Synthesis of Heterocyclic Compounds Using Amidines as Their Ene-1,1-diamine Tautomers. I. Synthesis of 4,5-Dihydro-3*H*-pyridin-2-one, 3,4-Dihydropyrrol-2-one and 1,3-Dihydropyrrol-2-one Derivatives by the Reaction of Amidines with α,β-Unsaturated Esters

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N-*t*-Butylacetamidines **1** on heating with methyl acrylate (**2**) at 200° gave the 4,5-dihydro-3*H*-pyridin-2-one derivatives **5**. Michael addition of the acetamidines **1** as their ene-1,1-diamine tautomers **1'** to **2** and the subsequent cyclization of the adducts gave derivatives **5**. Amidines **1** on reaction with trimethyl ethylenetricarboxylate (**9**) or dimethyl acetylenedicarboxylate (**12**) afforded 3,4-dihydropyrrol-2-one **11** or 1,3-dihydropyrrol-2-one derivatives **13**.

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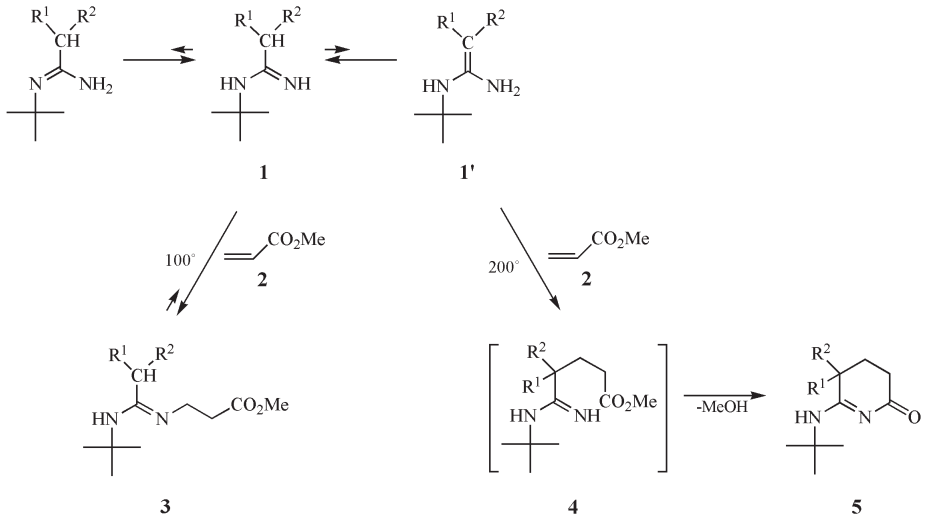
Reaction of amidines with electrophiles generally results in *N*-alkylated products, with reaction occurring *via* the *N,N'*-tautomer azaenamine [1]. For *C*-alkylation in which the amidines react *via* the *N,C*-tautomers ene-1,1-diamines, there is only one report on the reaction of trisubstituted cyclic amidine 1-methyl-2-benzyliminopyrrolidine [2]. There are no reports in which *C*-alkylation products are obtained from monosubstituted or disubstituted amidines. The present study describes reaction between monosubstituted acetamidines with a *t*-butyl group on the nitrogen atom and α,β-unsaturated esters. We report that amidines, reacting as their *N,C*-tautomer ene-1,1-diamine, take place Michael addition to α,β-unsaturated esters, and subsequently the Michael adducts underwent cyclization with elimination of alcohol to afforded 4,5-dihydro-3*H*-pyridin-2-one, 3,4-dihydropyrrol-2-one, or 1,3-dihydropyrrol-2-one derivatives.

N-*t*-butylbenzylamidine (**1a**) was heated with methyl acrylate (**2**) at 100° for 10 hours in diglyme. After the solvent and low-boiling materials were removed under reduced pressure, *N*-alkylated product **3a**, formed by addition of the amidine *via* the *N,N'*-tautomer azaenamine, was obtained in near quantitative yield (97 %).

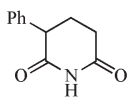
Scheme 1



	R^1	R^2
a	Ph	H
b	4-Cl-C_6H_4	H
c	4-Br-C_6H_4	H
d	4-MeO-C_6H_4	H
e	4-Me-C_6H_4	H
f	Ph-CH_2	H

	R^1	R^2
g	H	H
h	Me	H
i	Et	H
j	Me	Me
k	-$(CH_2)_5$-	

A solution of **3a** in triglyme was heated in an autoclave at 200˚ for 5 hours. 4,5-Dihydro-3*H*-pyridin-2-one derivative **5a**, derived from *C*-alkylation of amidine **1a**, was obtained (60 %). The structure of **5a** was confirmed by elemental analysis, spectroscopic measurements, and derivatization to known compound **6** [3].



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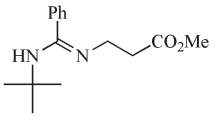

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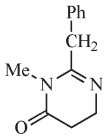

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As shown in Scheme 1, the reaction tends toward *N*-alkylation at 100˚. At 200˚, however, the *N*-alkylated product **3a** undergoes the retro-Michael reaction. A small amount of the *N*,*C*-tautomer of the amidine **1a**, that is ene-1,1-diamine **1'a**, then reacts with **2** by Michael addition to produce the *C*-alkylated product **4a**. Subsequently, cyclization with irreversible elimination of alcohol from **4a** yields the product **5a**. Thus, the reaction proceeds in the direction of *C*-alkylation, producing the pyridin-2-one derivative **5a**.

The existence of the ene-1,1-diamine tautomer **1'** was confirmed by the method of Pfau and Ribière [4]. Observation of the ^{1}H-nmr spectrum of *N*-*t*-butylbenzylamidine (**1a**) in CD_3OD revealed that the methylene singlet (δ = 3.44) intensity fell by 80% after 5 minutes at room temperature because of deuteration, and completely disappeared after 30 minutes. This indicates that there is a very fast tautomeric equilibrium between the azaenamine and ene-1,1-diamine in the monosubstituted acetamidine, as in the case between imine and secondary enamine.

