 1H, 3-H), 4.02 (ddd, J = 3.1, 8.8, 12.9 Hz, 1H, 5-H); ^{13}C nmr (deuteriochloroform): δ, ppm 18.4, 18.8 (CH_3), 22.9 (C-4), 34.1 (CH), 36.5 (C-3), 43.9 (C-5), 115.4 (CN), 165.8, 178.0 (C=O); ms: m/z 181[M+H]$^+$.

Anal. Calcd. for $C_9H_{12}N_2O_2$ (MW 180.2): C, 59.99; H, 6.71; N, 15.55. Found: C, 59.78; H, 6.73; N, 15.49.

1-Cyclobutanecarbonyl-2-oxo-3-pyrrolidinecarbonitrile (**2d**).

This compound was obtained as colorless scales (1.56 g, 81%), mp 68-69° (acetone-petroleum ether); ir (potassium bromide): ν 2259 (CN), 1749, 1672 cm^{-1} (C=O); ^{1}H nmr (deuteriochloroform): δ, ppm 1.80-2.55 (m, 8H, 4-H, $3CH_2$), 3.67-3.73 (m, 2H, 5-H), 3.71 (dd, J = 9.2, 10.4 Hz, 1H, 3-H), 3.95-4.04 (m, 2H, 5-H, CH); ^{13}C nmr (deuteriochloroform): δ, ppm 17.9 (CH_2), 23.1 (C-4), 24.2, 24.6 (CH_2), 36.2 (C-3), 39.7 (CH), 43.6 (C-5), 115.4 (CN), 165.7, 175.0 (C=O); ms: m/z 193[M+H]$^+$.

Anal. Calcd. for $C_{10}H_{12}N_2O_2$ (MW 192.2): C, 62.49; H, 6.29; N, 14.57. Found: C, 62.36; H, 6.31; N, 14.48.

1-Cyclopentanecarbonyl-2-oxo-3-pyrrolidinecarbonitrile (**2e**).

This compound was obtained as colorless columns (1.67 g, 81%), mp 63-64° (diethyl ether-petroleum ether); ir (potassium bromide): ν 2256 (CN), 1751, 1679 cm^{-1} (C=O); ^{1}H nmr (deuteriochloroform): δ, ppm 1.60-2.00 (m, 8H, $4CH_2$), 2.30-2.40 (m, 1H, 4-H), 2.50-2.55 (m, 1H, 4-H), 3.68-3.78 (m, 3H, 3-H, 5-H, CH), 4.02 (ddd, J = 3.1, 8.9, 11.9 Hz, 1H, 5-H); ^{13}C nmr (deuteriochloroform): δ, ppm 22.8 (C-4), 25.91, 25.94, 29.4, 29.9 (CH_2), 36.5 (C-3), 43.9 (C-5), 44.4 (CH), 115.5 (CN), 165.9, 176.9 (C=O); ms: m/z 207[M+H]$^+$.

Anal. Calcd. for $C_{11}H_{14}N_2O_2$ (MW 206.2): C, 64.06; H, 6.84; N, 13.58. Found: C, 63.84; H, 6.82; N, 13.53.

1-Cyclohexanecarbonyl-2-oxo-3-pyrrolidinecarbonitrile (**2f**).

This compound was obtained as colorless scales (1.94 g, 88%), mp 142-143° (acetone-petroleum ether); ir (potassium bromide): ν 2261 (CN), 1756, 1673 cm^{-1} (C=O); ^{1}H nmr (deuteriochloroform): δ, ppm 1.20-1.90 (m, 10H, $5CH_2$), 2.30-2.40 (m, 1H, 4-H), 2.50-2.55 (m, 1H, 4-H), 3.30-3.40 (m, 1H, CH), 3.68 (ddd, J = 7.4, 9.2, 11.9 Hz, 1H, 5-H), 3.73 (dd, J = 9.2, 10.4 Hz, 1H, 3-H), 4.01 (ddd, J = 3.1, 8.9, 11.9 Hz, 1H, 5-H); ^{13}C nmr (deuteriochloroform): δ, ppm 22.9 (C-4), 25.4, 25.5, 25.7, 28.6, 29.1 (CH_2), 36.5 (C-3), 43.6 (CH), 43.9 (C-5), 115.4 (CN), 165.8, 176.9 (C=O); ms: m/z 221 [M+H]$^+$.

