ADDITION OF 1-BOC-2-*tert*-BUTYLDIMETHYLSILYLOXYPYRROLE TO *N*-METHYLENEAMINE EQUIVALENTS: SYNTHESIS OF 1-BOC-5-AMINOMETHYL-2,5-DIHYDROPYRROL-2-ONES AND 1-BOC-2-OXO-1,7,9-TRIAZASPIRO[4,5]DEC-3-ENES[1,†]

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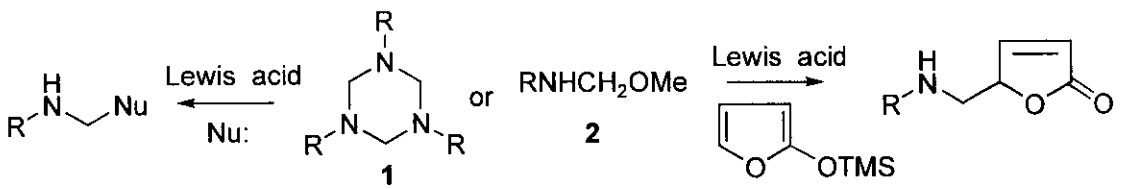
Abstract - *N*-Methyleneamine equivalents generated from 1,3,5-triphenylhexahydro-1,3,5-triazines or *N*-methoxymethylanilines reacted with 1-Boc-2-*tert*-butyldimethylsilyloxypyrrole to give 1-Boc-5-anilinomethyl-2,5-dihydropyrrol-2-ones. However, the same reaction from 1,3,5-trialkylhexahydro-1,3,5-triazines yielded unexpected product of 1-Boc-7,9-dialkyl-2-oxo-1,7,9-triazaspiro[4,5]dec-3-enes.

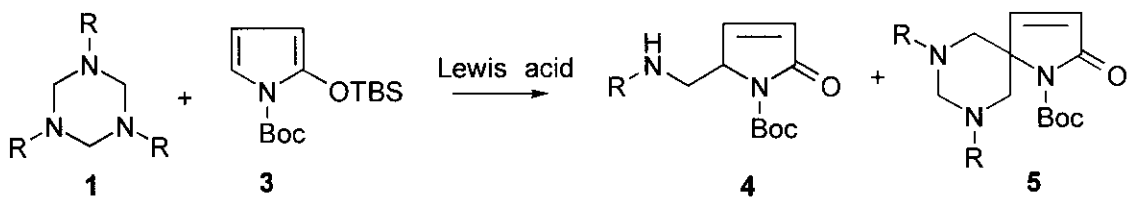
The Mannich reaction[2] involving one of the simplest imines, *N*-methyleneamine (monomeric formaldehyde imine), is very limited from a synthetic viewpoint because it is difficult to generate the methyleneamine. Recently we reported that *N*-methyleneamine equivalents can be generated from hexahydro-1,3,5-triazenes and (or) *N*-methoxymethylamines in the presence of a Lewis acid and used for aminomethylation reaction with various nucleophiles.[3]



Scheme 1

† To celebrate on the occasion to publish the Volume 50 of this journal.

Heteroatom nucleophiles of phosphorus[3a,b] and azide[3d] gave aminomethylphosphonates and aminomethyl azide. Hydride addition to *N*-methyleneamine equivalents afforded *N*-methylamines in good yield.[3g] Reaction with cyanotrimethylsilane gave a facile route to aminoacetonitrile.[3c] Synthetically useful aziridine-2-carboxylates were also prepared from the reaction with alkyldiazoacetate.[3f,i] Other carbon nucleophiles of allyltrimethylsilane, tri-*n*-butylallyltin, and propargyltrimethylsilane yielded allylated and propargylated products at the α-position of amine with some cyclized quinoline derivatives from branching of the cationic intermediates.[3e,h] Another nucleophile of 2-trimethylsilyloxyfuran with catalytically generated *N*-methyleneamine equivalents yielded the aminomethylated product of 5-aminomethyl-2,5-dihydrofuran-2-one in good yield as shown in Scheme 1.[4] Based on this reaction the similar nucleophile of 1-Boc-2-*tert*-butyldimethylsilyloxypyrrole[5] was applied to *N*-methyleneamine equivalents with expectation getting the simple aminomethylated product of 1-Boc-5-aminomethyl-2,5-dihydropyrrol-2-ones. The expected product is valuable not only for the versatile synthetic template[6] but for the precursor toward homologous of pharmaceutically important 5-benzamidomethyl-1-ethyl-2-pyrrolidine[7] represented by remoxipride and raclopride.



Scheme 2

In this report is described the reaction between hexahydro-1,3,5-triazenes (**1**) and (or) *N*-methoxymethylamines (**2**) in the presence of a Lewis acid with the nucleophile of 1-Boc-2-*tert*-butyldimethylsilyloxypyrrole (**3**). Based on the previous knowledge from the reaction with 2-trimethylsilyloxyfuran we carried out the reaction of 1,3,5-triphenylhexahydro-1,3,5-triazine (**1a**) with 1-Boc-2-*tert*-butyldimethylsilyloxypyrrole in the presence of the catalytic amount of several different Lewis acids.[8] Lewis acids such as $TiCl_4$, $SnCl_4$ and $AlCl_3$ showed poor reaction yields to get 1-Boc-5-aminomethyl-2,5-dihydropyrrol-2-one. Instead significant amount of the desilylated nucleophile of 1-Boc-2,5-dihydropyrrol-2-one was obtained (entries 1, 2 and 3). $Ti(O\textit{i}Pr)_4$ was not good while it was the best as a catalyst for the reaction of 1,3,5-triphenylhexahydro-1,3,5-triazine with the similar nucleophile of 2-trimethylsilyloxyfuran (entries 4 and 5). This means that the reaction depends on the characteristics of the Lewis acid used that has dual roles on the reaction not only generating *N*-methyleneamine equivalents from hexahydro-1,3,5-triazenes but also catalyzing the coupling with the nucleophile. Non-metallic catalysts of TMSOTf and $BF_3 \cdot OEt_2$ improved the reaction to obtain the expected product in 67 and 78%