The product **5a** was also directly obtained by heating **1a** and **2** at 200˚. When a triglyme solution of **1a** and **2** was heated with stirring in an autoclave at 200˚ for 5 hours, **5a** was obtained in 79 % yield. Table 1 shows the results of preparation of various 4,5-dihydro-3*H*-pyridin-2-one derivatives **5**, obtained from reaction between *N*-*t*-butylacetamidines **1** and methyl acrylate (**2**). When R^1 was aryl groups for compounds **5a**-**5e**, the pyridin-2-one derivatives **5** were obtained by comparatively higher yield compared with the case of alkyl groups. This result is due to the fact that the conjugation of double bond and aryl groups shifted the tautomeric equilibrium in the direction of the ene-1,1-diamine form **1'** in some measure.

Heating of *N*-*t*-butylbenzamidine or *N*-methylbenzylamidine with **2** at 200˚ showed a contrasting result to heating of **1** with **2**. Reaction of *N*-*t*-butylbenzamidine with **2** gave *N*-alkylated product **7** (40 %), and cyclization products such as pyrimidinone derivatives could not be isolated. Reaction of *N*-methylbenzylamidine with **2** gave 2-benzyl-3-methyl-5,6-dihydro-3*H*-pyrimidin-4-one (**8**) (65 %), derived from cyclization of the *N*-alkylated product. Therefore, it is considered that ring formation on the *t*-butyl nitrogen atom in **3** and **4** was controlled by the steric hindrance due to the bulky *t*-butyl group, *i.e.*, **5** was exclusively produced in the case of **1**.

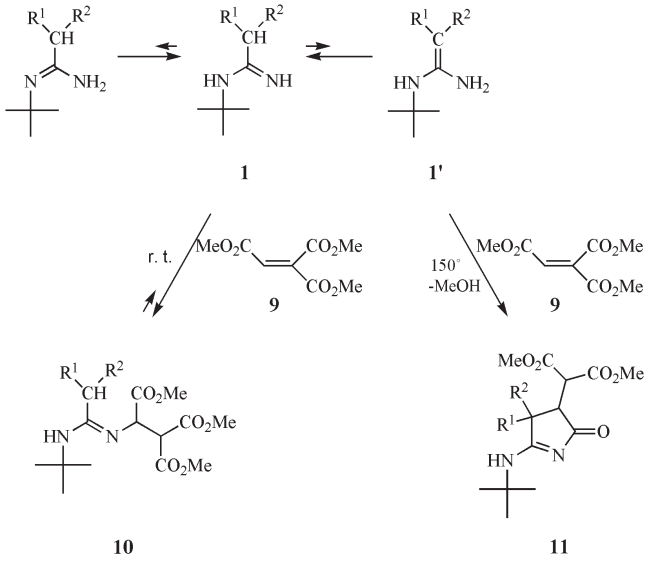
Table 1

Preparation of Compounds **5**

Compound	R^1	R^2	Yield %
5a	Ph	H	79
5b	4-Cl-C_6H_4	H	68
5c	4-Br-C_6H_4	H	71
5d	4-MeO-C_6H_4	H	59
5e	4-Me-C_6H_4	H	53
5f	Ph-CH_2	H	40
5g	H	H	14
5h	Me	H	40
5i	Et	H	19
5j	Me	Me	32
5k	-$(CH_2)_5$-		39

In a similar reaction to that between **1a** and **2**, the *N*-alkylated product **10a** was obtained by stirring an ether solution of **1a** and trimethyl ethylenetricarboxylate (**9**) for 2 hours at room temperature (93 %). When a diglyme solution of the obtained **10a** was heated at 150˚ for 3 hours, the 3,4-dihydropyrrol-2-one derivative **11a** was obtained (89 %). Separately, when a diglyme solution of the amidine **1a** and **9** was heated at 150˚ for 3 hours, **11a** was obtained in a yield of 87 % (Scheme 2). The results for preparation of various 3,4-dihydropyrrol-2-one derivatives

Scheme 2



1 **1'** **9** **9** **10** **11**

Scheme 3

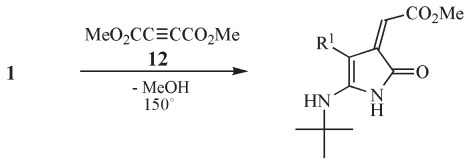


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Table 2

Preparation of Compounds **11** and **13**

Compound	R^1	R^2	Reaction Time [h]	Yield [%]
11a	Ph	H	3	87
11b	4-Cl-C_6H_4	H	3	71
11c	4-Br-C_6H_4	H	3	72
11d	4-MeO-C_6H_4	H	3	88
11e	4-Me-C_6H_4	H	3	56
11f	Ph-CH_2	H	3	51
11g	H	H	3	50
11j	Me	Me	3	50
13a	Ph	—	3	66
13b	4-Cl-C_6H_4	—	3	68
13c	4-Br-C_6H_4	—	3	58
13d	4-MeO-C_6H_4	—	2	65
13e	4-Me-C_6H_4	—	2	76
13f	Ph-CH_2	—	4	24
13i	Et	—	7	15

11 obtained from reaction of **1** and **9** are shown in Table 2.

When a diglyme solution of **1** and dimethyl acetylenedicarboxylate (**12**) was heated at 150˚, 1,3-dihydropyrrol-2-one derivatives **13** were obtained (Scheme 3, Table 2). The structures of **11** and **13** were confirmed on the basis of their microanalyses and spectral data. Both compounds **11** and **13** were prepared by reaction *via* the *N,C*-tautomer of the amidines **1**, that is, ene-1,1-diamine **1'**. When R^1 was aryl groups for compounds **11a-11e** and **13a-13e**, as well as the case of pyridin-2-one derivatives **5**, pyrrol-2-one derivatives **11** and **13** were obtained in somewhat higher yield.

