Selected Paper

Nitrogen Fixation: Synthesis of Heterocycles Using Molecular Nitrogen as a Nitrogen Source

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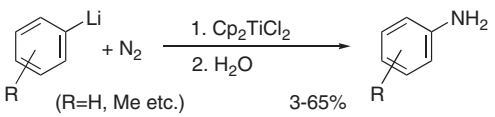
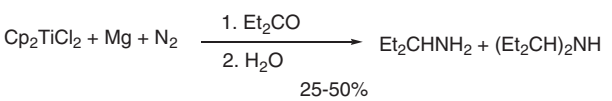
Nitrogen fixation using transition metals is a fascinating process. We have already reported on the incorporation of molecular nitrogen into organic compounds using a titanium–nitrogen complex reported by Yamamoto. We developed a novel titanium-catalyzed nitrogenation procedure using $TiCl_4$ in the presence of an excess amount of Li and TMSCl. In this reaction, a 1 atm pressure of nitrogen gas can be used and the reaction proceeds at room temperature. The procedure is very simple. A THF solution of $TiCl_4$ or $Ti(O^iPr)_4$ (1 equiv.), Li (10 equiv.), and TMSCl (10 equiv.) was stirred under an atmosphere of nitrogen at room temperature overnight to give titanium–nitrogen complexes. Although the structures of the titanium–nitrogen complexes have not yet been determined, they would consist of $N(TMS)_3$, $X_2TiN(TMS)_2$, and XTi=NTMS. Using this procedure, various heterocycles, such as indole, quinoline, pyrrole, pyrrolizine, and indolizine derivatives, could be synthesized from molecular nitrogen in good-to-moderate yields as a stoichiometric reaction based on a titanium complex by a one-pot reaction. Furthermore, monomorine I and pumiliotoxin C were synthesized from molecular nitrogen as a nitrogen source. This procedure was further extended for the syntheses of heterocycles using a catalytic amount of titanium complex; also, indole and pyrrole derivatives were obtained in high yields.

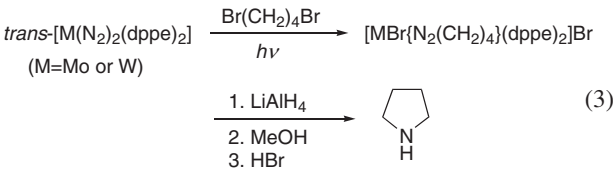
Since the discovery by Vol'pin and Shur that molecular nitrogen could be fixed by transition metals[1] and reducing agents under mild conditions, various systems of nitrogen fixation have been reported.[2] In 1967, Yamamoto reported on the synthesis of a cobalt–nitrogen complex[3] and then a titanium–nitrogen complex.[4] Hidai[5] and Bercaw[6] later reported on the synthesis of a molybdenum–nitrogen complex and a zirconium–nitrogen complex, respectively. However, there have been few reports on the incorporation of molecular nitrogen into organic compounds. In 1968, Vol'pin reported the synthesis of aniline from Cp_2TiCl_2 and phenyllithium under a high pressure of nitrogen (Eq. 1).[7] Later, van Tamelen succeeded to obtain diethylamine and banzonitrile from diethyl ketone and benzoyl chloride, respectively, using Cp_2TiCl_2 and Mg under nitrogen (Eq. 2).[8] In 1977, Chatt synthesized pyrrolidine and isopropylamine from 1,4-dibromobutane and acetone, respectively, using a molybdenum– or tungsten–nitrogen complex (Eqs. 3 and 4).[9] Hidai et al. synthesized pyrrole from a tungsten–nitrogen complex (Eq. 5).[10]



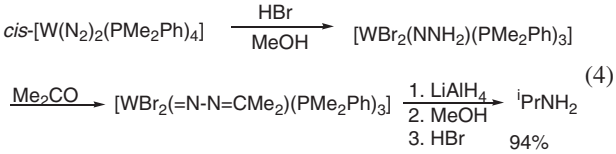
(1)



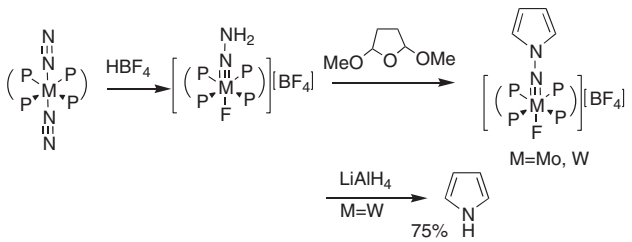
(2)



(3)



(4)



(5)

These results prompted us to utilize molecular nitrogen in organic synthesis. Yamamoto reported on the synthesis of a very interesting titanium–nitrogen complex **1** from $TiCl_4$ or $TiCl_3$ and Mg as a reducing agent (Eq. 6).[4] In this reaction, the nitrogen–nitrogen triple bond was cleaved by a titanium complex and a reducing agent to give a Ti–N complex. The result is very attractive for the synthesis of nitrogen heterocycles from molecular nitrogen because one nitrogen can be intro-

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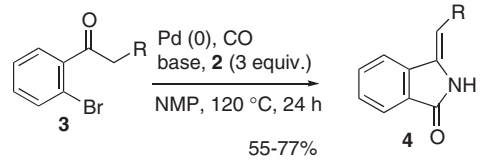
duced into the molecule. Sobota reported that the reaction of **1** with CO_2 gave titanium–isocyanate complex **2** (Eq. 7).[11]

$$\underset{\text{or } TiCl_3}{TiCl_4} \xrightarrow[THF]{Mg,\ N_2} \underset{\mathbf{1}}{[THF{\bullet}Mg_2Cl_2{\bullet}TiN]} \quad (6)$$

$$\mathbf{1} \xrightarrow{CO_2} \underset{\mathbf{2}}{[THF{\bullet}Mg_2Cl_2O{\bullet}TiNCO]} \quad (7)$$

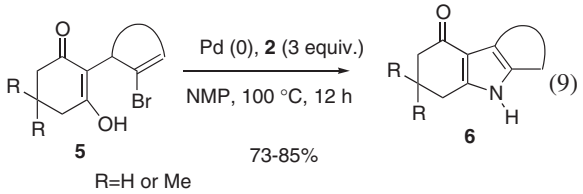
Since the handling of the latter complex **2** was easier than that of **1**, we used **2** as a nitrogenation agent, and succeeded to synthesize various heterocycles (Eqs. 8 and 9).[12a–e] Although the synthesis of heterocycles using titanium–nitrogen complex **2** was achieved, an extension of this reaction to a catalytic reaction based on a transition metal was difficult because titanium–nitrogen complexes **1** and **2** were used after their isolation. Thus, various attempts were made, and we succeeded to develop a titanium-catalyzed nitrogen fixation method using TiX_4–TMSCl–Li.[12f,g] That is, a THF solution of $TiCl_4$ was stirred in the presence of excess amounts of TMSCl and Li overnight under an atmosphere of nitrogen to give titanium–nitrogen complexes **7a** that would contain a titanium–imide complex, a titanium–amide complex, and $N(TMS)_3$.[13] After the hydrolysis of titanium–nitrogen complexes **7a** with 10% HCl, excess amounts of PhCOCl and K_2CO_3 were added and the solution was stirred overnight. After the usual workup, benzamide was obtained in more than 100% yield based on $TiCl_4$ (Scheme 1). This means that the reaction proceeds catalytically with regard to $TiCl_4$.

Nirtogenation-Carbonylation



(8)

Nitrogenation-Transmetalation



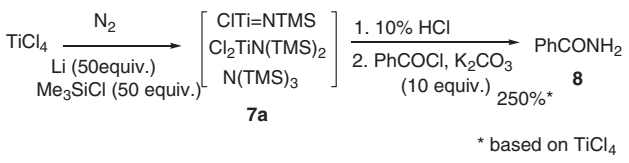
(9)

R=H or Me

Since molecular nitrogen can be fixed by this method and it is a very simple procedure, it was applied to the synthesis of heterocyclic compounds as a stoichiometric reaction.

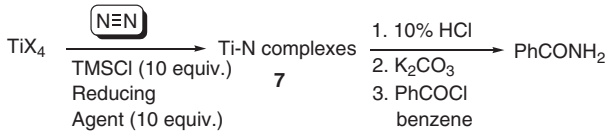
Results and Discussion

Effects of Titanium Complexes and Reducing Agents for Nitrogen Fixation. We previously examined the effect of various reducing agents,[12f,g] such as Mg, Na, K, Zn, and Li,



Scheme 1.

Table 1. Effects of Titanium Complex and Reducing Agents for Nitrogen Fixation



Run	TiX_4	Reducing agent	$PhCONH_2$/%
1	$TiCl_4$	Li	96
2	Cp_2TiCl_2	Li	46
3	$Ti(O^iPr)_4$	^{i}PrMgCl	4
4	$Ti(O^iPr)_4$	Li	91

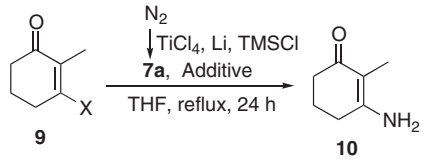
for nitrogen fixation, and it was found that Li gave good results. In this study, the effects of various titanium complexes were examined for nitrogen fixation. To measure the amount of fixed nitrogen, titanium–nitrogen complexes **7** were hydrolyzed with aqueous HCl to be converted into NH_4Cl, which reacted with benzoyl chloride in the presence of K_2CO_3 to give benzamide. The amount of nitrogen fixed by this method was estimated by the yield of benzamide. The results are given in Table 1.

A THF solution of $TiCl_4$ (1 equiv.), Li (10 equiv.), and TMSCl (10 equiv.) was stirred under an atmosphere of nitrogen overnight to give a black solution of titanium–nitrogen complexes **7a**, which was hydrolyzed with 10% HCl. To this solution was added a benzene solution of excess amounts of PhCOCl (10 equiv.) and K_2CO_3, and the solution was stirred at room temperature overnight to give benzamide in 96% yield (Table 1, run 1). When Cp_2TiCl_2 was used as a titanium complex, nitrogen could be fixed, but the results were not satisfactory. A low-valent titanium complex prepared from $Ti(O^iPr)_4$ and Grignard reagent, which was reported by Sato,[14] gave only a small amount of benzamide. It was very interesting that titanium–nitrogen complexes **7b**, prepared from $Ti(O^iPr)_4$ instead of $TiCl_4$, gave benzamide in 91% yield (run 4).

Synthesis of Indole and Quinoline Derivatives from 1,3-Diketone Bearing a Keto–Carbonyl Group in a Tether at the 2-Position. Since titanium–nitrogen complexes **7** were easily obtained from $TiCl_4$ or $Ti(O^iPr)_4$, TMSCl, and Li under nitrogen, an experiment was carried out to determine whether fixed nitrogen can be incorporated into organic compounds.[12h] As a model compound, cyclohexenone derivative **9** was chosen. To a THF solution of titanium–nitrogen complexes **7a**, which was prepared from $TiCl_4$ (1 equiv.), TMSCl (10 equiv.), and Li (10 equiv.) in THF under nitrogen, was added enol triflate **9a**, and the whole solution was refluxed overnight. After the usual workup, enaminone **10** was obtained in 35% yield (Table 2, run 1). This means that fixed nitrogen can be introduced directly into organic compounds. Various cyclohexenone derivatives **9** were examined, and enol triflate gave a good result. When CsF was added to this solution as an additive, the yields increased (runs 2 and 4). Provably, CsF would accelerate the cleavage of the nitrogen–silicon bond on titanium–nitrogen complexes. To clarify whether $N(TMS)_3$ in titanium–nitrogen complexes **7a** is an active species, the reaction of **9a** with $N(TMS)_3$ was carried out in the presence of CsF.

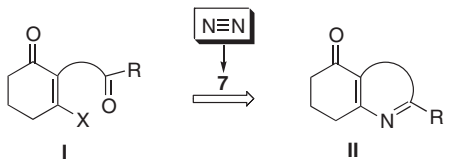
However, no product containing nitrogen was formed, indicating that the nitrogen source of **10** is derived from a titani-

Table 2. Synthesis of Heterocycles



Run	X		Additive	Yield[a)]/%
1	OTf	**9a**	—	35
2	OTf	**9a**	CsF	40
3	OMe	**9b**	—	14
4	OMe	**9b**	CsF	29
5	OMs	**9c**	CsF	11
6	OCOOMe	**9d**	CsF	10
7	OAc	**9e**	CsF	8
8	OCOOPh	**9f**	CsF	4
9	Cl	**9g**	CsF	—
10	OH	**9h**	CsF	6

a) Based on substrate.



