Substituent Effects on the Tautomer Ratios between the Enamine and Methylene Imine Forms in Side-chained Quinoxalines

Yoshihisa Kurasawa*, Ryuichiro Miyashita, and Atsushi Takada

School of Pharmaceutical Sciences, Kitasato University, Shirokane, Minato-ku, Tokyo 108, Japan

Ho Sik Kim

Department of Chemistry, Hyosung Women's University, Gyongsan, 713-702, Korea

Yoshihisa Okamoto

Department of Chemistry, College of Liberal Arts and Sciences, Kitasato University, Sagamihara, Kanagawa 228, Japan

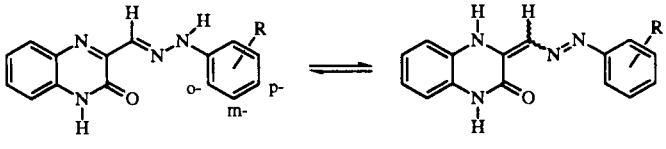
Received December 27, 1994

The *p*- and *m*-substituted 3-arylcarbamoylmethylene-2-oxo-1,2,3,4-tetrahydroquinoxalines **3a-o** showed the tautomeric equilibria between the enamine **C** and methylene imine **D** forms in dimethyl sulfoxide or dimethyl sulfoxide/trifluoroacetic acid media. The linear correlation of the Hammett σ_p and σ_m values with the log K_T values was observed in the dimethyl sulfoxide/trifluoroacetic acid (2:1) media of compounds **3a-o**, wherein K_T meaned the tautomeric equilibrium constants ([D]/[C]).

J. Heterocyclic Chem., **32**, 671 (1995).

In previous papers [1,2], we reported that the *p*- and *m*-substituted 3-(arylhydrazono)methyl-2-oxo-1,2-dihydroquinoxalines **1** exhibited tautomeric equilibria between the hydrazone imine **A** and diazenyl enamine **B** forms (Scheme 1) in a series of mixed dimethyl sulfoxide/trifluoroacetic acid media. Moreover, the substituent effects were studied by the nmr spectroscopy, and the linear correlation of the Hammett σ_p and σ_m values with the tautomeric equilibrium constants K_T ([A]/[B]) was observed in the dimethyl sulfoxide media of compounds **1**.

Scheme 1



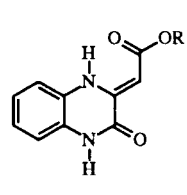
A **B**

1 R = *p*- and *m*-Substituents

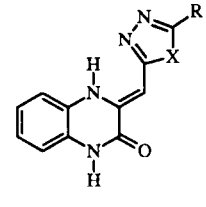
On the other hand, the side-chained quinoxaline derivatives **2a,b** [3] and related compounds **2c,d** [4,5] (Chart) have also been reported to show the tautomeric equilibria between the enamine **C** and methylene imine **D** forms (Scheme 2) in various solvents. For example, compounds **2a-d** existed as the enamine **C** and methylene imine **D** forms in dimethyl sulfoxide, and compounds **2a-c** exclusively existed as the methylene imine **D** form in trifluoroacetic acid. Recently, we have indicated that the tautomer ratios of **C** to **D** depend on the *p*Ka of the side chain moieties in the trifluoroacetic acid media of compunds **2e-g** [6]. However, there has seldom been a paper dealing with the correlation of the Hammett σ values with the tautomeric equilibrium constants K_T ([D]/[C]), because there may have been no appropriate model compounds necessary for the study on the substituent effects. In fact, the reaction of compound **2a** with aniline derivatives gave no products such as compounds **3** (Scheme 3), but recovered the starting materials. Since compounds **3** having *p*- or *m*-substituents were regarded as suitable model compounds for the study on the substituent effects, we devised the synthesis of compounds **3** in the present investigation. As the result, we accomplished the three step synthesis of compounds **3** from compound **2a** and found the linear correlation of the Hammett σ values with the log K_T values in the dimethyl sulfoxide/trifluoroacetic acid (2:1) media of compounds **3**. This paper describes the synthesis of compounds **3** and the substituent effects on the tautomeric equilibrium constants (K_T = [D]/[C]).