yields respectively (entries 6 and 7). One mole equivalent of $BF_3 \cdot OEt_2$ did not improve the reaction at all (entry 8). Under the condition with 5 mol % of $BF_3 \cdot OEt_2$ the reaction proceeded well with the most compounds bearing 2-Me, 2,5-Cl_2 and 4-F in the benzene ring with over 50% isolated yields (entries 9, 10 and 11).

Table 1. Reactions of 1,3,5-trisubstituted hexahydro-1,3,5-triazines (**1**) with 1-Boc-2-*tert*-butyldimethylsilyloxypyrrole (**3**) in the presence of Lewis acid.

entry	Substrate	R	Lewis Acid	mol %	Temp (°C)	Time (h)	**4**	**5**
1	**1a**	Ph	$TiCl_4$	5	-78	1	12	
2	**1a**	Ph	$SnCl_4$	5	-78	1	22	
3	**1a**	Ph	$AlCl_3$	5	-78	1	45	
4	**1a**	Ph	$Ti(OiPr)_4$	5	-78	1	56	
5	**1a**	Ph	$Ti(OiPr)_4$	100	-78	0.5	38	
6	**1a**	Ph	TMSOTf	5	-78	1	67	
7	**1a**	Ph	$BF_3 \cdot OEt_2$	5	-78	1	78	
8	**1a**	Ph	$BF_3 \cdot OEt_2$	100	-78	0.2	61	
9	**1b**	2-Me-C_6H_4	$BF_3 \cdot OEt_2$	5	-78	1	51	
10	**1c**	2,5-Cl_2-C_6H_3	$BF_3 \cdot OEt_2$	5	-78	1	68	
11	**1d**	4-F-C_6H_4	$BF_3 \cdot OEt_2$	5	-78	1	54	
12	**1f**	$PhCH_2$	$BF_3 \cdot OEt_2$	100	-78	8		nr
13	**1f**	$PhCH_2$	$BF_3 \cdot OEt_2$	100	rt	5		60
14	**1g**	(R)-PhMeCH	$BF_3 \cdot OEt_2$	100	rt	5	17	46
15	**1h**	Et	$BF_3 \cdot OEt_2$	100	rt	4		79
16	**1i**	C_6H_{11}	$BF_3 \cdot OEt_2$	100	rt	4		74

Once we have found that the reactions with 1,3,5-triphenylhexahydro-1,3,5-triazines worked well, another substrate of 1,3,5-tribenzylhexahydro-1,3,5-triazine (**1f**) was applied. Under the same reaction condition of -78 °C with $BF_3 \cdot OEt_2$ the reaction did not proceed at all leaving all starting material unreacted (entry 12). This implied that *N*-methyleneamine equivalents to be reacted with nucleophile were not generated with one mole equivalent of $BF_3 \cdot OEt_2$ at -78 °C. Therefore other Lewis acids such as $TiCl_4$, $SnCl_4$, $AlCl_3$ and $Ti(OiPr)_4$ were applied to the reaction at -78 °C to yield complex mixture of reaction products including some of hydrolyzed benzylamine without formation of our expected product of 1-Boc-5-benzylaminomethyl-2,5-dihydropyrrol-2-one. One equivalent of the Lewis acid $BF_3 \cdot OEt_2$ at room

temperature proceeded the reaction to give one major product (entry 13). This product was not 1-Boc-5-aminomethyl-2,5-dihydropyrrol-2-one (**4f**) of what we expected. ^{1}H NMR recorded twice amount of benzylic protons in the absence of one proton peak at 4.5 – 4.8 ppm corresponding to the proton at C-5 of dihydropyrrole. Based on the spectral date we deduced the structure of the product as 1-Boc-7,9-dibenzyl-2-oxo-1,7,9-triazaspiro[4,5]dec-3-ene (**5f**) that was further identified by X-Ray analysis of single crystals as in Figure 1.[9]

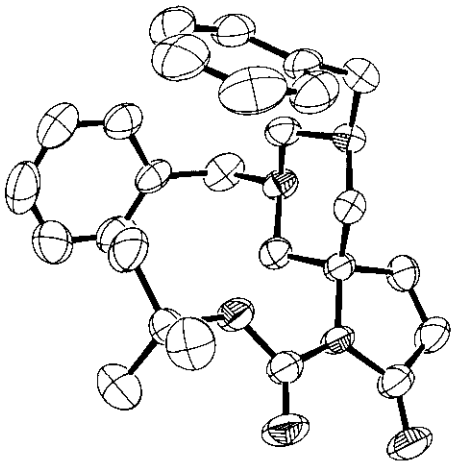


Figure 1. X-Ray structure of **5f**.

