REACTIONS OF 3,3-DIAMINO-2-CYANOACRYLATES WITH SUBSTITUTED UREAS AND DICHLOROMETHYLENEDIALKYLIMINIUM CHLORIDES

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Abstract - Reaction of 3,3-diamino-2-cyanoacrylates (**1**) with *N,N*-disubstituted ureas (**2**) leads only to (*Z*)-3-amino-3-*N.N*-disubstituted carbamido-2-cyanoacrylates (**3a-l**), but with monosubstituted ureas to *Z*- and *E*-tautomers (**3m-n**). A ready one-pot preparation for pyrimido[4,5-*d*][3,1]oxazines (**6a-b**) from **1** and dichloromethylenedialkyliminium chlorides (**4**) is also reported.

INTRODUCTION

After our report on the convenient preparation of 2-(alkyloxycarbonyl cyanomethylene)-1,3-dioxolane,[1] we have synthesized a series of heterocyclic compounds starting from 2-(alkyloxycarbonylcyanomethylene)- and dicyanomethylene-1,3-dioxolanes.[2] 3,3-Diamino-2-cyanoacrylic acid esters (**1**) can be easily obtained from 2-(alkyloxycarbonylcyanomethylene)-1,3-dioxolanes by replacement of the ethylenedioxy group with amino groups, similar to the preparation of 1,1-diamino-2,2-dicyanoethylene by W. J. Middleton and V. A. Engelhardt.[3] They can also be prepared by ammation of 3-amino-3-methoxy-2-cyanoacrylates.[4] Since closely related 1,1-diamino-2,2-dicyanoethylene has already been utilized in heterocyclic synthesis,[5] it is of interest to investigate the reactions of **1** with substituted ureas (**2**) and dichloromethylenedialkyliminium chlorides (**4**). Furthermore, P. Judson *et al.*[6] reported that 3-amino-3-alkyl(and aryl)amino-2-cyanoacrylates have been shown to possess fungicidal and herbicidal activites. The condensation products **3** may probably be biologically active because of their similar structures with the above mentioned acrylates.

Phosgeneiminium chlorides are valuable strong electrophilic one carbon reagents, they react with α-aminonitrile compounds affording pyrimidine derivatives.[2f,5,7] On the other hand, we found that methyl 3-amino-3-chloro-2-cyanoacrylate reacted with dichloromethylenedimethyliminium

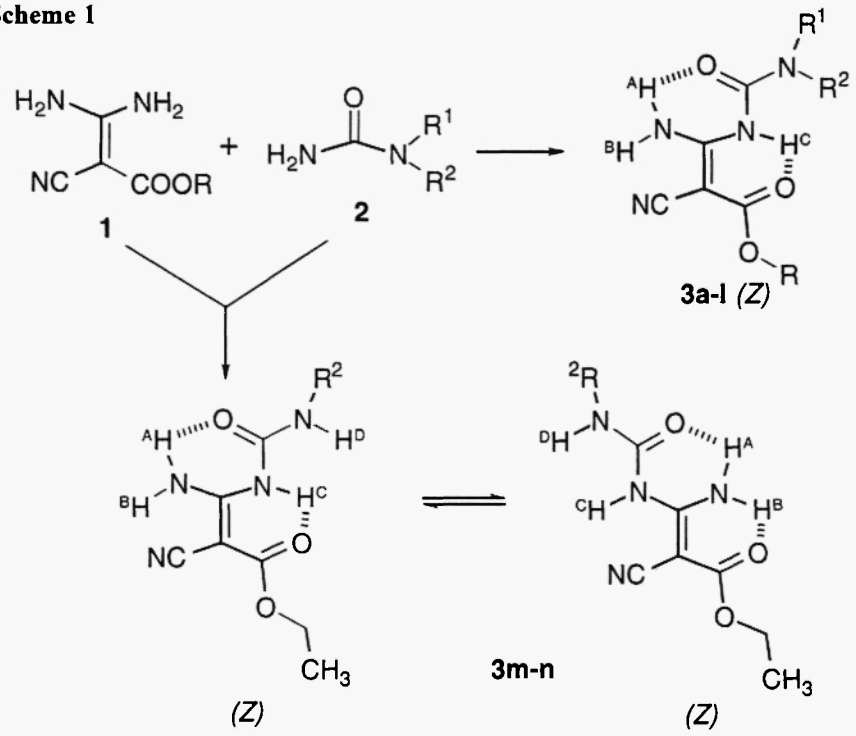
chloride (**4a**) giving 4-chloro-5-cyano-2-dimethylamino-6*H*-1,3-oxazin-6-one.[8] These stimulated us to investigate the reaction of **1** with **4** in order to obtain bicyclic oxazine derivatives.

RESULTS AND DISCUSSION

Condensation reaction of 1 and substituted ureas (2):

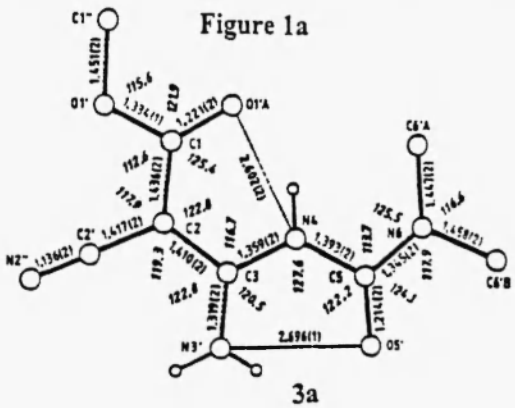
3,3-Diamino-2-cyanoacrylic acid esters (**1**) reacted with different *N,N*-disubstituted ureas (**2**), which are easily available by the method of T. L. Davis and K. C. Blanchard,[9] in DMF under reflux providing 3-amino-3-*N,N*-disubstituted carbamido-2-cyanoacrylates (**3a-l**) (see Scheme 1). The X-ray diffraction study of **3a** and **3b** (Figure 1) shows that they exist only in *Z*- configuration, which is stabilized by intramolecular hydrogen bonds. As shown in Figure 1a (**3a**), e.g., the distance between the oxygen atom in ester carbonyl group and the nitrogen atom in carbamido group (O1′A-N4) and the distance between the oxygen atom in carbamido group and the nitrogen atom in amino group (O5′-N3′) are 2.602 and 2.696 Å respectively, which is beneficial to the formation of the corresponding hydrogen bonds. Furthermore, the ^{1}H-NMR spectrum confirms the existence of the hydrogen bonds. There are three NH signals, one of them is at δ= 11.61 ppm (for H^C), which is in deeper field than normal amide NH signal, indicating the hydrogen bond of C=O...H^C-N. The other two are at δ= 9.29 ppm (for H^A) and δ = 8.11 ppm (for H^B). The difference between H^A and H^B is due to the formation of C=O...H^A-N hydrogen bond (see Figure 2a).

