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Rhodium(II) Acetate-Catalyzed Reaction of 2-Amino-4,5-dihydro-3-furancarbonitriles with α-Diazo-β-keto Esters

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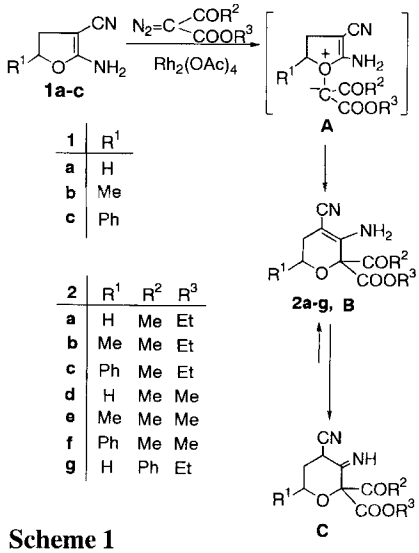
Abstract. 2-Amino-4,5-dihydro-3-furancarbonitriles (**1**) react with α-diazo-β-keto esters in the presence of rhodium (II) acetate to give alkyl 2*H*-pyran-2-carboxylates (**2**) in good yields. Benzoylation of **2** with benzoyl chloride provided alkyl 3-benzoylimino-2*H*-pyran-2-carboxylates (**4**). The formation of **2** could be explained by a mechanism involving an oxonium ylide derived from the rhodium carbenoids and **1**

Rhodium(II)-catalyzed decomposition of α-diazo carbonyl compounds has become an important methodology in organic synthesis [1–5].The reactions in which the intermediate metal-carbene participates include cyclopropanation, C–H insertion, and ylide formation. In the previous paper, we showed that 2-amino-4,5-dihydro-3-thiophenecarbonitriles react with ethyl diazoacetoacetate in the presence of rhodium(II) acetate to form sulfonium ylides or 1,4-oxathiocines, and both products are heated at 140 °C to give ethyl thiopyran-6-carboxylates [6]. As a sequel to this study, we investigated the reactions of 2-amino-4,5-dihydro-3-furancarbonitriles **1** [7] with α-diazo-β-keto esters. α-Diazo-β-keto esters used in this study include ethyl diazoacetoacetate [8], methyl diazoacetoacetate [9], and ethyl diazobenzoylacetate [10].

When a mixture of 3-furancarbonitrile **1a**, ethyl diazoacetoacetate, and a catalytic amount of rhodium(II) acetate in 1,2-dichloroethane was refluxed for 1 h, the ethyl 2*H*-pyran-2-carboxylate **2a** was obtained in 82% yield (Scheme 1).The IR and ^{1}H NMR spectra indicated that **2a** exists in the imine form **C** rather than the enamine form **B**. The formation of **2a** is considered to proceed through the oxonium ylide **A**. Examples of the ring expansion which proceeds *via* an oxonium ylide formed by the reaction of carbene or carbenoid with cyclic ethers have been reported by West [11] and Kirmse [12].

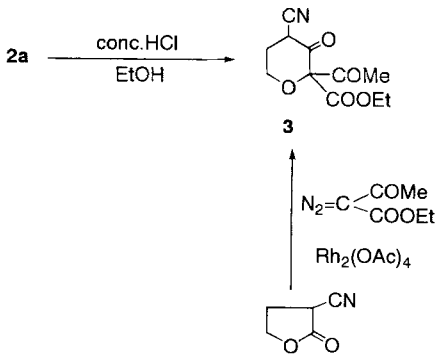
In order to confirm the structure of **2a**, hydrolysis of **2a** with hydrochloric acid led to ethyl 3-oxo-2*H*-pyran-2-carboxylate **3** which was identical with an authentic sample prepared by the reaction of tetrahydro-2-oxo-3-furancarbonitrile [13] with ethyl diazoacetoacetate (Scheme 2). Similarly, the reaction of 5-methyl-3-furancarbonitrile **1b** with ethyl diazoacetoacetate gave the ethyl 6-methyl-2*H*-pyran-2-carboxylate **2b** as a pale yel-low oil. The ^{1}H NMR spectrum of **2b** indicates that **2b** consists of approximately a 3:2 mixture of diastereo-mers. Separation of the diastereomers was attempted by column chromatography on silica gel, but was not