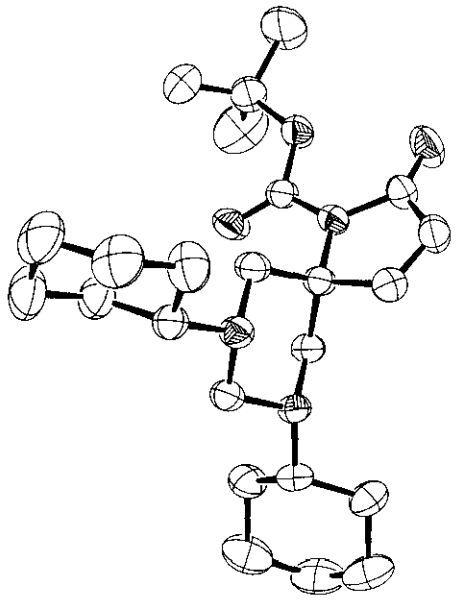
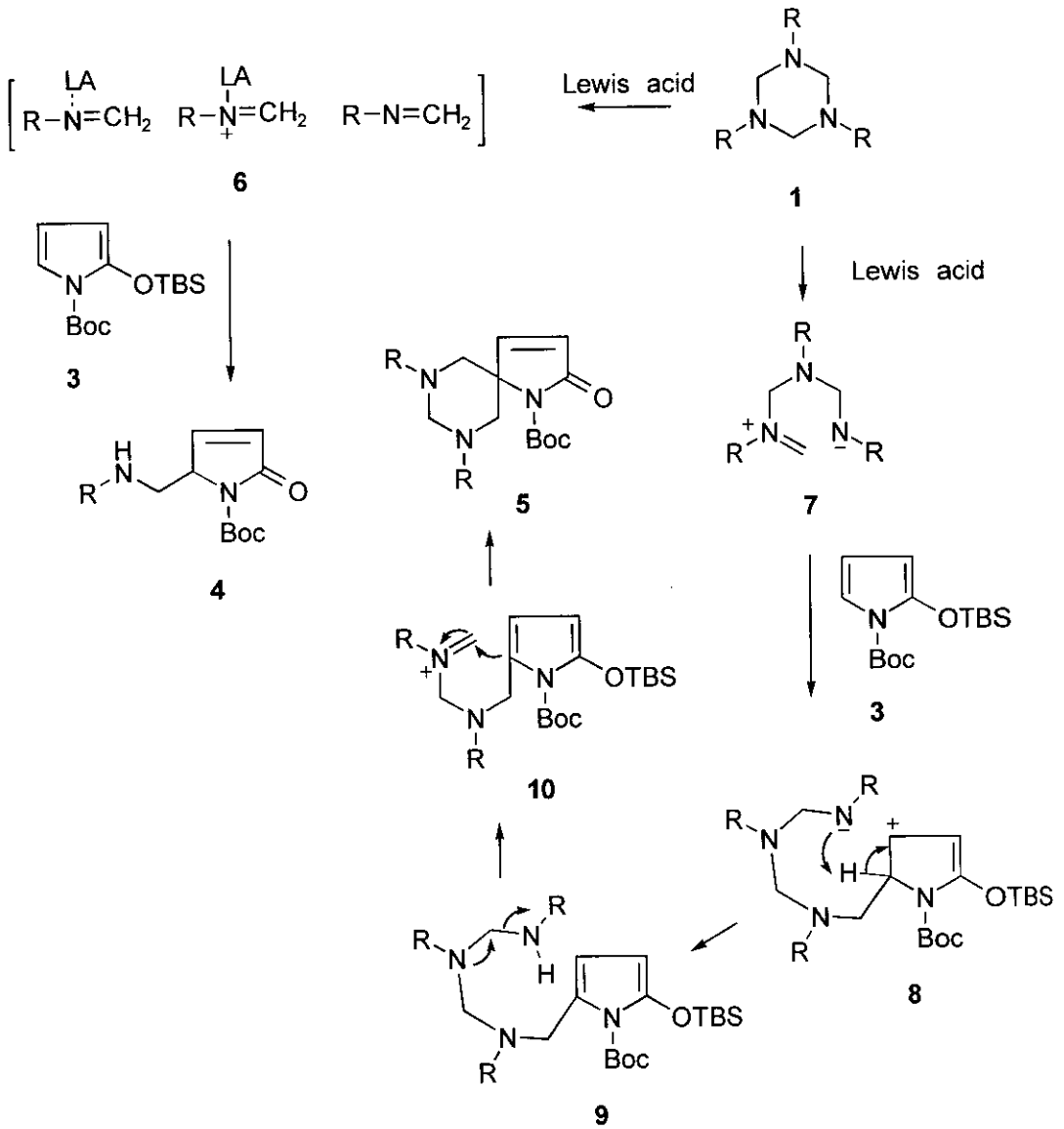


Figure 2. X-Ray structure of **5i**.