Scheme 1



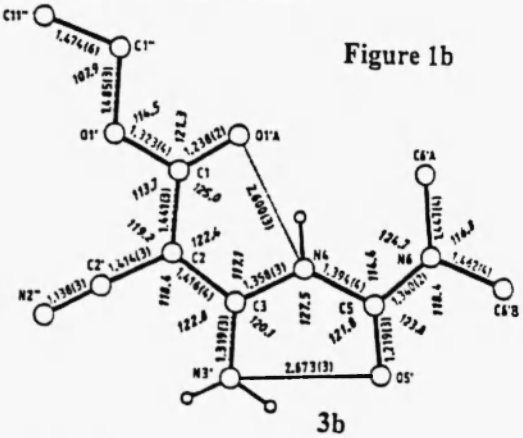
3	a	b	c	d	e	f	g
R	CH_3	C_2H_5	CH_3	C_2H_5	CH_3	C_2H_5	CH_3
R^1	CH_3	CH_3	C_2H_5	C_2H_5	CH_3	CH_3	CH_3
R^2	CH_3	CH_3	C_2H_5	C_2H_5	n-C_4H_9		CH_2Ph
3	**h**	**i**	**j**	**k**	**l**	**m**	**n**
R	C_2H_5	CH_3	C_2H_5	CH_3	C_2H_5	C_2H_5	C_2H_5
R^1	CH_3	CH_3	CH_3	CH_3	CH_3	H	H
R^2	CH_2Ph	c-C_6H_{11}		n-$C_{18}H_{35}$		C_2H_5	n-C_4H_9

Figure 1a



3a

Figure 1b



3b

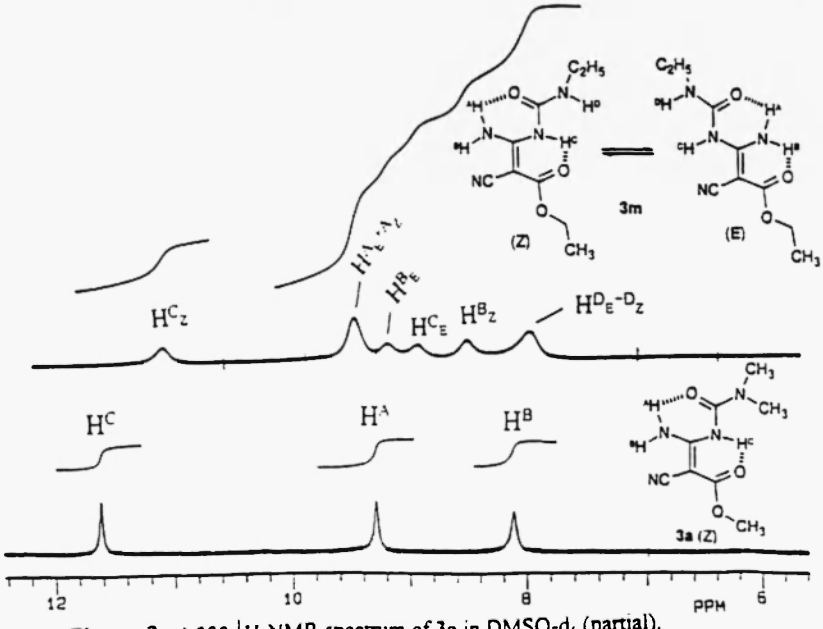


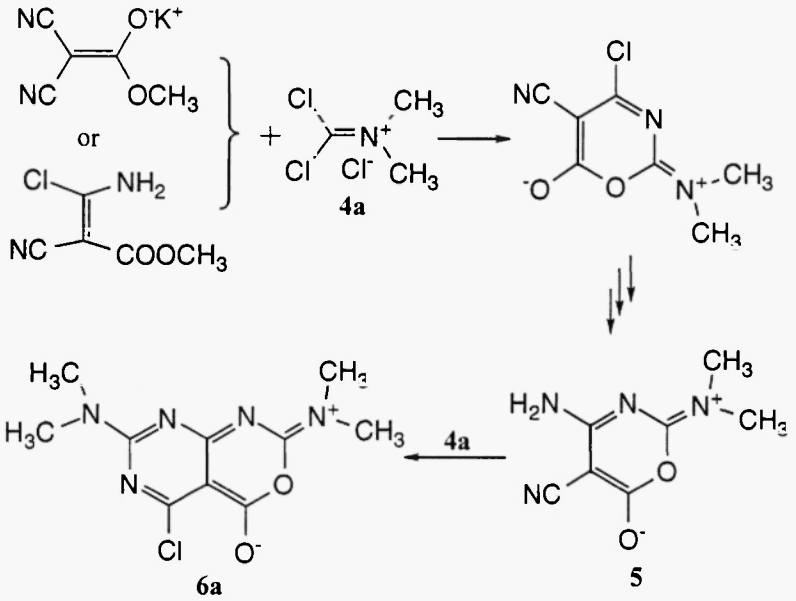
Figure 2. a) 300 ^{1}H-NMR spectrum of **3a** in DMSO-d_6 (partial).
b) 300 ^{1}H-NMR spectrum of **3m** in DMSO-d_6 (partial).

