Pyridine Ring Formation by the Reaction of Conjugated Carbodiimides with Enamines[1)]

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Abstract

The reaction of *N*-[6-methyl-2-oxo-4(2*H*)-pyranyl]-substituted carbodiimides **3**, generated by the treatment of [6-methyl-2-oxo-4(2*H*)-pyranyl]iminotriphenylphosphorane (**1**) with isocyanates **2** *in situ*, with 1-(1-pyrrolidinyl)cyclopentene (**4**) in refluxing toluene or dioxane gave cyclopenta[*d*]pyrano[4,3-*b*]pyridine derivatives **5**. A similar reaction of **3** with 1-(1-pyrrolidinyl)cyclohexene (**6**) afforded pyrano[4,3-*b*]isoquinoline derivatives **7** and **8**. Compound **8** corresponds formally to the adduct of **7** and isocyanate **2**.

Introduction

Since an aza-Witting reaction of iminophosphoranes with isocyanates exhibited a facile access to conjugated carbodiimides, much attention was focused on their chemistry as a useful and versatile tool for nitrogen heterocycle syntheses. Recently, Motoki *et al.* reported the intermolecular [4+2] cycloaddition reaction of α,β-unsaturated carbodiimides with tetracyanoethylene leading to pyridine derivatives.[2)] The intramolecular 6π-cyclization reaction of $\alpha,\beta,\gamma,\delta$-unsaturated carbodiimides gave pyridine derivatives[3)]. Similar 6π-cyclization reactions of conjugated carbodiimides in some carbo- and hetero-cyclic systems gave also pyridine derivatives fused by benzene,[4)] pyrazole,[5)] 1,2,3-triazole,[5)] furan,[6)] thiophene[6)], and pyrimidine.[7)]

Previously, we reported a facile preparation of quinoline derivatives by the reaction of *N*-(5,5-dimethyl-3-oxo-1-cyclohexenyl)-substituted carbodiimides with enamines.[8)] In the course of heterocycle syntheses using conjugated carbodiimides, we describe here a similar reaction of *N*-[6-methyl-2-oxo-4(2*H*)-pyranyl]-substituted carbodiimide with enamines leading to pyridine derivatives fused by pyran ring.

Results and Discussion

The preparation of *N*-[6-methyl-2-oxo-4(2*H*)-pyranyl]-*N'*-phenylcarbodiimide (**3a**) was accomplished easily by an aza-Witting reaction of iminophosphorane **1** with phenyl isocyanate (**2a**) (1.2 equiv.). Without isolation of carbodiimide **3a**, it was allowed to react with 1-(1-pyrrolidinyl)cyclopentene (**4**) (1.2 equiv.) in toluene under

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reflux for 22 h. Usual work-up of the reaction mixture gave 6-anilino-3-methyl-1-oxo-1,7,8,9-tetrahydrocyclopenta[*d*]pyrano[4,3-*b*]pyridine (**5a**) in 55% yield. Similar reaction of *N*-[6-methyl-2-oxo-4(2*H*)-pyranyl]-*N*'-(1-naphthyl)carbodiimide (**3b**), -*N*'-butylcarbodiimide (**3c**), and -*N*'-benzylcarbodiimide (**3d**) with **4** afforded also the same type of cyclopenetapyranopyridines **5b-d** in fair to moderate yields.