EXPERIMENTAL

All melting points are uncorrected. The ir spectra were recorded on a Horiba FT-720 spectrometer in potassium bromide pellets unless otherwise noted. The ^{1}H nmr data were obtained with a JEOL JNM-EX400 (400 MHz) spectrometer in deuteriochloroform by using tetramethylsilane as an internal standard. Mass spectra were measured with a Shimadzu GCMS-QP5050A spectrometer at 70 eV of ionization energy by use of a direct-inlet system. Elemental analyses were performed by using a Perkin-Elmer 2400 II CHN Analyzer.

N-t-Butylacetamidines **1**, *N-t*-Butylbenzamidine, and *N*-methylbenzylamidine were prepared by the method of Cooper and Partridge [5]. Methyl acrylate (**2**) and dimethyl acetylenedicarboxylate (**12**) were commercially available and used without further purification. Trimethyl ethylenetricarboxylate (**9**) was obtained according to the method of Hall and Ykman [6].

Methyl 3-[1-(*N-t*-Butylamino)-2-phenylethylidene]aminopropionate (**3a**).

A solution containing *N-t*-butylbenzylamidine (**1a**) (9.50 g, 50.0 mmoles) and methyl acrylate (**2**) (6.46 g, 75.0 mmoles) in diglyme (100 ml) was heated 100˚ for 10 hours. The solvent and the low boiling materials were removed under reduced pressure (at 0.15 mmHg), maintaining the bath temperature below 100˚, leaving 13.40 g (97 %) of *N*-alkylation product **3a** as a pale yellow liquid. This product obtained was of satisfactory purity as judged by ^{1}H nmr spectroscopy, which was used without further purification; ir (liquid film): 3411, 1736, 1647, 1600, 1525, 1504, 1444 cm^{-1}; ^{1}H nmr: δ 1.27 (9H, s, $C(CH_3)_3$), 2.53 and 3.47 (each 2H, t, J=6.6 Hz, CH_2), 3.48 (2H, s, CH_2), 3.63 (1H, br s, NH), 3.65 (3H, s, CO_2CH_3), 7.17-7.32 (5H, m, aromatic); ms: m/z 276 (M^+).

Anal. Calcd. for $C_{16}H_{24}N_2O_2$: C, 69.53; H, 8.75; N, 10.14. Found: C, 69.08; H, 9.22; N, 10.28.

Conversion to 4,5-Dihydro-3*H*-pyridin-2-one Derivative **5a** of *N*-Alkylation Product **3a**.

A solution of *N*-alkylation product **3a** (5.53 g, 20.0 mmoles) in triglyme (40 ml) was heated with stirring at 200˚ for 5 hours in an autoclave. The reaction mixture was cooled, and the precipitated product **5a** was collected by filtration and washed with carbon tetrachloride. Evaporation of the combined filtrates under reduced pressure and recrystallization of residual solid from a small amount of carbon tetrachloride, gave an additional amount of **5a**. The total yield of **5a** was 2.94 g (60 %), mp 202.5-205.0˚.

Derivatization to **6** by Hydrolysis of **5a**.

To a solution of **5a** (2.44 g, 10.0 mmoles) in 1,4-dioxane (10 ml) were added acetic acid (5.0 ml) and water (5.0 ml), and this mixture was heated under reflux for 50 hours. The resulting solution was concentrated under reduced pressure. To the residue was added 4 *N* aqueous sodium hydroxide, and the alkaline solution was extracted with chloroform (3 x 20 ml). The combined organic extracts were dried over anhydrous sodium sulfate and evaporated, leaving 0.87 g (46 %) of 3-phenyl-2,6-piperidinedione (**6**) as white needles. An analytical sample was prepared by recrystallization from ethyl acetate: mp 143.0-144.5˚ (reference [3a], mp 142-143˚); ir: 3405, 1716, 1697, 1492, 1454 cm^{-1}; ^{1}H nmr: δ 2.17-2.32 (2H, m, CH_2CH_2CO), 2.64 (1H, ddd, J=17.8, 9.3, 5.4 Hz, CH_2CO), 2.70 (1H, dt, J=17.8, 5.6 Hz, CH_2CO), 3.78 (1H, dd, J=9.3, 5.4 Hz, CH), 7.19-7.39 (5H, m, aromatic), 8.44 (1H, br s, NH); ms: m/z 189 (M^+).

Anal. Calcd. for $C_{11}H_{11}NO_2$: C, 69.83; H, 5.86; N, 7.40. Found: C, 69.66; H, 5.93; N, 7.39.

The ir and the ^{1}H nmr spectra of this compound are in complete agreement with the spectra of the sample synthesized according to the method of the reference [3b].

Methyl 3-[(*N-t*-Butylamino)benzylidene]aminopropionate (**7**).

A solution containing *N-t*-butylbenzamidine (5.29 g, 30.0 mmoles) and methyl acrylate (**2**) (3.10 g, 36.0 mmoles) in triglyme (60 ml) was heated with stirring at 200˚ for 5 hours in an autoclave. Removal of the solvent under reduced pressure and distillation of the residue gave 3.87 g (49 %) of **7**, which on standing crystallized. An analytical sample was prepared by recrystallization from hexane: bp 117-119˚ (0.35 mmHg), mp 43.0-44.0˚; ir: 3375, 1728, 1635, 1600, 1523, 1439 cm^{-1}; ^{1}H

nmr: δ 1.39 (9H, s, $C(CH_3)_3$), 2.45 and 3.28 (each 2H, t, J=6.8 Hz, CH_2), 3.63 (3H, s, CO_2CH_3), 3.81 (1H, br s, NH), 7.21-7.39 (5H, m, aromatic); ms: m/z 262 (M^+).