On the contrary, the condensation products of **1** and monosubstituted ureas exist as *E*- and *Z*-tautomers (see Scheme 1), which is confirmed by their ^{1}H-NMR spectra. The NH groups in **3m** may be assigned as shown in Figure 2b.

The preparation of pyrimido[4,5-d][3,1]oxazines (6a-b):

4-Amino-5-cyano-2-dimethylamino-6*H*-1,3-oxazin-6-one (**5**), which was synthesized in four steps starting from potassium methyl dicyanoacetate or methyl 3-amino-3-chloro-2-cyanoacrylate,[8] reacted with phosgeneiminium chloride (**4a**) in 1,2-dichlorethane under reflux for 4 h and subsequently treated with dry hydrogen chloride providing 5-chloro-2,7-bis(dimethylamino)-4*H*-pyrimido[4,5-*d*][3,1]oxazin-4-one (**6a**) (see Scheme 2).

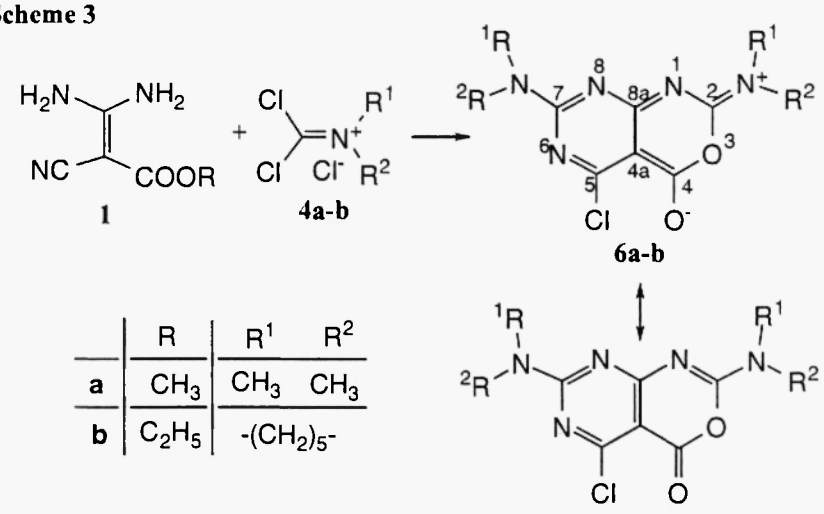
Scheme 2



On the other hand, pyrimido[4,5-*d*][3,1]oxazines (**6a-b**) can also be prepared by one-pot reaction under similar conditions from **1** and dichlormethyldialkyliminium chlorides (**4a-b**) as shown in Scheme 3.

The zwitter ionic structure of **6** is strongly suggested by ^{1}H-NMR and ^{13}C-NMR spectroscopy, which is consistent with our previous observation.[10] For example for **6b**, there is only one signal for -CH_2NCH_2- connected to the pyrimidine ring in ^{1}H-NMR (δ= 3.90 (s, 4H) ppm) and ^{13}C-NMR (δ= 45.3 (d, +) ppm) spectrum but two signals for -CH_2NCH_2- connected to the oxazine ring in ^{1}H-NMR (δ= 3.70 (s, 2H), 3.84 (s, 2H) ppm) and ^{13}C-NMR (δ= 45.1 (s, +), 45.9 (s, +) ppm) spectrum.

Scheme 3



	R	R^1	R^2
a	CH_3	CH_3	CH_3
b	C_2H_5	$-(CH_2)_5-$	

EXPERIMENTAL

Melting points were determined on a Reichert hot stage microscope and are uncorrected. IR-spectra were measured with a Perkin-Elmer spectrophotometer 283 using potassium bromide and are given as cm^{-1}. ^1H- and ^{13}C-NMR spectra were recorded on either a Bruker WM-250 (^1H-NMR: 250.13 MHz, ^{13}C-NMR: 62.89 MHz), WM-360 (^1H-NMR: 360 MHz, ^{13}C-NMR: 90.56 MHz) or a Varian XL 300 (^1H-NMR: 299.95 MHz, ^{13}C-NMR: 75.43 MHz) spectrometer in DMSO-d_6 or $CDCl_3$. The chemical shifts are reported in parts per million (ppm) downfield from internal tetramethylsilane. Electron impact MS spetra were obtained on a Varian MAT 311A instrument. Element analyses were performed on a Heraeus Vario EL CHNS apparatus.

(*Z*)-Methyl 3-amino-3-(*N,N*-dimethylcarbamido)-2-cyanacrylate (3a):

A solution of methyl 3,3-diamino-2-cyanoacrylate (1.41g, 10 mmol) and *N,N*-dimethylurea (0.88 g, 10 mmol) in DMF (5 mL) was refluxed under N_2 atmosphere for 4 h. After cooling to r.t., 110 mL chloroform was added. The mixture was washed with water. The solvent was removed and the residue was recrystallized from acetone/petroleum ether to yield 0.15 g **3a** (8%). mp 232-235°C. IR (KBr): 3332, 3192 (NH); 2201 (C=N); 1661, 1616 (C=O); 1496, 1437 (C=C). ^1H-NMR (299.95 MHz, DMSO-d_6): δ= 2.96 (s, 6H, $N(CH_3)_2$); 3.66 (s, 3H, OCH_3); 8.11 (s, 1H, H^B); 9.29 (s, 1H, H^A); 11.61 (s, 1H, H^C). ^{13}C-NMR (90.56 MHz, DMSO-d_6 + CF_3COOD): δ= 36.1 (-, $N(CH_3)_2$); 51.7 (-, OCH_3); 57.0 (+, C-2); 118.0 (+, CN); 154.7 (+, $C=O_{carb.}$); 162.3 (+, C-3); 170.1 (+, C-1). MS m/z (%): $[M+1]^+$: 213 (8); M^+: 212 (73); 181 (5); 136 (6); 72 (100); 44 (42); 42 (17). Anal. calcd for $C_8H_{12}N_4O_3$: C, 45.28; H, 5.70; N, 26.40. Found: C, 45.33; H, 5.41; N, 26.11.