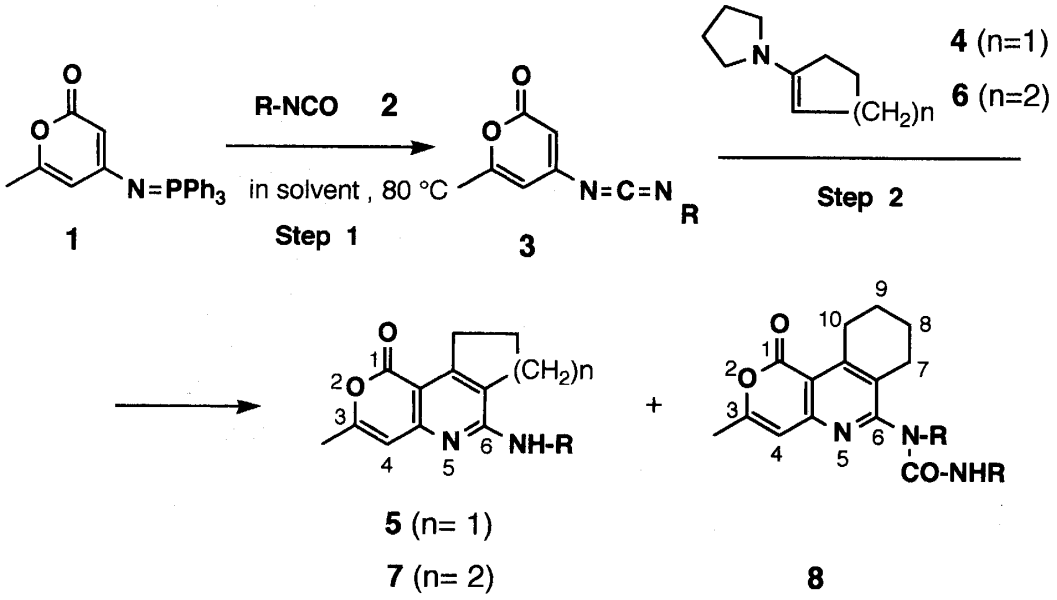
The structural elucidation of **5** was accomplished on the basis of their elemental analyses and spectral data. The IR spectra of **5** show absorption bands due to NH streching at 3340-3320 cm^{-1} and CO streching at 1705-1695 cm^{-1}. In their ^{1}H-NMR spectra the methyl group at 3-position and the bridged methylene ones appear characteristicly as signals at δ 2.2(singlet) and at δ 2.2(8-H, multiplet), 2.6(7-H, triplet, J=8 Hz), and 3.3(9-H, triplet, J=8 Hz), respectively. The existence of exocyclic NH group for **5** was also supported by their ^{1}H-NMR spectra; for **5d** the signal patterns of benzyl methylene were shown to be doublet and changed to be singlet after the treatment of deuterium oxide. The EI-mass spectra show the expected molecular ion peaks and the fragmentation patterns are in accord with the proposed structures.

6-Anilino-3-methyl-7,8,9,10-tetrahydropyrano[4,3-*c*]isoquinoline-1(1*H*)-one (**7a**) was formed in 46% yield by the reaction of **3a** with 1-(1-pyrrolidinyl)cyclohexene (**6**). Slightly different results were observed in the reactions of **3c** and **3d** with **6**. 6-(*N*,*N*'-dibutylureido)- (**8c**) and 6-(*N*,*N*'-dibenzylureido)-3-methyl-7,8,9,10-tetrahydropyrano[4,3-*c*]isoquinolin-1(1*H*)-one (**8d**)[9] were obtained as major products together wiht the expected **7c** and **7d**, respectively (Scheme 1). We suggest that compound **8** would be a secondary product from **7** and the unreacted or excess isocyanate **2**, but the details are still obscure. Although the ratio of **7** and **8** depended somewhat on the reaction conditions, the total yield of **7** and **8** was almost constant (Run 8 and 9). These results are summarized in Table 1.

Our next concerns were directed toward the extention of this reaction to that of *N*-[2-oxo-4(2*H*)-chromenyl]-substituted carbodiimides. *N*-[2-Oxo-4(2*H*)-chromenyl]-*N*'-phenylcarbodiimide (**10a**) reacted with enamine **4** in refluxing dioxane giving 11-anilino-6-oxo-6,7,8,9-tetrahydrocyclopenta[*d*]chromeno[4,3-*b*]-pyridine (**11a**) in 46% yield. 11-Anilino-7,8,9,10-tetrahydrochromeno[4,3-*c*]isoquinolin-6-(6*H*)-one (**12a**) were obtained in the reaction of **10a** with **6** in dioxane

Table 1. Reaction of Conjugated Carbodiimides **3** with Enamines **4** and **6**.

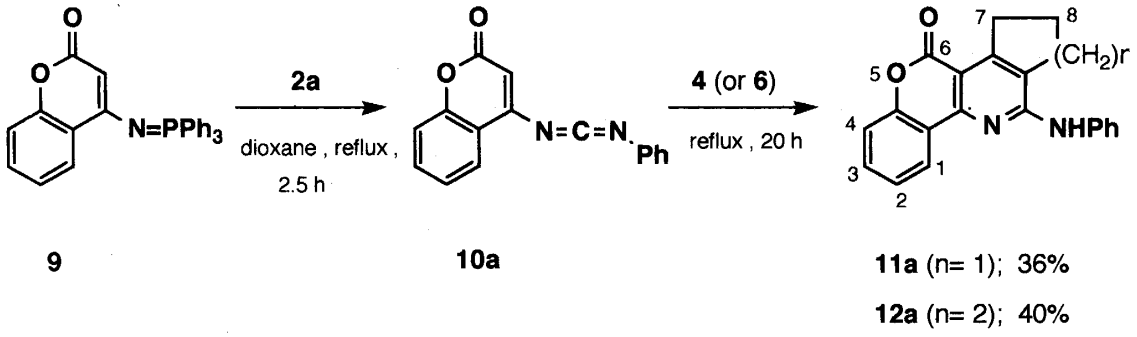
	Step 1			Step 2				
Run	R-NCO **2**	Solvent	Time(h)	Enamine	Temp.(℃)	Time(h)	Products	(Yield: %)
1	Ph	toluene	1	**4**	110	22	**5a**(55)	
2		xylene	1	**4**	140	4	**5a**(34)	
3	1-Naphthyl	toluene	2	**4**	110	20	**5b**(39)	
4		dioxane	1	**4**	80	20	**5b**(27)	
5	Bu	toluene	8	**4**	110	15	**5c**(31)	
6	CH_2Ph	toluene	7	**4**	110	15	**5d**(53)	
7	Ph	toluene	1.5	**6**	110	20	**7a**(46)	
8	Bu	toluene	8	**6**	room temp.	24	**7c**(23)	**8c**(33)
9		toluene	8	**6**	110	15	**7c**(17)	**8c**(40)
10	CH_2Ph	toluene	6	**6**	110	18	**7d**(15)	**8d**(36)