The reaction of compound **2a** with 10-fold molar amount of hydrazine hydrate has already been reported to

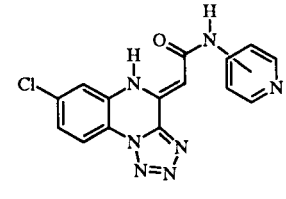
Chart



2a R = Me
2b R = Et



2c R = SH; X = N - R'
2d R = H, Me; X = O

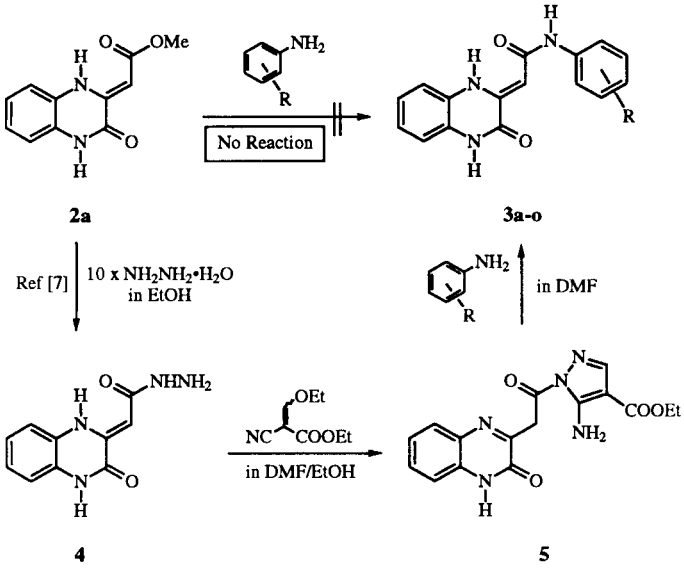


2e 2-Pyridyl
2f 3-Pyridyl
2g 4-Pyridyl

Scheme 2

C Enamine Form D Methylene Imine Form

Scheme 3



give the hydrazide **4** [7], whose reaction with ethyl ethoxymethylenecyanoacetate afforded ethyl 5-amino-1-(2-oxo-1,2-dihydroquinoxalin-3-yl)acetylpyrazole-4-carboxylate **5**. The reaction of compound **5** with various *p*- and *m*-substituted aniline derivatives provided the 3-arylcarbamoylmethylene-2-oxo-1,2,3,4-tetrahydroquinoxalines **3a-o**.

Since compound **5** was insoluble in dimethyl sulfoxide, the nmr spectrum of compound **5** was measured in a mixture of dimethyl sulfoxide/trifluoroacetic acid (1:3). The presence of the methylene proton signal at δ 2.55 ppm and the absence of the vinyl proton signal supported the exclusive existence of compound **5** as the methylene imine tautomer **D** in dimethyl sulfoxide/trifluoroacetic acid (1:3) medium.

The nmr spectra of compounds **3a-o** in dimethyl sulfox-

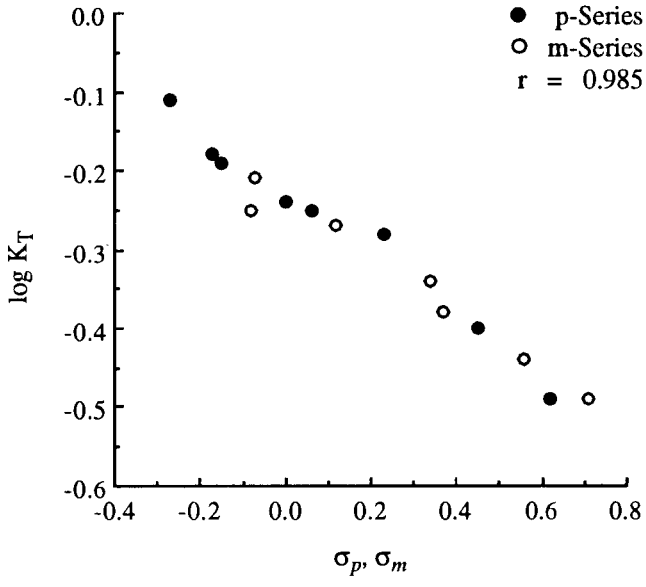


Figure. Correlation of the Hammett σ_p and σ_m values with the log K_T values in the DMSO/TFA (2:1) media of compounds **3a-o**.