General procedure for the preparation of 3-amino-3-substituted carbamido-2-cyanoacrylates (3b-l):

A solution of 3,3-diamino-2-cyanoacrylate (**1**) (10 mmol) and corresponding substituted urea (**2**) (10 mmol) in DMF (5-7 mL) was refluxed under N_2 atmosphere for 4-24 h. After cooling to r.t., the mixture was chromatographed on a silica column (70-230 mesh) using ethyl acetate/petroleum ether (1:1) as eluent to give **3b-l**.

(*Z*)-Ethyl 3-amino-3-(*N, N*-dimethylcarbamido)-2-cyanoacrylate (3b) (3.5%). mp 194-197°C. IR (KBr): 3350, 3185 (NH); 2197 (C=N); 1653, 1628 (C=O); 1559, 1496, 1476 (C=C); 1304. ^{1}H-NMR (299.95 MHz; $CDCl_3$): δ= 1.32 (t, 3H, $OCH_2\mathbf{CH_3}$); 3.08 (s, 6H, $N(\mathbf{CH_3})_2$); 3.98 (q, 2H, OCH_2CH_3); 6.04 (s, 1H, $\mathbf{H}^B$); 9.56 (s, 1H, $\mathbf{H}^A$); 11.92 (s, 1H, $\mathbf{H}^C$). ^{13}C-NMR (75.43 MHz, $CDCl_3$): δ= 14.4 (-, $OCH_2\mathbf{CH_3}$); 36.2 (-, $N(\mathbf{CH_3})_2$); 58.9 (+, C-2); 60.4 (+, $O\mathbf{CH_2}CH_3$); 117.5 (+, **C**N); 154.3 (+, $\mathbf{C}{=}O_{carb.}$); 162.0 (+, C-3); 169.3 (+, C-1). MS m/z (%): $[M+1]^+$: 227 (3); M^+: 226 (25); 72 (100); 44 (11). Anal. calcd for $C_9H_{14}N_4O_3$: C, 47.78; H, 6.24; N, 24.77. Found: C, 47.36; H, 6.15; N, 24.65. HRMS: Calcd. for $C_9H_{14}N_4O_3$: 226.1067. Found: 226.1068.

(*Z*)-Methyl 3-amino-3-(*N, N*-diethylcarbamido)-2-cyanoacrylate (3c) (6.5%). mp 147-149°C. IR (KBr): 3334, 3190 (NH); 2206 (CN); 1665, 1636 (C=O); 1599, 1438 (C=C); 1321. ^{1}H-NMR (250.13 MHz; $CDCl_3$): δ= 1.24 (s, 6H, $N(CH_2\mathbf{CH_3})_2$); 3.39 (q, J = 7.1 Hz, 4H, $N(\mathbf{CH_2}CH_3)_2$); 3.75 (s, 3H, $O\mathbf{CH_3}$); 5.94 (s, 1H, $\mathbf{H}^B$); 9.62 (s, 1H, $\mathbf{H}^A$); 11.80 (s, 1H, $\mathbf{H}^C$). ^{13}C-NMR (62.89 MHz, $CDCl_3$): δ= 13.5 (-, $N(CH_2\mathbf{CH_3})_2$); 42.0 (+, $N(\mathbf{CH_2}CH_3)_2$); 51.6 (-, $O\mathbf{CH_3}$); 58.7 (+, C-2); 117.8 (+, **C**N); 153.7 (+, $\mathbf{C}{=}O_{carb.}$); 162.5 (+, C-3); 169.8 (+, C-1). MS m/z (%): $[M+1]^+$: 241 (3); M^+: 240 (24); 100 (100); 72 (53); 58 (7); 44 (21). Anal. calcd for $C_{10}H_{16}N_4O_3$: C, 49.99; H, 6.71; N, 23.32. Found: C, 49.68; H, 6.73; N, 23.06.

(*Z*)-Ethyl 3-amino-3-(*N, N*-diethylcarbamido)-2-cyanoacrylate (3d) (5.5%). mp 105-107°C. IR (KBr): 3304, 3183 (NH); 2203 (CN); 1656, 1631 (C=O); 1596 (C=C); 1303; 1259. ^{1}H-NMR (250.13 MHz; $CDCl_3$): δ= 1.23-1.34 (m, 9H, $OCH_2C\mathbf{H_3}$, $N(CH_2C\mathbf{H_3})_2$); 3.38 (q, 4H, $N(\mathbf{CH_2}CH_3)_2$); 4.20 (q, 2H, $O\mathbf{CH_2}CH_3$); 5.91 (s, 1H, $\mathbf{H}^B$); 9.58 (s, 1H, $\mathbf{H}^A$); 11.87 (s, 1H, $\mathbf{H}^C$). ^{13}C-NMR (75.43 MHz, $CDCl_3$): δ= 13.4 (-, $OCH_2\mathbf{CH_3}$); 14.3(-, $N(CH_2\mathbf{CH_3})_2$); 41.8 (+, $N(\mathbf{CH_2}CH_3)_2$); 58.7 (+, C-2); 60.3 (+, $O\mathbf{CH_2}CH_3$); 117.6 (+, **C**N); 153.4 (+, $\mathbf{C}{=}O_{carb.}$); 162.2 (+, C-3); 169.1 (+, C-1). MS m/z (%): $[M+1]^+$: 255 (5); M^+: 254 (34); 100 (100); 72 (78); 58 (12); 44 (31). Anal. calcd for $C_{11}H_{18}N_4O_3$: C, 51.96; H, 7.14; N, 22.03. Found: C, 51.96; H, 7.11; N, 21.99.