Scheme 1

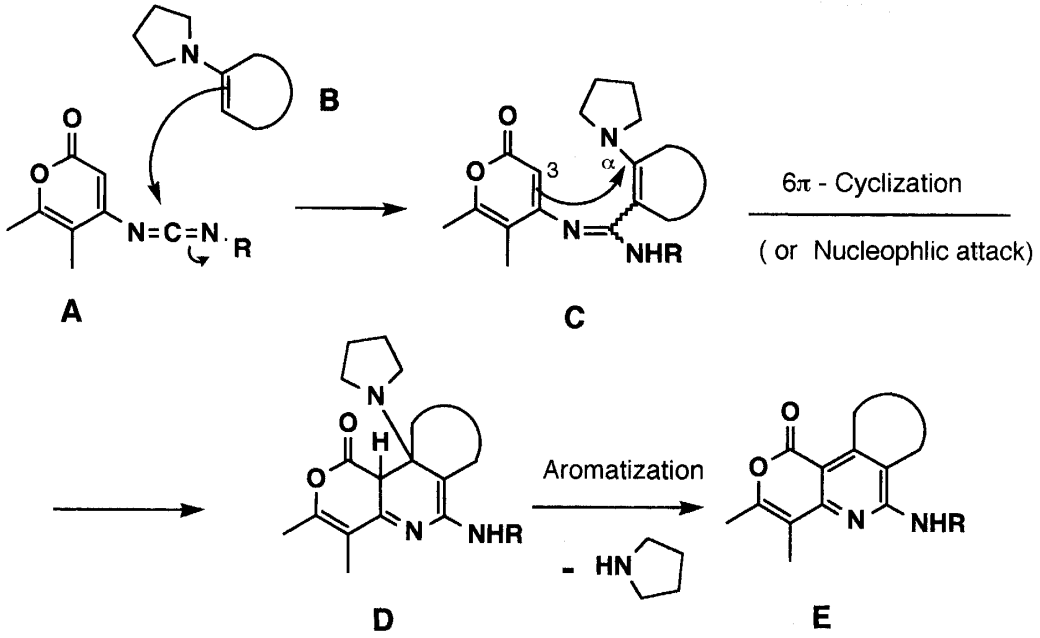
under reflux (Scheme 2).

As mentioned in a previous paper[8] amidine **C** is proposed to be an intermediate in this reaction, which undergoes a 6π-electrocyclic ring closure leading to dihydropyridine **D**. The aromatization of **D** with the elimination of pyrrolidine affords pyridine derivate **E** (Scheme 3). For another pathway, the nucleophilic attack of the carbon atom at 3-position in **C** to the α-position of the enemine moiety will initiate the ring closure giving **D**.