1	R^1
a	H
b	Me
c	Ph

2	R^1	R^2	R^3
a	H	Me	Et
b	Me	Me	Et
c	Ph	Me	Et
d	H	Me	Me
e	Me	Me	Me
f	Ph	Me	Me
g	H	Ph	Et

Scheme 1

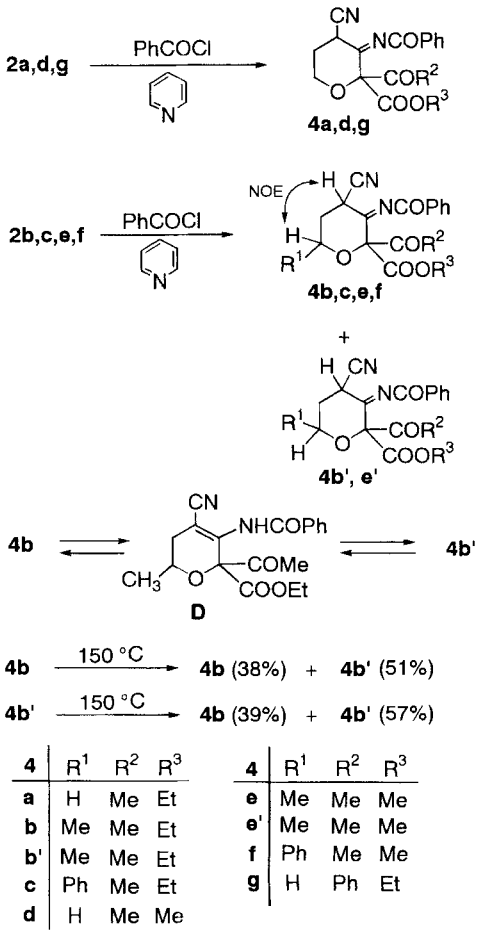


Scheme 2

successful. Treatment of **2b** with benzoyl chloride furnished the *N*-benzoyl derivatives (**4b** and **4b'**), which could be separated by fractional recrystallization. The mass spectra and the results of elemental analysis of **4b** and **4b'** indicate that both compounds have the same molecular composition $C_{19}H_{20}N_2O_5$. The IR and ^{1}H NMR spectra of **4b** are similar to those of **4b'**. In the NOESY spectra of **4b** and **4b'**, the NOE observed between 4-H and 6-H of **4b** indicates a *cis* relationship of both protones, while the absence of a NOE effect between 4-H and 6-H of **4b'** shows a *trans* relationship.

Compound **4b** was heated at 150 °C for 3 h to furnish a mixture of **4b** (38%) and **4b'** (51%). Under the same conditions, **4b'** was also converted into a mixture of **4b** (39%) and **4b'** (57%). Probably, this interconversion takes place through the intermediate enamine form **D** (Scheme 3). The rhodium(II) acetate-catalyzed reaction of 5-phenyl-3-furancarbonitrile (**1c**) with ethyl diazoacetoacetate gave ethyl 3-imino-6-phenyl-2*H*-pyran-2-carboxylate (**2c**) which was shown to be a 3:2 mixture of the diastereomers on the basis of the ^{1}H NMR spectrum. On benzoylation with benzoyl chloride, **2c** was converted into ethyl 3-benzoylimino-6-phenyl-2*H*-pyran-2-carboxylate (**4c**) in 85% yield as a single product. The presence of the NOE between 4-H and 6-H of **4c** suggests 4-H and 6-H to be in the *cis* configuration.

Subsequently, reactions of **1a–c** with methyl diazoacetoacetate were also examined. From compound **1a** the methyl 2*H*-pyran-2-carboxylate **2d** was obtained in 74% yield, while **1b** or **1c** furnished a diastereomeric mixture of methyl 6-methyl-2*H*-pyran-2-carboxylate (**2e**) or methyl 6-phenyl-2*H*-pyran-2-carboxylate (**2f**). In a similar manner, the reaction of **1a** with ethyl diazobenzoylacetate gave ethyl 2*H*-pyran-2-carboxylate **2g** in 72% yield. Benzoylation of **2a,d,f,g** with benzoyl chloride provided the corresponding alkyl 3-benzoylimino-2*H*-pyran-2-carboxylates **4a,d,f,g** as a single product, whereas the reaction of **2e** with benzoyl chloride gave a diastereomeric mixture of the *N*-benzoyl derivatives (**4e** and **4e'**). An NOE enhancement between 4-H and 6-H of **4e,f** is observed while an NOE is not evident between 4-H and 6-H of **4e'**. These findings suggest that 4-H of **4e,f** is *cis* to 6-H, whereas that of **4e'** is *trans* to 6-H.