Anal. Calcd. for $C_{12}H_{16}N_2O_2$ (MW 220.3): C, 65.43; H, 7.32; N, 12.72. Found: C, 65.29; H, 7.32; N, 12.65.

1-Phenylacetyl-2-oxo-3-pyrrolidinecarbonitrile (**2g**).

This compound was obtained as colorless needles (1.97 g, 86%), mp 124-125° (acetone-petroleum ether); ir (potassium bromide): ν 2250 (CN), 1736, 1714 cm^{-1} (C=O); ^{1}H nmr (deuteriochloroform): δ, ppm 2.30-2.37 (m, 1H, 4-H), 2.45-2.55 (m, 1H, 4-H), 3.68 (ddd, J = 7.4, 9.2, 11.8 Hz, 1H, 5-H), 3.72 (dd, J = 8.9, 10.4 Hz, 1H, 3-H), 4.02 (ddd, J = 3.2, 9.8, 12.8 Hz, 1H, 5-H); 4.23 (AB quartet, J = 15.4 Hz, NCH_2CO), 7.25-7.35 (m, 5H, aryl H); ^{13}C nmr (deuteriochloroform): δ, ppm 22.8 (C-4), 36.3 (C-3), 42.6 (CH_2), 43.8 (C-5), 115.3 (CN), 127.3, 128.6, 129.7, 133.0 (C aryl), 166.3, 171.4 (C=O); ms: m/z 229 [M+H]$^+$.

Anal. Calcd. for $C_{13}H_{12}N_2O_2$ (MW 228.3): C, 68.41; H, 5.30; N, 12.27. Found: C, 68.33; H, 5.36; N, 12.17.

1-(4-Fluorobenzoyl)-2-oxo-3-pyrrolidinecarbonitrile (**2h**).

This compound was obtained as colorless columns (1.80 g, 78%), mp 166-167° (acetone-petroleum ether); ir (potassium bromide): ν 2257 (CN), 1758, 1672 cm^{-1} (C=O); ^{1}H nmr (deuteriochloroform): δ, ppm 2.42-2.52 (m, 1H, 4-H), 2.58-2.66 (m, 1H, 4-H), 3.73 (dd, J = 9.5, 10.2 Hz, 1H, 3-H), 3.93 (ddd, J = 7.5, 9.0, 11.5 Hz, 1H, 5-H), 4.10 (ddd, J = 3.0, 8.5, 11.5 Hz, 1H, 5-H), 7.01-7.10 (m, 2H, aryl H), 7.65-7.69 (m, 2H, aryl H); ^{13}C nmr (deuteriochloroform): δ, ppm 23.2 (C-4), 35.9 (C-3), 44.7 (C-5), 115.2 (C aryl), 115.4 (CN), 128.9, 132.0 (C aryl), 164.5 (C=O), 166.0 (C aryl), 168.5 (C=O); ms: m/z 233 [M+H]$^+$.

Anal. Calcd. for $C_{12}H_9FN_2O_2$ (MW 232.2): C, 62.07; H, 3.91; N, 12.06. Found: C, 62.16; H, 3.95; N, 11.99.

1-(4-Chlorobenzoyl)-2-oxo-3-pyrrolidinecarbonitrile (**2i**).

This compound was obtained as colorless needles (1.93 g, 78%), mp 138-139° (acetone-petroleum ether); ir (potassium bromide): ν 2256 (CN), 1763, 1678 cm^{-1} (C=O); ^{1}H nmr (deuteriochloroform): δ, ppm 2.45-2.53 (m, 1H, 4-H), 2.60-2.67 (m, 1H, 4-H), 3.73 (dd, J = 8.9, 10.1 Hz, 1H, 3-H), 3.94 (ddd, J = 7.4, 8.9, 12.5 Hz, 1H, 5-H), 4.10 (ddd, J = 3.4, 8.6, 12.5 Hz, 1H, 5-H), 7.25-7.42 (m, 2H, aryl H), 7.56-7.60 (m, 2H, aryl H); ^{13}C nmr (deuteriochloroform): δ, ppm 23.2 (C-4), 35.9 (C-3), 44.6 (C-5), 115.2 (CN), 128.4, 130.7, 131.2, 139.3 (C aryl), 165.6, 168.7 (C=O); ms: m/z 249 [M+H]$^+$.