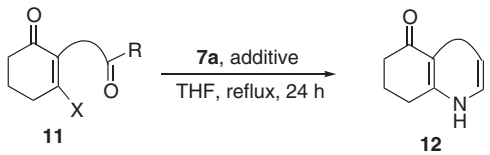
Scheme 2.

um–nitride complex or a titanium–amide complex. Thus, we next attempted to synthesize heterocycles from molecular nitrogen as a nitrogen source. Our plan is shown in Scheme 2. On the basis of the above results, if keto cyclohexenone **I** bearing a keto–carbonyl group in a tether at the 2-position is treated with titanium–nitrogen complexes **7a**, molecular nitrogen would be introduced at the 3-position of cyclohexenone, and then fixed nitrogen would further react with the carbonyl group in a tether to give cyclized compounds **II**.

We were very pleased to find that when a THF solution of **11a** and **7a** was refluxed overnight, indole derivative **12a** was obtained in 51% yield (Scheme 3, Table 3, run 1). In this reaction, the addition of CsF gave a good result (runs 2 or 3) and the hydroxy group was suitable as a leaving group (runs 3 and 5), although the reaction of **9h** with **7a** did not give a good result. Various indole derivatives were obtained in high yields. Elongation of the methylene group in a tether gave dihydroquinoline derivative **12f** in moderate yield. In this reaction, the spot on the TLC of the reaction mixture was different from that of the purified product **12f**. Presumably, tetrahydroquinoline derivative **13** would be formed, and then easily converted into dihydro-derivative **12f** by air oxidation. The treatment of triketone **11g** in a similar manner afforded **12f** in the same yield.

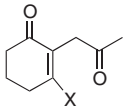
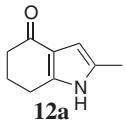
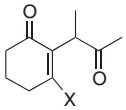
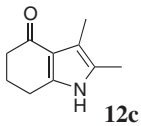
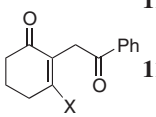
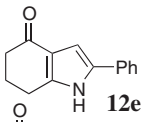
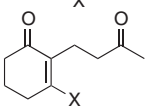
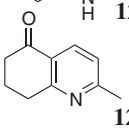
Synthesis of Pyrrole Derivatives from 1,4-Diketone. Since it was clear that titanium–nitrogen complexes **7a** could react with the carbonyl group of **I**, we next tried to synthesize pyrrole derivative **IV** from 1,4-diketone **III** (Scheme 4). If 1,4-diketone **III** were treated with titanium–nitrogen complexes **7**, pyrrole derivative **IV** would be formed.

When compound **14a** was treated with titanium–nitrogen

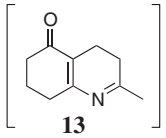


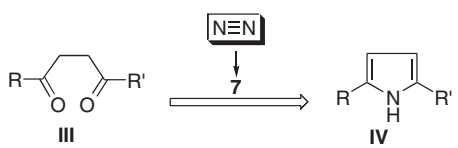
Scheme 3.

Table 3. Synthesis of Heterocycles

Run	Substrate		X	Additive	Product	Yield[a)]/%
1		**11a**	OTf	CsF		51
2		**11b**	OH	—	**12a**	71
3		**11b**	OH	CsF		86
4		**11c**	OTf	CsF		46
5		**11d**	OH	CsF	**12c**	86
6		**11e**	OH	CsF	 **12e**	57[b)]
7		**11f**	OTf	CsF	 **12f**	32
8		**11g**	OH			32

a) All reactions were carried out using a THF solution of titanium-nitrogen complexes **7a**, prepared from $TiCl_4$ (1.25 equiv.), Li (12.5 equiv.), and TMSCl (12.5 equiv.) and to this solution was added the substrate (1 equiv.) and the whole solution was refluxed in THF overnight. b) 2 equiv. of titanium-nitrogen complexes **7a** was used.





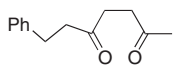
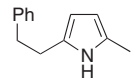
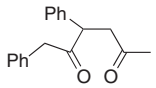
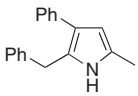
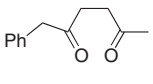
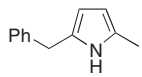
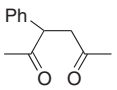
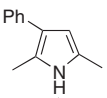
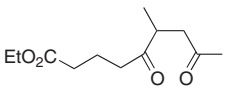
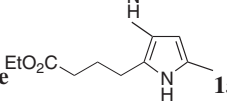
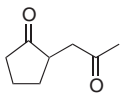
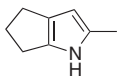
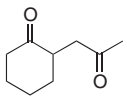
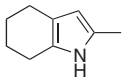
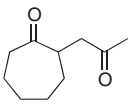
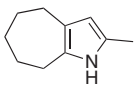
Scheme 4.

complexes **7a**, pyrrole derivative **15a** was obtained in 25% yield (Table 4, run 1). In a similar manner, various pyrroles **15b–e** (runs 2–5) or fuzed-pyrrole derivatives **15f–h** (runs 6–8) could be synthesized in good-to-moderate yields. The ester group of **14e** did not react with **7a** (run 5).

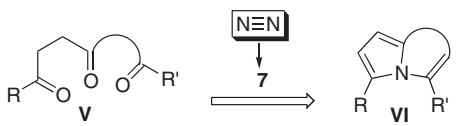
Synthesis of Pyrrolizine and Indolizine Derivatives. Since titanium–nitrogen complexes **7a** could react with two keto–carbonyl groups to give pyrrole derivatives, we next examined the reaction of titanium–nitrogen complexes **7** with triketone **V**. If this reaction proceeds, it would be possible to synthesize pyrrolizine or indolizine derivatives **VI** in one step from triketone (Scheme 5).

To a THF solution of **7a** was added triketone **16a** and CsF, and the whole solution was refluxed overnight to give a mix-

Table 4. Synthesis of Pyrrole Derivatives **15** Using **7a**

Run	Substrate		Product		Yield[a]/%
1		**14a**		**15a**	25
2		**14b**		**15b**	39
3		**14c**		**15c**	54
4		**14d**		**15d**	64
5		**14e**		**15e**	60
6		**14f**		**15f**	23
7		**14g**		**15g**	41
8		**14h**		**15h**	41

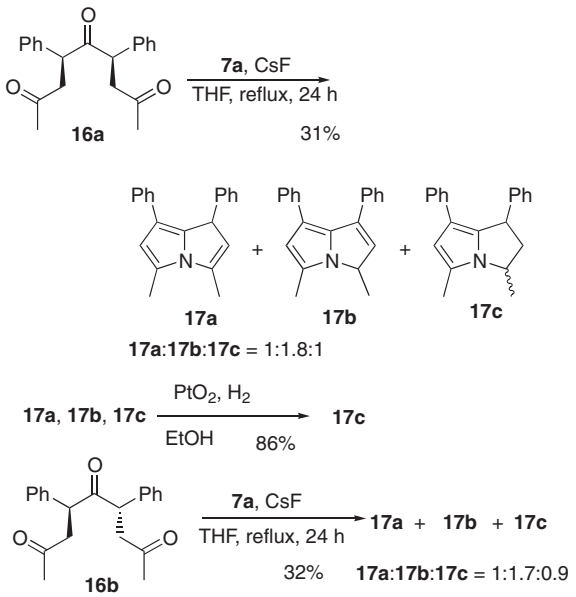
a) All reactions were carried out upon heating in THF for 24 h.



Scheme 5.

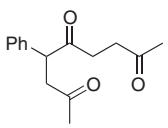
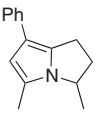
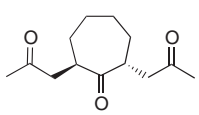
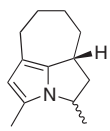
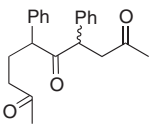
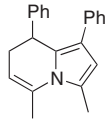
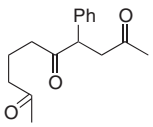
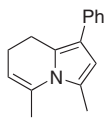
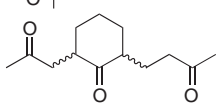
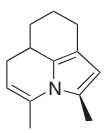
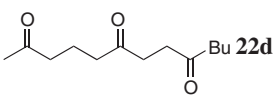
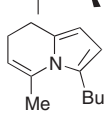
ture of pyrrolizine derivatives (**17a**, **17b**, and **17c**) as an inseparable mixture in 31% yield, whose ratio was determined to be 1:1.8:1 by a ^{1}H NMR spectrum (Scheme 6). The hydrogenation of these compounds with PtO_2 in EtOH afforded pyrrolizine derivative **17c** in 86% yield. In a similar manner, **16b** gave the same pyrrolizine derivatives (**17a**, **17b**, and **17c**) in the same ratio in 32% yield.

A treatment of triketone **18** with **7a** gave pyrrolizine derivative **19** in 30% yield (Table 5, run 1). Although the yield was moderate, it is very interesting that the pyrrolizine derivative **19** could be synthesized from triketone **18** and **7a** by a one-step reaction. Triketone **20** was treated with **7a** in a similar manner to give tricyclic compound **21** as a mixture of two inseparable isomers in 31% yield (run 2). Subsequently, the synthesis of an indolizidine derivative was examined. Triketone **22a**, whose one methylene was elongated compared with that of **18**, was treated with **7a** to give indolizine derivative **23a** in 29% yield. When 2 equiv. of **7a** was used for this reaction, the yield of **23a** increased to 41% (run 3). In a similar treatment of **22b**, **22c**, and **22d** with **7a** (2 equiv.), indolizine derivatives **23b**, **23c**, and **23d** were formed in 56%, 30%, and 30% yields, respectively (runs 4–6). From **23d**, monomorine I and indolizidine 195 B could be synthesized by hydrogenation (Fig. 1).[12i]



Scheme 6.

Table 5. Synthesis of Pyrrolizine and Indolizine Derivatives

Run	Triketone		Pyrrolizine or indolizine		Yield/%
1		**18**		**19**	30
2		**20**		**21**[a]	31
3		**22a**		**23a**	41[b]
4		**22b**		**23b**	56[b]
5		**22c**		**23c**	30[b]
6		**22d**		**23d**	30[b]

a) 3.4:1 (determined by ^{1}H NMR (500 MHz)). b) 2 equivalents of **7a** was used.

Synthesis of Heterocycles from Keto–Alkyne. Next, the Michael-type addition of titanium–nitrogen complexes **7** to α,β-unsaturated compound was examined. Our plan is shown in Scheme 7. If keto–alkyne **VII** reacts with **7**, imine complex should be formed, and it would then react with α,β-unsaturat-

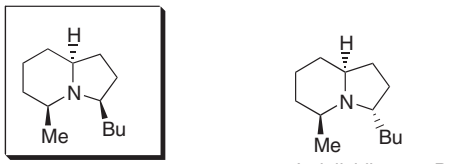
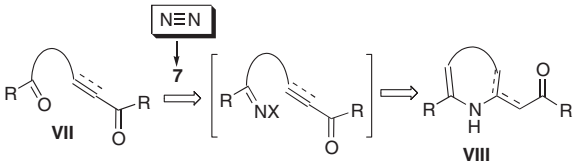


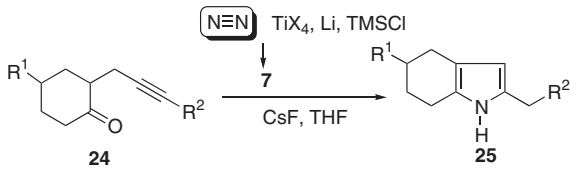
Fig. 1. Monomorine I and indolizine 195B.



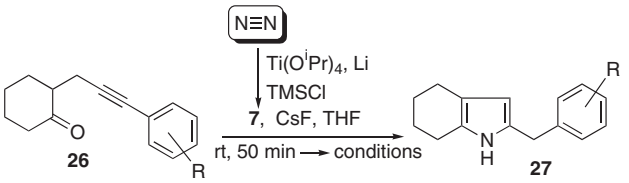
Scheme 7.

ed compound to give **VIII**.[12j]

A THF solution of keto–alkyne **24a** (1 equiv.) and titanium–nitrogen complexes **7a**, which was prepared from $TiCl_4$ (1.2 equiv.), Li (10 equiv.), and TMSCl (10 equiv.) under nitrogen, was refluxed in the presence of CsF (6 equiv.) for 17 h. Surprisingly, indole derivative **25a** was obtained in 90% yield (Scheme 8, Table 6, run 1). When the reaction was carried out at room temperature for 24 h, the desired indole derivative **25a** was obtained in 59% yield (run 2). On the other hand, when $Ti(O^iPr)_4$ was used for the preparation of titanium–nitrogen complexes **7b** in a similar manner, the reaction proceeded at room temperature for only 50 min and **25a** was obtained in 82% yield (run 3). In the absence of CsF, the yield slightly decreased (run 4). Indole derivative **25b**, having an acetoxy group on a six-membered ring, was also synthesized from keto–alkyne **24b** (run 5). Subsequently, the effect of a substitu-



Scheme 8.