Anal. Calcd. for $C_{15}H_{22}N_2O_2$: C, 68.67; H, 8.45; N, 10.68. Found: C, 69.06; H, 8.53; N, 10.87.

2-Benzyl-3-methyl-5,6-dihydro-3*H*-pyrimidin-4-one (**8**).

A solution containing *N*-methylbenzylamidine (4.45 g, 30.0 mmoles) and methyl acrylate (**2**) (3.10 g, 36.0 mmoles) in triglyme (60 ml) was heated with stirring at 200° for 5 hours in an autoclave. Removal of the solvent under reduced pressure and distillation of the residue gave 3.96 g (65 %) of **8**, which on standing crystallized. An analytical sample was prepared by recrystallization from carbon tetrachloride: bp 148-150° (1.15 mmHg), mp 67.3-68.2°; ir: 1685, 1655, 1458, 1365, 1296 cm^{-1}; ^1H nmr: δ 2.48 and 3.64 (each 2H, t, J=7.3 Hz, CH_2), 3.06 (3H, s, NCH_3), 3.82 (2H, s, CH_2), 7.24-7.35 (5H, m, aromatic); ms: m/z 202 (M^+).

Anal. Calcd. for $C_{12}H_{14}N_2O$: C, 71.26; H, 6.98; N, 13.85. Found: C, 70.91; H, 7.00; N, 13.82.

4,5-Dihydro-3*H*-pyridin-2-ones **5**.

A solution containing *N*-*t*-butylacetamidines **1** (30 mmoles) and methyl acrylate (**2**) (36.0 mmoles) in triglyme (60 ml) was heated with stirring at 200° for 5 hours in an autoclave. The reaction mixture was cooled, and the precipitated product was collected by filtration and washed with carbon tetrachloride. Evaporation of combined filtrates under reduced pressure and recrystallization of the residual solid from a small amount of carbon tetrachloride, gave an additional amount of product **5**. All the products obtained were of satisfactory purity as judged by ^1H nmr spectroscopy. Samples for analysis were recrystallized from chloroform.

6-*t*-Butylamino-5-phenyl-4,5-dihydro-3*H*-pyridin-2-one (**5a**).

This compound was obtained as white scales, mp 204.5-205.0°; ir: 3273, 1649, 1577, 1520, 1469, 1444, 1392 cm^{-1}; ^1H nmr: δ 1.39 (9H, s, $C(CH_3)_3$), 2.11 and 2.21 (each 1H, m, CH_2), 2.42-2.56 (2H, m, CH_2), 3.51 (1H, dd, J=9.3, 5.1 Hz, CH), 4.93 (1H, br s, NH), 7.20-7.42 (5H, m, aromatic); ms: m/z 244 (M^+).

Anal. Calcd. for $C_{15}H_{20}N_2O$: C, 73.74; H, 8.25; N, 11.47. Found: C, 73.59; H, 8.32; N, 11.37.

6-*t*-Butylamino-5-(4-chlorophenyl)-4,5-dihydro-3*H*-pyridin-2-one (**5b**).

This compound was obtained as a white powder, mp 171.0-172.0°; ir: 3271, 1645, 1583, 1537, 1500, 1448, 1387 cm^{-1}; ^1H nmr: δ 1.41 (9H, s, $C(CH_3)_3$), 2.05 and 2.20 (each 1H, m, CH_2), 2.42-2.47 (2H, m, CH_2), 3.51 (1H, dd, J=8.3, 5.1 Hz, CH), 4.99 (1H, br s, NH), 7.15 and 7.37 (each 2H, d, J=8.3 Hz, aromatic); ms: m/z 278 (M^+).

Anal. Calcd. for $C_{15}H_{19}ClN_2O$: C, 64.63; H, 6.87; N, 10.05. Found: C, 64.65; H, 6.95; N, 10.13.

5-(4-Bromophenyl)-6-*t*-butylamino-4,5-dihydro-3*H*-pyridin-2-one (**5c**).

This compound was obtained as a white powder, mp 186.5-187.0°; ir: 3255, 1641, 1595, 1545, 1500, 1456, 1392 cm^{-1}; ^1H nmr: δ 1.41 (9H, s, $C(CH_3)_3$), 2.02 and 2.19 (each 1H, m, CH_2), 2.39 (2H, t, J=6.6 Hz, CH_2), 3.52 (1H, dd, J=7.8, 5.1 Hz, CH), 5.20 (1H, br s, NH), 7.09 and 7.51 (each 2H, d, J=8.3 Hz, aromatic); ms: m/z 322 and 324 (M^+).

Anal. Calcd. for $C_{15}H_{19}BrN_2O$: C, 55.74; H, 5.92; N, 8.67. Found: C, 55.38; H, 6.00; N, 9.00.

6-*t*-Butylamino-5-(4-methoxyphenyl)-4,5-dihydro-3*H*-pyridin-2-one (**5d**).

This compound was obtained as white needles, mp 150.0-151.0°; ir: 3249, 1639, 1606, 1545, 1510, 1469, 1392 cm^{-1}; ^1H nmr: δ 1.39 (9H, s, $C(CH_3)_3$), 2.07 and 2.15 (each 1H, m, CH_2), 2.40-2.54 (2H, m, CH_2), 3.46 (1H, dd, J=8.9, 5.1 Hz, CH), 3.82 (3H, s, OCH_3), 5.06 (1H, br s, NH), 6.92 and 7.12 (each 2H, d, J=8.8 Hz, aromatic); ms: m/z 274 (M^+).

Anal. Calcd. for $C_{16}H_{22}N_2O_2$: C, 70.04; H, 8.08; N, 1021. Found: C, 70.48; H, 8.17; N, 10.12.

6-*t*-Butylamino-5-(4-methylphenyl)-4,5-dihydro-3*H*-pyridin-2-one (**5e**).