The plausible reaction mechanism can be drawn as shown in Scheme 3 with comparison to the formation of 1-Boc-5-anilinomethyl-2,5-dihydropyrrol-2-ones. Under the condition to break down the trimeric unit of 1,3,5-triphenylhexahydro-1,3,5-triazine (**1**, R = Ph) completely the monomer of *N*-methyleneamine equivalents (**6**) is generated and reacted with the nucleophile of 1-Boc-2-*tert*-butyldimethylsilyloxypyrrole to form only aminomethylated product of 1-Boc-5-anilinomethyl-2,5-dihydropyrrol-2-ones. When the fragmentation of 1,3,5-trisubstituted hexahydro-1,3,5-triazine (**1**, R = alkyl) is not completed to generate *N*-methyleneamine equivalents as a monomer drawn in the bracket of **6**, zwiterionic intermediate like **7** as a possibly coordinated complex with the Lewis acid can be formed by breaking one single bond of carbon and nitrogen.[10] The reaction of **7** with the nucleophile of 1-Boc-2-*tert*-butyldimethylsilyloxypyrrole gives an adduct (**8**) bearing an electron rich anionic nitrogen that may complex with the Lewis acid in anyhow. Immediate abstraction of proton at C-5 by the basic nitrogen regenerates another type of nucleophile like

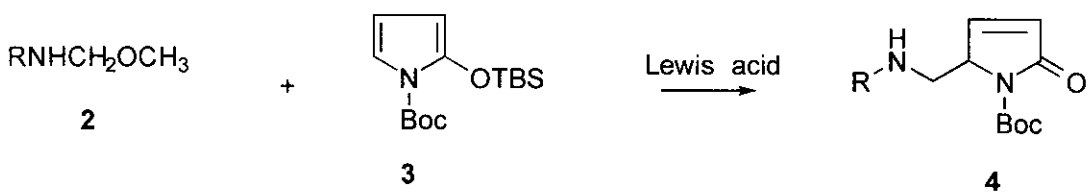
9. Mannich base is generated again from **9** in the presence of Lewis acid with the removal of one amine that is ready to be reacted with internally pre-formed nucleophile. One more intramolecular aminomethylation at C-5 of the reactive intermediate by Mannich base like **10** gives a double aminomethylated product of 1-Boc-2-oxo-7,9-dibenzyl-1,7,9-triazaspiro[4,5]dec-3-ene. Under this condition could not be obtained mono-aminomethylated product of 1-Boc-5-aminomethyl-2,5-dihydropyrrol-2-ones.[10]



Scheme 3

This implies that two pathways giving different products are not competing each other. Instead these two pathways are pre-determined by characteristics of R, the substituent of 1,3,5-trisubstituted hexahydro-1,3,5-triazine (**1**). When R is phenyl, the monomeric fragments of **6** from 1,3,5-triphenylhexahydro-1,3,5-trazine were stabilized by conjugation with phenyl. This seems the most important driving force to intrude the reaction starting from 1,3,5-triphenylhexahydro-1,3,5-trazine to yield monoaminomethylated product (**4**). While R is alkyl no extra stabilization exists to drive the fragmentation up to the monomers like **6**. Instead there is equilibrium between break and formation of one carbon-nitrogen bond like **7** derived by the Lewis acid of $BF_3 \cdot OEt_2$. This may be a reason why the reaction requires one mole equivalent of Lewis acid. In a case of the substrate with the phenylethyl substituent (**1g**) both pathways were allowed to yield two products of **4g** and **5g** in 17 and 46% yields respectively. Monoaminomethylated product of **4g** was obtained as a diastereomeric mixture with the ratio of 58:42. Formation of double aminomethylated product at C-5 of nucleophile was observed as a major product. Under this condition did work the reaction from all substrates bearing the alkyl substituents like ethyl (**1h**), and cyclohexyl (**1i**) in good yield (entries 15 and 16). The X-Ray crystal structure[11] of 7,9-dicyclohexyl-2-oxo-1,7,9-triazaspiro[4,5]dec-3-ene (**5i**) is shown in Figure 2.

Another known source to get *N*-methyleneamine equivalents is from *N*-methoxymethylanilines in the presence of Lewis acid. The previous reaction characteristics of *N*-methyleneamine equivalents from *N*-methoxymethylanilines suggest the formation of monoaminomethylated product of 1-Boc-5-anilinomethyl-2,5-dihydropyrrol-2-ones (Table 2).



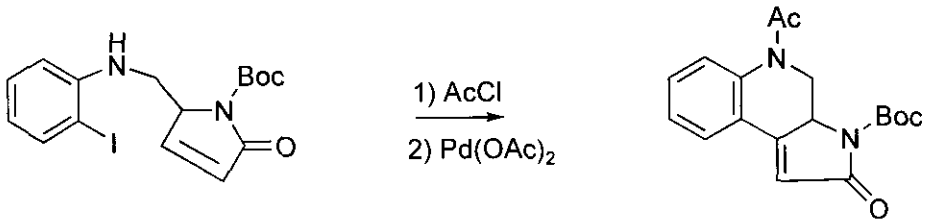
Scheme 4

Table 2. Reactions of *N*-methoxymethylanilines (**2**) with 1-Boc-2-*tert*-butyldimethylsilyloxypyrrole (**3**).