Table

Data of the K_T and Log K_T Values for Compounds **3a-o**

Compound	R	σ [a]	in DMSO K_T [b]	in DMSO Chemical Shift (δ) Vinyl	in DMSO Chemical Shift (δ) Methylene	in DMSO/TFA (2:1) K_T [b]	in DMSO/TFA (2:1) Chemical Shift (δ) Vinyl	in DMSO/TFA (2:1) Chemical Shift (δ) Methylene	Log K_T
3a	*p*-SO_2NH_2	+0.62	0.30	5.88	3.91	0.32	5.82	3.83	-0.49
3b	*p*-COOEt	+0.45	0.28	5.89	3.92	0.40	5.84	3.86	-0.40
3c	*p*-Cl	+0.23	0.36	5.84	3.88	0.52	5.79	3.83	-0.28
3d	*p*-F	+0.06	0.42	5.83	3.87	0.56	5.80	3.82	-0.25
3e	*p*-H	+0.00	0.40	5.86	3.88	0.58	5.81	3.82	-0.24
3f	*p*-Et	-0.15	0.36	5.85	3.86	0.64	5.80	3.81	-0.19
3g	*p*-Me	-0.17	0.40	5.84	3.86	0.66	5.80	3.81	-0.18
3h	*p*-OMe	-0.27	0.38	5.82	3.84	0.78	5.77	3.80	-0.11
3i	*m*-NO_2	+0.71	0.26	5.87	3.92	0.32	5.81	3.84	-0.49
3j	*m*-CN	+0.56	0.26	5.85	3.90	0.36	5.80	3.83	-0.44
3k	*m*-Cl	+0.37	0.32	5.84	3.88	0.42	5.80	3.83	-0.38
3l	*m*-F	+0.34	0.32	5.85	3.88	0.46	5.81	3.84	-0.34
3m	*m*-OMe	+0.12	0.34	5.85	3.87	0.54	5.81	3.82	-0.27
3n	*m*-Me	-0.07	0.34	5.86	3.86	0.56	5.81	3.83	-0.25
3o	*m*-Et	-0.08	0.36	5.86	3.86	0.62	5.80	3.81	-0.21

[a] Hammett σ values shown herein were selected from several literature sources [8-13]. [b] Tautomeric equilibrium constants K_T ([D]/[C]).

ide or dimethyl sulfoxide/trifluoroacetic acid (2:1) showed the vinyl and methylene proton signals (Table), indicating the coexistence of the enamine **C** and methylene imine **D** tautomers. The tautomer ratios of **C** to **D** calculated from the integral ratios of the vinyl and methylene proton signals afforded the K_T ([D]/[C]) values in dimethyl sulfoxide or dimethyl sulfoxide/trifluoroacetic acid (2:1) media. The K_T values in dimethyl sulfoxide/trifluoroacetic acid (2:1) media gradually increased with the stepwise decrease in the Hammett σ values (Table), but the K_T values in dimethyl sulfoxide media did not exhibit such a correlation. The Table and Figure show the linear correlation of the Hammett σ_p and σ_m values with the log K_T values in dimethyl sulfoxide/trifluoroacetic acid (2:1) media (correlation coefficient, r = 0.985). The above results indicate that the difference in the *p*Ka of the side chain aniline moieties is well reflected in acidic media, but not in dimethyl sulfoxide media.

EXPERIMENTAL

All melting points were determined on a Yazawa micro melting point BY-2 apparatus and are uncorrected. The ir spectra (potassium bromide) were recorded with a JASCO IRA-1 spectrophotometer. The mass spectra (ms) were determined with a JEOL JMS-01S spectrometer. The nmr spectra were measured at 25° with a VXR-300 spectrometer at 300 MHz. Chemical shifts were given in the δ scale. Elemental analyses were performed on a Perkin-Elmer 240B instrument.

Ethyl 5-Amino-1-(2-oxo-1,2-dihydroquinoxalin-3-yl)acetylpyrazole-4-carboxylate **5**.