4	R^1	R^2	R^3
a	H	Me	Et
b	Me	Me	Et
b'	Me	Me	Et
c	Ph	Me	Et
d	H	Me	Me

4	R^1	R^2	R^3
e	Me	Me	Me
e'	Me	Me	Me
f	Ph	Me	Me
g	H	Ph	Et

Scheme 3

Experimental

All melting points are uncorrected. IR spectra were recorded with a Jasco A-302 instrument. ^{1}H and ^{13}C NMR spectra were measured on a Hitachi R22 (90 MHz), Jeol JNM-GX-400 (400 MHz), and Jeol JNM-A500 (500 MHz) in $CDCl_3$ with TMS as internal standard, δ scale; coupling constants in Hz. Mass spectra were recorded with a Jeol JMS-D300, 70 eV.

Reactions of 2-Amino-4,5-dihydro-3-furancarbonitriles (1) with α-Diazo-β-keto Esters (General Procedure)

A mixture of **1** (20 mmol), α-diazo-β-keto ester (22 mmol), and $Rh_2(OAc)_4$ (0.05 g) in 1,2-dichloroethane (40 ml) was refluxed for 1 h. The solvent was removed, and the residue was chromatographed on silica gel with CH_2Cl_2/acetone (4:1) as eluent, to afford **2**.

Ethyl 2-Acetyl-4-cyanotetrahydro-3-imino-2H-pyran-2-carboxylate (**2a**)

From 2-amino-4,5-dihydro-3-furancarbonitrile (2.20 g, 20 mmol) and ethyl diazoacetoacetate (3.43 g, 22 mmol). Yield 3.92 g (82%), pale yellow oil. – IR (neat): ν/cm^{-1} = 3410 (NH), 2250 (C≡N), 1735 (sh), 1720 (C=O). – ^{1}H NMR (90 MHz): δ/ppm = 1.40 (t, J = 7 Hz, 3H, $OCH_2C\underline{H}_3$), 2.30–2.60 (br., 1H, NH), 2.35 (dt, J = 7/9 Hz, 2H, 5-H), 2.66 (s, 3H, $COCH_3$), 3.87 (t, J = 7 Hz, 2H, 6-H), 4.40 (t, J = 9 Hz, 1H, 4-H), 4.38 (q, J = 7 Hz, 2 H, $OC\underline{H}_2CH_3$). – MS (EI) *m/z* (%): 238 (48) [M$^+$].

$C_{11}H_{14}N_2O_4$	Calcd.:	C 55.46	H 5.92	N 11.76
(238.2)	Found:	C 55.62	H 5.95	N 11.70.

Ethyl 2-Acetyl-4-cyanotetrahydro-3-imino-6-methyl-2H-pyran-2-carboxylate (**2b**)

From 2-amino-4,5-dihydro-5-methyl-3-furancarbonitrile (2.48 g, 20 mmol) and ethyl diazoacetoacetate (3.43 g, 22 mmol). Yield 4.43 g (88%), pale yellow oil. – IR (neat): ν/cm^{-1} = 3480 (NH), 2245 (C≡N), 1738 (sh), 1722 (C=O). – ^{1}H NMR (90 MHz): δ/ppm = 1.26 (d, J = 6.5 Hz, 1.2H, CH_3), 1.30 (d, J = 6.5 Hz, 1.8H, CH_3), 1.40 (t, J = 7 Hz, 3H, $OCH_2C\underline{H}_3$), 2.00–2.45 (m, 3H, NH/5-H), 2.65 (s, 3H, $COCH_3$), 4.00–4.50 (m, 2H, 4-H/6-H), 4.38 (q, J = 7 Hz, 2H, $OC\underline{H}_2CH_3$).

$C_{12}H_{16}N_2O_4$	Calcd.:	C 57.13	H 6.39	N 11.10
(252.3)	Found:	C 57.39	H 6.39	N 10.95.