Entry	Substrate	R	Lewis Acid	mol %	Temp (°C)	Time (h)	**4**
1	**2a**	Ph	$BF_3 \cdot OEt_2$	5	-78	1	67
2	**2b**	2-Me-C_6H_4	$BF_3 \cdot OEt_2$	5	-78	1	52
3	**2c**	2,5-Cl_2-C_6H_3	$BF_3 \cdot OEt_2$	5	-78	1	72
4	**2e**	2-I-C_6H_4	$BF_3 \cdot OEt_2$	5	-78	1	80

As we expected we could obtained 1-Boc-5-anilinomethyl-2,5-dihydropyrrol-2-one (**4a**) from the reaction of *N*-methoxymethylaniline (**2a**) with the nucleophile of 1-Boc-2-*tert*-butyldimethylsilyloxypyrrole (**3**) in 67% yield (entry 1). Under the same condition of 5 mol % of $BF_3 \cdot OEt_2$ at -78 °C did work the reactions from the substrates with the substituents (**2b-c**, **2e**) on the phenyl ring such as 2-Me, 2,5-Cl_2 and 2-I (entries 2, 3 and 4).

1-Boc-5-(2-iodoanilinomethyl)-2,5-dihydropyrrol-2-one (**4e**) elaborated further to noble tricyclic compound through *N*-acetyl protection and Heck reaction[13] with $Pd(OAc)_2$, PPh_3 and Et_3N in MeCN to give 5-acetyl-3-Boc–2-oxo-3,3a,4,5-tetrahydropyrrolo[2,3-*c*]quinoline (**11**) in 84% yield.



4e **11**

Scheme 5

In conclusion *N*-Methyleneamine equivalents generated from 1,3,5-trisubstituted hexahydro-1,3,5-triazines reacted with the nucleophile of 1-Boc-2-*tert*-butyldimethylsilyloxypyrrole yielded either 1-Boc-5-anilinomethyl-2,5-dihydropyrrol-2-ones or 1-Boc-7,9-dialkyl-2-oxo-1,7,9-triazaspiro[4,5]dec-3-enes depending on the substituents of phenyl and alkyl respectively. The same reaction starting from *N*-methoxymethylanilines also gave 1-Boc-5-anilinomethyl-2,5-dihydropyrrol-2-ones.

EXPERIMENTAL

^1H NMR and ^{13}C-NMR spectra were recorded on a Varian Gemini 200 (200 MHz for ^1H and 50.3 MHz for ^{13}C). Chemical shifts were given in ppm using TMS as internal standard. IR spectra were obtained using Perken-Elmer System 2000 FT-IR spectrophotometer. Elemental analysis was taken on a Perkin-Elmer 240 DS elemental analyzer. Melting point was measured by Mel-II capillary melting point apparatus. The silica gel used for column chromatography was Merck 200-230 mesh. TLC was carried out with Merck 60F-254 plates with 0.25 mm thickness. *N*-Methoxymethylanilines[3a] and 1-Boc-2-*tert*-butyldimethylsilyloxypyrrole[5] were prepared by the reported method. 1,3,5-Hexahydrotriazines were obtained by the conventional method with amine and formaldehyde. Some of *N*-methyoxymethylanilines and 1,3,5-triphenylhexahydro-1,3,5-triazines were interconvertible.[3c] All the other chemicals were reagent grade and used without further purification.

General Procedure: To a stirred solution of 1,3,5-trisubstituted hexahydro-1,3,5-triazine (3.0 mmol) or *N*-methoxymethylanilines (9.0 mmol) in CH_2Cl_2 (30 mL) was added slowly the specified Lewis acid in certain amount under the specified temperature. After being stirred for 10 min 1-Boc-2-*tert*-butyldimethylsilyloxypyrrole (2.65 g, 9.0 mmol) was added to it. The resulting solution was stirred at the specified temperature until all starting materials disappeared on TLC. The reaction mixture was poured into ice-water. The resulting solution was neutralized with cold sat. $NaHCO_3$ solution. The reaction product was extracted with CH_2Cl_2. Organic layer was washed successively with water and brine, dried over anhydrous Na_2SO_4, filtered, and concentrated under reduced pressure. The crude product was purified by flash chromatography.

1-Boc-5-anilinomethyl-2,5-dihydropyrrol-2-one (4a): mp 111-113 °C (EtOAc + Hexane); ^{1}H-NMR ($CDCl_3$) δ: 1.52 (9H, s), 3.27 (1H, dd, J = 13.6 and 7.6 Hz), 3.83 (1H, dd, J = 13.6 and 4.0 Hz), 3.91 (1H, br s), 4.74 - 4.78 (1H, m), 6.05 (1H, dd, J = 6.2 and 1.2 Hz), 6.56 - 6.68 (3H, m), 7.10 (2H, t, J = 7.6 Hz) and 7.19 (1H, dd, J = 6.2 and 1.8 Hz); ^{13}C-NMR ($CDCl_3$) δ: 28.0, 45.2, 61.7, 83.4, 112.6, 117.9, 127.1, 129.3, 147.4, 149.6, 149.9 and 169.2. IR (KBr) ν 3365, 1772, 1604, 1369 and 1160 cm^{-1}. Anal. Calcd for $C_{16}H_{20}N_2O_3$: C, 66.7; H, 6.99; N, 9.72. Found: C, 66.6; H, 7.16; N, 9.64.