Anal. Calcd. for $C_{12}H_9ClN_2O_2$ (MW 248.7): C, 57.96; H, 3.65; N, 11.27. Found: C, 57.98; H, 3.74; N, 11.20.

1-(4-Methoxybenzoyl)-2-oxo-3-pyrrolidinecarbonitrile (**2j**).

This compound was obtained as colorless needles (1.90 g, 78%), mp 106-107° (acetone-petroleum ether); ir (potassium bromide): ν 2253 (CN), 1758, 1673 cm^{-1} (C=O); ^{1}H nmr (deuteriochloroform): δ, ppm 2.40-2.50 (m, 1H, 4-H), 2.57-2.65 (m, 1H, 4-H), 3.71 (dd, J

= 8.9, 10.4 Hz, 1H, 3-H), 3.87 (s, 3H, OCH$_3$), 3.93 (ddd, J = 6.7, 9.2, 11.5 Hz, 1H, 5-H), 4.06 (ddd, J = 3.4, 8.3, 11.5 Hz, 1H, 5-H), 6.90-6.94 (m, 2H, aryl H), 7.65-7.68 (m, 2H, aryl H); ^{13}C nmr (deuteriochloroform): δ, ppm 23.4 (C-4), 36.0 (C-3), 44.8 (C-5), 55.5 (OCH$_3$), 113.4 (C aryl), 115.5 (CN), 124.7, 132.1, 163.7 (C aryl), 165.6, 168.9 (C=O); ms: m/z 245[M+H]$^+$.

Anal. Calcd. for $C_{13}H_{12}N_2O_3$ (MW 244.3): C, 63.93; H, 4.95; N, 11.47. Found: C, 63.86; H, 4.95; N, 11.38.

General Procedure for the Preparation of *N*-Acyl-4-chloro-2-cyanobutanamides **2**.

Titanium(IV) chloride (9.12 g, 48 mmoles) was added dropwise to an ice-cooled and stirred solution of **1b-j** (40 mmoles) in chloroform (80 ml). After the mixture was refluxed for 1 hour, the precipitate was dissolved in 5% hydrochloric acid (50 ml) with stirring and ice-cooling, and then the chloroform layer was separated. The aqueous layer was extracted with chloroform. The organic layer was washed with water, dried over anhydrous sodium sulfate and concentrated *in vacuo*. The residue was purified by column chromatography on silica gel with dichloromethane as the eluent to yield **3b-j**.

4-Chloro-2-cyano-*N*-cyclopropanecarbonylbutanamide (**3b**).

This compound was obtained as colorless needles (4.58 g, 54%), mp 134-135° (acetone-petroleum ether); ir (potassium bromide): ν 3258, 3169 (NH), 2253 (CN), 1735, 1694 cm^{-1} (C=O); ^{1}H nmr (deuteriochloroform): δ, ppm 1.00-1.10 (m, 2H, CH$_2$), 1.15-1.25 (m, 2H, CH$_2$), 1.95-2.05 (m, 1H, CH), 2.35-2.50 (m, 2H, 3-H), 3.70-3.80 (m, 2H, 4-H), 4.59 (t, J = 8.0 Hz, 1H, 2-H), 9.22 (br. s, 1H, NH); ^{13}C nmr (deuteriochloroform): δ, ppm 10.9, 11.0 (CH$_2$), 15.4 (CH), 31.9 (C-3), 36.9 (C-2), 40.8 (C-4), 115.5 (CN), 165.7, 174.4 (C=O); ms: m/z 215 [M+H]$^+$.

Anal. Calcd. for $C_9H_{11}ClN_2O_2$ (MW 214.7): C, 50.36; H, 5.17; N, 13.05. Found: C, 50.41; H, 5.07; N, 12.82.

4-Chloro-2-cyano-*N*-(2-propanecarbonyl)butanamide (**3c**).