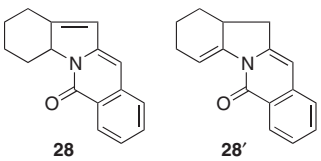


Scheme 9.

Table 7. Effects of Substituents on the Aromatic Ring

Run	Substrate	R	Conditions	Yield/%	**26**/%
1	**26a**	*p*-CH_3	reflux, 20 h	32	31
2	**26b**	*p*-CO_2Me	reflux, 20 h	42	30
3	**26c**	*p*-CN	reflux, 5 h	45	21
4	**26d**	*p*-CF_3	reflux, 20 h	49	14
5	**26e**	*p*-NO_2	reflux, 12 h	—	8
6	**26f**	*o*-CO_2Me	40 °C, 20 h	35[a)]	19
7	**26f**	*o*-CO_2Me	reflux, 20 h	18[b)]	6

a) **28** was obtained in 3% yield. b) **28** and **28′** were obtained in 7% and 5% yields.



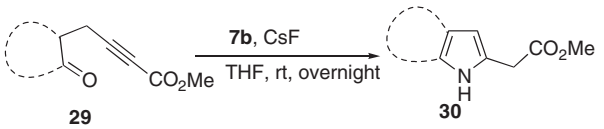
ent on alkyne was examined. In the case of the nitrile group, the yield was also high (run 6), and **24d** or **24e** bearing the amide or keto–carbonyl group on alkyne gave the desired indole derivative, **25d** or **25e**, in moderate yields (runs 7 and 8). Although, keto–alkyne **24f** having the alkyl group on an alkyne part gave only a trace amount of the desired product **25f** (run 9), keto–alkyne **24g** having a phenyl group afforded indole derivative **25g** in moderate yield (runs 9 and 10). These results indicate that the electron-withdrawing group on the alkyne gives a good result.

Thus, the substituent effect of the aromatic ring on the alkyne was examined (Scheme 9). The results are given in Table 7. The electron-withdrawing group on the aromatic ring gave good results (runs 2–4), but keto–alkyne **26e** having the

Table 6. Synthesis of Indole Derivatives

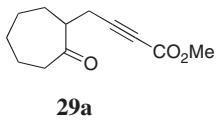
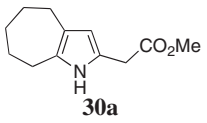
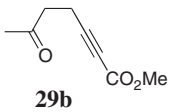
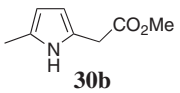
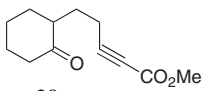
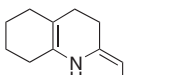
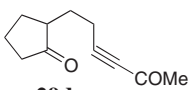
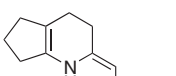
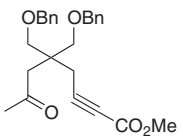
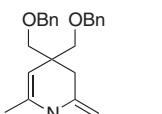
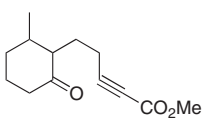
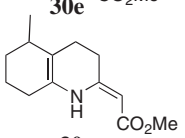
Run	Substrate	X	R^1	R^2	Temp.	Time/h	Yield[a)]/%
1	**24a**	Cl	H	CO_2Me	reflux	17	90
2	**24a**	Cl	H	CO_2Me	rt	24	59[b)]
3	**24a**	O^iPr	H	CO_2Me	rt	50 (min)	82
4	**24a**	O^iPr	H	CO_2Me	rt	2	77[c)]
5	**24b**	O^iPr	OAc	CO_2Me	rt	50 (min)	62
6	**24c**	O^iPr	H	CN	rt	12	92
7	**24d**	O^iPr	H	$CONEt_2$	rt	24	45
8	**24e**	O^iPr	H	$COCH_3$	rt	1.5	35
9	**24f**	O^iPr	H	Me	reflux	20[d)]	3[f)]
10	**24g**	O^iPr	H	Ph	reflux	20[e)]	35[g)]

a) **7a** or **7b** were prepared from TiX_4 (1 equiv.), Li (10 equiv.), and TMSCl (10 equiv.). All reactions were carried out using **24** (1 equiv.), CsF (6 equiv.), and **7a** or **7b** (1.25 equiv.). b) **24a** was recovered in 30% yield. c) In the absence of CsF. d) The solution was stirred at rt for 2 h and then refluxed. e) The solution was stirred at rt for 70 min and then refluxed. f) **24f** was recovered in 45% yield. g) **24g** was recovered in 21% yield.



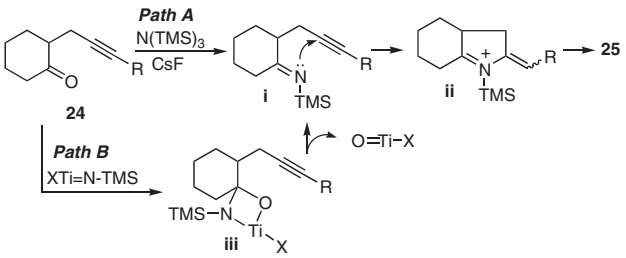
Scheme 10.

Table 8. Synthesis of Heterocycles from Keto–Alkyne

Run	Substrate	Product	Yield/%
1	 **29a**	 **30a**	72
2	 **29b**	 **30b**	39
3	 **29c**	 **30c**	66
4	 **29d**	 **30d**	34
5	 **29e**	 **30e**	63
6	 **29g**	 **30g**	79

nitro group did not give the desire product (run 5). In the case of keto–alkyne **26f** having the methoxycarbonyl group at the ortho-position on the aromatic ring, small amounts of tetracyclic compounds **28** and **28′** were obtained (runs 6 and 7). Various mono- and bicyclic heterocycles were synthesized from keto–alkyne **29** using **7b** (Scheme 10), the results are given in Table 8. The desired heterocyclic compounds, such as pyrroles **30a** and **30b**, quinolines **30c**, and piperidine derivatives **30d** and **30e**, were obtained in good-to-moderate yields.

The possible reaction course for the formation of heterocyclic compounds from keto–alkyne is shown in Scheme 11. There are two possible pathways. If the reaction of keto–alkyne **24** with $N(TMS)_3$ proceeds in the presence of CsF, imine **i** would be formed. Then, a Michael addition of nitrogen of imine would afford **ii**, which would isomerize to give **25** (path A). However, when **24a** was reacted with $N(TMS)_3$ in the presence of CsF at room temperature for 16 h, no cyclized product was formed, indicating that $N(TMS)_3$ in titanium–nitrogen complexes **7b** is not an active species. Thus, the active species in this reaction would be a titanium–imide complex [XTi=N(TMS)] or titanium–amide complex [X_2Ti–



Scheme 11.

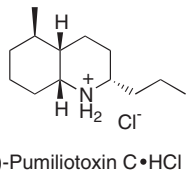
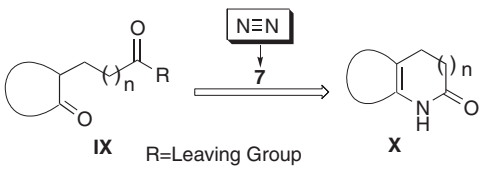


Fig. 2.



Scheme 12.

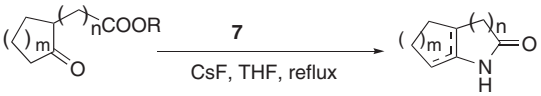
$N(TMS)_2$], and the complex would react with the carbonyl carbon to give imine **i** via **iii**.[15,16] Then, the Michael addition of nitrogen gives **25**. The mechanism of this reaction is similar to that in the synthesis of a pyrrole derivative by Arcadi, who obtained a pyrrole derivative from keto–alkyne and primary amine.[17] The total synthesis of (±)-pumiliotoxin C was achieved from **30g** (Fig. 2).[12l]

Synthesis of Lactams from Keto–Carboxylic Acid. Next, we tried to synthesize lactam **X** from keto–carboxylic acid **IX** and **7** (Scheme 12). At first, a THF solution of acid chloride **31b** and **7a**, which was prepared using a $TiCl_4$–Li–TMSCl system under nitrogen, was refluxed in the presence of CsF to give lactam **32** in 28% yield (Scheme 13, Table 9, run 1). The use of titanium–nitrogen complexes **7b**, prepared by a $Ti(O^iPr)_4$–Li–TMSCl system, slightly increased the yield of **32** (run 2). In this reaction, various carboxylic acid derivatives, such as chloride **31b**, mixed anhydrides (**31c** and **31d**, ester **31e**), and even the carboxylic acid **31a**, could be used and lactam **32** was produced in good yields (runs 1–7). Various bicyclic lactams (**34**, **36**, and **38**) were obtained in good yields using this method. In a similar manner, piperidone derivatives **40**, **42**, and **44** were also obtained in moderate yields from the corresponding keto–esters (**39**, **41**, and **43**).

Investigation of Titanium-Catalyzed Nitrogenation. As described in Scheme 1, this nitrogenation method was developed as a catalytic reaction based on a titanium complex. Although the reaction species are not clear, the possible reaction course is considered as shown in Fig. 3. TiX_4 would be reduced with Li and converted into TiX_2 **XI**, which would react with N_2 to give **XII**. This would then be converted into titanium–nitride complex **XIII** by Li and TMSCl and **XIII** would

react with TMSCl to give titanium–amide complex **XIV**. In the presence of Li, **XIV** reacts with TMSCl to give $N(TMS)_3$ and TiX_2 **XI** would be regenerated.

Thus, an experiment was carried out to determine whether nitrogen-heterocycles could be catalytically synthesized based on TiX_4 from molecular nitrogen (Scheme 14). To determine whether $TiCl_4$ acts as a catalyst, titanium–nitrogen complexes **7a** were synthesized from $TiCl_4$ (1 equiv.) in the presence of excess amounts of Li (50 equiv.) and TMSCl (50 equiv.) under an atmosphere of nitrogen. To this solution was added a THF solution of an excess amount of 1,3-diketone derivative **9a** (10 equiv.), and the solution was refluxed overnight. After the usual workup, enamide **10** was obtained in 189% yield based on $TiCl_4$. This means that $TiCl_4$ acts as a catalytic reagent in this



Scheme 13.

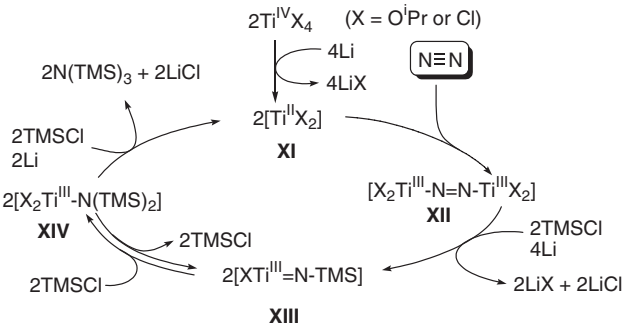
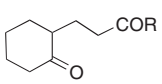
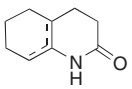
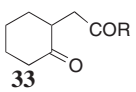
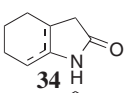
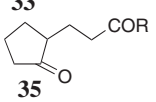
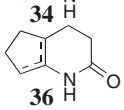
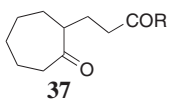
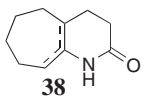
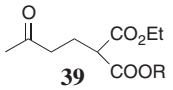
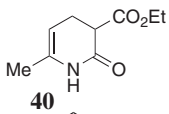
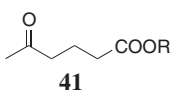
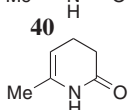
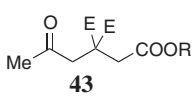
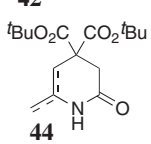
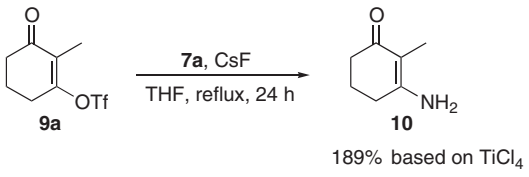


Fig. 3. Possible reaction course.