1-Boc-5-(2-methylanilinomethyl)-2,5-dihydropyrrol-2-one (4b): mp 95-96 °C (EtOAc + Hexane); ^{1}H-NMR ($CDCl_3$) δ: 1.52 (9H, s), 2.03 (3H, s), 3.32 (1H, dd, J = 11.6 and 8.2 Hz), 3.79 – 3.88 (m, 2H), 4.78 - 4.83 (1H, m), 6.05 (1H, dd, J = 6.4 and 1.6 Hz), 6.56 - 6.68 (2H, m), 7.06 - 7.14 (2H, m) and 7.19 (1H, dd, J = 6.2 and 1.8 Hz); ^{13}C-NMR ($CDCl_3$) δ: 17.2, 28.0, 45.5, 61.5, 83.4, 109.5, 117.5, 121.9, 127.0, 127.1, 130.3, 145.2, 149.8, 149.9 and 169.0. IR (KBr) ν 3417, 1775, 1605, 1369, 1317 and 1158 cm^{-1}. Anal. Calcd for $C_{17}H_{22}N_2O_3$: C, 67.5; H, 7.33; N, 9.26. Found: C, 67.1; H, 7.08; N, 9.48.

1-Boc-5-(2,5-dichloroanilinomethyl)-2,5-dihydropyrrol-2-one (4c): mp 122-124 °C (EtOAc + Hexane); ^{1}H-NMR ($CDCl_3$) δ: 1.53 (9H, s), 3.37 - 3.47 (1H, m), 3.77 - 3.84 (1H, m), 4.55 (1H, t, J = 6.4 Hz), 4.76 - 4.82 (1H, m), 6.12 (1H, dd, J = 6.0 and 1.4 Hz), 6.56 (1H, dd, J = 8.4 and 2.0 Hz), 6.70 (1H, d, J = 2.2 Hz), 7.09 (1H, d, J = 8.4 Hz) and 7.18 (1H, dd, J = 6.1 and 2.0 Hz); ^{13}C-NMR ($CDCl_3$) δ: 28.1, 44.5, 61.1, 83.8, 111.0, 117.5, 117.8, 128.0, 130.1, 133.8, 144.1, 148.8, 149.8 and 168.7. IR (KBr) ν 3383, 1764, 1596, 1371 and 1160 cm^{-1}. Anal. Calcd for $C_{16}H_{18}N_2O_3Cl_2$: C, 53.8; H, 5.08; N, 7.84. Found: C, 54.0; H, 4.89; N, 7.67.

1-Boc-5-(4-fluoroanilinomethyl)-2,5-dihydropyrrol-2-one (4d): mp 128-129 °C (EtOAc + Hexane); ^{1}H-NMR ($CDCl_3$) δ: 1.50 (9H, s), 3.29 (1H, dd, J = 13.5 and 7.4), 3.75 (1H, dd, J = 13.5 and 3.8), 3.83 (1H, br s), 4.72 - 4.77 (1H, m), 6.05 (1H, dd, J = 6.0 and 1.6 Hz), 6.40 - 6.55 (2H, m), 6.76 – 6.85 (2H, m) and 7.20 (1H, dd, J = 6.0 and 2.0 Hz); ^{13}C-NMR ($CDCl_3$) δ: 27.9, 45.8, 61.8, 83.5, 113.5, 113.6, 115.5, 115.9, 127.2, 143.8, 143.9, 149.7, 149.8, 153.6, 158.3 and 169.1. IR (KBr) ν 3395, 1775, 1526, 1386 and

1162 cm^{-1}. Anal. Calcd for $C_{16}H_{19}N_2O_3F$: C, 62.7; H, 6.25; N, 9.14. Found: C, 62.4; H, 6.11; N, 9.31.

1-Boc-5-(2-iodoanilinomethyl)-2,5-dihydropyrrol-2-one (4e): mp 91-93 °C (EtOAc + Hexane); ^{1}H-NMR ($CDCl_3$) δ: 1.60 (9H, s), 3.20 – 3.46 (1H, m), 3.93 - 4.13 (1H, m), 4.35 (1H, t, *J* = 6.2 Hz), 4.81 - 4.87 (1H, m), 6.18 (1H, dd, *J* = 7.6 and 1.4 Hz), 6.48 (1H, t, *J* = 7.6 Hz), 6.76 (1H, d, *J* = 8.2 Hz), 7.18 - 7.31 (2H, m) and 7.65 (1H, dd, *J* = 8.2 and 1.4 Hz); ^{13}C-NMR ($CDCl_3$) δ: 28.0, 45.5, 61.1, 83.6, 85.5, 110.7, 119.4, 127.6, 129.5, 139.3, 146.3, 149.4, 149.7 and 168.8. IR (KBr) ν 3369, 1784, 1585, 1358 and 1162 cm^{-1}. Anal. Calcd for $C_{16}H_{19}N_2O_3I$: C, 46.4; H, 4.62; N,6.76. Found: C, 46.6; H, 4.53; N, 6.95.

1-Boc-5-(1-phenylethylaminomethyl)-2,5-dihydropyrrol-2-one (4g): oil; ^{1}H-NMR ($CDCl_3$) δ: 1.24 (3H, d, *J* = 6.6 Hz), 1.40 (9H, s), 1.67 (1H, br s), 2.60 - 2.80 (1H, m), 2.89 - 3.05 (1H, m), 3.65 (1H, dd, *J* = 13.2 and 6.6 Hz), 4.47 - 4.54 (1H, m), 6.00 - 6.06 (1H, m) and 7.12 - 7.27 (6H, m); ^{13}C-NMR ($CDCl_3$) δ: 24.3, 27.9, 48.0, 48.5, 58.3, 58.5, 62.8, 82.9, 83.0, 126.4, 126.5, 126.8, 126.9, 127.1, 128.6, 145.0, 145.3, 149.4, 150.2, 150.4, 169.6 and 169.7. IR (neat) ν 3433, 1765, 1370 and 1159 cm^{-1}. Anal. Calcd for $C_{18}H_{24}N_2O_3$: C, 68.3; H, 7.65; N, 8.85. Found: C, 68.1; H, 7.49; N, 8.92.