This compound was obtained as white needles, mp 180.0-181.0°; ir: 3252, 1647, 1601, 1547, 1510, 1471, 1450, 1390 cm^{-1}; ^1H nmr: δ 1.39 (9H, s, $C(CH_3)_3$), 2.08 and 2.16 (each 1H, m, CH_2), 2.36 (3H, s, CH_3), 2.40-2.54 (2H, m, CH_2), 3.47 (1H, dd, J=9.3, 5.1 Hz, CH), 4.99 (1H, br s, NH), 7.09 and 7.19 (each 2H, d, J=8.1 Hz, aromatic); ms: m/z 258 (M^+).

Anal. Calcd. for $C_{16}H_{22}N_2O$: C, 74.38; H, 8.58; N, 10.84. Found: C, 74.08; H, 8.81; N, 11.32.

5-Benzyl-6-*t*-butylamino-4,5-dihydro-3*H*-pyridin-2-one (**5f**).

This compound was obtained as a white powder, mp 184.5-185.0°; ir: 3249, 1635, 1599, 1545, 1500, 1475, 1456, 1392 cm^{-1}; ^1H nmr: δ 1.27 (9H, s, $C(CH_3)_3$), 1.85 and 2.02 (each 1H, m, CH_2), 2.43-2.61 (3H, m, CH_2 and CH), 2.85 (1H, dd, J=13.6, 6.8 Hz, CH_2), 2.91 (1H, dd, J=13.6, 9.3 Hz, CH_2), 5.09 (1H, br s, NH), 7.17-7.35 (5H, m, aromatic); ms: m/z 258 (M^+).

Anal. Calcd. for $C_{16}H_{22}N_2O$: C, 74.38; H, 8.58; N, 10.84. Found: C, 74.50; H, 8.68; N, 10.90.

6-*t*-Butylamino-4,5-dihydro-3*H*-pyridin-2-one (**5g**).

This compound was obtained as a white powder, mp 219.0-220.0°; ir: 3276, 1651, 1585, 1527, 1473, 1448, 1421, 1390 cm^{-1}; ^1H nmr: δ 1.46 (9H, s, $C(CH_3)_3$), 1.88 (2H, quin, J=6.6 Hz, CH_2), 2.34 and 2.40 (each 2H, t, J=6.6 Hz, CH_2), 6.35 (1H, br s, NH); ms: m/z 168 (M^+).

Anal. Calcd. for $C_9H_{16}N_2O$: C, 64.25; H, 9.59; N, 16.65. Found: C, 64.13; H, 9.72; N, 16.50.

6-*t*-Butylamino-5-methyl-4,5-dihydro-3*H*-pyridin-2-one (**5h**).

This compound was obtained as a white powder, mp 180.0-180.5°; ir: 3253, 1639, 1601, 1547, 1500, 1473, 1451, 1398 cm^{-1}; ^1H nmr: δ 1.26 (3H, d, J=7.3 Hz, CH_3), 1.46 (9H, s, $C(CH_3)_3$), 1.69 and 2.00 (each 1H, m, CH_2), 2.37-2.55 (3H, m, CH_2 and CH), 5.85 (1H, br s, NH); ms: m/z 182 (M^+).

Anal. Calcd. for $C_{10}H_{18}N_2O$: C, 64.90; H, 9.95; N, 15.37. Found: C, 65.90; H, 10.23; N, 15.27.

6-*t*-Butylamino-5-ethyl-4,5-dihydro-3*H*-pyridin-2-one (**5i**).

This compound was obtained as a white powder, mp 184.0-184.5°; ir: 3252, 1643, 1592, 1547, 1500, 1475, 1452, 1394 cm^{-1}; ^1H nmr: δ 0.99 (3H, t, J=7.4 Hz, CH_3), 1.47 (9H, s, $C(CH_3)_3$), 1.54 –1.71 (2H, m, CH_2), 1.82, 1.95 and 2.12 (each 1H, m, CH_2 and CH), 2.38-2.51 (2H, m, CH_2), 5.66 (1H, br s, NH); ms: m/z 196 (M^+).

Anal. Calcd. for $C_{11}H_{20}N_2O$: C, 67.31; H, 10.27; N, 14.27. Found: C, 67.01; H, 10.48; N, 14.07.

6-*t*-Butylamino-5,5-dimethyl-4,5-dihydro-3*H*-pyridin-2-one (**5j**).

This compound was obtained as a white powder, mp 181.0-

182.0°; ir: 3336, 1738, 1647, 1558, 1514, 1469, 1444 cm^{-1}; ^1H nmr: δ 1.24 (6H, s, $2CH_3$), 1.46 (9H, s, $C(CH_3)_3$), 1.75 and 2.51 (each 2H, t, J=6.8 Hz, CH_2), 5.27 (1H, br s, NH); ms: m/z 196 (M^+).

Anal. Calcd. for $C_{11}H_{20}N_2O$: C, 67.31; H, 10.27; N, 14.27. Found: C, 67.30; H, 10.55; N, 14.38.

1-*t*-Butylamino-2-azaspiro[5,5]undec-1-en-3-one (**5k**).

This compound was obtained as a white powder, mp 193.5-194.5°; ir: 3342, 1639, 1552, 1502, 1477, 1442 cm^{-1}; ^1H nmr: δ 1.46 (9H, s, $C(CH_3)_3$), 1.45-1.73 (10H, m, $(CH_2)_5$), 1.86 and 2.47 (each 2H, t, J=6.8 Hz, CH_2), 5.45 (1H, br s, NH); ms: m/z 236 (M^+).

Anal. Calcd. for $C_{14}H_{24}N_2O$: C, 71.14; H, 10.23; N, 11.85. Found: C, 71.11; H, 10.52; N, 11.99.

Trimethyl 2-[1-(*N*-*t*-Butylamino)-2-phenylethylidene])amino-1,1,2-ethanetricarboxylate (**10a**).