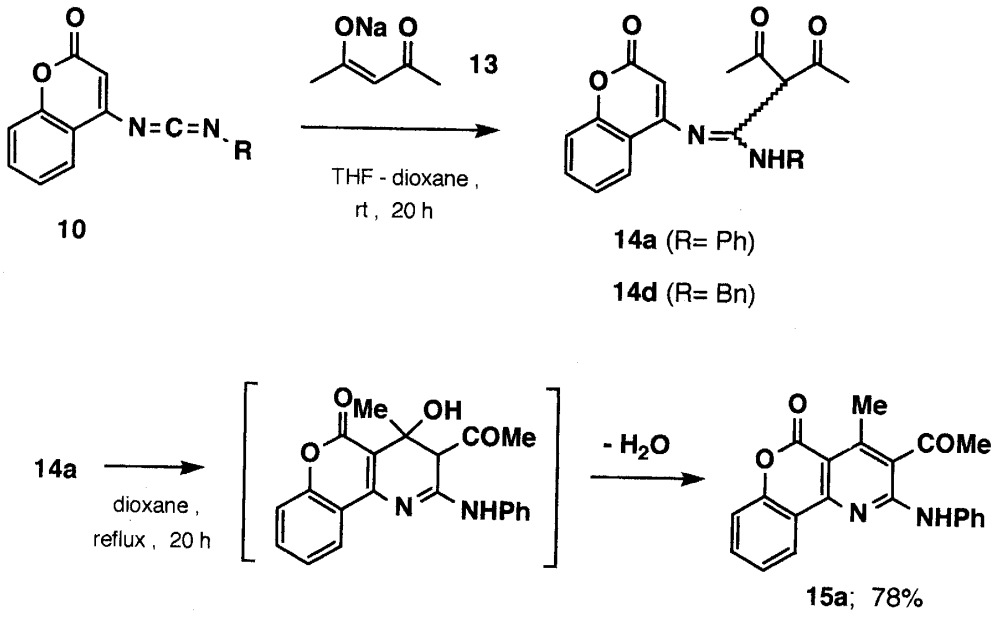
Scheme 2

In order to obtain better understandings for the reaction pathway, we examined the reaction of carbodiimides with enolate. The reaction of **10a** and **10d** with sodium acetylacetonate (**13**) in toluene gave the desired amidine **14a** and **14d** in low yields.[10] Heating **14a** in dioxane for 40 h afforded the final product **15a** in 78% yield with the elimination of water (Scheme 4). This means that the nucleophilic ring closure of **C** as well as the electrocyclic one is a plausible route to dihydropyridine **D**.



Scheme 3

This paper demonstrated that the intermolecular cyclization reaction of conjugated carbodiimides **3** and **10** with electron-rich olefins was a useful synthetic tool for the pyridine derivatives fused by heterocyclic system.



Scheme 4

Experimental

General.

All melting points are uncorrected. The IR spectra were measured on a JASCO IR-Report-100 spectrophotometer as potassium bromide pellets. The ^{1}H-NMR spectra were obtained on JEOL GSX-270 and/or JMH-MH-100 spectrometers for deuteriochloroform solution unless otherwise stated. Splitting patterns are indicated as s, singlet; d, doublet; t, triplet; q, quartet; ov, overlapping each other. The ^{13}C-NMR spectra were obtained on a JEOL GSX-270 spectrometer for deuteriochloroform solution. The mass spectra were recorded on a JEOL JMS-D spectrometer at an ionization energy of 75 eV. Elemental analyses were performed on a Hitachi 026 CHN analyzer. All nonaqueous reactions were run under a positive pressure of argon. All solvents were dried by standard methods before use. The progress of reactions was monitored by thin-layer chromatography (Silica Gel 60F-254, Merck). Chromatographic purification was performed with Wakogel C-200 (Wako Pure Chemical Industries, Ltd) and/or Silica Gel 60(230-234 mesh, Merck).

The starting iminophosphorane **9** was prepared from 4-hydroxy-2-oxo-2*H*-chromene similar to the reported method for **1**.[1b]

A solution of methanesulfonyl chloride (2.74 g, 22 mM) in THF (5 mL) was added to a solution of 4-hydroxycoumarin (3.24 g, 20 mM) and triethylamine (3.6 mL, 24 mM) in THF (50 mL) at 0 ℃ and the reaction mixture was stirred for additional 1 h. The resulting triethylamine hydrochloride was filtered off and the filtrate was evaporated to give 4-methanesulfonyloxy-2-oxo-2*H*-chromene in a quantitative yield. To a solution of the sulfone ester in methanol (100 mL) and DMF (50 mL) was added sodium azide (1.30 g, 20 mM) in water (100 mL) and the mixture was stirred at room temperature for 40 h. Extracted with dichloromethane (5 ×30 mL) and the orgaic layer was washed with water (10×20 mL) and dried with anhydrous magnesium sulfate. Concentration of the solution *in vacuo* gave 4-azido-2-oxo-2*H*-chromene (1.87 g, 10 mM). To a solution of the azide (10 mM) in benzene (10 mL) was added triphenylphosphine (4.0 g, 15.3 mM) in benzene (10 mL) and the mixture was stirred at 0 ℃ for 5 h. The benzene was evaporated to dryness, which was chromatographed on silica gel to give **9** (2.85 g, 34% based on the starting material) as an eluent of hexane/ethyl acetate (1/4)

N-[2-Oxo-4(2*H*)-chromenyl]iminotriphenylphosphorane (**9**). ^{1}H-NMR δ: 5.15 (1H, s, 3-H), 7.2-8.0(18H, ov, aromatic-H), 8.54(1H, d, 8-H, J=7 Hz).