Ethyl 2-Acetyl-4-cyanotetrahydro-3-imino-6-phenyl-2H-pyran-2-carboxylate (**2c**)

From 2-amino-4,5-dihydro-5-phenyl-3-furancarbonitrile (3.72 g, 20 mmol) and ethyl diazoacetoacetate (3.43 g, 22 mmol). Yield 5.03 g (80%), pale yellow oil. – IR (neat): ν/cm^{-1} = 3480 (NH), 2245 (C≡N), 1735 (sh), 1720 (C=O). – ^{1}H NMR (90 MHz): δ/ppm = 1.36 (t, J = 7 Hz, 3H, $OCH_2C\underline{H}_3$), 2.43 (t, J = 6.5 Hz, 2H, 5-H), 2.50–2.85 (br., 1H, NH), 2.61 (s, 1.8H, $COCH_3$), 2.64 (s, 1.2H, $COCH_3$), 4.36 (q, J = 7 Hz, 2 H, $OC\underline{H}_2CH_3$), 4.53 (t, J = 6.5 Hz, 1H, 4-H), 4.79 (t, J = 6.5 Hz, 0.4H, 6-H), 5.00 (t, J = 6.5 Hz, 0.6H, 6-H), 7.35 (s, 5H, aryl).

$C_{17}H_{18}N_2O_4$	Calcd.:	C 64.96	H 5.77	N 8.91
(314.3)	Found:	C 64.98	H 5.81	N 8.71.

Methyl 2-Acetyl-4-cyanotetrahydro-3-imino-2H-pyran-2-carboxylate (**2d**)

From 2-amino-4,5-dihydro-3-furancarbonitrile (2.20 g, 20 mmol) and methyl diazoacetoacetate (3.12 g, 22 mmol). Yield 3.32 g (74%), pale yellow oil. – IR (neat): ν/cm^{-1} = 3420 (NH), 2255 (C≡N), 1740 (sh), 1720 (C=O). – ^{1}H NMR (90 MHz): δ/ppm = 2.20–2.50 (br., 1H, NH), 2.33 (dt, J = 6/7 Hz, 2H, 5-H), 2.65 (s, 3H, $COCH_3$), 3.86 (t, J = 6 Hz, 2H, 6-H), 3.92 (s, 3H, OCH_3), 4.40 (t, J = 7 Hz, 1H, 4-H). – MS (EI) *m/z* (%): 224 (79) [M$^+$].

$C_{10}H_{12}N_2O_4$	Calcd.:	C 53.57	H 5.39	N 12.49
(224.2)	Found:	C 53.82	H 5.59	N 12.24.

Methyl 2-Acetyl-4-cyanotetrahydro-3-imino-6-methyl-2H-pyran-2-carboxylate (**2e**)

From 2-amino-4,5-dihydro-5-methyl-3-furancarbonitrile (2.48 g, 20 mmol) and methyl diazoacetoacetate (3.12 g, 22 mmol). Yield 3.90 g (82%), pale yellow oil. – IR (neat): ν/cm^{-1} = 3460 (NH), 2260 (C≡N), 1740 (sh), 1725 (C=O). – ^{1}H NMR (90 MHz): δ/ppm = 1.26 (d, J = 6 Hz, 1.2H, CH_3), 1.31 (d, J = 6 Hz, 1.8H, CH_3), 1.85–2.45 (m, 4H, NH/5-H/6-H), 2.66 (s, 3H, $COCH_3$), 3.94 (s, 3H, OCH_3), 4.37 (t, J = 6 Hz, 0.6H, 4-H), 4.49 (t, J = 6 Hz, 0.4H, 4-H). – MS (EI) *m/z* (%): 238 (61) [M$^+$].

$C_{11}H_{14}N_2O_4$	Calcd.:	C 55.46	H 5.92	N 11.76
(238.2)	Found:	C 55.29	H 6.07	N 11.52.