This compound was obtained as colorless needles (3.12 g, 36%), mp 104-105° (acetone-petroleum ether); ir (potassium bromide): ν 3273, 3189 (NH), 2255 (CN), 1740, 1700 cm^{-1} (C=O); ^{1}H nmr (deuteriochloroform): δ, ppm 1.23 (d, J = 5.2 Hz, 3H, CH$_3$), 1.24 (d, J = 5.5 Hz, 3H, CH$_3$), 2.35-2.50 (m, 2H, 3-H), 2.70-2.80 (m, 1H, CH), 3.70-3.80 (m, 2H, 4-H), 4.67 (dd, J = 5.8, 8.6 Hz, 1H, 2-H), 8.78 (br. s, 1H, NH); ^{13}C nmr (deuteriochloroform): δ, ppm 18.56, 18.6 (CH$_3$), 31.8 (C-3), 36.3 (CH), 37.0 (C-2), 40.8 (C-4), 115.5 (CN), 166.3, 176.7 (C=O); ms: m/z 217 [M+H]$^+$.

Anal. Calcd. for $C_9H_{13}ClN_2O_2$ (MW 216.7): C, 49.89; H, 6.05; N, 12.93. Found: C, 49.95; H, 6.12; N, 12.90.

4-Chloro-2-cyano-*N*-cyclobutanecarbonylbutanamide (**3d**).

This compound was obtained as colorless needles (4.51 g, 47%), mp 82-84° (diethyl ether-petroleum ether); ir (potassium bromide): ν 3267, 3181 (NH), 2251 (CN), 1738, 1702 cm^{-1} (C=O); ^{1}H nmr (deuteriochloroform): δ, ppm 1.90-2.50 (m, 8H, 3-H, 3CH$_2$), 3.35-3.45 (m, 1H, CH), 3.70-3.75 (m, 2H, 4-H), 4.57 (t, J = 7.9 Hz, 1H, 2-H), 8.79 (br. s, 1H, NH); ^{13}C nmr (deuteriochloroform): δ, ppm 17.8, 24.5, 24.6 (CH$_2$), 31.9 (C-3), 36.9 (CH), 40.4 (C-2), 40.8 (C-4), 115.5 (CN), 165.6, 174.9 (C=O); ms: m/z 229 [M+H]$^+$.

Anal. Calcd. for $C_{10}H_{13}ClN_2O_2$ (MW 228.7): C, 52.52; H, 5.73; N, 12.25. Found: C, 52.93; H, 5.82; N, 11.64.

4-Chloro-2-cyano-*N*-cyclopentanecarbonylbutanamide (**3e**).

This compound was obtained as colorless needles (5.88 g, 61%), mp 124-125° (acetone-petroleum ether); ir (potassium bromide): ν 3269, 3184 (NH), 2260 (CN), 1739, 1712 cm^{-1} (C=O); ^{1}H nmr (deuteriochloroform): δ, ppm 1.60-2.00 (m, 8H, 4CH$_2$), 2.30-2.50 (m, 2H, 3-H), 2.85-2.95 (m, 1H, CH), 3.70-3.80 (m, 2H, 4-H), 4.66 (dd, J = 6.1, 8.6 Hz, 1H, 2-H), 8.65 (br. s, 1H, NH); ^{13}C nmr (deuteriochloroform): δ, ppm 25.9, 29.7, 29.8 (CH$_2$), 31.8 (C-3), 36.9 (CH), 40.8 (C-4), 46.3 (C-2), 115.5 (CN), 166.0, 175.8 (C=O); ms: m/z 243 [M+H]$^+$.

Anal. Calcd. for $C_{11}H_{15}ClN_2O_2$ (MW 242.7): C, 54.44; H, 6.23; N, 11.54. Found: C, 54.44; H, 6.19; N, 11.47.

4-Chloro-2-cyano-*N*-cyclohexanecarbonylbutanamide (**3f**).

This compound was obtained as colorless needles (6.79 g, 66%), mp 128-129° (acetone-petroleum ether); ir (potassium bromide): ν 3266, 3181 (NH), 2253 (CN), 1739, 1712 cm^{-1} (C=O); ^{1}H nmr (deuteriochloroform): δ, ppm 1.20-1.95 (m, 10H, 5CH$_2$), 2.35-2.50 (m, 3H, 3-H, CH), 3.70-3.80 (m, 2H, 4-H), 4.67 (dd, J = 5.8, 8.6 Hz, 1H, 2-H), 8.60 (br. s, 1H, NH); ^{13}C nmr (deuteriochloroform): δ, ppm 25.2, 25.4, 28.77, 28.8 (CH$_2$), 31.8 (C-3), 37.0 (CH), 40.8 (C-4), 45.8 (C-2), 115.5 (CN), 166.2, 175.5 (C=O); ms: m/z 257 [M+H]$^+$.