One-pot Procedure for The Preparation of Fused Pyridine Derivatives: Phenyl isocyanate (**2a**) (59 μL, 0.54 mM) was added to a solution of iminophosphorane **1**(0.208 g, 0.54 mM) in dry toluene(5 mL). The reaction mixture was heated at 80 ℃ for 1 h. A solution of enemine **4**(79 μL, 0.54 mM) in dry toluene (2 mL) was added to the above solution. The resulting mixture was heated under reflux for 22 h and concentrated to dryness *in vacuo*. The residue was chromatographed on silica gel to give **5a** (0.086 g, 55%) using chloroform as an eluent.

6-Anilino-3-methyl-1-oxo-1,7,8,9-tetrahydrocyclopenta[*d*]pyrano [4,3-*b*]-pyridine (**5a**). Colorless needles from ethanol; mp 275-277 ℃; IR cm^{-1}: 3325(NH), 1695(CO); ^{1}H-NMR δ: 2.25(3H, s, 3-CH_3), 2.3(2H, ov, 8-H), 2.80(2H, t, 7-H, J=8

Hz), 3.43(2H, 9-H, J =8 Hz), 6.32(1H, br s, 6-H), 6.45(1H, br, NH), 7.1-7.8(5H, ov, phenyl-H); ^{13}C-NMR δ: 19.8(CH_3), 23.9(8-C), 29.1(7-C), 34.5(9-C), 106.1(4-C), 106.6(4b-C), 120.3, 123.4, 129.0, 139.2(phenyl-C), 124.2(6a-C), 155.2, 155.5, 156.8, 158.0(3-, 4a-, 6-, and 9-C), 162.5(1-C); MS m/z: 292(M^+), 222, 177, 119. Anal. Calcd for $C_{18}H_{16}N_2O_2$(292.3): C, 73.95; H, 5.52; N, 9.58. Found: C, 74.17; H, 5.65; N, 9.53.

3-Methyl-6-(1-naphthyl)amino-1-oxo-1,7,8,9-tetrahydrocyclopeta[*d*]pyrano-[4,3-*b*]pyridine (**5b**). Colorless needles from ethanol; mp 224-225 ℃; IR cm^{-1}: 3320(NH), 1695(CO); ^{1}H-NMR δ: 2.20(3H, s, 3-CH_3), 2.18(2H, ov, 8-H), 2.70(2H, t, 7-H, J=8 Hz), 3.40(2H, 9-H, J=8 Hz), 6.22(1, br s, 6-H), 6.95(1H, br, NH), 7.7-8.0(7H, ov, aroamtic-H); ^{13}C-NMR δ: 19.8(CH_3), 24.0(8-C), 29.5(7-C), 34.3(9-C), 105.9(4-C), 106.6(4b-C), 120.8, 121.1, 121.6, 125.4, 125.6, 126.1, 126.3, 128.1, 128.8, 134.0, 134.3(aromatic-C), 124.2(6a-C), 155.4, 156.4, 157.5, 157.9(3-, 4a-, 6-, and 9-C), 162.5(1-C); MS m/z: 342(M^+), 326, 314, 229, 127. Anal. Calcd for $C_{22}H_{18}N_2O_2$(342.4): C, 77.17; H, 5.30; N, 8.18. Found: C, 77.27; H, 5.40; N, 8.16.

6-Butylamino-3-methyl-1-oxo-1,7,8,9-tetrahydrocyclopenta[*d*]pyrano [4,3-*d*]-pyridine (**5c**). Colorless needles from ethanol; mp 164 ℃; IR cm^{-1}: 3340(NH), 1695(CO); 0.90(3H, m, -CH_3), 1.2-1.8(4H, ov, -CH_2- and 8-H), 2.22(3H, s, 3-CH_3), 2.65(2H, br t, 7-H, J=8 Hz), 3.1-3.7(4H, ov, -CH_2- and 9-H), 4.8(1H, br, NH), 6.20(1H, br s, 6-H); MS m/z: 272(M^+), 243(M^+-C_2H_5), 229(M^+-C_3H_7). Anal. Calcd for $C_{16}H_{20}N_2O_2$(272.3): C, 70.56; H, 7.40; N, 10.29. Found: C, 69.77; H, 7.46; N, 9.87.

6-Benzylamino-3-methyl-1-oxo-1,7,8,9-tetrahydrocyclopenta[*d*]pyrano[4,3-*b*] pyrine (**5d**). Colorless needles from ethanol; mp 194-195 ℃; IR cm^{-1}: 3325(NH), 1705, 1690(CO); ^{1}H-NMR δ: 2.2(2H, ov, 8-H), 2.24(3H, s, 3-CH_3), 2.64(2H, t, 7-H, J=8 Hz), 3.36(2H, t, 9-H, J=8 Hz), 4.78(2H, d, CH_2Ph, J=4 Hz), 5.0(1H, br, NH), 6.26 (1H, s, 6-H), 7.2-7.4(10H, ov, phenyl-H); ^{13}C-NMR δ: 19.8(CH_3), 23.8(8-C), 28.8(7-C), 34.4(9-C), 45.1(CH_2), 105.1(4b-C), 106.1(4-C), 123.0(6a-C), 127.5, 127.9, 128.8, 139.0(phenyl-C), 155.6, 156.0, 157.6, 157.7(3-, 4a-, 6-, and 9-C), 162.8(1-C); MS m/z: 306(M^+), 215(M^+-C_7H_7), 106(NHC_7H_7), 91. Anal. Calcd for $C_{19}H_{18}N_2O_2$ (306.4): C, 74.79; H, 5.92; N, 9.15. Found: C, 74.56; H, 5.96; N, 9.10.