(*Z*)-Methyl 3-amino-3-[(*N*-*n*-butyl-*N*-methyl)carbamido]-2-cyanoacrylate (3e) (9.8%). mp 153-155°C. IR (KBr): 3322, 3180 (NH); 2207 (CN); 1665, 1600 (C=O); 1499, 1437 (C=C); 1323. ^{1}H-NMR (360.13 MHz; $CDCl_3$): δ= 0.96 (t, J = 7.3 Hz, 3H, $(CH_2)_3C\mathbf{H_3}$); 1.36 (s, 2H, $(CH_2)_2C\mathbf{H_2}CH_3$); 1.57 (s, 2H, $CH_2C\mathbf{H_2}CH_2CH_3$); 3.04 (d, 3H, $NC\mathbf{H_3}$); 3.36 (t, J = 7.3 Hz, 2H,

$CH_2(CH_2)_2CH_3$); 3.75 (s, 3H, OCH_3); 5.94 (s, 1H, H^B); 9.58 (s, 1H, H^A); 11.83 (s, 1H, H^C). ^{13}C-NMR (62.89 MHz, $CDCl_3$): δ= 13.8 (-, $(CH_2)_3CH_3$); 19.9 (+, $CH_2(CH_2)_2CH_3$); 29.7 (+, $CH_2(CH_2)_2CH_3$); 34.6 (-, NCH_3); 51.5 (-, OCH_3); 58.8 (+, C-2); 117.7 (+, CN); 154.3 (+, $C{=}O_{carb.}$); 162.4 (+, C-3); 169.8 (+, C-1). MS m/z (%): $[M+1]^+$: 255 (5); M^+: 254 (34); 114 (65); 58 (23); 57 (100); 44 (31); 41 (18). Anal. calcd for $C_{11}H_{18}N_4O_3$: C, 51.96; H, 7.14; N, 22.03. Found: C, 52.05; H, 6.80; N, 22.00.

(*Z*)-Ethyl 3-amino-3-[(*N*-*n*-butyl-*N*-methyl)carbamido]-2-cyanoacrylate (3f) (7.1%). mp 174-176°C. IR (KBr): 3331, 3184 (NH); 2206 (CN); 1665, 1643 (C=O); 1599, 1499 (C=C); 1313. ^{1}H-NMR (250.13 MHz; $CDCl_3$): δ= 0.95 (t, J = 7.2 Hz, 3H, $(CH_2)_3CH_3$); 1.31 (t, J = 7.2 Hz, 3H, OCH_2CH_3); 1.37 (2H, $(CH_2)_2CH_2CH_3$); 1.58 (2H, $CH_2CH_2CH_2CH_3$); 3.02 (s, 3H, NCH_3); 3.35 (t, J = 7.4 Hz, 2H, $CH_2(CH_2)_2CH_3$); 4.19 (q, J = 7.0 Hz, 2H, OCH_2CH_3); 5.90 (s, 1H, H^B); 9.54 (s, 1H, H^A); 11.90 (s, 1H, H^C). ^{13}C-NMR (62.89 MHz, $CDCl_3$): δ= 13.6, 14.4 (2-, OCH_2CH_3, $(CH_2)_3CH_3$); 19.9 (+, $CH_2(CH_2)_2CH_3$); 29.8 (+, $CH_2(CH_2)_2CH_3$); 34.6 (-, NCH_3); 59.0 (+, C-2); 60.5 (+, OCH_2); 117.8 (+, CN); 154.3 (+, $C{=}O_{carb.}$); 162.4 (+, C-3); 169.9 (+, C-1). MS m/z (%): $[M+1]^+$: 269 (4); M^+: 268 (27); 114 (54); 58 (22); 57 (100); 44 (34); 41 (19). Anal. calcd for $C_{12}H_{20}N_4O_3$: C, 53.72; H, 7.51; N, 20.88. Found: C, 53.38; H, 7.56; N, 20.53.

(*Z*)-Methyl 3-amino-3-[(*N*-benzyl-*N*-methyl)carbamido]-2-cyanoacrylate (3g) (8.7%). mp 183-185°C. IR (KBr): 3325, 3185 (NH); 2206 (CN); 1668, 1645 (C=O); 1597, 1496 (C=C); 1322. ^{1}H-NMR (360.13 MHz; $CDCl_3$): δ= 3.03 (s, 3H, NCH_3); 3.74 (s, 3H, OCH_3); 4.58 (s, 2H, CH_2Ph); 6.06 (s, 1H, H^B); 7.24-7.38 (m, 5H, $H_{arom.}$); 9.58 (s, 1H, H^A); 11.96 (s, 1H, H^C). ^{13}C-NMR (62.89 MHz, $CDCl_3$): δ= 34.2 (-, NCH_3); 51.7 (-, OCH_3); 52.0 (+, CH_2Ph); 59.1 (+, C-2); 117.5 (+, CN); 127.9 (-, C-4′); 128.3 (-, C-3′); 129.0 (-, C-2′); 154.7 (+, $C{=}O_{carb.}$); 162.4 (+, C-3); 169.9 (+, C-1). MS m/z (%): $[M+1]^+$: 289 (7); M^+: 288 (42); 172 (5); 120 (14); 91 (100); 65 (18), 42(11). Anal. calcd for $C_{14}H_{16}N_4O_3$: C, 58.32; H, 5.59; N, 19.43. Found: C, 58.58; H, 5.46; N, 19.42.