A suspension of 3-hydrazinocarbonylmethylene-2-oxo-1,2,3,4-tetrahydroquinoxaline (10 g, 45.9 mmoles) and ethyl ethoxymethylenecyanoacetate (11.63 g, 68.8 mmoles) in *N,N*-dimethylformamide (150 ml)/ethanol (100 ml) was refluxed on a boiling water bath for 3 hours to precipitate yellow needles **5**, which were collected by suction filtration and washed with ethanol to give an analytically pure sample (9.90 g, 63%), mp 302-303°; ir: ν cm^{-1} 3420, 3300, 1660, 1600; ms: m/z 341 (M^+); nmr [deuteriodimethyl sulfoxide/trifluoroacetic acid (1:3)]: 7.84 (s, 1H, pyrazole C_3-H), 7.60 (dd, J = 8.0 Hz, J = 1.0 Hz, 1H, C_5-H), 7.47 (ddd, J = 8.0 Hz, J = 8.0 Hz, J = 1.0 Hz, 1H, C_7-H), 7.24 (dd, J = 8.0 Hz, J = 1.0 Hz, 1H, C_8-H), 7.23 (ddd, J = 8.0 Hz, J = 8.0 Hz, J = 1.0 Hz, 1H, C_6-H), 3.99 (q, J = 7.0 Hz, 2H, CH_2), 2.55 (s, 2H, CH_2), 0.97 (t, J = 7.0 Hz, 3H, CH_3). The NH and NH_2 proton signals were unobservable.

Anal. Calcd. for $C_{16}H_{15}N_5O_4$: C, 56.30; H, 4.43; N, 20.52. Found: C, 56.45; H, 4.55; N, 20.49.

General Procedure for the Synthesis of Compounds **3a-o**.

A solution of the pyrazole derivative **5** (2 g, 5.87 mmoles) and the appropriate aniline derivative (17.6 mmoles, 3-fold molar amount) in *N,N*-dimethylformamide (100 ml) was refluxed for 3 hours. Evaporation of the solvent *in vacuo* gave yellow crystals, whose recrystallization from *N,N*-dimethylformamide/ethanol/water afforded yellow needles.

In the synthesis of compound **3i**, 5-fold molar amount of *m*-nitroaniline was allowed to react with compound **5** under 5 hour reflux.

Compound **3a** (yield, 46%) had mp 310-311°; ir: ν cm^{-1} 3540, 3360, 3240, 1675, 1640, 1605; ms: m/z 358 (M^+); nmr (deuteriodimethyl sulfoxide): (signals due to the enamine form **C**) 11.69 (s, N_4-H), 11.66 (s, N_1-H), 10.34 (s, amide NH), 5.88 (s, vinylic H); (signals due to the methylene imine form **D**) 10.55 (s, amide NH), 3.91 (s, CH_2), (N_1-H)-unobservable; (other signals) 7.80-6.95 (aromatic), 7.20 (s, *p*-SO_2NH_2).

Anal. Calcd. for $C_{16}H_{14}N_4O_4S$: C, 53.62; H, 3.94; N, 15.63. Found: C, 53.73; H, 4.03; N, 15.81.

Compound **3b** (yield, 59%) had mp 273-274°; ir: ν cm^{-1} 3370, 1680, 1640, 1600; ms: m/z 351 (M^+); nmr (deuteriodimethyl sulfoxide): (signals due to the enamine form **C**) 11.70 (s, N_4-H), 11.58 (s, N_1-H), 10.34 (s, amide NH), 5.89 (s, vinylic H); (signals due to the methylene imine form **D**) 12.42 (s, N_1-H), 10.58 (s, amide NH), 3.92 (s, CH_2); (other signals) 7.89-6.94 (aromatic), 4.26 (q, J = 7.0 Hz, CH_2), 1.29 (t, J = 7.0 Hz, CH_3).

Anal. Calcd. for $C_{19}H_{17}N_3O_4$: C, 64.95; H, 4.88; N, 11.96. Found: C, 64.93; H, 4.99; N, 12.05.

Compound **3c** (yield, 60%) had mp 302-303°; ir: ν cm^{-1} 3300, 3240, 1660, 1640; ms: m/z 313 (M^+), 315 (M^+ + 2); nmr (deuteriodimethyl sulfoxide): (signals due to the enamine form **C**) 11.68 (s, N_4-H), 11.54 (s, N_1-H), 10.14 (s, amide NH), 5.84 (s, vinylic H); (signals due to the methylene imine form **D**) 12.40 (s, N_1-H), 10.34 (s, amide NH), 3.88 (s, CH_2); (other signals) 7.73-6.93 (aromatic).