6-Anilino-3-methyl-7,8,9,10-tetrahydropyrano[4,3-*c*]isoquinolin-1(1*H*)-one (**7a**). Colorless needles from ethanol; 249-250 ℃: IR cm^{-1}: 3350(NH), 1695(CO); ^{1}H-NMR δ: 1.6-2.0(4H, ov, 8- and 9-H), 2.20(3H, s, 3-CH_3), 2.4-2.5(2H, ov, 7-H), 3.1-3.2(2H, ov, 10-H), 6.16(1H, s, 4-H), 6.6(1H, br, NH), 6.9-7.6(5H, ov, phenyl-H); ^{13}C-NMR δ: 19.6(CH_3), 21.6, 21.9(8-, and 9-C), 24.3(7-C), 28.9(10-C), 106.3(4-C), 107.1(4b-C), 116.8, 121.0, 128.9, 139.3(phenyl-C), 123.5(6a-C), 150.2, 154.6, 156.5, 157.7(3-, 4a, 6-, and 10a-C), 162.4(1-C); MS m/z: 306(M^+), 305(M^+-H), 291(M^+-CH_3). Anal. Calcd for $C_{19}H_{18}N_2O_2$ (306.4): C, 74.49; H, 5.92; N, 9.15. Found: C, 74.38; H, 6.24; N, 9.04.

6-Butylamino-3-methyl-7,8,9,10-tetrahydropyrano[4,3-*c*]isoquinolin-1(1*H*)-one (**7c**). Colorless prisms from hexane; 157 ℃; IR cm^{-1}: 3360(NH), 1690(CO); ^{1}H-NMR δ: 1.05(3H, t, -CH_3, J=7 Hz), 1.9(6H, ov, -CH_2- and 8- and 9-H), 2.30(3H, s, 3-CH_3), 2.4(2H, ov, 7-H), 3.25(2H, ov, 10-H), 2.70(2H, m, NH-CH_2-), 5.0(1H, br, NH), 6.40(1H, s, 4-H); MS m/z: 286(M^+-C_2H_5), 243(M^+-C_3H_7), 230(M^+-C_4H_8). Anal. Calcd for $C_{17}H_{22}N_2O_2$(286.4): C, 71.30; H, 7.74; N, 9.78. Found: C, 71.27; H, 7.72; N, 9.65.

6- (*N*,*N*'- Dibutylureido) -3- methyl -7,8,9,10- tetrahydropyrano [4,3- *c*] -isoquinolin-1(1*H*)-one (**8c**). Colorless prisms from hexane; mp 106 ℃; IR cm^{-1}: 3350(NH), 1710, 1670(CO); ^{1}H-NMR δ: 0.88(6H, br, t, 2x-CH_3, J=6 Hz), 1.1-2.6(8 H, ov, -CH_2-), 2.7-2.9(4H, ov, 8- and 9-H), 2.68(2H, ov, 7-H), 3.1-3.5(4H, ov, NH -CH_2- and 10-H), 3.8(2H, m, N-CH_2-), 4.6(1H, br, NH), 6.1(1H, s, 4-H); MS *m/z*: 385(M^+), 342(M^+-NCO), 286(M-C_4H_9NCO). Anal. Calcd for $C_{22}H_{31}N_2O_2$ (385.5): C, 68.54; H, 8.11; N, 10.90. Found: C, 68.67; H, 8.13; N, 10.94.