To a stirred solution of *N*-*t*-butylbenzylamidine (**1a**) (2.85 g, 15.0 mmoles) in ether (30 ml) at room temperature was added dropwise a solution of trimethyl ethylenetricarboxylate (**9**) (3.03 g 15.0 mmoles) in ether (30 ml) during 15 minutes. When the reaction mixture was further stirred for 30 minutes at room temperature a white precipitate began to separate from solution. The reaction mixture was further stirred at room temperature. After 2 hours, the crystalline solid was collected by filtration to give 4.46 g of *N*-alkylation product **10a**. Evaporation of the filtrate yielded an additional 0.99 g of **10a**. The total yield of **10a** was 5.45 g (93 %), as pale yellow needles. An analytical sample was prepared by further recrystallization from ether: mp 101.0-101.5°; ir: 3400, 1747, 1726, 1620, 1529, 1437 cm^{-1}; ^1H nmr: δ 1.20 (9H, s, $C(CH_3)_3$), 3.67 (3H, s, CO_2CH_3), 3.68 (5H, s, CO_2CH_3 and CH_2), 3.73 (3H, s, CO_2CH_3), 3.78 (1H, br s, NH), 4.20 and 4.83 (each 1H, d, J=9.3 Hz, CH), 7.18-7.30 (5H, m, aromatic); ms: m/z 392 (M^+).

Anal. Calcd. for $C_{20}H_{28}N_2O_4$: C, 61.21; H, 7.19; N, 7.14. Found: C, 61.16; H, 7.15; N, 7.16.

Conversion to 3,4-Dihydropyrrol-2-one derivative **11a** of *N*-Alkylation Product **10a**.

A solution of *N*-alkylation product **10a** (3.04 g, 8.0 mmoles) in diglyme (16 ml) was heated with stirring at 150° for 3 hours. The solvent was removed under reduced pressure and the residual solid was recrystallized from carbon tetrachloride to give 2.57 g (89 %) of **11a** as a white powdery solid, mp 146.5-150.0°.

3,4-Dihydropyrrol-2-ones **11**.

A solution containing *N*-*t*-butylacetamidines **1** (10.0 mmoles) and trimethyl ethylenetricarboxylate (**9**) (10.5 mmoles) in diglyme (20 ml) was heated with stirring at 150° for 3 hours. After removal of the solvent under reduced pressure, the residual solid was recrystallized from carbon tetrachloride to give **11**. All the products obtained were of satisfactory purity as judged by ^1H nmr spectroscopy. Analytical samples were prepared by recrystallization from monoglyme.

Dimethyl 2-(5-*t*-Butylamino-2-oxo-4-phenyl-3,4-dihydro-2*H*-pyrrol-3-yl)-malonate (**11a**).

This compound was obtained as a white powder, mp 149.5-151.0°; ir: 3240, 1757, 1738, 1703, 1657, 1579, 1531, 1437 cm^{-1}; ^1H nmr: δ 1.41 (9H, s, $C(CH_3)_3$), 3.09 (1H, dd, J=5.9, 4.9 Hz, CH), 3.39 and 3.70 (each 3H, s, CO_2CH_3), 4.14 (1H, d, J=4.9 Hz, CH), 4.37 (1H, d, J=5.9 Hz, CH), 5.08 (1H, br s, NH), 7.10-7.39 (5H, m, aromatic); ms: m/z 360 (M^+).

Anal. Calcd. for $C_{19}H_{24}N_2O_5$: C, 63.32; H, 6.71; N, 7.77. Found: C, 63.46; H, 6.88; N, 7.74.

Dimethyl 2-[5-*t*-Butylamino-4-(4-chlorophenyl)-2-oxo-3,4-dihydro-2*H*-pyrrol-3-yl]malonate (**11b**).

This compound was obtained as white prisms, mp 139.5-140.5°; ir: 3294, 1755, 1736, 1703, 1574, 1529, 1491, 1438 cm^{-1}; ^1H nmr: δ 1.41 (9H, s, $C(CH_3)_3$), 3.01 (1H, dd, J=5.6, 4.6 Hz, CH), 3.46 and 3.71 (each 3H, s, CO_2CH_3), 4.15 (1H, d, J=4.6 Hz, CH), 4.37 (1H, d, J=5.6 Hz, CH), 5.04 (1H, br s, NH), 7.07 and 7.35 (each 2H, d, J=8.5 Hz, aromatic); ms: m/z 394 (M^+).

Anal. Calcd. for $C_{19}H_{23}ClN_2O_5$: C, 57.80; H, 5.87; N, 7.09. Found: C, 57.42; H, 5.92; N, 7.03.

Dimethyl 2-[4-(4-Bromophenyl)-5-*t*-butylamino-2-oxo-3,4-dihydro-2*H*-pyrrol-3-yl]malonate (**11c**).

This compound was obtained as white needles, mp 168.0-168.5°; ir: 3294, 1755, 1736, 1703, 1576, 1527, 1489, 1437 cm^{-1}; ^1H nmr: δ 1.41 (9H, s, $C(CH_3)_3$), 3.00 (1H, dd, J=5.4, 4.6 Hz, CH), 3.47 and 3.71 (each 3H, s, CO_2CH_3), 4.14 (1H, d, J=4.6 Hz, CH), 4.35 (1H, d, J=5.4 Hz, CH), 5.14 (1H, br s, NH), 7.01 and 7.50 (each 2H, d, J=8.3 Hz, aromatic); ms: m/z 438 and 440 (M^+).

Anal. Calcd. for $C_{19}H_{23}BrN_2O_5$: C, 51.95; H, 5.28; N, 6.38. Found: C, 52.24; H, 5.42; N, 6.39.

Dimethyl 2-[5-*t*-Butylamino-4-(4-methoxyphenyl)-2-oxo-3,4-dihydro-2*H*-pyrrol-3-yl]malonate (**11d**).