Anal. Calcd. for $C_{16}H_{12}ClN_3O_2$: C, 61.25; H, 3.86; N, 13.39. Found: C, 61.22; H, 4.06; N, 13.67.

Compound **3d** (yield, 45%) had mp 303-304°; ir: ν cm^{-1} 3410, 1660, 1645; ms: m/z 297 (M^+); nmr (deuteriodimethyl sulfoxide): (signals due to the enamine form **C**) 11.67 (s, N_4-H), 11.60 (s, N_1-H), 10.07 (s, amide NH), 5.83 (s, vinylic H); (signals due to the methylene imine form **D**) 10.26 (s, amide NH), 3.87 (s, CH_2), (N_1-H)-unobservable; (other signals) 7.73-6.90 (aromatic).

Anal. Calcd. for $C_{16}H_{12}FN_3O_2$: C, 64.64; H, 4.07; N, 14.13. Found: C, 64.35; H, 4.17; N, 14.32.

Compound **3e** (yield, 56%) had mp 304-305°; ir: ν cm^{-1} 1690, 1640, 1600; ms: m/z 279 (M^+); nmr (deuteriodimethyl sulfoxide): (signals due to the enamine form **C**) 11.70 (s, N_4-H), 11.51 (s, N_1-H), 10.01 (s, amide NH), 5.86 (s, vinylic H); (signals due to the methylene imine form **D**) 12.40 (s, N_1-H), 10.22 (s, amide NH), 3.88 (s, CH_2); (other signals) 7.73-6.92 (aromatic).

Anal. Calcd. for $C_{16}H_{13}N_3O_2$: C, 68.80; H, 4.69; N, 15.05. Found: C, 68.52; H, 4.67; N, 15.02.

Compound **3f** (yield, 68%) had mp 287-288°; ir: ν cm^{-1} 3240, 3210, 1690, 1635, 1600; ms: m/z 307 (M^+); nmr (deuteriodimethyl sulfoxide): (signals due to the enamine form **C**) 11.71 (s, N_4-H), 11.51 (s, N_1-H), 9.95 (s, amide NH), 5.85 (s, vinylic H) 1.14 (t, J = 7.0 Hz, CH_3); (signals due to the methylene imine form **D**) 10.15 (s, amide NH), 3.86 (s, CH_2), 1.13 (t, J = 7.0 Hz, CH_3), (N_1-H)-unobservable; (other signals) 7.73-6.90 (aromatic), 2.53 (q, J = 7.0 Hz, CH_2).

Anal. Calcd. for $C_{18}H_{17}N_3O_2$: C, 70.34; H, 5.58; N 13.67. Found: C, 70.13; H, 5.58; N, 13.72.

Compound **3g** (yield, 45%) had mp 282-283°; ir: ν cm^{-1} 3300, 1660, 1640, 1600; ms: m/z 293 (M^+); nmr (deuteriodimethyl sulfoxide): (signals due to the enamine form **C**) 11.71 (s,

N_4-H), 11.49 (s, N_1-H), 9.94 (s, amide NH), 5.84 (s, vinylic H); (signals due to the methylene imine form **D**) 12.40 (s, N_1-H), 10.11 (s, amide NH), 3.86 (s, CH_2); (other signals) 7.73-6.91 (aromatic), 2.23 (s, CH_3).

Anal. Calcd. for $C_{17}H_{15}N_3O_2$: C, 69.61; H, 5.15; N, 14.33. Found: C, 69.39; H, 5.25; N, 14.61.

Compound **3h** (yield, 83%) had mp 286-288°; ir: ν cm^{-1} 3230, 1690, 1635, 1600; ms: m/z 309 (M^+); nmr (deuteriodimethyl sulfoxide): (signals due to the enamine form **C**) 11.70 (s, N_4-H), 11.47 (s, N_1-H), 9.90 (s, amide NH), 5.82 (s, vinylic H), 3.70 (s, OCH_3); (signals due to the methylene imine form **D**) 12.39 (s, N_1-H), 10.05 (s, amide NH), 3.84 (s, CH_2), 3.69 (s, OCH_3); (other signals) 7.73-6.86 (aromatic).