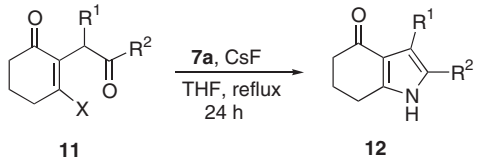
reaction. It was already reported that the reaction of **9a** with $N(TMS)_3$ did not afford **10**. However, in this reaction, the use of 1 equiv. of $TiCl_4$ in the presence of the excess amounts of Li and TMSCl afforded 189% yield of **10**. Although the reason why $TiCl_4$ acts as a catalytic reagent is not clear, the possibility for a catalytic reaction is that the titanium species acts as a Lewis acid in this reaction, or generated titanium-oxide

Table 9. Synthesis of Lactams

Run	Substrate		R	Ti=NX	Time/h	Product	Yield/%
1	 **31**	**31b**	Cl	**7a**	24	 **32**	28
2		**31b**	Cl	**7b**	24		31
3		**31c**	OCO_2Et	**7a**	24		25
4		**31c**	OCO_2Et	**7b**	24		55
5		**31d**	$OPO(OEt)_2$	**7b**	24		58
6		**31a**	OH	**7b**	24		53
7		**31e**	OEt	**7b**	12		50
8	 **33**	**33**	OEt	**7b**	1	 **34**	24
9	 **35**	**35a**	OH	**7b**	24	 **36**	22
10		**35d**	$OPO(OEt)_2$	**7b**	24		38
11	 **37**	**37a**	OH	**7b**	24	 **38**	32
12		**37d**	$OPO(OEt)_2$	**7b**	24		42
13	 **39**		$OPO(OEt)_2$	**7b**		 **40**	19
14	 **41**		$OPO(OEt)_2$	**7b**		 **42**	29
15	 **43** E = $CO_2{}^t$Bu,		$OPO(OEt)_2$	**7b**		 **44**	51



Scheme 14.



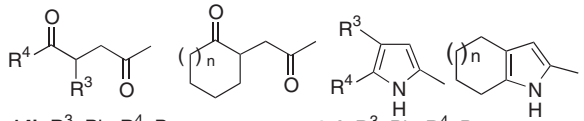
Scheme 15.

Table 10. Synthesis of Indole Derivative Using Titanium-Catalyzed Nitrogenation

Run	SM	R^1	R^2	X	Product	Yield[a)]/%
1	**11a**	H	Me	OTf	**12a**	129
2	**11b**	H	Me	OH	**12a**	273
3	**11d**	Me	Me	OH	**12d**	369
4	**11e**	H	Ph	OH	**12e**	208

a) Based on $TiCl_4$.

Table 11. Synthesis of Pyrrole and Indole Derivatives Using Titanium-Catalyzed Nitrogenation



14b R^3=Ph, R^4=Bn **14g** n=1
14c R^3=H, R^4=Bn **14h** n=2
14d R^3=Ph, R^4=Me

15b R^3=Ph, R^4=Bn **15g** n=1
15c R^3=H, R^4=Bn **15h** n=2
15d R^3=Ph, R^4=Me

Run	Substrate	Product	Yield[a)]/%
1	**14b**	**15b**	247
2	**14c**	**15c**	354
3	**14d**	**15d**	280
4	**14g**	**15g**	350
5	**14h**	**15h**	335

a) Based on $TiCl_4$.

complexes would be reduced by the reducing agent.

Subsequently, the synthesis of indole derivatives was carried out using a catalytic amount of TiX_4 (Scheme 15). The reaction procedure was similar to that used in the synthesis of **10**, the results are given in Table 10. In a similar manner, pyrrole derivatives were synthesized using a catalytic amount of $TiCl_4$, as shown in Table 11. In all cases, indole and pyrrole derivatives were obtained in more than 100% yield. These results mean that these heterocycles could be synthesized from molecular nitrogen as a nitrogen source using a catalytic amount of TiX_4.

Conclusion

Nitrogen fixation is a very interesting and useful method for synthetic organic chemistry, and studies concerning for the utilization of molecular nitrogen in organic synthesis are exciting. It is known that various transition metals can fix nitrogen, but there have been few reports on the incorporation of nitrogen into organic compounds. We previously reported that the heterocycles could be synthesized using the titanium–nitrogen complex reported by Yamamoto. Next, we considered whether nitrogen can be catalytically introduced in regard to the metal. After various attempts had been made, a novel $TiCl_4$ or $Ti(O^iPr)_4$–Li–TMSCl system was developed for nitrogen fixation, and it was found that the reaction proceeded catalytically based on TiX_4 in the presence of excess amounts of Li and TMSCl under nitrogen (1 atm). This method was then extended to the synthesis of heterocycles as a stoichiometric reaction, and various heterocycles, such as indole, quinoline, pyrrole, pyrrolizine, indolizine derivatives, and lactams, could be synthesized from molecular nitrogen as a nitrogen source. Furthermore, various heterocycles were obtained by a catalytic amount of titanium–nitrogen complexes in the presence of excess amounts of Li and TMSCl. The results mean that titanium–nitrogen complexes could be used as nitrogenation reagents for the synthesis of nitrogen containing compounds and heterocycles.

Experimental

All manipulations were performed under a nitrogen atmosphere using standard Schlenk techniques, and all of the reaction solutions were degassed through a freeze–pump–thaw cycle. THF and TMSCl were distilled under an argon atmosphere from sodium diphenylketyl (THF) or CaH_2 (TMSCl). All other reagents and solvents were purified when necessary using standard procedures. Column chromatography was performed on silica gel 60 (70–230 mesh, 60 Å), and flash chromatography was performed on silica gel 60 (230–400 mesh, 60 Å) using the indicated solvent. The melting points are uncorrected.

Typical Procedure for Synthesis of Titanium–Nitrogen Complexes 7. To a suspension of Li (10 equiv.) in THF was added $TiCl_4$ or $Ti(O^iPr)_4$ (1 equiv.) and TMSCl (10 or 16 equiv.) at -78 °C, and the solution was degassed by a freeze–pump–thaw cycle. The atmosphere of the reaction vessel was changed to nitrogen, and the solution was stirred at room temperature under nitrogen (1 atm) overnight. The resultant black solution was used as titanium–nitrogen complexes **7**.

General Procedure for the Synthesis of Nitrogen Heterocycles. To a black solution of **7** (1.25 equiv.) were added a substrate (1 equiv.) and CsF (6 equiv.); the solution was then stirred at an appropriate temperature. After cooling, water was added and the solution was stirred at room temperature until the black precipitate had disappeared. The aqueous solution was made basic by K_2CO_3, and the solution was extracted with ethyl acetate. The organic layer was washed with brine, dried over Na_2SO_4, and concentrated. The residue was purified by column chromatography on silica gel to give a nitrogen-fixation product.

General Procedure for Titanium-Catalyzed Nitrogen Fixation. A THF suspension of $TiCl_4$ or $Ti(O^iPr)_4$ (1 equiv.), Li (50 equiv.), and TMSCl (50 equiv.) was stirred at room temperature for 24 h. To the solution were added a substrate (10 equiv.) and CsF (10 equiv.), and the solution was refluxed for 24 h. After cooling, water was added and the solution was stirred at room temperature until the black precipitate had disappeared. The solution was extracted with ethyl acetate. The organic layer was washed with brine, dried over Na_2SO_4, and concentrated. The residue

was purified by column chromatography on silica gel to give the nitrogen-fixation product. The yields were calculated based on the titanium complex.

Synthesis of Heterocycles from Di- and Triketones. General Procedure for the Synthesis of Triflates (9 and 11): To a solution of 1,3-diketone derivatives (1 equiv.) and pyridine (1.1 equiv.) in CH_2Cl_2 was added trifuloromethylsulfonyloxy anhydride (Tf_2O, 1.1 equiv.) at -78 °C, and the solution was stirred at 0 °C for 2 h. Ether was added and the ether layer was washed with a 3% HCl solution, a saturated $NaHCO_3$ solution, and brine, dried over Na_2SO_4, and concentrated. The residue was purified by silica-gel chromatography to give the desired product.

2-Methyl-3-trifuloromethanesulfonyloxy-2-cyclohexenone (9a): A crude product, which was prepared from **9h** (630 mg, 5.0 mmol), pyridine (0.445 mmol, 5.5 mmol), and Tf_2O (0.95 mL, 5.5 mmol) in CH_2Cl_2 (50 mL), was purified by column chromatography on silica gel (hexane/ethyl acetate, 3/1) to give a colorless oil of **9a** (778 mg, 60%). IR (neat) 1693, 1668, 1419, 1215 cm^{-1}; ^1H NMR (270 MHz, $CDCl_3$) δ 1.86 (t, $J = 2.1$ Hz, 3H), 2.02–2.13 (m, 2H), 2.46–2.51 (m, 2H), 2.71–2.78 (m, 2H); MS m/z 258 (M^+), 257, 225, 123, 98, 83, 55, 43. Anal. Calcd for $C_8H_9F_3O_4S$: C, 37.21; H, 3.51; S, 12.42; F, 22.07%. Found: C, 37.10; H, 3.50; S, 12.27; F, 22.23%.

2-(2-Oxypropyl)-3-trifluoromethylsulfonyloxy-2-cyclohexenone (11a): A crude product, which prepared from triketone **11b**[1] (168 mg, 1.0 mmol), pyridine (0.089 mL, 1.1 mmol), and Tf_2O (0.19 mL, 1.1 mmol) in CH_2Cl_2 (10 mL), was purified by column chromatography on silica gel (hexane/ethyl acetate, 3/1) to give a colorless oil of **11a** (279 mg, 93%). IR (neat) 1724, 1690, 1671, 1420, 1216 cm^{-1}; ^1H NMR (270 MHz, $CDCl_3$) δ 2.09–2.18 (m, 2H), 2.24 (s, 3H), 2.48–2.55 (m, 2H), 2.79–2.86 (m, 2H), 3.50 (s, 2H); MS m/z 300 (M^+), 258, 167, 150, 125, 109; HRMS (EI, m/z) for $C_{10}H_{11}F_3O_5S$ calcd 300.0280, found 300.0274.

2-(1-Methyl-2-oxopropyl)-3-trifluoromethanesulfonyloxy-2-cyclohexeneone (11c): A crude product, which was prepared from triketone **11d**[1] (364 mg, 2.0 mmol), pyridine (0.18 mL, 2.2 mmol), and Tf_2O (0.37 mL, 2.2 mmol) in CH_2Cl_2 (20 mL), was purified by column chromatography on silica gel (hexane/ethyl acetate, 3/1) to give a colorless oil of **11c** (534 mg, 85%). IR (neat) 1722, 1688, 1654, 1418, 1216 cm^{-1}; ^1H NMR (270 MHz, $CDCl_3$) δ 1.34 (d, $J = 7.0$ Hz, 3H), 2.08–2.18 (m, 2H), 2.12 (s, 3H), 2.48–2.53 (m, 2H), 2.81–2.87 (m, 2H), 3.51 (q, $J = 7.0$ Hz, 1H); MS m/z 314 (M^+), 299, 271, 181, 139, 123, 93, 69, 43; HRMS m/z for $C_{11}H_{13}F_3O_5S$ calcd 314.0436, found 314.0430.

2-(2-Oxophenethyl)cyclohexane-1,3-dione (11e): To a solution of 1,3-cyclohexanedione (1.12 g, 10 mmol) in MeOH (4 mL) were added an aq. KOH (678.3 mg, 12 mmol, 1 mL) solution and phenacyl bromide (1.855 mg, 12 mmol) at 0 °C; the solution was stirred at room temperature for 48 h. KBr was filtered off, and to the filtrate was added a 10% NaOH solution, and the solvent was evaporated. The residue was extracted with ethyl ether. The aqueous layer was acidified by 10% HCl and extracted with ethyl acetate. The organic layer was washed with brine, dried over Na_2SO_4, and concentrated. The residue was purified by column chromatography on silica gel (hexane/ethyl acetate, 1/1) to give a colorless crystal (836.1 mg, 36%). mp 148–150 °C (from Et_2O); IR (neat) 3172, 1727, 1688, 1598 cm^{-1}; ^1H NMR (270 MHz, $CDCl_3$) δ 1.85–1.99 (m, 2H), 2.38–2.50 and 2.70–2.79 (m and m, 4H), 3.67–4.02 (d, $J = 4.6$ Hz, and s, 1H), 3.93 (s and t, $J = 4.6$ Hz), 7.43–7.92 and 7.58–7.62 (m and m, 3H), 8.17–8.22 and 7.99–8.01 (m and m, 2H); MS m/z 230 (M^+), 125, 105, 97, 77.