1-Boc-7,9-dibenzyl-2-oxo-1,7,9-triazaspiro[4,5]dec-3-ene (5f): mp 141-143 °C (EtOAc); ^{1}H-NMR ($CDCl_3$) δ: 1.44 (9H, s), 2.54 (2H, d, *J* = 10.2), 2.72 (1H, d, *J* = 9.0 Hz), 3.11 (2H, d, *J* = 11.0 Hz), 3.42 (2H, d, *J* = 13.4 Hz), 3.59 (2H, d, *J* = 13.4 Hz), 3.71 (1H, d, *J* = 8.8 Hz), 5.95 (1H, d, *J* = 6.2 Hz), 7.16 - 7.24 (10H, m) and 8.05 (1H, d, *J* = 6.2 Hz); ^{13}C-NMR ($CDCl_3$) δ: 28.0, 57.0, 59.4, 66.5, 74.9, 83.3, 123.9, 127.3, 128.4, 128.6, 137.6, 149.8, 157.3 and 169.3. IR (KBr) ν 1785, 1217 and 1159 cm^{-1}. Anal. Calcd for $C_{26}H_{31}N_3O_3$: C, 72.0; H, 7.21; N, 9.69. Found: C, 71.8; H, 7.54; N, 9.83.

1-Boc-7,9-bis(1-phenylethyl)-2-oxo-1,7,9-triazaspiro[4,5]dec-3-ene (5g): mp 189-191 °C (EtOAc); ^{1}H-NMR ($CDCl_3$) δ: 1.14 (3H, d, *J* = 6.8), 1.22 (3H, d, *J* = 6.6), 1.38 (9H, s), 2.49 - 2.65 (3H, m), 3.01 (1H, d, *J* = 8.2 Hz), 3.06 (1H, d, *J* = 7.6 Hz), 3.48 (2H, q, *J* = 6.4 Hz), 3.80 (1H, d, *J* = 9.0 Hz), 5.95 (1H, d, *J* = 6.1 Hz), 7.10 - 7.23 (10H, m) and 8.04 (1H, d, *J* = 6.0 Hz); ^{13}C-NMR ($CDCl_3$) δ: 19.1, 19.7, 28.0, 54.2, 54.6, 61.6, 61.8, 66.9, 70.5, 83.1, 123.6, 127.1, 127.3, 128.4, 143.4, 143.5, 149.6, 157.8 and 169.7. IR (KBr) ν 1765, 1274 and 1159 cm^{-1}. Anal. Calcd for $C_{28}H_{35}N_3O_3$: C, 72.9; H, 7.64; N, 9.10. Found: C, 72.7; H, 7.88; N, 8.93.

1-Boc-7,9-diethyl-2-oxo-1,7,9-triazaspiro[4,5]dec-3-ene (5h): mp 130-132 °C (EtOAc); ^{1}H-NMR ($CDCl_3$) δ: 1.06 (6H, t, *J* = 7.0 Hz), 1.48 (9H, s), 2.27 - 2.42 (4H, m), 2.52 (1H, d, *J* = 8.7 Hz), 2.57 (2H, d, *J* = 10.7 Hz), 3.01 (2H, d, *J* = 10.6 Hz), 3.68 (1H, d, *J* = 9.0 Hz), 5.95 (1H, d, *J* = 6.2 Hz) and 7.87 (1H, d, *J* = 6.2 Hz); ^{13}C-NMR ($CDCl_3$) δ: 12.2, 28.1, 49.2, 56.9, 66.4, 75.3, 83.3, 123.7, 128.4, 149.8, 157.7 and 169.5. IR (KBr) ν 1796, 1715, 1306 and 1164 cm^{-1}. Anal. Calcd for $C_{16}H_{27}N_3O_3$: C, 62.1; H, 8.80; N, 13.6. Found: C, 62.3; H, 8.72; N, 13.7.

1-Boc-7,9-dicyclohexyl-2-oxo-1,7,9-triazaspiro[4,5]dec-3-ene (5i): mp 118-119 °C (EtOAc); ^{1}H-NMR

($CDCl_3$) δ: 1.09 - 1.40 (12H, m), 1.57 (9H, s), 1.69 - 1.85 (8H, m), 2.41 (2H, br s), 2.65 (2H, d, J = 10.2 Hz), 3.15 (1H, d, J = 8.4 Hz), 3.33 (2H, d, J = 10.4 Hz), 3.85 (1H, d, J = 8.8 Hz), 6.02 (1H, d, J = 6.0 Hz) and 8.00 (1H, d, J = 6.0 Hz); ^{13}C-NMR ($CDCl_3$) δ: 25.4, 25.6, 26.0, 28.0, 28.5, 29.8, 53.2, 61.4, 66.9, 70.0, 82.9, 123.3, 149.7, 158.4 and 169.7. IR (KBr) ν 1738, 1712, 1304 and 1155 cm^{-1}. Anal. Calcd for $C_{24}H_{39}N_3O_3$: C, 69.0; H, 9.41; N, 10.1. Found: C, 68.8; H, 9.31; N, 10.3.