Anal. Calcd. for $C_{12}H_{17}ClN_2O_2$ (MW 256.7): C, 56.14; H, 6.67; N, 10.91. Found: C, 56.23; H, 6.65; N, 10.84.

4-Chloro-2-cyano-*N*-phenylacetylbutanamide (**3g**).

This compound was obtained as colorless needles (5.12 g, 48%), mp 113-114° (acetone-petroleum ether); ir (potassium bromide): ν 3267, 3183 (NH), 2252 (CN), 1745, 1707 cm^{-1} (C=O); ^{1}H nmr (deuteriochloroform): δ, ppm 2.30-2.50 (m, 2H, 3-H), 3.70 (t, J = 5.5 Hz, 2H, 4-H), 3.85 (s, 2H, COCH$_2$), 4.55 (dd, J = 6.1, 8.2 Hz, 1H, 2-H), 7.26-7.40 (m, 5H, aryl H), 8.51 (br. s, 1H, NH); ^{13}C nmr (deuteriochloroform): δ, ppm 31.8 (C-3), 36.9 (C-2), 40.8 (C-4), 44.4 (CH$_2$), 115.3 (CN), 128.2, 129.3, 129.5, 132.0 (C aryl), 165.5, 170.7 (C=O); ms: m/z 265 [M+H]$^+$.

Anal. Calcd. for $C_{13}H_{13}ClN_2O_2$ (MW 264.7): C, 58.99; H, 4.95; N, 10.58. Found: C, 58.96; H, 4.83; N, 10.51.

4-Chloro-2-cyano-*N*-(4-fluorobenzoyl)butanamide (**3h**).

This compound was obtained as colorless prisms (4.69 g, 44%), mp 127-128° (acetone-petroleum ether); ir (potassium bromide): ν 3303, 3168 (NH), 2248 (CN), 1732, 1686 cm^{-1} (C=O); ^{1}H nmr (deuteriochloroform): δ, ppm 2.40-2.60 (m, 2H, 3-H), 3.70-3.82 (m, 2H, 4-H), 5.00 (dd, J = 5.5, 8.9 Hz, 1H, 2-H), 7.20-7.25 (m, 2H, aryl H), 7.95-7.99 (m, 2H, aryl H), 9.21 (br. s, 1H, NH); ^{13}C nmr (deuteriochloroform): δ, ppm 31.9 (C-3), 37.3 (C-2), 40.8 (C-4), 115.5 (CN), 116.5, 127.5, 130.8, 164.2 (C aryl), 165.3, 167.3 (C=O); ms: m/z 269 [M+H]$^+$.

Anal. Calcd. for $C_{12}H_{10}ClFN_2O_2$ (MW 268.7): C, 53.65; H, 3.75; N, 10.43. Found: C, 53.61; H, 3.78; N, 10.38.

4-Chloro-*N*-(4-chlorobenzoyl)-2-cyanobutanamide (**3i**).

This compound was obtained as colorless prisms (6.01 g, 53%), mp 112-113° (acetone-petroleum ether); ir (potassium bromide): ν 3327 (NH), 2251 (CN), 1715, 1688 cm^{-1} (C=O); ^{1}H nmr (deuteriochloroform): δ, ppm 2.40-2.60 (m, 2H, 3-H), 3.70-3.80 (m, 2H, 4-H), 4.98 (dd, J = 5.8, 8.5 Hz, 1H, 2-H), 7.50-7.54 (m, 2H, aryl H), 7.86-7.90 (m, 2H, aryl H), 9.32 (br. s, 1H, NH); ^{13}C nmr (deuteriochloroform): δ, ppm 31.9 (C-3), 37.4 (C-2), 40.8 (C-4), 115.5 (CN), 129.46, 129.56, 129.6, 140.9 (C aryl), 164.5, 167.4 (C=O); ms: m/z 285 [M+H]$^+$.

Anal. Calcd. for $C_{12}H_{10}Cl_2N_2O_2$ (MW 285.1): C, 50.55; H, 3.54; N, 9.82. Found: C, 50.51; H, 3.55; N, 9.84.

4-Chloro-2-cyano-*N*-(4-methoxybenzoyl)butanamide (**3j**).