2-(3-Oxobutyl)-3-trifluoromethylsulfonyloxy-2-cyclohexanone (11f): A crude product, which was prepared from triketone **11g** (364 mg, 2.0 mmol), pyridine (0.18 mL, 2.2 mmol), and Tf_2O (0.37 mL, 2.2 mmol) in CH_2Cl_2(20 mL), was purified by column chromatography on silica gel (hexane/ethyl acetate, 3/1) to give a colorless oil of **11f** (547 mg, 87%). IR (neat) 1717, 1688, 1662, 1418, 1216 cm^{-1}; ^1H NMR (270 MHz, $CDCl_3$) δ 2.05–2.11 (m, 2H), 2.13 (s, 3H), 2.45–2.50 (m, 2H), 2.55–2.60 (m, 4H), 2.73–2.79 (m, 2H). MS m/z 314 (M^+), 181, 163, 150, 139, 121, 43 (base peak); Anal. Calcd for for $C_{11}H_{13}F_3O_5S$: C, 41.88; H, 4.15; S, 10.26; F, 18.08%. Found: C, 42.03; H, 4.17; S, 10.20; F, 18.14%.

1,3-Diphenylhexane-2,5-dione (14b): To a solution of NH(^{i}Pr)$_2$ (4.4 mL, 36 mmol) in THF (70 mL) was added BuLi (19 mL, 33 mmol, 1.74 M) at 0 °C; the solution was stirred at the same temperature for 30 min. To this solution was added dibenzyl ketone (6.3 g, 30 mmol) at -78 °C. The solution was allowed to remain at 0 °C for 1 h. To this solution was added allyl bromide (6.5 mL, 45 mmol) at -78 °C, and the solution was stirred at 0 °C for 4 h. A saturated NH_4Cl solution was added and the aqueous layer was extracted with Et_2O. The organic layer was washed with brine, dried over Na_2SO_4, and concentrated. The residue was purified by column chromatography on silica gel (hexane/ethyl acetate, 15/1) to give a colorless oil of 1,3-diphenyl-5-hexen-2-one (5.23 g, 70%). IR (neat) 1714, 1640, 1600 cm^{-1}; ^1H NMR (500 MHz, $CDCl_3$) δ 2.41(ddd, $J = 7.4$, 7.4, 14.3 Hz, 1H), 2.76 (ddd, $J = 7.0$, 7.4, 14.3 Hz, 1H), 3.62 (d, $J = 2.7$ Hz, 2H), 3.79 (dd, $J = 7.4$, 7.4 Hz, 1H), 4.89 ($J = 10.0$ Hz, 1H), 4.94 (d, $J = 17.2$ Hz, 1H), 5.99 (dddd, $J = 7.0$, 7.4, 10.0, 17.2 Hz, 1H), 7.00–7.20 (m, 2H), 7.14–7.16 (m, 2H), 7.19–7.47 (m, 6H); To a solution of 1,3-diphenyl-5-hexen-2-one (2.5 g, 10 mmol) in DMF–H_2O (10:1, 3.3 mL) was added $PdCl_2$ (328 mg, 2.0 mmol) and CuCl (2.22 g, 22.4 mmol), and the solution was stirred under oxygen at room temperature for 26 h. Ether was added and the organic layer was washed with a 10% HCl solution, a sat. $NaHCO_3$ solution and brine, dried over Na_2SO_4, and concentrated. The residue was purified by column chromatography on silica gel (hexane/ethyl acetate, 5/1) to give a colorless oil of **14b** (1.59 g, 60%). IR (neat) 1712, 1702, 1600 cm^{-1}; ^1H NMR (500 MHz, $CDCl_3$) δ 2.13 (s, 3H), 2.58 (dd, $J = 3.9$, 18.0 Hz, 1H), 3.43 (dd, $J = 10.3$, 18.0 Hz, 1H), 3.71 (d, $J = 16.4$ Hz, 1H), 3.74 (d, $J = 16.4$ Hz, 1H), 4.31 (dd, $J = 3.9$, 10.3 Hz, 1H), 7.00–7.20 (m, 2H), 7.14–7.16 (m, 2H), 7.19–7.47 (m, 6H); MS m/z 266 (M^+), 175, 147, 91, 65, 43; HRMS (EI, m/z) for $C_{18}H_{18}O_2$, calcd 266.1307, found 266.1295. Anal. Calcd for $C_{18}H_{18}O_2$: C, 81.13; H, 6.81%. Found: C, 81.12; H, 6.97%.

Ethyl 5,8-dioxo-6-methylnonanoate (14e): IR (neat) 2972, 1734, 1712 cm^{-1}; ^1H NMR (500 MHz, $CDCl_3$) δ 4.13 (q, $J = 7.0$ Hz, 2H), 2.86–3.05 (m, 2H), 2.64 (t, $J = 7.2$ Hz, 1H), 2.63 (t, $J = 7.2$ Hz, 1H), 2.41 (m, 1H), 2.32 (t, $J = 7.2$ Hz, 2H), 2.13 (s, 3H), 1.90 (tt, $J = 7.2$, 7.2 Hz, 2H), 1.25 (t, $J = 7.0$ Hz, 3H), 1.08 (d, $J = 6.9$ Hz, 3H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 212.6, 207.0, 173.2, 60.2, 46.5, 40.9, 40.0, 33.2, 29.8, 18.8, 16.5, 14.2; MS m/z 228 (M^+), 183, 143, 115; HRMS calcd for $C_{12}H_{20}O_4$ 228.1362, found 228.1363.

4,6-Disphenylnonane-2,5,8-trione (16a, 16b): A crude product that was prepared from 4,6-diphenyl-1,8-nonadiene-5-one (3.2 g, 11.2 mmol), $PdCl_2$ (400 mg, 2.44 mmol), and CuCl (2.22 g, 22.4 mmol) in DMF (5 mL)–H_2O (0.3 mL) under oxygen was purified by column chromatography on silica gel (hexane/ethyl acetate, 4/1) to give **16a** (536.7 mg, 15%) and **16b** (771.4 mg, 21%).

16a: mp 77–78 °C (from Et_2O); IR (neat) 1718, 1706, 1598 cm^{-1}; ^1H NMR (500 MHz, $CDCl_3$) δ 2.09 (s, 6H), 2.44 (dd, $J = 4.6$, 17.6 Hz, 2H), 3.27 (dd, $J = 9.6$, 17.6 Hz, 2H), 4.12 (dd, $J = 4.6$, 9.6 Hz, 2H), 7.09–7.10 (m, 4H), 7.29–7.38 (m, 6H); ^{13}C NMR (67.8 MHz, $CDCl_3$) δ 29.98, 46.00, 51.07, 127.58, 128.73, 129.00, 137.86, 206.20, 207.24; MS m/z: 322 (M^+), 175, 147, 104, 77, 43; HRMS m/z for $C_{21}H_{22}O_3$, calcd 322.1569, found 322.1541; Anal. Calcd for $C_{21}H_{22}O_3$: C, 78.23; H, 6.88%. Found: C, 78.23; H, 6.99%. **16b**: mp 87–89 °C (recrystallized from Et_2O); IR (neat) 1716, 1704, 1600 cm^{-1}; ^1H NMR (500 MHz, $CDCl_3$) δ 2.13 (s, 6H), 2.67 (dd, $J = 5.2$, 17.9 Hz, 2H), 3.34 (dd, $J = 8.9$, 17.9 Hz, 2H), 4.41 (dd, $J = 5.2$, 8.9 Hz, 2H), 6.84–6.86 (m, 4H), 7.03–7.08 (m, 6H); ^{13}C NMR (67.8 MHz, $CDCl_3$) δ 29.9, 47.1, 52.9, 126.9, 128.3, 128.4, 137.3, 206.3, 208.8; MS m/z 322 (M^+), 175, 147, 104, 77, 43; HRMS m/z for $C_{21}H_{22}O_3$, calcd 322.1569, found 322.1580; Anal. Calcd for $C_{21}H_{22}O_3$: C, 78.23; H, 6.88%. Found: C, 78.27; H, 6.88%.

4-Phenyl-nonane-2,5,8-trione (18): Compound **18** was prepared from 4-phenyl-1,8-nonadien-5-one (1.28 g, 6.0 mmol), $PdCl_2$ (213 mg, 1.2 mmol), and CuCl (1.3 g, 13.2 mmol) in DMF–H_2O (10:1, 8.8 mL) under oxygen. The crude product was purified by column chromatography on silica gel (hexane/ethyl acetate, 3/1) to give a pale yellow oil of **18** (154.5 mg, 10%). IR (neat) 1715, 1712, 1670, 1600 cm^{-1}; ^1H NMR (500 MHz, $CDCl_3$) δ 2.12 (s, 3H), 2.14 (s, 3H), 2.60 (dd, $J = 3.9$, 18.0 Hz, 1H), 2.63 (dd, $J = 6.2$, 6.2 Hz, 2H), 2.68 (dt, $J = 6.2$, 25.4 Hz, 1H), 2.78 (dt, $J = 6.2$, 25.4 Hz, 1H), 3.42 (dd, $J = 10.0$, 18.0 Hz, 1H), 4.23 (dd, $J = 3.9$, 10.0 Hz, 1H), 7.19–7.20 (m, 2H), 7.27–2.78 (m, 1H), 7.33–7.34 (m, 2H); MS m/z 246 (M^+), 228, 185, 148, 99, 91, 77; HRMS m/z for $C_{15}H_{18}O_3$, calcd 246.1256, found 246.1249. Anal. Calcd for $C_{15}H_{18}O_3$: C, 73.15; H, 7.37%. Found: C, 73.14; H, 7.36%.

2,6-Bis(2-oxopropyl)cycloheptane-1-one (20): Compound **16c** was prepared from 2,7-di(2-propenyl)cycloheptane-1-one (1.73 g, 9.0 mmol), $PdCl_2$ (190 mg, 0.9 mmol), and CuCl (1.78 mg, 0.18 mmol) in DMF–H_2O (7:1, 7.2 mL) under oxygen. The crude product was purified by column chromatography on silica gel (hexane/ethyl acetate, 3/1) to give a pale yellow oil of **20** (711 mg, 35%). IR (neat) 1714, 1702 cm^{-1}; ^1H NMR (270 MHz, $CDCl_3$) δ 1.23–1.49 (m, 4H), 1.70–1.95 (m, 4H), 2.13 (s, 6H), 2.49 (dd, $J = 7.3$, 15.4 Hz, 2H), 2.95 (dd, $J = 7.3$, 21.6 Hz, 2H), 2.96–3.07 (m, 2H); MS m/z 224 (M^+), 206, 181, 166, 95, 43. HRMS m/z for $C_{13}H_2O_3$ calcd 224.1413, found 224.1402. Anal. Calcd for $C_{13}H_{20}O_3$: C, 69.61; H, 8.99%. Found: C, 69.61; H, 9.12%.

4,6-Diphenyldecane-2,5,9-trione (22a): Compound **22a** was prepared from 4,6-diphenyl-1,9-decadien-5-one (1.58 g, 5.2 mmol), $PdCl_2$ (177.3 mg, 1 mmol), and CuCl (1.13 g, 11.4 mmol) in DMF–H_2O (10:1, 3.3 mL) under oxygen. The crude product was purified by column chromatography on silica gel (hexane/ethyl acetate, 5/1) to give a pale-yellow oil of **22a** (786.3 mg, 45%, major/minor = 4). **22a**: IR (neat) 1712, 1600 cm^{-1}; ^1H NMR (500 MHz, $CDCl_3$) [major product] δ 1.87–1.92 (m, 1H), 2.05–2.15 (m, 1H), 2.09 (s, 3H), 2.16 (s, 3H), 2.34–2.39 (m, 2H), 2.59 (dd, $J = 3.5$, 18.1 Hz, 1H), 3.42 (dd, $J = 10.7$, 18.1 Hz, 1H), 3.93 (dd, $J = 6.9$, 6.9 Hz, 1H), 4.22 (dd, $J = 3.5$, 10.7 Hz, 1H), 6.82–6.86 (m, 4H), 7.00–7.08 (m, 6H), [minor product] δ 1.87–1.92 (m, 21H), 1.88 (s, 3H), 2.05 (s, 3H), 2.05–2.15 (m, 1H), 2.30–2.35 (m, 2H), 2.54 (dd, $J = 5.0$, 17.7 Hz, 1H), 3.26 (dd, $J = 9.1$, 17.7 Hz, 1H), 3.60 (dd, $J = 7.2$, 7.2 Hz, 1H), 4.16 (dd, $J = 5.0$, 9.1 Hz, 1H), 7.10–7.16 (m, 4H), 7.28–7.31 (m, 2H), 7.34–7.38 (m, 4H); MS m/z: 336 (M^+), 318, 260, 189, 175, 161, 147, 104, 91, 43; HRMS m/z: for $C_{22}H_{24}O_3$, calcd 336.1725, found 336.1716; Anal. Calcd for $C_{22}H_{24}O_3$: C, 78.54; H, 7.19%. Found: C, 78.55; H, 7.21%.