Methyl 2-Acetyl-4-cyanotetrahydro-3-imino-6-phenyl-2H-pyran-2-carboxylate (**2f**)

From 2-amino-4,5-dihydro-5-phenyl-3-furancarbonitrile (3.72 g, 20 mmol) and methyl diazoacetoacetate (3.12 g, 22 mmol). Yield 4.65 g (78%), pale yellow oil. – IR (neat): ν/cm^{-1} = 3480 (NH), 2255 (C≡N), 1740 (sh), 1720 (C=O). – ^{1}H NMR (90 MHz): δ/ppm = 2.15–2.80 (m, 3H, NH/5-H), 2.61 (s, 1.8H, $COCH_3$), 2.63 (s, 1.2H, $COCH_3$), 3.88 (s, 1.8H, OCH_3), 3.90 (s, 1.2H, OCH_3), 4.23 (t, J = 8 Hz, 0.4H, 4-H), 4.52 (dd, J = 8/11 Hz, 0.6H, 4-H), 4.77 (t, J = 8 Hz, 0.4H, 6-H), 5.00 (dd, J = 7.5/10 Hz, 0.6H, 6-H), 7.33 (s, 5 H, aryl). – MS (EI) *m/z* (%): 300 (18) [M$^+$].

$C_{16}H_{16}N_2O_4$	Calcd.:	C 63.99	H 5.37	N 9.33
(300.3)	Found:	C 63.70	H 5.41	N 9.22.

Ethyl 2-Benzoyl-4-cyanotetrahydro-3-imino-2H-pyran-2-carboxylate (**2g**)

From 2-amino-4,5-dihydro-3-furancarbonitrile (2.20 g, 20 mmol) and ethyl diazobenzoylacetate (4.80 g, 22 mmol). Yield 4.29 g (72%), pale yellow oil. – IR (neat): ν/cm^{-1} = 3440 (NH), 2260 (C≡N), 1740 (sh), 1720 (C=O). – ^{1}H NMR (90 MHz): δ/ppm = 1.38 (t, J = 7 Hz, 3H, $OCH_2C\underline{H}_3$), 2.25–2.55 (m, 2H, 5-H), 3.88 (t, J = 6 Hz, 2H, 6-H), 4.41 (q, J = 7 Hz, 2H, $OC\underline{H}_2CH_3$), 4.55 (t, J = 7 Hz, 1H, 4-H), 4.65 (s, 1H, NH), 7.35–7.60 (m, 3H, aryl), 7.85–8.15 (m, 2H, aryl).

$C_{16}H_{16}N_2O_4$	Calcd.:	C 63.99	H 5.37	N 9.33
(300.3)	Found:	C 63.94	H 5.48	N 9.12.

Preparation of Ethyl 2-Acetyl-4-cyanotetrahydro-3-oxo-2*H*-pyran-2-carboxylate (3)

Procedure A: A mixture of **2a** (3.41 g, 14 mmol) and conc. HCl (5 ml) in EtOH (15 ml) was heated at 50 °C with stirring for 4 h. The solvent was removed, and H_2O was added to the residue. The mixture was extracted with CH_2Cl_2. The extract was washed with H_2O and dried with Na_2SO_4, and concentrated. The residue was purified by column chromatography on silica gel with CH_2Cl_2/acetone (4:1) as eluent to give **3** (1.24 g, 36%).

Procedure B: A mixture of tetrahydro-2-*oxo*-3-furan-carbonitrile (2.22 g, 20 mmol), ethyl diazoacetoacetate (6.24 g, 40 mmol), and $Rh_2(OAc)_4$ (0.10 g) in C_6H_5F (30 ml) was heated at 50 °C with stirring for 15 min. The solvent was removed, and the residue was chromatographed on silica gel with CH_2Cl_2/acetone (4:1) as eluent to afford **3** (0.45 g, 9%).

Colorless columns; *m.p.* 78–79 °C (Et_2O/petroleum ether). – IR (KBr): ν/cm^{-1} = 1760, 1735 cm^{-1} (C=O). – ^{1}H NMR (90 MHz): δ/ppm = 1.37 (t, J = 7.5 Hz, 3H, $OCH_2C\underline{H}_3$), 2.62 (s, 3H, $COCH_3$), 2.55–3.10 (m, 2H, 5-H), 4.05 (t, J = 10 Hz, 1H, 4-H), 4.38 (q, J = 7.5 Hz, 2H, $OC\underline{H}_2CH_3$), 4.30–4.70 (m, 2H, 6-H). – ^{13}C NMR (125.65 MHz) 12.0, 14.3, 27.6, 39.9, 61.0, 67.1, 128.1 (C≡N), 156.7, 157.3 (C=O), 161.9 (C=O), 172.4 (C=O). – MS (EI) *m/z* (%): 239 (23) [M$^+$].