This compound was obtained as colorless columns (5.52 g, 49%), mp 113-114° (acetone-petroleum ether); ir (potassium bromide): ν 3289, 3170 (NH), 2254 (CN), 1721, 1670 cm^{-1} (C=O); ^{1}H nmr (deuteriochloroform): δ, ppm 2.40-2.60 (m, 2H, 3-H), 3.75-3.82 (m, 2H, 4-H), 3.89 (s, 3H, OCH_3), 5.04 (dd, J = 5.5, 8.8 Hz, 1H, 2-H), 6.95-7.02 (m, 2H, aryl H), 7.80-7.92 (m, 2H, aryl H), 9.18 (br. s, 1H, NH); ^{13}C nmr (deuteriochloroform): δ, ppm 32.0 (C-3), 37.3 (C-2), 40.9 (C-4), 55.6 (OCH_3), 114.5 (C aryl), 115.7 (CN), 123.2, 130.3, 164.4 (C aryl), 164.6, 167.4 (C=O); ms: m/z 281 [M+H]$^+$.

Anal. Calcd. for $C_{13}H_{13}ClN_2O_3$(MW 280.7): C, 55.62; H, 4.67; N, 9.98. Found: C, 55.61; H, 4.63; N, 9.97.

General Procedure for the Preparation of *N*-Acylcyclopropanecarboxamides **4**.

A suspension of **3b-j** (15 mmoles) and potassium carbonate (2.07 g, 15 mmoles) in acetone (50 ml) was refluxed for l hour. After the solvent had been removed under reduced pressure, cold water was added to the residue. The mixture was acidified 5% hydrochloric acid. The precipitate was collected by filtration, washed with water and dried to give the corresponding **4b-j**.

1-Cyano-*N*-cyclopropanecarbonylcyclopropanecarboxamide (**4b**).

This compound was obtained as colorless needles (2.01 g, 75%), mp 162-163° (acetone-petroleum ether); ir (potassium bromide): ν 3266, 3175 (NH), 2246 (CN), 1728, 1693 cm^{-1} (C=O); ^{1}H nmr (deuteriochloroform): δ, ppm 1.00-1.10 (m, 2H, CH_2), 1.18-1.24 (m, 2H, CH_2), 1.65-1.70 (m, 2H, CH_2), 1.79-1.84 (m, 2H, CH_2), 2.62-2.68 (m, 1H, CH), 8.65 (br. s, 1H, NH); ^{13}C nmr (deuteriochloroform): δ, ppm 11.1 (CH_2), 14.6 (CH), 14.8 (C-1), 19.6 (CH_2), 118.7 (CN), 164.8, 174.5 (C=O); ms: m/z 179 [M+H]$^+$.

Anal. Calcd. for $C_9H_{10}N_2O_2$ (MW 178.2): C, 60.66; H, 5.66; N, 15.72. Found: C, 60.54; H, 5.72; N, 15.66.

1-Cyano-*N*-(2-propanecarbonyl)cyclopropanecarboxamide (**4c**).

This compound was obtained as colorless needles (1.85 g, 69%), mp 121-122° (acetone-petroleum ether); ir (potassium bromide): ν 3258, 3175 (NH), 2247 (CN), 1737, 1694 cm^{-1} (C=O); ^{1}H nmr (deuteriochloroform): δ, ppm 1.99 (d, J = 6.7 Hz, 6H, $2CH_3$), 1.65-1.70 (m, 2H, CH_2), 1.75-1.80 (m, 2H, CH_2), 3.18-3.26 (m, 1H, CH), 8.55 (br. s, 1H, NH); ^{13}C nmr (deuteriochloroform): δ, ppm 14.8 (C-1), 18.5 (CH_3), 19.6 (CH_2), 35.4 (CH), 118.8 (CN), 164.2, 177.1 (C=O); ms: m/z 181 [M+H]$^+$.

Anal. Calcd. for $C_9H_{12}N_2O_2$ (MW 180.2): C, 59.99; H, 6.71; N, 15.55. Found: C, 59.94; H, 6.71; N, 15.55.

1-Cyano-*N*-cyclobutanecarbonylcyclopropanecarboxamide (**4d**).