4-Phenyl-decane-2,5,9-trione (22b): Compound **22b** was prepared from 4-phenyl-1,9-decadien-5-one (1.5 g, 6.58 mmol), $PdCl_2$ (233 mg, 1.32 mmol), and CuCl (1.43 g, 14.5 mmol) in DMF–H_2O (10:1, 8.8 mL) under oxygen. The crude product was purified by column chromatography on silica gel (hexane/ethyl acetate, 3/1) to give a pale-yellow oil of **22b** (783 mg, 46%). IR (neat) 1714, 1712, 1675, 1600 cm^{-1}; ^1H NMR (500 MHz, $CDCl_3$) δ 1.75 (ddddd, $J = 6.7$, 7.0, 7.0, 7.3, 14.2 Hz, 1H), 1.80 (ddddd, $J = 6.7$, 7.0, 7.0, 7.3, 14.3 Hz, 1H), 2.03 (s, 3H), 2.16 (s, 3H), 2.29 (ddd, $J = 7.0$, 7.0, 17.5 Hz, 1H), 2.35 (ddd, $J = 7.3$, 7.3, 17.5 Hz, 1H), 2.42 (ddd, $J = 7.0$, 7.0, 17.5 Hz, 1H), 2.55 (ddd, $J = 6.7$, 6.7, 17.5 Hz, 1H), 2.59 (dd, $J = 3.6$, 14.5 Hz, 1H), 3.46 (dd, $J = 10.5$, 14.5 Hz, 1H), 4.17 (dd, $J = 3.6$, 14.5 Hz, 1H), 7.17–7.18 (m, 2H), 7.27–7.28 (m, 1H), 7.32–7.33 (m, 2H); MS m/z 260 (M^+), 243, 199, 184, 171, 159, 148, 113, 104, 85; HRMS m/z for $C_{16}H_{20}O_3$ calcd 260.1413, found 260.1408. Anal. Calcd for $C_{16}H_2O_3$: C, 73.82; H, 7.74%. Found: C, 73.87; H, 7.93%.

2-(3-Oxobutyl)-6-(2-oxopropyl)cyclohexanone (22c): Compound **22c** was prepared from 2-(3-oxobutyl)-6-(2-propenyl)cyclohexanone (4.16 g, 20 mmol), $PdCl_2$ (354 mg, 2 mmol), and CuCl (2.2 g, 22 mmol) in DMF–H_2O (10:1, 11 mL) under oxygen. The crude product was purified by column chromatography on silica gel (hexane/ethyl acetate, 4/1 to 3/1) to give a pale-yellow oil of **22c** (2.8 mg, 63%). IR (neat) 1710, 1702 cm^{-1}; ^1H NMR (500 MHz, $CDCl_3$) [major product] δ 1.30–1.40 (m, 3H), 1.78–1.95 (m, 4H), 2.10–2.20 (m, 1H), 2.12 (s, 3H), 2.20 (s, 3H), 2.36–2.45 (m, 3H), 2.89–3.00 (m, 3H); [minor product] δ 1.47–1.55 (m, 3H), 1.69–1.70 (m, 1H), 1.92–2.02 (m, 1H), 2.04–2.20 (m, 6H), 2.15 (s, 3H), 2.17 (s, 3H), 2.53–2.59 (m, 2H), 3.05–3.11 (m, 1H); MS m/z 224 (M^+), 206, 166, 148, 135, 123, 109, 96, 81, 71, 43; HRMS m/z for $C_{13}H_{20}O_3$, calcd 224.1313, found 224.1420; Anal. Calcd for $C_{13}H_{20}O_3$: C, 69.61; H, 8.99%. Found: C, 69.65; H, 9.08%.

Synthesis of Nitrogen Containing Compounds from Di- or Triketone. 2-Methyl-5-(phenethyl)pyrrole (15a): A crude product that was prepared from $TiCl_4$ (0.055 mL, 0.5 mmol), TMSCl (0.63 mL, 5.0 mmol), Li (37 mg, 5.0 mmol), **14a** (82 mg, 0.4 mmol), and CsF (369 mg, 2.5 mmol) in THF (7.5 mL) was purified by column chromatography on silica gel [hexane/ethyl acetate (10/1) which was contained 3% Et_3N] to give **15a** (19 mg, 25%). IR (neat) 3372, 1602 cm^{-1}; ^1H NMR (500 MHz, $CDCl_3$) δ 2.21 (s, 3H), 2.85–2.94 (m, 4H), 5.76 (d, $J = 2.0$ Hz, 1H), 5.18 (dd, $J = 2.0$, 2.7 Hz, 1H), 7.18–7.23 (m, 3H), 7.27–7.31 (m, 2H), 7.47 (brs, 1H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 13.0, 29.7, 36.3, 105.2, 105.7, 126.1, 126.2, 128.4, 130.6, 141.8; MS m/z 185 (M^+), 150, 122, 99, 91, 77; HRMS m/z for $C_{13}H_{15}N$, calcd 185.1205, found 185.1197.

2-Benzyl-5-methyl-3-phenylpyrrole (15b): A crude product that was prepared from $TiCl_4$ (0.055 mL, 0.5 mmol), TMSCl (0.63 mL, 5.0 mmol), Li (37 mg, 5.0 mmol), **15a** (106 mg, 0.4 mmol), and CsF (376 mg, 2.5 mmol) in THF (7.5 mL) was purified by column chromatography on silica gel [hexane/ethyl acetate (10/1), which was contained 3% Et_3N] to give **14b** (39 mg, 39%). IR (neat) 3412, 1600 cm^{-1}; ^1H NMR (500 MHz, $CDCl_3$) δ 2.21 (s, 3H), 4.10 (s, 2H), 6.04 (d, $J = 2.5$ Hz, 1H), 7.17–7.25 (m, 4H), 7.30–7.34 (m, 4H), 7.40–7.41 (m, 2H), 7.44 (brs, 1H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 12.7, 32.4, 106.4, 122.0, 124.5, 125.1, 126.3, 126.5, 127.5, 128.3, 128.5, 128.6, 137.0, 139.7; MS m/z

247 (M^+), 232, 202, 170, 154, 128; HRMS m/z for $C_{18}H_{17}N$, calcd 247.1361, found 247.1345.

2-Benzyl-5-methylpyrrole (15c): A crude product, which was prepared from $TiCl_4$ (0.055 mL, 0.5 mmol), TMSCl (0.63 mL, 5.2 mmol), Li (37 mg, 5.0 mmol), **14c** (76 mg, 0.4 mmol), and CsF (378 mg, 2.5 mmol) in THF (7.5 mL), was purified by column chromatography on silica gel [hexane/ethyl acetate (10/1) which was contained 3% Et_3N] to give **15c** (37 mg, 54%). IR (neat) 3366, 1592 cm^{-1}; ^1H NMR (500 MHz, $CDCl_3$) δ 2.28 (d, $J = 3.1$ Hz, 3H), 4.02 (s, 2H), 5.87 (d, $J = 2.1$ Hz, 1H), 5.94 (d, $J = 2.1$ Hz, 1H), 7.31–7.33 (m, 3H), 7.37–7.42 (m, 2H), 7.58 (brs, 1H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 13.0, 34.2, 105.8, 106.5, 127.0, 128.6, 128.7, 129.2, 139.8; MS m/z 171 (M^+), 156, 128, 115, 102, 94, 91, 85, 77, 65, 51; HRMS (EI, m/z) for $C_{12}H_{13}N$, calcd 171.1048, found 171.1038.

2,5-Dimethyl-3-phenyl-1*H*-pyrrole (15d): A crude product, which was prepared from $TiCl_4$ (0.055 mL, 0.5 mmol), TMSCl (0.63 mL, 5.2 mmol), Li (36.9 mg, 5.0 mmol), **14d** (76.4 mg, 0.4 mmol), and CsF (377.9 mg, 2.5 mmol) in THF (7.5 mL), was purified by column chromatography on silica gel [hexane/ethyl acetate (10/1) that was contained 3% Et_3N] to give **15d** (44.1 mg, 64%). IR (neat) 3366, 1602 cm^{-1}; ^1H NMR (500 MHz, $CDCl_3$) δ 2.25 (s, 3H), 2.35 (s, 3H), 6.00 (d, $J = 2.5$ Hz, 1H), 7.30–7.40 (m, 5H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 12.5, 12.9, 106.3, 120.9, 122.4, 124.8, 125.7, 127.4, 128.3, 137.2; MS m/z 171 (M^+), 170, 156, 128, 115, 102, 94, 77, 63, 43; HRMS m/z for $C_{12}H_{13}N$, calcd 171.1048, found 171.1030.

2-(3-Ethoxycarbonylpropyl)-3,5-dimethylpyrrole (15e): IR (neat) 3386, 3086, 2928, 1718, 1636 cm^{-1}; ^1H NMR (270 MHz, $CDCl_3$) δ 7.98 (d, $J = 2.6$ Hz, 1H), 7.57 (brs, 1H), 4.15 (q, $J = 7.1$ Hz, 2H), 2.54 (t, $J = 7.3$ Hz, 2H), 2.31 (t, $J = 7.3$ Hz, 2H), 2.20 (d, $J = 2.6$ Hz, 3H), 1.96 (s, 3H), 1.85 (tt, $J = 7.3$, 7.3 Hz, 2H), 1.26 (t, $J = 7.1$ Hz, 3H); ^{13}C NMR (100 MHz, C_6D_6) δ 173.1, 125.1, 124.6, 114.4, 108.4, 60.2, 33.5, 26.2, 25.1, 14.4, 13.2, 11.4; MS m/z 209 (M^+), 164, 108; HRMS calcd for $C_{12}H_{19}NO_2$ 209.1416, found 209.1417.

2-Methyl-1,4,5,6-tetrahydrocyclopenta[*b*]pyrrole (15f): A crude product, which was prepared from $TiCl_4$ (0.055 mL, 0.5 mmol), TMSCl (0.63 mL, 5.0 mmol), Li (37 mg, 5.0 mmol), **14f** (56 mg, 0.4 mmol), and CsF (379 mg, 2.5 mmol) in THF (7.5 mL), was purified by column chromatography on silica gel [hexane/ethyl acetate (10/1) that was contained 3% Et_3N] to give **15f** (11 mg, 23%). IR (neat) 3362, 1613 cm^{-1}; ^1H NMR (500 MHz, $CDCl_3$) δ 2.25 (s, 3H), 2.32–2.43 (m, 2H), 2.57–2.60 (m, 2H), 2.65–2.69 (m, 2H), 5.78 (s, 1H), 7.53 (brs, 1H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 13.6, 25.4, 25.6, 29.0, 101.7, 126.6, 130.6, 134.7; MS m/z 121 (M^+), 120, 106, 93, 91, 79, 67; HRMS m/z for $C_8H_{11}N$, calcd 121.0891, found 121.0897.

2-Methyl-4,5,6,7-tetrahydro-1*H*-indole (15g): A crude product, which was prepared from $TiCl_4$ (0.055 mL, 0.5 mmol), TMSCl (0.63 mL, 5.0 mmol), Li (37 mg, 5.0 mmol), **14g** (62 mg, 0.4 mmol), and CsF (376 mg, 2.5 mmol) in THF (7.5 mL), was purified by column chromatography on silica gel [hexane/ethyl acetate (10/1) which was contained 3% Et_3N] to give **15g** (22 mg, 41%). IR (neat) 3362, 1606 cm^{-1}; ^1H NMR (500 MHz, $CDCl_3$) δ 1.70–1.84 (m, 4H), 2.22 (s, 3H), 2.43–2.55 (m, 4H), 5.63 (d, $J = 1.4$ Hz, 1H), 7.38 (brs, 1H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 13.0, 22.7, 22.9, 23.6, 23.9, 105.1, 117.0, 125.4, 125.8; MS m/z 135 (M^+), 117, 107, 94, 91, 77; HRMS m/z for $C_9H_{13}N$, calcd 135.1048, found 135.1049.