Anal. Calcd. for $C_{17}H_{15}N_3O_3$: C, 66.01; H, 4.89; N, 13.59. Found: C, 65.91; H, 4.88; N, 13.74.

Compound **3i** (yield, 35%) had mp 282-283°; ir: ν cm^{-1} 3410, 3380, 3320, 1690, 1650; ms: m/z 324 (M^+); nmr (deuteriodimethyl sulfoxide): (signals due to the enamine form **C**) 11.63 (s, N_4-H), 11.61 (s, N_1-H), 10.48 (s, amide NH), 5.87 (s, vinylic H); (signals due to the methylene imine form **D**) 10.80 (s, amide NH), 3.92 (s, CH_2), (N_1-H)-unobservable; (other signals) 8.82-6.95 (aromatic).

Anal. Calcd. for $C_{16}H_{12}N_4O_4$: C, 59.26; H, 3.73; N, 17.28. Found: C, 59.01; H, 3.86; N, 17.22.

Compound **3j** (yield, 46%) had mp 296-297°; ir: ν cm^{-1} 3360, 2240, 1680, 1645; ms: m/z 304 (M^+); nmr (deuteriodimethyl sulfoxide): (signals due to the enamine form **C**) 11.66 (s, N_4-H), 11.59 (s, N_1-H), 10.34 (s, amide NH), 5.85 (s, vinylic H); (signals due to the methylene imine form **D**) 12.43 (s, N_1-H), 10.59 (s, amide NH), 3.90 (s, CH_2); (other signals) 8.24-6.95 (aromatic).

Anal. Calcd. for $C_{17}H_{12}N_4O_2$: C, 67.09; H, 3.98; N, 18.41. Found: C, 66.84; H, 4.10; N, 18.39.

Compound **3k** (yield, 57%) had mp 251-252°; ir: ν cm^{-1} 3270, 1650, 1605; ms: m/z 313 (M^+), 315 ($M^+ + 2$); nmr (deuteriodimethyl sulfoxide): (signals due to the enamine form **C**) 11.66 (s, N_4-H), 11.56 (s, N_1-H), 10.19 (s, amide NH), 5.84 (s, vinylic H); (signals due to the methylene imine form **D**) 12.43 (s, N_1-H), 10.42 (s, amide NH), 3.88 (s, CH_2); (other signals) 7.88-6.87 (aromatic).

Anal. Calcd. for $C_{16}H_{12}ClN_3O_2$: C, 61.25; H, 3.86; N, 13.39. Found: C, 60.97; H, 3.89; N, 13.67.

Compound **3l** (yield, 52%) had mp 262-263°; ir: ν cm^{-1} 3290, 1650; ms: m/z 297 (M^+); nmr (deuteriodimethyl sulfoxide): (signals due to the enamine form **C**) 11.65 (s, N_4-H), 11.55 (s, N_1-H), 10.21 (s, amide NH), 5.85 (s, vinylic H); (signals due to the methylene imine form **D**) 12.44 (s, N_1-H), 10.43 (s, amide NH), 3.88 (s, CH_2); (other signals) 7.67-6.78 (aromatic).

Anal. Calcd. for $C_{16}H_{12}FN_3O_2$: C, 64.64; H, 4.07; N, 14.13. Found: C, 64.35; H, 4.08; N, 14.27.

Compound **3m** (yield, 66%) had mp 224-225°; ir: ν cm^{-1} 3300, 1650, 1600; ms: m/z 309 (M^+); nmr (deuteriodimethyl sulfoxide): (signals due to the enamine form **C**) 11.67 (s, N_4-H), 11.56 (s, N_1-H), 10.00 (s, amide NH), 5.85 (s, vinylic H), 3.72 (s, OCH_3); (signals due to the methylene imine form **D**) 12.40 (s, N_1-H), 10.20 (s, amide NH), 3.87 (s, CH_2), 3.69 (s, OCH_3); (other signals) 7.74-6.57 (aromatic).