(*Z*)-Ethyl 3-amino-3-[(*N*-benzyl-*N*-methyl)carbamido)]-2-cyanoacrylate (3h) (6.6%). mp 207-210°C. IR (KBr): 3329, 3184 (NH); 2206 (CN); 1666, 1643 (C=O); 1597, 1496 (C=C); 1311. ^{1}H-NMR (250.13 MHz; $CDCl_3$): δ= 1.30 (t, J = 7.1 Hz, 3H, OCH_2CH_3); 3.03 (s, 3H, NCH_3); 4.18 (q, J = 7.1 Hz, 3H, OCH_2CH_3); 4.58 (s, 2H, CH_2Ph); 5.89 (s, 1H, H^B); 7.23-7.37 (m, 5H, $H_{arom.}$); 9.57 (s, 1H, H^A); 12.04 (s, 1H, H^C). ^{13}C-NMR (75.43 MHz, $CDCl_3$): δ= 14.36 (-, OCH_2CH_3); 34.1 (-, NCH_3); 51.8 (+, CH_2Ph); 59.1 (+, C-2); 60.4 (+, OCH_2); 117.4 (+, CN); 127.3 (-, C-4′); 127.6 (-, C-3′); 128.7 (-, C-2′); 154.4 (+, $C{=}O_{carb.}$); 162.1 (+, C-3); 169.2 (+, C-1). MS m/z (%): $[M+1]^+$: 303 (3); M^+: 302 (19); 120 (7); 91 (100); 65 (5), 44(3). Anal. calcd for $C_{15}H_{18}N_4O_3$: C, 59.59; H, 6.00; N, 18.53. Found: C, 59.50; H, 6.14; N, 18.47.

(*Z*)-Methyl 3-amino-3-[(*N*-cyclohexyl-*N*-methyl)carbamido]-2-cyanoacrylate (3i) (11.4%). mp 209-212°C. IR (KBr): 3325, 3184 (NH); 2209 (CN); 1663, 1645 (C=O); 1597, 1490 (C=C); 1322. ^{1}H-NMR (250.13 MHz; $CDCl_3$): δ= 1.42 (t, 4H, H-3′); 1.79 (d, 4H, H-2′); 1.84 (d, 2H, H-4′); 2.89 (s, 3H, NCH_3); 3.76 (s, 3H, OCH_3); 5.92 (s, 1H, H^B); 9.62 (s, 1H, H^A); 11.81 (s, 1H, H^C). ^{13}C-NMR (75.43 MHz, $CDCl_3$): δ= 25.4 (+, C-3′,4′); 28.6 (-, C-1′); 30.1 (+, C-2′); 51.5 (-, OCH_3); 58.7 (+, C-2); 117.6 (+, CN); 153.9 (+, $C{=}O_{carb.}$); 162.2 (+, C-3); 169.6 (+, C-1). MS m/z (%): $[M+1]^+$: 281 (8); M^+: 280 (48); 141 (31); 140 (85); 110 (19); 83 (100); 70 (23); 55 (70); 42 (25); 41 (35). Anal. calcd for $C_{13}H_{20}N_4O_3$: C, 55.70; H, 7.19; N, 19.99. Found: C, 55.70; H, 7.29; N, 19.82.

(*Z*)-Ethyl 3-amino-3-[(*N*-cyclohexyl-*N*-methyl)carbamido]-2-cyanoacrylate (3j) (8.5%). mp 195-198°C. IR (KBr): 3327, 3180 (NH); 2207 (CN); 1664, 1643 (C=O); 1594, 1480 (C=C); 1316. ^{1}H-NMR (250.13 MHz; $CDCl_3$): δ= 1.31 (t, J = 7.2 Hz, 3H, OCH_2CH_3); 1.44 (m, 4H, H-3′); 1.71 (m, 4H, H-2′); 1.83 (m, 2H, H-4′); 2.90 (s, 3H, NCH_3); 4.20 (q, 2H, OCH_2); 5.88 (s, 1H, H^B); 9.60 (s, 1H, H^A); 11.89 (s, 1H, H^C). ^{13}C-NMR (62.89 MHz, $CDCl_3$): δ= 14.5 (-, OCH_2CH_3); 25.3 (+, C-4′); 25.5 (+, C-3′); 28.5 (-, C-1′); 30.3 (+, C-2′); 59.1 (+, C-2); 60.5 (+, OCH_2); 117.8 (+, CN); 154.2 (+, $C{=}O_{carb.}$); 162.5 (+, C-3); 169.5 (+, C-1). MS m/z (%): $[M+1]^+$: 295 (5); M^+: 294 (34); 155 (8); 140 (42); 83 (100); 70 (11); 55 (32); 42 (10); 41 (18). Anal. calcd for $C_{14}H_{22}N_4O_3$: C, 57.13; H, 7.53; N, 19.03. Found: C, 56.96; H, 7.45; N, 18.98.

(*Z*)-Methyl 3-amino-3-[(*N*-methyl-*N*-octadecyl)carbamido]-2-cyanoacrylate (3k) (9.2%). mp 117-119°C. IR (KBr): 3327, 3183 (NH); 2206 (CN); 1666, 1647 (C=O); 1601, 1501 (C=C); 1325. ^{1}H-NMR (250.13 MHz; $CDCl_3$): δ= 0.88 (t, J = 5.8 Hz, 3H, $(CH_2)_{17}CH_3$); 1.25 (s, 32H, $CH_2(CH_2)_{16}CH_3$); 3.03 (d, 3H, NCH_3); 3.75 (s, 3H, OCH_3); 5.87 (s, 1H, H^B); 9.58 (s, 1H, H^A); 11.83 (s, 1H, H^C). ^{13}C-NMR (62.89 MHz, $CDCl_3$): δ= 14.1 (-, $(CH_2)_{17}CH_3$); 22.7 (+, $(CH_2)_{16}CH_2CH_3$); 26.6-29.7 (+, m, $CH_2(CH_2)_{16}CH_3$); 31.9 (+, $CH_2(CH_2)_{16}CH_3$); 34.6 (-, NCH_3); 51.6 (-, OCH_3); 58.8 (+, C-2); 117.6 (+, CN); 154.2 (+, $C{=}O_{carb.}$); 162.4 (+, C-3); 169.8 (+, C-1). MS m/z (%): $[M+1]^+$: 451 (30); M^+: 450 (97); 310 (22); 282 (14); 85 (38); 71 (56); 57 (99); 44 (100); 43 (61). Anal. calcd for $C_{25}H_{46}N_4O_3$: C, 66.63; H, 10.29; N, 12.43. Found: C, 66.53; H, 10.01; N, 12.29.