$C_{11}H_{13}NO_5$	Calcd.:	C 55.23	H 5.48	N 5.86
(239.2)	Found:	C 55.33	H 5.55	N 5.96.

Reactions of Alkyl 3-Imino-2*H*-pyran-2-carboxylates (2) with Benzoyl Chloride: Synthesis of Alkyl 3-Benzoylimino-2*H*-pyran-2-carboxylates (4) (General Procedures)

Procedure A: To an ice-cooled and stirred solution of **2a,c,d,f,g** (5 mmol) in pyridine (3 ml) benzoyl chloride (0.78 g, 5.5 mmol) was added. The mixture was stirred at 80 °C for 3 h. The solvent was removed, and H_2O was added to the residue. The mixture was extracted with CH_2Cl_2. The extract was washed with H_2O and dried with Na_2SO_4, and concentrated. The solvent was evaporated, and the residue was purified by column chromatography on silica gel with CH_2Cl_2 as eluent. Yields **4a** (0.98 g, 57%), **4c** (1.78 g, 85%), **4d** (1.32 g, 80%), **4f** (1.80 g, 89%), and **4g** (1.52 g, 75%).

Procedure B: From **2b** (1.26 g, 5 mmol) and benzoyl chloride (0.78 g, 5.5 mmol) as described for *procedure A*. Fractional recrystallization from CH_2Cl_2/petroleum ether gave colorless needles (**4b**, 0.49 g, 28%) and colorless prisms (**4b'**, 0.91 g, 51%). –The analogous treatment of **2e** (1.19g, 5mmol) afforded colorless needles (**4e**, 0.60 g, 35%) and colorless prisms (**4e'**, 0.91 g, 53%).

Ethyl 2-Acetyl-3-benzoylimino-4-cyanotetrahydro-2H-pyran-2-carboxylate (**4a**)

From **2a** (1.19 g, 5 mmol). Colorless prisms; *m.p.* 59–61 °C (Et_2O/petroleum ether). – IR (KBr): ν/cm^{-1} = 2240 (C≡N), 1720, 1620 (C=O). – ^{1}H NMR (400 MHz): δ/ppm = 1.38 (t, J = 7 Hz, 3H, $OCH_2C\underline{H}_3$), 2.57 (s, 3H, $COCH_3$), 2.56–2.65 (m, 2H, 5-H), 4.35 (t, J = 6 Hz, 1H, 4-H), 4.37 (q, J = 7 Hz, 2H, $OC\underline{H}_2CH_3$), 4.50–4.58 (m, 2H, 6-H), 7.41–7.45 (m, 2H, aryl), 7.55–7.59 (m, 1H, aryl), 7.97–8.00 (m, 2H, aryl). – MS (EI) m/z (%): 342 (0.9) [M$^+$].

$C_{18}H_{18}N_2O_5$	Calcd.:	C 63.15	H 5.30	N 8.18
(342.4)	Found:	C 63.09	H 5.34	N 8.14.

Ethyl cis-2-Acetyl-3-benzoylimino-4-cyanotetrahydro-6-methyl-2H-pyran-2-carboxylate (**4b**)

m.p. 87–88 °C. – IR (KBr): ν/cm^{-1} 2245 (C≡N), 1720, 1620 (C=O). – ^{1}H NMR (400 MHz): 1.38 (t, J = 6.5 Hz, 3H, $OCH_2C\underline{H}_3$), 1.46 (d, J = 5.5 Hz, 3H, CH_3), 2.47 (s, 3H, $COCH_3$), 2.51–2.63 (m, 2H, 5-H), 4.26 (t, J = 7 Hz, 1H, 4-H), 4.36 (q, J = 6.5 Hz, 2H, $OC\underline{H}_2CH_3$), 5.24–5.29 (m, 1H, 6-H), 7.40–7.44 (m, 2H, aryl), 7.54–7.58 (m, 1H, aryl), 7.95–7.97 (m, 2H, aryl). – MS (FAB): m/z (%): 357 (100) [M$^+$ + H].

$C_{19}H_{20}N_2O_5$	Calcd.:	C 64.04	H 5.66	N 7.86
(356.4)	Found:	C 64.20	H 5.61	N 7.91.