Anal. Calcd. for $C_{17}H_{15}N_3O_3$: C, 66.01; H, 4.89; N, 13.59. Found: C, 65.79; H, 4.87; N, 13.71.

Compound **3n** (yield, 61%) had mp 242-243°; ir: ν cm^{-1} 3290, 1650, 1610; ms: m/z 293 (M^+); nmr (deuteriodimethyl sulfoxide): (signals due to the enamine form **C**) 11.71 (s, N_4-H), 11.50 (s, N_1-H), 9.94 (s, amide NH), 5.86 (s, vinylic H), 2.26 (s, CH_3); (signals due to the methylene imine form **D**) 12.40 (s, N_1-H), 10.13 (s, amide NH), 3.86 (s, CH_2), 2.25 (s, CH_3); (other signals) 7.73-6.82 (aromatic).

Anal. Calcd. for $C_{17}H_{15}N_3O_2$: C, 69.61; H, 5.15; N, 14.33. Found: C, 69.37; H, 5.14; N, 14.39.

Compound **3o** (yield, 41%) had mp 266-267°; ir: ν cm^{-1} 3300, 1670, 1630, 1610; ms: m/z 307 (M^+); nmr (deuteriodimethyl sulfoxide): (signals due to the enamine form **C**) 11.69 (s, N_4-H), 11.51 (s, N_1-H), 9.96 (s, amide NH), 5.86 (s, vinylic H), 2.56 (q, J = 7.0 Hz, CH_2), 1.16 (t, J = 7.0 Hz, CH_3); (signals due to the methylene imine form **D**) 12.40 (s, N_1-H), 10.19 (s, amide NH), 3.86 (s, CH_2), 2.54 (q, J = 7.0 Hz, CH_2), 1.14 (t, J = 7.0 Hz, CH_3); (other signals) 7.73-6.85 (aromatic).

Anal. Calcd. for $C_{18}H_{17}N_3O_2$: C, 70.34; H, 5.58; N, 13.67. Found: C, 70.42; H, 5.64; N, 13.79.

REFERENCES AND NOTES

[1] Y. Kurasawa, T. Hosaka, A. Takada, H. S. Kim, and Y. Okamoto, *J. Heterocyclic Chem.*, in press.

[2] Y. Kurasawa, T. Hosaka, A. Takada, H. S. Kim, and Y. Okamoto, *J. Heterocyclic Chem.*, **31**, 1661 (1994).

[3] R. Mondelli and L. Merlini, *Tetrahedron*, **22**, 3253 (1966).

[4] Y. Kurasawa and A. Takada, *Heterocycles*, **20**, 1917 (1983).

[5] Y. Kurasawa, Y. Okamoto, and A. Takada, *Chem. Pharm. Bull.*, **33**, 1249 (1984).

[6] Y. Kurasawa, Y. Matsumoto, A. Ishikura, K. Ikeda, T. Hosaka, A. Takada, H. S. Kim, and Y. Okamoto, *J. Heterocyclic Chem.*, **30**, 1463 (1993).

[7] Y. Kurasawa, Y. Moritaki, T. Ebukuro, and A. Takada, *Chem. Pharm. Bull.*, **31**, 3897 (1983).

[8] Physical Organic Chemistry, Reaction Rates, Equilibria and Mechanism, 2nd ed, L. P. Hammett, ed, McGraw-Hill Book Company, New York, St. Louis, San Francisco, Duesseldorf, London, Mexico, Panama, Sydney, Toronto, 1970, pp 355-357.

[9] O. Exner, Correlation Analysis in Chemistry, N. B. Chapman and J. Shorter, eds, Plenum Press, New York, London, 1978, pp 439-540.

[10] D. H. McDaniel and H. C. Brown, *J. Org. Chem.*, **23**, 420 (1958).

[11] H. Zollinger and C. Wittwer, *Helv. Chim. Acta*, **39**, 347 (1956).

[12] Correlation Analysis of Organic Reactivity, J. Shorter, ed, Research Studies Press, John Wiley and Sons, Chichester, New York, Brisbane, Toronto, Singapore, 1982, pp 27-72.

[13] Correlation Analysis of Chemical Data, O. Exner, ed, Plenum Press, New York, London, 1988, pp 60-64.