(*Z*)-Ethyl 3-amino-3-[(*N*-methyl-*N*-octadecyl)carbamido]-2-cyanoacrylate (3l) (10.8%). mp 122°C. IR (KBr): 3336, 3185 (NH); 2205 (CN); 1667, 1645 (C=O); 1600, 1560 (C=C);. ^{1}H-NMR (250.13 MHz; $CDCl_3$): δ= 0.88 (t, 3H, $(CH_2)_{17}CH_3$); 1.26-1.34 (m, 32H, $CH_2(CH_2)_{16}CH_3$); 3.02 (d, 3H, NCH_3); 3.35 (t, 2H, $CH_2(CH_2)_{16}CH_3$); 4.19 (q, 2H, OCH_2); 5.89 (s, 1H, H^B); 9.56 (s, 1H, H^A); 11.90 (s, 1H, H^C). ^{13}C-NMR (62.89 MHz, $CDCl_3$): δ= 14.1 (-, $(CH_2)_{17}CH_3$); 22.7 (+, $(CH_2)_{16}CH_2CH_3$); 26.7 (+, $(CH_2)_{16}CH_2CH_3$); 29.3-29.7 (+, m, $CH_2CH_2(CH_2)_{15}CH_3$); 32.0 (+, $CH_2(CH_2)_{16}CH_3$); 34.6 (-, NCH_3); 59.1 (+, C-2); 60.5 (+, OCH_2); 117.8 (+, CN); 154.3 (+, $C{=}O_{carb.}$); 162.4 (+, C-3); 169.5 (+, C-1). MS m/z (%): $[M+1]^+$: 465 (26); M^+: 464 (83); 310 (12); 282 (11); 71 (45); 57 (82); 44 (100). Anal. calcd for $C_{26}H_{48}N_4O_3$: C, 67.20; H, 10.41; N, 12.06. Found: C, 67.22; H, 10.29; N, 12.05.

(*E, Z*)-Ethyl 3-amino-3-(ethylcarbamido)-2-cyanoacrylate (3m) (2.7%). mp 230-233°C. IR (KBr): 3387, 3291 (NH); 2209 (CN); 1718, 1653 (C=O); 1620, 1560 (C=C);. ^{1}H-NMR (299.95 MHz; DMSO-d_6): δ= 1.06 (t, 3H, $NCH_2C\mathbf{H}_3$); 1.21 (t, 3H, $OCH_2C\mathbf{H}_3$); 3.10 (m, 2H, $NC\mathbf{H}_2CH_3$); 4.11 (q, 2H, $OC\mathbf{H}_2CH_3$); 7.83 (s, 1H, $\mathbf{H}^{D_E+D_Z}$); 8.36 (s, 1/2H, $\mathbf{H}^{B_Z}$); 8.83 (s, 1/2H, $\mathbf{H}^{C_E}$); 9.05 (s, 1/2H, $\mathbf{H}^{B_E}$); 9.28 (s, 1H, $\mathbf{H}^{A_E+A_Z}$); 10.98 (s, 1/2H, $\mathbf{H}^{C_Z}$). ^{13}C-NMR (62.89 MHz; DMSO-d_6): δ= 14.3 (-, $NCH_2\mathbf{C}H_3$, $OCH_2\mathbf{C}H_3$); 34.0 (+, $N\mathbf{C}H_2CH_3$); 56.3 (+, C-2); 59.3 (+, $O\mathbf{C}H_2CH_3$); 117.6 (+, **C**N); 154.2 (+, $\mathbf{C}{=}O_{carb.}$); 161.6 (+, C-3); 168.0 (+, C-1). MS m/z (%): $[M+1]^+$: 227 (5); M^+: 226 (53); 155 (100); 127 (49); 110 (65); 83 (72); 72 (22); 44 (28); 43 (33). Anal. calcd for $C_9H_{14}N_4O_3$: C, 47.78; H, 6.24; N, 24.77. Found: C, 47.50; H, 6.13; N, 24.80.