This compound was obtained as colorless needles (1.99 g, 69%), mp 131-132° (acetone-petroleum ether); ir (potassium bromide): ν 3257, 3178 (NH), 2246 (CN), 1737, 1705 cm^{-1} (C=O); ^{1}H nmr (deuteriochloroform): δ, ppm 1.64-1.67 (m, 2H, CH_2), 1.74-1.78 (m, 2H, CH_2), 1.86-2.37 (m, 6H, $3CH_2$), 3.72-3.76 (m, 1H, CH), 8.52 (br. s, 1H, NH); ^{13}C nmr (deuteriochloroform): δ, ppm 14.6 (C-1), 17.8, 19.6, 24.4 (CH_2), 40.4 (CH), 118.7 (CN), 164.2, 175.0 (C=O); ms: m/z 193 [M+H]$^+$.

Anal. Calcd. for $C_{10}H_{12}N_2O_2$ (MW 192.2): C, 62.49; H, 6.29; N, 14.57. Found: C, 62.26; H, 6.36; N, 14.43.

1-Cyano-*N*-cyclopentanecarbonylcyclopropanecarboxamide (**4e**).

This compound was obtained as colorless needles (2.58 g, 83%), mp 152-153° (acetone-petroleum ether); ir (potassium bromide): ν 3268, 3176 (NH), 2247 (CN), 1736, 1695 cm^{-1} (C=O); ^{1}H nmr (deuteriochloroform): δ, ppm 1.56-1.96 (m, 12H, $6CH_2$), 3.35-3.42 (m, 1H, CH), 8.54 (br. s, 1H, NH); ^{13}C nmr (deuteriochloroform): δ, ppm 14.8 (C-1), 19.5, 25.9, 29.6 (CH_2), 45.6 (CH), 118.8 (CN), 164.2, 176.2 (C=O); ms: m/z 207 [M+H]$^+$.

Anal. Calcd. for $C_{11}H_{14}N_2O_2$ (MW 206.2): C, 64.06; H, 6.84; N, 13.58. Found: C, 63.85; H, 6.74; N, 13.54.

1-Cyano-*N*-cyclohexanecarbonylcyclopropanecarboxamide (**4f**).

This compound was obtained as colorless needles (3.09 g, 94%), mp 152-153° (acetone-petroleum ether); ir (potassium bromide): ν 3263, 3177 (NH), 2242 (CN), 1740, 1702 cm^{-1} (C=O); ^{1}H nmr (deuteriochloroform): δ, ppm 1.20-1.93 (m, 14H, $7CH_2$), 2.90-2.97 (m, 1H, CH), 8.55 (br. s, 1H, NH); ^{13}C nmr (deuteriochloroform): δ, ppm 14.8 (C-1), 19.5, 25.4, 25.6, 28.7 (CH_2), 44.9 (CH), 118.8 (CN), 164.2, 175.9 (C=O); ms: m/z 221 [M+H]$^+$.

Anal. Calcd. for $C_{12}H_{16}N_2O_2$ (MW 220.3): C, 65.43; H, 7.32; N, 12.72. Found: C, 65.40; H, 7.24; N, 12.73.

1-Cyano-*N*-phenylacetylcyclopropanecarboxamide (**4g**).

This compound was obtained as colorless needles (2.76 g, 80%), mp 145-146° (acetone-petroleum ether); ir (potassium bromide): ν 3245, 3173 (NH), 2241 (CN), 1742, 1685 cm^{-1} (C=O); ^{1}H nmr (deuteriochloroform): δ, ppm 1.62-1.66 (m, 2H, CH_2), 1.75-1.78 (m, 2H, CH_2), 4.06 (s, 2H, $COCH_2$), 7.25-7.37 (m, 5H, aryl H), 8.69 (br. s, 1H, NH); ^{13}C nmr (deuteriochloroform): δ, ppm 14.8 (C-1), 19.8, 43.9 (CH_2), 118.5 (CN), 127.6, 128.8, 129.5, 132.7 (C aryl), 164.5, 171.0 (C=O); ms: m/z 229 [M+H]$^+$.

Anal. Calcd. for $C_{13}H_{12}N_2O_2 \bullet 0.1H_20$ (MW 228.3): C, 67.87; H, 5.35; N, 12.18. Found: C, 67.93; H, 5.33; N, 12.16.

1-Cyano-*N*-(4-fluorobenzoyl)cyclopropanecarboxamide (**4h**).