Ethyl trans-2-Acetyl-3-benzoylimino-4-cyanotetrahydro-6-methyl-2H-pyran-2-carboxylate (**4b'**)

m.p. 121–123 °C. – IR (KBr): ν/cm^{-1} = 2245 (C≡N), 1725, 1625 (C=O). – ^{1}H NMR (400 MHz): δ/ppm = 1.38 (t, J = 7 Hz, 3H, $OCH_2C\underline{H}_3$), 1.46 (d, J = 6 Hz, 3H, CH_3), 2.43–2.60 (m, 2H, 5-H), 2.57 (s, 3H, $COCH_3$), 4.26 (dd, J = 7/11 Hz, 1H, 4-H), 4.36 (q, J = 7 Hz, 2H, $OC\underline{H}_2CH_3$). 5.36–5.41 (m, 1H, 6-H), 7.41–7.45 (m, 2H, aryl), 7.55–7.59 (m, 1H, aryl), 7.95–8.00 (m, 2H, aryl). – MS (FAB) m/z (%): 357 (100) [M$^+$ + H].

$C_{19}H_{20}N_2O_5$	Calcd.:	C 64.04	H 5.66	N 7.86
(356.4)	Found:	C 64.09	H 5.93	N 7.85.

Ethyl 2-Acetyl-3-benzoylimino-4-cyanotetrahydro-6-phenyl-2H-pyran-2-carboxylate (**4c**)

From **2c** (1.57 g, 5 mmol). Colorless prisms; *m.p.* 143–145 °C (CH_2Cl_2/petroleum ether). – IR (KBr): ν/cm^{-1} = 2240 (C≡N), 1730, 1715, 1600 (C=O). – ^{1}H NMR (500 MHz): δ/ppm = 1.37 (t, J = 7 Hz, 3H, $OCH_2C\underline{H}_3$), 2.58 (s, 3H, $COCH_3$), 2.60–2.90 (m, 2H, 5-H), 4.30 (dd, J = 7.5/12 Hz, 1H, 4-H), 4.38 (q, J = 7 Hz, 2H, $OC\underline{H}_2CH_3$), 6.25 (dd, J = 4.5/10.5 Hz, 1H, 6-H), 7.30–7.70 (m, 8H, aryl), 7.95–8.15 (m, 2H, aryl). – MS (FAB) m/z (%): 419 (18) [M$^+$ + H].

$C_{24}H_{22}N_2O_5$	Calcd.:	C 68.89	H 5.30	N 6.69
(418.4)	Found:	C 68.77	H 5.43	N 6.66.

Methyl 2-Acetyl-3-benzoylimino-4-cyanotetrahydro-2H-pyran-2-carboxylate (**4d**)

From **2d** (1.12 g, 5 mmol). Colorless needles; *m.p.* 99–100 °C (CH_2Cl_2/petroleum ether). – IR (KBr): ν/cm^{-1} = 2245 (C≡N), 1730 (sh), 1720, 1618 (C=O). – ^{1}H NMR (90 MHz) δ/ppm = 2.58 (s, 3H, $COCH_3$), 2.60 (dt, J = 5.5/7 Hz, 2H, 5-H), 3.90 (s, 3H, OCH_3), 4.35 (t, J = 7 Hz, 1H, 4-H), 4.55 (t, J = 5.5 Hz, 2H, 6-H), 7.30–7.70 (m, 3H, aryl), 7.90–8.10 (m, 2H, aryl). – MS (EI) m/z (%): 328 (0.1) [M$^+$].

$C_{17}H_{16}N_2O_5$	Calcd.:	C 62.19	H 4.91	N 8.53
(328.3)	Found:	C 62.47	H 4.97	N 8.59.

Methyl cis-2-Acetyl-3-benzoylimino-4-cyanotetrahydro-6-methyl-2H-pyran-2-carboxylate (**4e**)

m.p. 84–86 °C. – IR (KBr): ν/cm^{-1} = 2250 (C≡N), 1725, 1626 (C=O). – ^{1}H NMR (500 MHz) δ/ppm = 1.44 (d, J = 6.5 Hz, 3H, CH_3), 2.47 (s, 3H, $COCH_3$), 2.50–2.65 (m, 2H, 5-H), 3.90 (s, 3H, OCH_3), 4.28 (t, J = 7 Hz, 1H, 4-H), 5.16–5.45 (m, 1H, 6-H), 7.30–7.70 (m, 3H, aryl), 7.85–8.10 (m, 2H, aryl). – MS (EI) m/z (%): 342 (0.2) [M$^+$].