2-Methyl-1,4,5,6,7,8-hexahydrocyclopenta[*b*]pyrrole (15h): A crude product, which was prepared from $TiCl_4$ (0.055 mL, 0.5 mmol), TMSCl (0.63 mL, 5.0 mmol), Li (37 mg, 5.0 mmol), **14h** (67 mg, 0.4 mmol), and CsF (378 mg, 2.5 mmol) in THF (7.5 mL), was purified by column chromatography on silica gel [hexane/ethyl acetate (10/1) that contained 3% Et_3N] to give **15h** (25 mg, 41%). IR (neat) 3364, 1602 cm^{-1}; ^1H NMR (500 MHz, $CDCl_3$) δ 1.64–1.70 (m, 4H), 1.76–1.79 (m, 2H), 2.19 (s, 3H), 2.49–2.55 (m, 2H), 2.57–2.63 (m, 2H), 5.63 (d, $J = 2.2$ Hz, 1H), 7.38 (brs, 1H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 12.7, 28.2, 28.3, 29.2, 29.4, 31.9, 108.0, 121.5, 123.2, 128.7; MS (EI, m/z) 149 (M^+), 134, 120, 107, 94, 91, 79, 67; HRMS m/z for $C_{10}H_{15}N$, calcd 149.1204, found 149.1178.

3,5-Dimethyl-1,7-diphenyl-1*H*-, -3*H*-, and -1*H*-2,3-dihydropyrrolizines (17a, 17b, and 17c): A crude product, which was prepared from $TiCl_4$ (0.055 mL, 0.5 mmol), TMSCl (0.63 mL, 5.0 mmol), Li (37 mg, 5.0 mmol), triketone **16a** (67 mg, 0.4 mmol), and CsF (378 mg, 2.5 mmol) in THF (7.5 mL), was purified by column chromatography on silica gel [hexane/ethyl acetate (10/1) that contained 3% Et_3N] to give **17** (35.4 mg, 31%, ratio of **17a**:**17b**:**17c** = 1:1.8:1). **17a**: IR (neat) 1602 cm^{-1}; ^1H NMR (500 MHz, $CDCl_3$) δ 2.30 (t, $J = 1.3$ Hz, 3H), 2.47 (s, 3H), 4.80 (d, $J = 1.3$ Hz, 1H), 5.47 (d, $J = 1.3$ Hz, 1H), 6.11 (s, 1H), 6.91–7.25 (m, 10H); MS m/z 322 (M^+) 270, 254, 228, 208, 194, 165, 143, 115, 104, 91, 77; HRMS m/z: for $C_{21}H_{22}N$, calcd 285.1518, found 285.1514. **17b**: IR (neat) 1602 cm^{-1}; ^1H NMR (500 MHz, $CDCl_3$) δ 1.57 (d, $J = 6.8$ Hz, 3H), 2.40 (s, 3H), 4.77 (dt, $J = 6.8$, 6.8 Hz, 1H), 6.12 (d, $J = 6.8$ Hz, 1H), 6.12 (s, 1H), 6.91–7.25 (m, 10H); MS m/z 285 (M^+), 270, 254, 208, 165, 143, 115, 104, 91, 77; HRMS m/z for $C_{21}H_{22}N$, calcd 285.1518, found 285.1514. **17c**: IR (neat) 1608 cm^{-1}; ^1H NMR (500 MHz, $CDCl_3$) [major product] δ 1.31 (d, $J = 6.5$ Hz, 3H), 2.18 (ddd, $J = 3.2$, 6.5, 12.8 Hz, 1H), 2.31 (s, 3H), 3.31 (ddd, $J = 4.2$, 9.3, 12.8 Hz, 1H), 4.30 (ddt, $J = 4.2$, 6.5, 6.5 Hz, 1H), 4.57 (dd, $J = 3.2$, 9.3 Hz, 1H), 6.32 (s, 1H), 6.95–7.24 (m, 10H), [minor project] δ 1.47 (d, $J = 6.3$ Hz, 3H), 2.34 (s, 3H), 2.56 (ddd, $J = 5.3$, 6.8, 12.5 Hz, 1H), 2.64 (ddd, $J = 6.8$, 8.0, 12.5 Hz, 1H), 4.40 (ddt, $J = 6.3$, 6.8, 6.8 Hz, 1H), 4.61 (dd, $J = 5.3$, 8.0 Hz, 1H), 6.28 (s, 1H), 6.95–7.24 (m, 10H); ^{13}C NMR (100 MHz, $CDCl_3$) [major product] δ 12.1, 22.3, 43.2, 46.9, 52.2, 108.5, 115.6, 123.8, 124.1, 125.3, 126.3, 127.6, 128.2, 128.5, 133.0, 136.0, 144.6, [minor product] δ 12.5, 20.8, 29.7, 48.4, 51.9, 108.9, 124.6, 126.4, 127.3, 128.0, 133.7, 143.9, 149.0; MS m/z 287 (M^+) 272, 256, 244, 230, 210, 194, 180, 167, 144, 115, 102; HRMS m/z for $C_{21}H_{22}N$, calcd 287.1674, found 287.1652.

3,5-Dimethyl-7-phenyl-2,3-dihydro-1*H*-pyrrolizine (19): A crude product, which was prepared from $TiCl_4$ (0.055 mL, 0.5 mmol), TMSCl (0.63 mL, 5.0 mmol), Li (37 mg, 5.0 mmol), **18** (98 mg, 0.4 mmol), and CsF (375 mg, 2.5 mmol) in THF (7.5 mL), was purified by column chromatography on silica gel [hexane/ethyl acetate (10/1) that contained 3% Et_3N] to give **19** (26 mg, 30%). IR (neat) 1602 cm^{-1}; ^1H NMR (500 MHz, $CDCl_3$) δ 1.39 (d, $J = 6.5$ Hz, 3H), 2.13–2.18 (m, 1H), 2.27 (s, 3H), 2.70–2.75 (m, 1H), 2.96–3.01 (m, 1H), 3.08–3.14 (m, 1H), 4.30–4.33 (m, 1H), 6.20 (s, 1H), 7.06–7.09 (m, 1H), 7.28–7.30 (m, 3H), 7.42–7.43 (m, 1H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 12.1, 21.1, 24.3, 36.2, 52.6, 107.8, 114.0, 123.6, 124.1, 124.9, 128.4, 132.1, 136.9; MS m/z 211 (M^+), 196, 180, 168, 154, 141, 134, 128, 115, 105, 90, 77; HRMS m/z for $C_{15}H_{17}N$, calcd 211.1361, found 211.1352.

2,3-Dimethyl-5,5a,6,7,8,9-hexahydro-4*H*-3-azacyclopenta[*cd*]azulene (21): A crude product, which was prepared from $TiCl_4$ (0.055 mL, 0.5 mmol), TMSCl (0.63 mL, 5.0 mmol), Li (37 mg, 5.0 mmol), **20** (90 mg, 0.4 mmol), and CsF (379 mg,

2.5 mmol) in THF (7.5 mL), was purified by column chromatography on silica gel [hexane/ethyl acetate (10/1) that contained 3% Et_3N] to give **21** (23 mg, 31%). IR (neat) 1608 cm^{-1}; ^1H NMR (500 MHz, $CDCl_3$) [major product] δ 1.15–1.25 (m, 1H), 1.44–1.53 (m, 2H), 1.49 (d, $J = 6.5$ Hz, 3H), 1.64–1.70 (m, 1H), 1.95–2.02 (m, 2H), 2.09–2.12 (m, 1H), 2.21 (s, 3H), 2.39–2.46 (m, 1H), 2.51 (dd, $J = 3.7$, 15.7 Hz, 1H), 2.63–2.68 (m, 1H), 2.93 (dddd, $J = 5.2$, 10.7, 17.5, 21.7 Hz, 1H), 4.18–4.25 (m, 1H), 5.68 (s, 1H), [minor product] δ 0.88–0.92 (m, 1H), 1.31 (d, $J = 6.5$ Hz, 3H), 1.39–1.45 (m, 2H), 1.64–1.70 (m, 1H), 1.95–2.02 (m, 2H), 2.16–2.25 (m, 1H), 2.17 (s, 3H), 2.39–2.46 (m, 1H), 2.50–2.53 (m, 1H), 2.63–2.67 (m, 1H), 3.19 (dddd, $J = 5.1$, 10.4, 14.3, 22.2 Hz, 1H), 4.28–4.33 (m, 1H), 5.66 (s, 1H); ^{13}C NMR (100 MHz, $CDCl_3$) [major product] δ 12.6, 20.8, 27.7, 30.3, 30.5, 34.7, 39.0, 45.9, 54.9, 109.8, 114.6, 121.9, 138.5, [minor product] δ 11.5, 21.3, 27.7, 30.2, 30.7, 34.7, 38.1, 44.1, 52.9, 108.9, 113.1, 121.0, 136.9; MS m/z 189 (M^+) 174, 160, 146, 118, 105, 91; HRMS m/z for $C_{13}H_{19}N$, calcd 189.1517, found 189.1537.

3,5-Dimethyl-1,8-diphenyl-7,8-dihydroindolizine (23a): A crude product, which was prepared from $TiCl_4$ (0.11 mL, 1.0 mmol), TMSCl (1.26 mL, 10.0 mmol), Li (73.1 mg, 10.0 mmol), **22a** (168.0 mg, 0.5 mmol), and CsF (377 mg, 2.5 mmol) in THF (7.5 mL), was purified by column chromatography on silica gel [hexane/ethyl acetate (10/1) that contained 3% Et_3N] to give **23a** (60.8 mg, 41%); IR (neat) 1666, 1602 cm^{-1}; ^1H NMR (500 MHz, $CDCl_3$) δ 2.28 (s, 3H), (ddd, $J = 6.0$, 6.2, 16.2 Hz, 1H), 2.51 (s, 3H), 2.65 (ddd, $J = 6.0$, 6.2, 16.2 Hz, 1H), 4.36 (dd, $J = 6.0$, 6.2 Hz, 1H), 4.95 (dd, $J = 6.2$, 6.2 Hz, 1H), 6.16 (s, 1H), 7.05–7.29 (m, 10H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 16.3, 20.9, 30.4, 108.7, 109.3, 120.2, 125.3, 126.1, 127.5, 127.6, 128.2, 129.0, 134.7, 136.1, 144.2; MS m/z 299 (M^+), 284, 268, 222, 207, 194, 180, 165, 141, 128, 115, 102, 91; HRMS m/z for $C_{22}H_{22}N$, calcd 299.1674, found 299.1673.

3,5-Dimethyl-1-phenyl-7,8-dihydroindolizine (23b): A crude product, which was prepared from $TiCl_4$ (0.11 mL, 1.0 mmol), TMSCl (1.26 mL, 10.0 mmol), Li (73.7 mg, 10.0 mmol), **22b** (130.0 mg, 0.5 mmol), and CsF (376 mg, 2.5 mmol) in THF (7.5 mL), was purified by column chromatography on silica gel [hexane/ethyl acetate (5/1) which was contained 3% Et_3N] to give **23b** (62.3 mg, 56%). IR (neat) 1664, 1604 cm^{-1}; ^1H NMR (500 MHz, $CDCl_3$) δ 2.07–2.12 (m, 2H), 2.24 (s, 3H), 2.41 (s, 3H), 2.84 (t, $J = 7.2$ Hz, 2H), 5.18 (t, $J = 4.8$ Hz, 1H), 6.04 (s, 1H), 7.15–7.17 (m, 2H), 7.31–7.33 (m, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 16.2, 21.1, 21.5, 21.6, 108.9, 110.9, 119.1, 125.2, 126.7, 127.0, 127.8, 128.3, 134.6, 136.5; MS m/z 223 (M^+), 208, 193, 167, 152, 141, 128, 121, 115, 102, 91, 77; HRMS m/z for $C_{16}H_{17}N$, calcd 223.1361, found 223.1362.

2,4-Dimethyl-6a,7,8,9-tetrahydro-6*H*-pyrolo[3,2,1-*ij*]quinoline (23c): A crude product, which was prepared from $TiCl_4$ (0.11 mL, 1.0 mmol), TMSCl (1.26 mL, 10.0 mmol), Li (72.9 mg, 10.0 mmol), **22c** (112.1 mg, 0.5 mmol), and CsF (376 mg, 2.5 mmol) in THF (7.5 mL), was purified by column chromatography on silica gel [hexane/ethyl acetate (5/1) that contained 3% Et_3N] to give **23c** (28.4 mg, 30%). IR (neat) 1654, 1604 cm^{-1}; ^1H NMR (500 MHz, $CDCl_3$) δ 1.23–1.31 (m, 1H), 1.65–1.82 (m, 2H), 1.93–2.01 (m, 2H), 2.10–2.17 (m, 1H), 2.19 (s, 3H), 2.37 (s, 3H), 2.46–2.50 (m, 2H), 2.68–2.73 (m, 1H), 5.02 (d, $J = 7.0$ Hz, 1H), 5.68 (s, 1H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 15.6, 20.6, 22.4, 24.0, 28.5, 303, 31.1, 107.9, 108.9, 114.4, 126.3, 134.2, 165.2; MS m/z 187 (M^+), 172, 158, 147, 134, 117, 105, 91, 77, 73; HRMS m/z for $C_{13}H_{17}N$, calcd 187.1361, found 187.1334.