This compound was obtained as white needles, mp 147.0-148.0°; ir: 3238, 1736, 1703, 1579, 1541, 1510, 1458 cm^{-1}; ^1H nmr: δ 1.41 (9H, s, $C(CH_3)_3$), 3.05 (1H, dd, J=5.9, 4.9 Hz, CH), 3.42 (3H, s, OCH_3), 3.70 and 3.81 (each 3H, s, CO_2CH_3), 4.13 (1H, d, J=4.9 Hz, CH), 4.32 (1H, d, J=5.9 Hz, CH), 5.09 (1H, br s, NH), 6.89 and 7.03 (each 2H, d, J=8.7 Hz,, aromatic); ms: m/z 390 (M^+).

Anal. Calcd. for $C_{20}H_{26}N_2O_6$: C, 61.53; H, 6.71; N, 7.18. Found: C, 61.88; H, 6.92; N, 7.22.

Dimethyl 2-[5-*t*-Butylamino-4-(4-methylphenyl)-2-oxo-3,4-dihydro-2*H*-pyrrol-3-yl]malonate (**11e**).

This compound was obtained as white needles, mp 168.5-169.5°; ir: 3240, 1749, 1697, 1591, 1545, 1514, 1431 cm^{-1}; ^1H nmr: δ 1.40 (9H, s, $C(CH_3)_3$), 2.35 (3H, s, CH_3), 3.07 (1H, dd, J=5.9, 4.9 Hz, CH), 3.40 and 3.70 (each 3H, s, CO_2CH_3), 4.13 (1H, d, J=4.9 Hz, CH), 4.33 (1H, d, J=5.9 Hz, CH), 5.05 (1H, br s, NH), 6.99 and 7.17 (each 2H, d, J=8.1 Hz, aromatic); ms: m/z 374 (M^+).

Anal. Calcd. for $C_{20}H_{26}N_2O_5$: C, 64.15; H, 7.00; N, 7.48. Found: C, 64.24; H, 7.22; N, 7.44.

Dimethyl 2-(4-Benzyl-5-*t*-butylamino-2-oxo-3,4-dihydro-2*H*-pyrrol-3-yl)-malonate (**11f**).

This compound was obtained as white needles, mp 189.0-190.5°; ir: 3230, 1759, 1738, 1697, 1595, 1522, 1446 cm^{-1}; ^1H nmr: δ 1.24 (9H, s, $C(CH_3)_3$), 2.62 (1H, dd, J=13.7, 11.2 Hz, CH_2), 2.81 (1H, t, J=4.4 Hz, CH), 3.29 (1H, dd, J=13.7, 4.4 Hz, CH_2), 3.39 (1H, dt, J=11.2, 4.4 Hz, CH), 3.68 and 3.79 (each 3H, s, CO_2CH_3), 4.13 (1H, d, J=4.4 Hz, CH), 4.89 (1H, br s, NH), 7.25-7.40 (5H, m, aromatic); ms: m/z 374 (M^+).

Anal. Calcd. for $C_{20}H_{26}N_2O_5$: C, 64.15; H, 7.00; N, 7.48. Found: C, 64.08; H, 7.01; N, 7.49.

Dimethyl 2-(5-*t*-Butylamino-2-oxo-3,4-dihydro-2*H*-pyrrol-3-yl)malonate (**11g**).

This compound was obtained as white needles, mp 173.0-174.0°; ir: 3234, 1741, 1699, 1597, 1520, 1490, 1465, 1437 cm^{-1}; ^1H nmr: δ 1.46 (9H, s, $C(CH_3)_3$), 2.88 (1H, dd, J=13.0, 6.3 Hz, CH_2), 2.91 (1H, dd, J=13.0, 7.8 Hz, CH_2), 3.10 (1H, ddd, J=7.8, 6.3, 5.4, Hz, CH), 3.69 and 3.76 (each 3H, s, CO_2CH_3), 4.01 (1H, d, J=5.4 Hz, CH), 6.71 (1H, br s, NH); ms: m/z 284 (M^+).

Anal. Calcd. for $C_{13}H_{20}N_2O_5$: C, 54.92; H, 7.09; N, 9.85. Found: C, 55.18; H, 7.10; N, 9.75.

Dimethyl 2-(5-*t*-Butylamino-4,4-dimethyl-2-oxo-3,4-dihydro-2*H*-pyrrol-3-yl)-malonate (**11j**).

This compound was obtained as white needles, mp 176.0-177.0°; ir: 3294, 1747, 1693, 1572, 1531, 1460, 1435 cm^{-1}; ^1H nmr: δ 1.17 and 1.39 (each 3H, s, CH_3), 1.49 (9H, s, $C(CH_3)_3$), 3.20 and 3.61 (each 1H, d, J=10.6 Hz, CH), 3.75 and 3.80 (each 3H, s, CO_2CH_3), 5.84 (1H, br s, NH); ms: m/z 312 (M^+).

Anal. Calcd. for $C_{15}H_{24}N_2O_5$: C, 57.68; H, 7.74; N, 8.97. Found: C, 57.76; H, 7.85; N, 9.02.

1,3-Dihydropyrrol-2-ons **13**.

A solution containing *N*-*t*-butylacetamidines **1** (20.0 mmoles) and dimethyl acetylenedicarboxylate (**12**) (20.0 mmoles) in diglyme (40 ml) was heated with stirring at 150° for the time indicated in Table 2. After removal of the solvent under reduced pressure, the residue was recrystallized from ethyl acetate–hexane to give **13**. All the products obtained were of satisfactory purity as judged by ^1H nmr spectroscopy. Samples for analysis were recrystallized from monoglyme.

Methyl (5-*t*-Butylamino-2-oxo-4-phenyl-1,2-dihydropyrrol-3-ylidene)acetate (**13a**).