6-Benzylamino-3-methyl-7,8,9,10-tetrahydropyrano[4,3-*c*]isoquinolin-1(1*H*)-one (**7d**). Colorless prisms from hexane and ethyl acetate; mp 151 ℃; IR cm^{-1}: 3350(NH), 1690(CO); ^{1}H-NMR δ: 1.6-1.8(4H, ov, 8- and 9-H), 2.16(3H, s, 3-CH_3), 2.33(2H, t, 7-H, J=6 Hz), 3.25(2H, t, 10-H, J=6 Hz), 4.65(2H, d, NH-CH_2Ph, J=5Hz), 5.0(1H, br, NH), 6.24(1H, s, 4-H), 7.0-7.3(5H, ov, phenyl-H); ^{13}C-NMR δ: 19.6(CH_3), 21.5, 22.1(8- and 9-C), 24.0(7-C), 28.8(10-C), 45.5(-CH_2Ph), 105.7(4b-C), 106.4(4-C), 116.0, 128.0, 128.8, 139.2(phenyl-C), 127.6(6a-C), 149.0, 155.3, 157.6, 158.7(3-, 4a-, 6-, and 9-C), 162.8(1-C); MS *m/z*: 320(M^+), 229(M^+-C_7H_7). Anal. Calcd for $C_{20}H_{20}N_2O_2$ (320.4): C, 74.97; H, 6.29; N, 8.74. Found: C, 74.93; H, 6.36N, 8.64.

6-(*N*,*N*'-Dibutylureido)-3-methyl-7, 8, 9, 10-tetrahydropyrano [4, 3-*c*]-isoquinolin-1(1*H*)-one (**8d**). Colorless plates from ethanol and ethyl acetate; mp 198 ℃; IR cm^{-1}: 3350(NH), 1730, 1660(CO); ^{1}H-NMR δ: 1.3-1.8(4H, ov, 8- and 9-H), 2.14(3H, s, 3-CH_3), 2.34(2H, br, t, 7-H, J=6 Hz), 3.10(2H, br t, 10-H, J=6 Hz), 4.16(2H, d, NH-CH_2Ph, J=6 Hz), 4.7(1H, br, NH), 4.77(2H, s, CH_2Ph), 6.04(1H, s, 4-H), 6.9-7.0(10H, ov, phenyl-H); ^{13}C-NMR δ: 19.6(CH_3), 21.1, 21.9(8- and 9-C), 25.6(10-C), 29.2(7-C), 44.9, 52.1(CH_2Ph), 105.8(4-C). 113.2(4b-C), 127.3(6a-C), 127.5-138.8(phenyl-C), 154.0, 155.0, 156.0, 158.0, 158.3(3-, 4a-, and 6-C and CO), 161.5(1-C); MS *m/z*: 453(M^+), 362(M^+-C_7H_7), 319(M^+-C_7H_7NHCO), 229, 133. Anal. Calcd for $C_{28}H_{27}N_3O_3$ (453.5): C, 74.15; H, 6.00; N, 9.27. Found: C, 74.11; H, 6.04; N, 9.14.

10-Anilino-6-oxo-6,7,8,9-tetrahydrocyclopeta[*d*]chromeno[4,3-*b*]pyridine (**11a**). Colorless needles from ethanol; mp 253-254℃; IR cm^{-1}: 3320(NH), 1695, 1690(CO); ^{1}H-NMR($CDCl_3$+DMSO-d_6) δ: 2.22(2H, m, 8-H), 2.97(2H, t, 7-H, J=7 Hz), 3.38(2H, t, 10-H, J=7 Hz), 7.0-8.0(8H, ov, aromatic-H), 8.32(1H, br d, 4-H, J=8 Hz), 8.59(1H, br, NH); ^{13}C-NMR($CDCl_3$+DMSO-d_6) δ: 23.6(8-C), 29.4(8-C), 34.4(7-C), 106.6(6a-C), 116.4-139.8(4b- and 9a-C and aromatic-C), 150.9, 152.5, 155.0, 156.3(4a-, 9b-, 10-, and 11a-C), 160.1(6-C); MS *m/z*: 328(M^+), 251(M^+-Ph), 164, 77.

11-Anilino-7,8,9,10-tetrahydrochromeno[4,3-*c*]isoquinolin-6(6*H*)-one (**12a**). Colorless needles from ethanol; mp 234-235 ℃; IR cm^{-1}: 3370(NH), 1690(CO); ^{1}H-NMR δ: 1.8-2.0(4H, ov, 8- and 9-H), 2.58(2H, t, 7-H, J=6 Hz), 3.35(2H, t, 10-H, J=6 Hz), 6.7(1H, br, NH), 7.1-7.9(7H, ov, aromatic-H), 8.37(1H, dd, 4-H, J=7 and 2 Hz); ^{13}C-NMR δ: 21.4, 21.9(8- and 9-C), 24.3(10-C), 29.2(7-C), 108.3(6a-C), 116.3-139.1(4b- and 10a-C and aromatic-C), 150.8, 150.9, 152.6, 156.0(4a-, 10b-, 11-, and 12a-C), 160.7(6-C); MS *m/z*: 342(M^+), 327(M^+-NH), 251(M^+-NPh), 77. Anal. Calcd for $C_{22}H_{18}N_2O_2$ (324.4): C, 77.17; H, 5.30; N, 8.18. Found: C, 76.82; H, 5.22; N, 8.06.