5-Acetyl-3-Boc-2-oxo-2,3a,4,5-tetrahydropyrrolo[2,3-c]quinoline (11): Acetyl chloride (157 mg, 2.0 mmol) was added to 1-Boc-5-(2-iodoanilinomethyl)-2,5-dihydropyrrol-2-one (828 mg, 2.0 mmol) in ether (8 mL) under nitrogen atmosphere. The resultant solution was stirred until all starting materials disappeared on TLC. The reaction mixture was poured into water. The resulting solution was neutralized with cold sat. $NaHCO_3$ solution. The reaction product was extracted with ether. Organic layer was washed successively with water and brine, dried over anhydrous Na_2SO_4, filtered, and concentrated under reduced pressure. The crude product was dissolved in Me_3CN. Into this solution were added triethylamine (607 mg, 6.0 mmol), Ph_3P (105 mg, 0.4 mmol) and $Pd(OAc)_2$ (45 mg, 0.2 mmol). The resultant solution was refluxed for 2 h. The reaction mixture was poured into water. The reaction product was extracted with EtOAc. Organic layer was washed successively with water and brine, dried over anhydrous Na_2SO_4, filtered, and concentrated under reduced pressure. The crude product was purified by flash chromatography to give 552 mg of the purified titled compound in 84% yield. mp 166-168 °C (EtOAc + Hexane); ^{1}H-NMR ($CDCl_3$) δ: 1.55 (9H, s), 2.33 (3H, s), 3.12 (1H, t, J = 11.8 Hz), 4.63 (1H, ddd, J = 11.6, 4.6 and 1.6 Hz), 5.25 - 5.30 (1H, m), 6.17 (1H, d, J = 1.4 Hz) and 7.14 - 7.62 (4H, m); ^{13}C-NMR ($CDCl_3$) δ: 23.5, 28.1, 49.7, 58.1, 83.8, 116.9, 121.0, 125.1, 125.9, 126.7, 131.5, 138.8, 149.5, 155.4, 169.0 and 170.4. Anal. Calcd for $C_{18}H_{20}N_2O_4$: C, 65.8; H, 6.14; N, 8.53. Found: C, 65.5; H, 6.22; N, 8.41.

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REFERENCES AND NOTES

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9. Crystallographic data for **5f** : $C_{26}H_{31}N_3O_3$, Mw = 433.60, Orthorhombic, Space group Pnma, a = 16.482(5) Å, b = 14.258(5) Å, c = 9.838(4) Å , V = 2312.0(1) $Å^3$, F(000) = 928, Z = 4, Dc = 1.246 g/cm^3, μ = 0.082 mm^{-1}. Preliminary examination and data collection were performed on an Mac Science MXC3 diffractometer equipped with graphite monochromatized MoKα radiation (λ (Kα) = 0.7107 Å). The cell constants were determined from least-squares refinement of the setting angles of 18 reflections in the range $24^\circ \leq 2\theta \leq 30^\circ$ that had been automatically centered. Intensity data were collected by the ω-2θ scan technique. Diffraction data +h, -k, +l were collected from the inner sphere ($3^\circ \leq 2\theta$(MoKα) $\leq 46^\circ$) at rt (293(2)K). The structure was solved by direct methods and refined by full-matrix least-square methods with wR2 (F_o^2) with 1462 unique reflections afforded residuals 0.0954 and the conventional R index based on the reflections having $F_o^2 > 2\sigma(F_o^2)$ is 0.0427.[12] This compound has crystallographically imposed

m symmetry that is compatiable with undistinguishable benzylic peaks in ^{1}H and ^{13}C NMR spectra. Detailed crystallographic data will be published elsewhere in due course.

10. This observation may give a clue to explain why the reaction of 1,3,5-trialkylhexahydro-1,3,5-triazine with various nucleophiles showed relatively poor yield compared to the same reaction starting from 1,3,5-triphenylhexahydro-1,3,5-triazine with significant amount of starting amine recovered.[3b,c,d,g]

11. Crystallographic data for **5i** : $C_{23}H_{39}N_3O_3$, Mw = 405.65 , Monoclinic, Space group $P2_1/a$, a = 11.094(3) Å, b = 22.927(8) Å, c = 10.487(3) Å, β = 114.50(2) Å, V = 2427.1(1) $Å^3$, F(000) = 912, Z = 4, Dc = 1.143 g/cm^3, μ = 0.075 mm^{-1}. Preliminary examination and data collection were performed on an Mac Science MXC3 diffractometer equipped with graphite monochromatized MoKα radiation (λ (Kα) = 0.7107 Å). The cell constants were determined from least-squares refinement of the setting angles of 22 reflections in the range $20^\circ \leq 2\theta \leq 30^\circ$ that had been automatically centered. Intensity data were collected by the ω-2θ scan technique. Diffraction data +h, -k, $\pm$l were collected from the inner sphere ($3^\circ \leq 2\theta$(MoKα) $\leq 48^\circ$) at rt (293(2)K). The structure was solved by direct methods and refined by full-matrix least-square methods with wR2 (F_o^2) with 3553 unique reflections afforded residuals 0.1272 and the conventional R index based on the reflections having $F_o^2 > 2\sigma(F_o^2)$ is 0.0444.[12] Detailed crystallographic data will be published elsewhere in due course.

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