This compound was obtained as dark red prisms, mp 189.0-189.5°; ir: 3411, 1668, 1579, 1523, 1442 cm^{-1}; ^1H nmr: δ 1.55 (9H, s, $C(CH_3)_3$), 3.80 (3H, s, CO_2CH_3), 5.85 (1H, br s, NH), 5.94 (1H, s, CH), 7.17-7.27 and 7.37-7.42 (5H, m, aromatic) 9.05 (1H, br s, NH); ms: m/z 300 (M^+).

Anal. Calcd. for $C_{17}H_{20}N_2O_3$: C, 67.98; H, 6.71; N, 9.33. Found: C, 67.80; H, 6.77; N, 9.47.

Methyl [5-*t*-Butylamino-4-(4-chlorophenyl)-2-oxo-1,2-dihydropyrrol-3-ylidene]acetate (**13b**).

This compound was obtained as as red needles, mp 222.0-222.5°; ir: 3400, 1689, 1670, 1597, 1523, 1437 cm^{-1}; ^1H nmr: δ 1.56 (9H, s, $C(CH_3)_3$), 3.81 (3H, s, CO_2CH_3), 5.75 (1H, br s, NH), 5.93 (1H, s, CH), 7.35 (4H, s, aromatic) 9.09 (1H, br s, NH); ms: m/z 334 (M^+).

Anal. Calcd. for $C_{17}H_{19}ClN_2O_3$: C, 60.99; H, 5.72; N, 8.37. Found: C, 60.75; H, 5.80; N, 8.26.

Methyl [4-(4-Bromophenyl)-5-*t*-butylamino-2-oxo-1,2-dihydropyrrol-3-ylidene]acetate (**13c**).

This compound was obtained as light red needles, mp 227.5-228.5°; ir: 3415, 1692, 1672, 1597, 1522, 1439 cm^{-1}; ^1H nmr: δ 1.56 (9H, s, $C(CH_3)_3$), 3.81 (3H, s, CO_2CH_3), 5.78 (1H, br s, NH), 5.92 (1H, s, CH), 7.28 and 7.49 (each 2H, d, J=8.5 Hz, aromatic) 9.08 (1H, br s, NH); ms: m/z 378 and 380 (M^+).

Anal. Calcd. for $C_{17}H_{19}BrN_2O_3$: C, 53.84; H, 5.05; N, 7.39. Found: C, 53.97; H, 5.04; N, 7.36.

Methyl [5-*t*-Butylamino-4-(4-methoxyphenyl)-2-oxo-1,2-dihydropyrrol-3-ylidene]acetate (**13d**).

This compound was obtained as dark red needles, mp 207.0-207.5; ir: 3413, 1693, 1664, 1587, 1533, 1439 cm^{-1}; ^1H nmr: δ 1.54 (9H, s, $C(CH_3)_3$), 3.80 and 3.81 (each 3H, s, OCH_3 or CO_2CH_3), 5.69 (1H, br s, NH), 5.94 (1H, s, CH), 6.95 and 7.31 (each 2H, d, J=8.8 Hz, aromatic) 9.00 (1H, br s, NH); ms: m/z 330 (M^+).

Anal. Calcd. for $C_{18}H_{22}N_2O_4$: C, 65.44; H, 6.71; N, 8.48. Found: C, 65.64; H, 6.73; N, 8.55.

Methyl [5-*t*-Butylamino-4-(4-methylphenyl)-2-oxo-1,2-dihydropyrrol-3-ylidene]acetate (**13e**).

This compound was obtained as red needles, mp 204.5-205.0°; ir: 3396, 1690, 1657, 1583, 1533, 1442 cm^{-1}; ^1H nmr: δ 1.54 (9H, s, $C(CH_3)_3$), 2.34 (3H, s, CH_3), 3.80 (3H, s, CO_2CH_3), 5.79 (1H, br s, NH), 5.94 (1H, s, CH), 7.21 and 7.29 (each 2H, d, J=8.1 Hz, aromatic) 9.02 (1H, br s, NH); ms: m/z 314 (M^+).

Anal. Calcd. for $C_{18}H_{22}N_2O_3$: C, 68.77; H, 7.05; N, 8.91. Found: C, 68.72; H, 7.13; N, 8.93.

Methyl (4-Benzyl-5-*t*-butylamino-2-oxo-1,2-dihydropyrrol-3-ylidene)acetate (**13f**).

This compound was obtained as orange needles, mp 192.5-193.5°; ir: 3406, 1693, 1662, 1587, 1550, 1437 cm^{-1}; ^1H nmr: δ 1.27 (9H, s, $C(CH_3)_3$), 3.59 (2H, s, CH_2), 3.77 (3H, s, CO_2CH_3), 4.79 (1H, br s, NH), 5.89 (1H, s, CH), 7.19-7.31 (5H, m, aromatic), 8.69 (1H, br s, NH); ms: m/z 314 (M^+).

Anal. Calcd. for $C_{18}H_{22}N_2O_3$: C, 68.77; H, 7.05; N, 8.91. Found: C, 69.08; H, 7.27; N, 9.02.

Methyl (5-*t*-Butylamino-4-ethyl-2-oxo-1,2-dihydropyrrol-3-ylidene)acetate (**13i**).

This compound was obtained as orange needles, mp 180.0-180.5°; ir: 3413, 1682, 1658, 1585, 1543, 1437 cm^{-1}; ^1H nmr: δ 1.02 (3H, t, J=7.6 Hz, CH_3), 1.54 (9H, s, $C(CH_3)_3$), 2.14 (2H, q, J=7.6 Hz, CH_2), 3.77 (3H, s, CO_2CH_3), 5.20 (1H, br s, NH), 5.82 (1H, s, CH), 8.72 (1H, br s, NH); ms: m/z 252 (M^+).

Anal. Calcd. for $C_{13}H_{20}N_2O_3$: C, 61.88; H, 7.99; N, 11.10. Found: C, 62.00; H, 8.04; N, 10.99.

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