To a solution of carbodiimide **10a**, prepared from **9** (1.0 mM) and **2a** (1.0 mM), in THF (8 mL) and dioxane (3 mL) was added sodium acetylacetonate (**13**), prepared from sodium hydride and acetylacetone in THF (5 mL). The resulting mixture was stirred at room temperature for 20 h. Usual work-up with column chromatography gave **14a** (0.066 g, 18%).

3-(N^1-Phenyl-N^2-[2-oxo-4(2*H*)-chromenyl])amidino-2,4-pentanedione (**14a**). Colorless crystals; IR cm^{-1}: 3280, 3200(OH and NH), 1685(CO); MS *m/z*: 362(M^+), 344(M^+-H_2O), 329.

3-(N^1-Benzyl-N^2-[2-oxo-4(2*H*)-chromenyl])amidino-2,4-pentanedione (**14d**). Yield 26%; colorless prisms from ethanol; mp 204℃; IR cm^{-1}: 3250(OH and NH), 1680(CO); MS *m/z*: 376(M^+), 358(M^+-H_2O), 267, 106, 91.

A solution of **14a** (0.066 g) in dioxane (5 mL) was heated under reflux for 40 h. Concentration to dryness *in vacuo* and crystallization gave **15a** (0.044 g, 78%).

3-Acetyl-2-anilino-4-methylchromeno[4,3-*b*]pyridin-5(5*H*)-one (**15a**). Yellow needles from methanol; mp 157-158℃; IR cm^{-1}: 3330(NH), 1720, 1690(CO); ^{1}H-NMR δ: 2.62, 2.83(each 3H, 2s, $-CH_3$), 7.1-7.8(8H, ov, aromatic-H), 8.22(1H, br d, 7-H, J = 8 Hz), 8.6(1H, br, NH); MS *m/z*: 344(M^+), 329(M^+-CH_3), 301($M-COCH_3$), 77.

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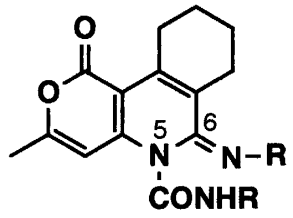
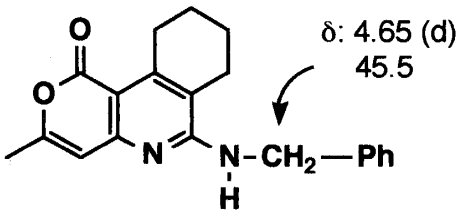
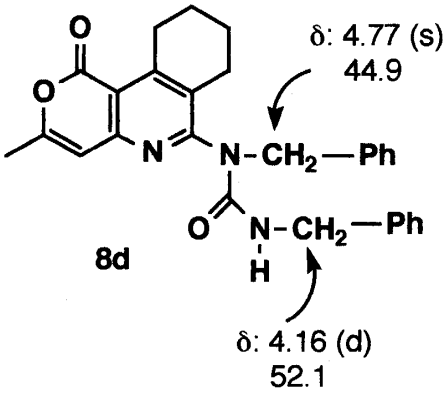
9) For the product **8**, 5-benzylcarbamoyl-6-imino-5,6,7,8,9,10-hexahydropyrano[4,3-*c*]isoquinolin-1(1*H*)-one structure (**8'**) is also possible. However, the comparison of the chemical shifts of the benzyl methylene signals for **8d** with that of **7d** indicates that both of **7** and **8** have same ring structures.
10) The ^{1}H-NMR spectra show that **14** exist as mixtures of their isomers. Due to many signals assigned to methyl groups and relatively smaller intensity of 3-H signals, we suggest a facile interconversion between **14** and **14'** as below.



8'



7d



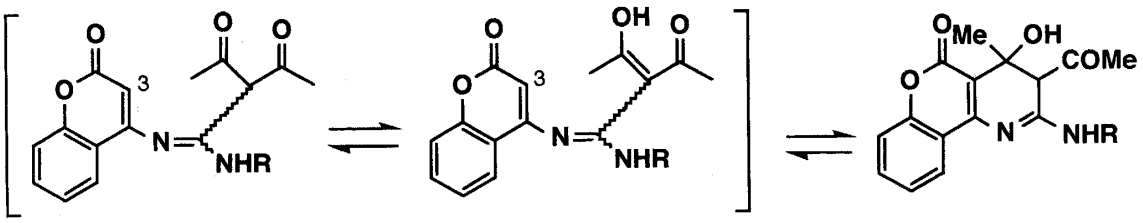
8d

δ: 4.65 (d)
45.5

δ: 4.77 (s)
44.9

δ: 4.16 (d)
52.1

^{1}H- and ^{13}C-NMR Spectral Data for Benzyl Methylene Signals of **7d** and **8d**.



14

14'

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