This compound was obtained as colorless columns (3.07 g, 88%), mp 118-119° (acetone-petroleum ether); ir (potassium bromide): ν 3249, 3153 (NH), 2248 (CN), 1725, 1685 cm^{-1} (C=O); ^{1}H nmr (deuteriochloroform): δ, ppm 1.69-1.72 (m, 2H, CH_2), 1.84-1.87 (m, 2H, CH_2), 7.16-7.22 (m, 2H, aryl H), 7.88-7.92 (m, 2H, aryl H), 9.33 (br. s, 1H, NH); ^{13}C nmr (deuteriochloroform): δ, ppm 15.3 (C-1), 19.6 (CH_2), 116.3 (C aryl), 119.2 (CN), 128.5, 130.6, 163.2, 164.6 (C aryl), 164.9, 166.9 (C=O); ms: m/z 233 [M+H]$^+$.

Anal. Calcd. for $C_{12}H_9FN_2O_2$ (MW 232.2): C, 62.07; H, 3.91; N, 12.06. Found: C, 62.15; H, 3.85; N, 12.06.

N-(4-Chlorobenzoyl)-1-cyanocyclopropanecarboxamide (**4i**).

This compound was obtained as colorless scales (3.55 g, 95%), mp 127-128° (acetone-petroleum ether); ir (potassium bromide): ν 3243, 3150 (NH), 2249 (CN), 1725, 1683 cm^{-1} (C=O); ^{1}H nmr (deuteriochloroform): δ, ppm 1.69-1.72 (m, 2H, CH_2), 1.84-1.87 (m, 2H, CH_2), 7.47-7.51 (m, 2H, aryl H), 7.80-7.82 (m, 2H, aryl

H), 9.32 (br. s, 1H, NH); ^{13}C nmr (deuteriochloroform): δ, ppm 15.3 (C-1), 19.6 (CH_2), 119.1 (CN), 129.3, 129.4, 130.6, 140.2 (C aryl), 163.4, 164.2 (C=O); ms: m/z 249 $[M+H]^+$.

Anal. Calcd. for $C_{12}H_9ClN_2O_2$ (MW 248.7): C, 57.96; H, 3.65; N, 11.27. Found: C, 57.94; H, 3.64; N, 11.23.

1-Cyano-*N*-(4-methoxybenzoyl)cyclopropanecarboxamide (**4j**).

This compound was obtained as colorless needles (3.35 g, 92%), mp 114-115° (acetone-petroleum ether); ir (potassium bromide): ν 3307, 3170 (NH), 2240 (CN), 1740, 1685 cm^{-1} (C=O); ^{1}H nmr (deuteriochloroform): δ, ppm 1.67-1.70 (m, 2H, CH_2), 1.84-1.87 (m, 2H, CH_2), 3.88 (s, 3H, OCH_3), 6.97-7.01 (m, 2H, aryl H), 7.83-7.87 (m, 2H, aryl H), 9.28 (br. s, 1H, NH); ^{13}C nmr (deuteriochloroform): δ, ppm 15.2 (C-1), 19.4 (CH_2), 55.6 (OCH_3), 114.4 (C aryl), 119.4 (CN), 124.4, 130.1, 163.3 (C aryl), 163.96, 164.0 (C=O); ms: m/z 245 $[M+H]^+$.

Anal. Calcd. for $C_{13}H_{12}N_2O_3$ (MW 244.3): C, 63.93; H, 4.95; N, 11.47. Found: C, 63.96; H, 5.00; N, 11.39.

General Procedure for the Reaction of **4** with Sodium Iodide.

A solution of **4a-j** (5 mmoles) and sodium iodide (1.50 g, 10 mmoles) in DMF (5 ml) was stirred at 150° for 1 hour. After removal of the solvent *in vacuo*, cold water was added to the residue. The mixture was extracted with ethyl acetate. The extract was washed with water, dried over anhydrous sodium sulfate and concentrated *in vacuo*. The residue was chromatographed on silica gel with dichloromethane as the eluent to yield **2a** (0.66 g, 87%), **2b** (0.75 g, 84%), **2c** (0.78 g, 87%), **2d** (0.80 g, 83%), **2e** (0.90 g, 87%), **2f** (0.98 g, 89%), **2g** (1.01 g, 89%), **2h** (1.00 g, 86%), **2i** (1.05 g, 84%) and **2j** (1.07 g, 88%).

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