$C_{18}H_{18}N_2O_5$	Calcd.:	C 63.15	H 5.30	N 8.18
(342.4)	Found:	C 63.33	H 5.40	N 8.21.

Methyl trans-2-Acetyl-3-benzoylimino-4-cyanotetrahydro-6-methyl-2H-pyran-2-carboxylate (**4e'**)

m.p. 107–108 °C. – IR (KBr): ν/cm^{-1} = 2250 (C≡N), 1726, 1626 (C=O). – ^{1}H NMR (500 MHz) δ/ppm = 1.43 (d, J = 6.5 Hz, 3H, CH_3), 2.40–2.65 (m, 2H, 5-H), 2.57 (s, 3H, $COCH_3$), 3.90 (s, 3H, OCH_3), 4.28 (dd, J = 8/11 Hz, 1H, 4-H), 5.20–5.50 (m, 1H, 6-H), 7.30–7.65 (m, 3H, aryl), 7.90–8.10 (m, 2H, aryl). – MS (EI) m/z (%): 342 (0.1) [M$^+$].

$C_{18}H_{18}N_2O_5$	Calcd.:	C 63.15	H 5.30	N 8.18
(342.4)	Found:	C 63.31	H 5.47	N 8.21.

Methyl 2-Acetyl-3-benzoylimino-4-cyanotetrahydro-6-phenyl-2H-pyran-2-carboxylate (**4f**)

From **2f** (1.50 g, 5 mmol). Colorless prisms; *m.p.* 129–131 °C (CH_2Cl_2/petroleum ether). – IR (KBr): ν/cm^{-1} = 2250 (C≡N), 1735, 1725, 1603 (C=O). – ^{1}H NMR (500 MHz) δ/ppm = 2.57 (s, 3H, $COCH_3$), 2.65–3.05 (m, 2H, 5-H), 3.91 (s, 3H, OCH_3), 4.28 (dd, J = 7/10 Hz, 1H, 4-H), 6.25 (dd, J = 4.5/8 Hz, 1H, 6-H), 7.30–7.60 (m, 8H, aryl), 8.00–8.15 (m, 2H, aryl). – MS (FAB) m/z (%): 405 (14) [M$^+$ + H].

$C_{23}H_{20}N_2O_5$	Calcd.:	C 68.31	H 4.98	N 6.93
(404.4)	Found:	C 68.35	H 5.10	N 7.03.

Ethyl 2-Benzoyl-3-benzoylimino-4-cyanotetrahydro-2H-pyran-2-carboxylate (**4g**)

From **2g** (1.50 g, 5 mmol). Colorless columns; *m.p.* 68–70 °C (Et_2O/petroleum ether). – IR (KBr): ν/cm^{-1} = 2250 (C≡N), 1728, 1716 (sh), 1602 (C=O). – ^{1}H NMR (500 MHz) : δ/ppm = 1.38 (t,

J = 6 Hz, 3H, $OCH_2C\underline{H}_3$), 2.62–2.75 (m, 2H, 5-H), 4.40 (q, J = 6 Hz, 2H, $OC\underline{H}_2CH_3$), 4.44 (dd, J = 7/9 Hz, 1H, 4-H), 4.54–4.64 (m, 2H, 6-H), 7.38–7.56 (m, 6H, aryl), 7.96–8.00 (m, 4H, aryl).

$C_{23}H_{20}N_2O_5$	Calcd.:	C 68.31	H 4.98	N 6.93
(404.4)	Found:	C 68.49	H 5.04	N 6.93.

Isomerization of 4b or 4b'

Compound **4b** (1.00 g) was heated at 150 °C for 3h. The crude products were recrystallized from CH_2Cl_2/petroleum ether to give **4b** (0.38 g, 38%) as colorless needles and **4b'** (0.51 g, 51%) as colorless prisms. – The analogous treatment of **4b'** (1.00g) gave a mixture of **4b** (0.39 g, 39%) and **4b'** (0.57 g, 57%).

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