(*E, Z*)-Ethyl 3-amino-3-(*N-n*-butylcarbamido)-2-cyanoacrylate (3n) (4.2%). mp 200-202°C. IR (KBr): 3382, 3288 (NH); 2211 (CN); 1718, 1654 (C=O); 1622 (C=C);. ^{1}H-NMR (299.95 MHz; DMSO-d_6): δ= 0.89 (t, J = 7.2 Hz, 3H, $N(CH_2)_3C\mathbf{H}_3$); 1.21 (t, J = 7.2 Hz, 3H, $OCH_2C\mathbf{H}_3$); 1.30 (q, J = 7.2 Hz, 2H, $N(CH_2)_2C\mathbf{H}_2CH_3$); 1.37 (t, J = 7.2 Hz, 2H, $NCH_2C\mathbf{H}_2CH_2CH_3$); 3.08 (m, 2H, $NC\mathbf{H}_2(CH_2)_2CH_3$); 4.11 (q, J = 7.2 Hz, 2H, $OC\mathbf{H}_2CH_3$); 7.83 (s, 1H, $\mathbf{H}^{D_E+D_Z}$); 8.18 (s, 1/2H, $\mathbf{H}^{B_Z}$); 8.81 (s, 1/2H, $\mathbf{H}^{C_E}$); 9.08 (s, 1/2H, $\mathbf{H}^{B_E}$); 9.36 (s, 1H, $\mathbf{H}^{A_E+A_Z}$); 10.98 (s, 1/2H, $\mathbf{H}^{C_Z}$). ^{13}C-NMR (62.89 MHz; DMSO-d_6): δ= 13.5 (-, $N(CH_2)_3\mathbf{C}H_3$); 14.4 (-, $OCH_2\mathbf{C}H_3$); 14.5 (+, $N(CH_2)_2\mathbf{C}H_2CH_3$); 30.8 (+, $NCH_2\mathbf{C}H_2CH_2CH_3$); 32.2 (+, $N\mathbf{C}H_2(CH_2)_2CH_3$); 56.5 (+, C-2); 59.4 (+, $O\mathbf{C}H_2CH_3$); 117.7 (+, **C**N); 154.3 (+, $\mathbf{C}{=}O_{carb.}$); 161.6 (+, C-3); 168.0 (+, C-1). MS m/z (%): $[M+1]^+$: 255 (3); M^+: 254 (30); 155 (100); 127 (34); 110 (35); 83 (46); 43 (16); 41 (15). Anal. calcd for $C_{11}H_{18}N_4O_3$: C, 51.96; H, 7.14; N, 22.03. Found: C, 51.95; H, 7.18; N, 21.70.

5-Chloro-2,7-bis(dimethylamino)-4*H*-pyrimido[4,5-*d*][3,1]oxazin-4-one (6a)

Method A: A solution of methyl 3,3-diamino-2-cyanoacrylate (**1a**) (1.42g, 10 mmol) and dichloromethylenedimethylimmonium chloride (**4a**) in 1,2-dichlorethane (150 mL) was refluxed for 4h. A stream of dry hydrogen chloride gas was passed the mixture for 4h. After cooling to r.t., it was stirred overnight. The solvent was removed under reduced pressure and the residue was chromatographed on a silica column (70-230 mesh) using ethyl acetate as eluent to give 165 mg **6a** (6.1%).

Method B: From **5** (0.18 g, 1 mmol) and **4a** (0.4 g, 2.5 mmol) in 1,2-dichlorethane (20 mL) analogous to methode A to yield 80 mg **6a** (29.7%). mp 232-235°C. IR (KBr): 1757 (C=O); 1628, 1559 (C=C, C=N); 1382. ^{1}H-NMR (250.13 MHz; $CDCl_3$): δ= 3.14 (s, 3H, $N^+C\mathbf{H}_3$); 3.269, 3,275, 3.284 (3s, 9H, $N(C\mathbf{H}_3)_2$, $N^+C\mathbf{H}_3$). ^{13}C-NMR (90.56 MHz, $CDCl_3$); δ= 36.6 (-, $N^+\mathbf{C}H_3$); 37.6 (-, $N(\mathbf{C}H_3)_2$); 37.8 (-, $N^+\mathbf{C}H_3$); 92.6 (+, C-4a); 155.4 (+, C-5); 158.5 (+, C-8a); 162.2 (+, C-7); 163.0 (+, C-4); 168.1 (+, C-2). MS m/z (%): $[M+2]^+$: 271 (27); M^+: 269 (94); 240 (10); 227 (80); 225 (100); 72 (46); 44 (24); 42 (21). Anal. calcd for $C_{10}H_{12}N_5ClO_2$: C, 44.54; H, 4.19; N, 25.97. Found: C, 44.62; H, 4.45; N, 25.55. HRMS: Calcd. for $C_{10}H_{12}N_5ClO_2$: 269.0681. Found: 269.0682.

5-Chloro-2,7-dipiperidino-4*H*-pyrimido[4,5-*d*][3,1]oxazin-4-one (6b):

From *N*-(dichloromethylene)piperidinium chloride (**4b**), prepared from bis(piperidinthiocarbamoyl)disulfide in absol. CCl_4 by the method of B. U. Schlottmann,[11] and ethyl 3,3-diamino-2-cyanoacrylate (**1b**) (0.47 g, 3 mmol) in 1,2-dichlorethane (50 mL) analogous to method A to yield 466 mg **6b** (44.5%). mp 179-182°C. IR (KBr): 1778 (C=O); 1616, 1566, 1544 (C=C, C=N); 1296. ^{1}H-NMR (360.13 MHz; $CDCl_3$): δ= 1.67 (s, br, 12H, H-3′,4′,5′,3′′,4′′,5′′); 3.70 (s, 2H, H-6′); 3.84 (s, 2H, H-2′); 3.90 (s, 4H, H-2′′,6′′). ^{13}C-NMR (90.56 MHz, $CDCl_3$); δ= 23.95, 24.43 (2+, C-4′,4′′); 25.44, 25.76, 25.93 (3+, C-3′,3′′,5′,5′′); 45.08 (+, C-6′); 45.30, 45.38 (2+, C-2′′,6′′); 45.86 (+, C-2′); 92.35 (+, C-4a); 155.3 (+, C-5); 157.0 (+, C-8a); 161.0 (+, C-7); 163.0 (+, C-4); 168.4 (+, C-2). MS m/z (%): $[M+2]^+$: 351 (30); M^+: 349 (87); 320 (16); 267 (40); 265 (100); 84 (64); 69 (25); 55 (15); 41 (40). Anal. calcd for $C_{16}H_{20}N_5ClO_2$: C, 54.94; H, 5.76; N, 20.02. Found: C, 54.86; H, 5.87; N, 19.78. HRMS: Calcd. for $C_{16}H_{20}N_5ClO_2$: 349.1306. Found: 349.1306.

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