Synthesis of Heterocycles from 7 and Keto–Alkyne. Methyl 4-(2-Oxocyclohexyl)-2-butynoate (24a): IR (neat) 2940, 2862, 2238, 1714, 1436, 1260, 1078 cm^{-1}; ^1H NMR (500 MHz, $CDCl_3$) δ 1.42 (dddd, $J = 12.8$, 12.8, 12.8, 3.7 Hz, 1H), 1.68 (m, 1H), 1.93 (m, 1H), 2.11 (m, 1H), 2.3 1 (m, 1H), 2.33 (dd, $J = 17.5$, 8.5 Hz, 1H), 2.37–2.46 (m, 2H), 2.54–2.60 (m, 2H), 2.77 (dd, $J = 17.5$, 4.6 Hz, 1H), 3.75 (s, 3H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 209.6, 153.8, 87.6, 73.7, 52.4, 48.7, 41.6, 33.2, 27.5, 24.8, 18.9; EIMS m/z 194 (M^+), 179; HRMS calcd for $C_{11}H_{14}O_3$ 194.0943, found 194.0938.

Methyl 4-(5-Acetoxy-2-oxocyclohexyl)-2-butynoate (24b): IR (neat) 2238, 1714 cm^{-1}; ^1H NMR (500 MHz, $CDCl_3$) δ 1.58–1.95 (m, 2H), 2.04 (s, 33/13H), 2.12 (s, 6/13H), 2.57–2.97 (m, 7H), 3.72 (s, 3H), 5.17 (dddd, $J = 4.4$, 4.4, 11.0, 11.0 Hz, 11/13H), 5.23 (m, 2/13H); ^{13}C NMR (68 MHz, $CDCl_3$) [major product] δ 207.0, 170.2, 153.8, 86.5, 74.3, 69.6, 52.5, 45.0, 37.8, 36.4, 31.1, 21.1, 18.8. LRMS m/z 252 (M^+), 237, 43; HRMS calcd for $C_{13}H_{16}O_5$ 252.0997, found 252.0991.

4-(2-Oxocyclohexyl)-2-butynenitrile (24c): IR (neat) 2318, 2264, 1712 cm^{-1}; ^1H NMR (270 MHz, $CDCl_3$) δ 1.44 (m, 1H), 1.58–1.80 (m, 2H), 1.94 (m, 1H), 2.12 (m, 1H), 2.23–2.50 (m, 4H), 2.57 (m, 1H), 2.72 (dd, $J = 17.8$, 5.3 Hz, 1H); ^{13}C NMR (68 MHz, $CDCl_3$) δ 19.4, 24.9, 27.5, 33.4, 41.7, 48.4, 56.2, 85.6, 105.1, 209.0; LRMS m/z 161 (M^+), 133, 97, 77; HRMS calcd for $C_{10}H_{11}NO$ 161.0892, found 161.0831.

***N*,*N*-Diethyl-4-(2-oxocyclohexyl)-2-butynamide (24d):** IR (neat) 2226, 1710, 1622 cm^{-1}; ^1H NMR (270 MHz, $CDCl_3$) δ 1.12 (t, $J = 7.2$ Hz, 3H), 1.91 (t, $J = 7.2$ Hz, 3H), 1.44 (m, 1H), 1.54–1.79 (m, 2H), 1.92 (m, 1H), 2.12 (m, 1H), 2.24–2.49 (m, 3H), 2.35 (dd, $J = 17.1$, 8.1 Hz, 1H), 2.56 (m, 1H), 2.75 (dd, $J = 17.1$, 4.7 Hz, 1H), 3.40 (q, $J = 7.2$ Hz, 2H), 3.55 (q, $J = 7.2$ Hz, 2H); ^{13}C NMR (68 MHz, $CDCl_3$) δ 209.5, 153.3, 89.1, 74.9, 48.5, 43.0, 41.3, 38.6, 33.0, 27.2, 24.5, 18.8, 13.9, 12.3; EIMS m/z 235 (M^+), 135; HRMS calcd for $C_{14}H_{21}NO$ 235.1583, found 235.1569.

5-(2-Oxocyclohexyl)-3-pentyne-2-one (24e): IR (neat) 2210, 1712, 1676 cm^{-1}; ^1H NMR (270 MHz, $CDCl_3$) δ 1.42 (dddd, $J = 12.6$, 12.6, 3.6 Hz, 1H), 1.60–1.80 (m, 2H), 1.95 (m, 1H), 2.11 (m, 1H), 2.25–2.50 (m, 4H), 2.31 (s, 3H), 2.56 (m, 1H), 2.78 (dd, $J = 17.6$, 4.6 Hz, 1H); ^{13}C NMR (68 MHz, $CDCl_3$) δ 209.9, 184.6, 91.9, 82.2, 48.8, 41.7, 33.3, 32.6, 27.6, 24.9, 19.3; LRMS m/z 178 (M^+), 163, 135, 43; HRMS calcd for $C_{11}H_{14}O_2$ 178.0993, found 178.1006.

2-(2-Butynyl)cyclohexanone (24f): IR (neat) 1710 cm^{-1}; ^1H NMR (270 MHz, $CDCl_3$) δ 1.38 (m, 1H), 1.53–1.80 (m, 3H), 1.77 (dd, $J = 2.5$, 2.5 Hz, 3H), 1.80–1.97 (m, 1H), 2.00–2.18 (m, 2H), 2.21–2.48 (m, 3H), 2.56 (ddq, $J = 16.4$, 5.0, 2.5 Hz, 1H); ^{13}C NMR (68 MHz, C_6D_6) δ 3.3, 19.5, 25.1, 27.7, 33.3, 41.7, 49.9, 76.6, 77.7, 208.8; LRMS m/z 150 (M^+), 149, 135; HRMS calcd for $C_{10}H_{14}O$ 150.1045, found 150.1036.

2-(3-Phenyl-2-propynyl)cyclohexanone (24g): mp 48 °C (from hexane); IR (nujol) 2220, 1702, 1490 cm^{-1}; ^1H NMR (270 MHz, $CDCl_3$) δ 1.47 (m, 1H), 1.62–1.78 (m, 2H), 1.94 (m, 1H), 2.11 (m, 1H), 2.26–2.66 (m, 4H), 2.40 (dd, $J = 16.9$, 8.6 Hz, 1H), 2.85 (dd, $J = 16.9$, 4.1 Hz, 1H), 7.24–7.30 (m, 3H), 7.34–7.42 (m, 2H); ^{13}C NMR (68 MHz, $CDCl_3$) δ 19.6, 24.9, 27.6, 32.2, 41.7, 49.6, 81.6, 88.0, 123.6, 127.4, 128.0, 131.4, 210.7; EI-LRMS m/z 212 (M^+), 183, 135; EI-HRMS calcd for $C_{15}H_{16}O$ 212.1202, found 212.1208; Anal. Calcd for $C_{15}H_{16}O$: C, 84.87; H, 7.60%. Found: C, 85.08; H, 7.73%.

2-[3-(*p*-Methylphenyl)-2-propynyl]cyclohexanone (26a):

mp 46 °C (from hexane); IR (nujol) 2230, 1705, 1518 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$) δ 1.45 (m, 1H), 1.60–1.80 (m, 2H), 1.95 (m, 1H), 2.12 (m, 1H), 2.30–2.62 (m, 5H), 2.54 (s, 3H), 2.84 (dd, $J = 17.1$, 4.3 Hz, 1H), 7.05–7.12 (m, 2H), 7.25–7.30 (m, 2H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 210.4, 137.2, 131.1, 128.6, 120.4, 87.1, 81.5, 49.5, 41.7, 33.2, 27.6, 24.9, 21.1, 19.5; LRMS m/z 226 (M^+), 211; HRMS calcd for $C_{16}H_{18}O$ 226.1358, found 226.1347; Anal. Calcd for $C_{16}H_{18}O$: C, 84.91; H, 8.02%. Found: C, 85.08; H, 8.11%.

Methyl *p*-[3-(2-Oxocyclohexyl)-2propynyl]benzoate (26b): mp 69–70 °C (from MeOH); IR (nujol) 2220, 1714, 1702, 1606 cm^{-1}; ^1H NMR (270 MHz, $CDCl_3$) δ 1.50 (m, 1H), 1.60–1.82 (m, 2H), 1.95 (m, 1H), 2.11 (m, 1H), 2.28–2.67 (m, 5H), 2.87 (dd, $J = 17.1$, 4.4 Hz, 1H), 3.91 (m, 3H), 7.41–7.48 (m, 2H), 7.93–7.99 (m, 2H); ^{13}C NMR (68 MHz, $CDCl_3$) δ 210.5, 166.4, 131.3, 129.1, 128.8, 128.4, 91.6, 81.1, 52.0, 49.5, 41.8, 33.3, 27.7, 25.0, 19.7; EIMS m/z 270 (M^+), 255, 241; HRMS calcd for $C_{17}H_{18}O_3$ 270.2156, found 270.2154; Anal. Calcd for $C_{17}H_{18}O_3$: C, 75.53; H, 6.71%. Found: C, 75.49; H, 6.76%.

2-[3-(*p*-Cyanophenyl)-2-propynyl]cyclohexanone (26c): mp 97–98 °C (from MeOH); IR (nujol) 2224, 1698, 1604 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$) δ 1.47 (ddd, $J = 12.7$, 12.7, 3.4 Hz, 1H), 1.60–1.79 (m, 2H), 1.94 (m, 1H), 2.12 (m, 1H), 2.39–2.49 (m, 4H), 2.59 (m, 1H), 2.84 (dd, $J = 17.3$, 4.6 Hz, 1H), 7.44 (d, $J = 8.3$ Hz, 2H), 7.55 (d, $J = 8.3$ Hz, 2H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 210.2, 131.8, 131.6, 128.6, 118.3, 110.7, 93.3, 80.3, 49.4, 41.8, 33.3, 27.7, 25.0, 19.8; LRMS m/z 237 (M^+), 135, 55; HRMS calcd for $C_{16}H_{15}NO$ 237.1153, found 237.1158; Anal. Calcd for $C_{16}H_{15}NO$: C, 80.98; H, 6.37; N, 5.90%. Found: C, 81.10; H, 6.51; N, 5.88%.

2-[3-(*p*-Trifluolomethylphenyl)-2-propynyl]cyclohexanone (26d): mp 45–46 °C (from hexane); IR (nujol) 2240, 1734, 1614 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$) δ 1.50 (m, 1H), 1.64–1.80 (m, 2H), 1.95 (m, 1H), 2.13 (m, 1H), 2.30–2.50 (m, 4H), 2.60 (m, 1H), 2.86 (dd, $J = 17.0$, 4.5 Hz, 1H), 7.47 (d, $J = 8.5$ Hz, 2H), 7.53 (d, $J = 8.5$ Hz, 2H); ^{13}C NMR (68 MHz, $CDCl_3$) δ 210.7, 131.9, 129.4 (q, $J_{C-F} = 33$ Hz), 127.0, 125.1, 124.1 (q, $J_{C-F} = 272$ Hz), 91.2, 80.7, 49.7, 42.0, 33.5, 27.9, 25.2, 19.9; MS m/z 280 (M^+), 261, 183; HRMS calcd for $C_{16}H_{15}F_3O$ 280.175, found 280.171; Anal. Calcd for $C_{16}H_{15}F_3O$: C, 68.56; H, 5.39%. Found: C, 68.62; H, 5.49%.

Methyl *o*-[3-(2-Oxocyclohexyl)-2-propynyl]benzoate (26f): IR (neat) 2245, 1735, 1720 cm^{-1}; ^1H NMR (500 MHz, $CDCl_3$) δ 1.50 (ddd, $J = 12.6$, 12.6, 3.5 Hz, 1H), 1.65–1.79 (m, 2H), 1.95 (m, 1H), 2.11 (m, 1H), 2.35 (ddd, $J = 13.0$, 13.0, 6.0 Hz, 1H), 2.41–2.51 (m, 2H), 2.55 (m, 1H), 2.63 (m, 1H), 2.91 (dd, $J = 17.2$, 4.3 Hz, 1H), 3.91 (s, 3H), 7.30 (dd, $J = 7.6$, 7.6 Hz, 1H), 7.41 (dd, $J = 7.6$, 7.6 Hz, 1H), 7.50 (d, $J = 7.9$ Hz, 1H), 7.87 (d, $J = 7.6$ Hz, 1H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 210.4, 166.4, 133.8, 131.7, 131.1, 129.8, 127.0, 123.8, 93.5, 80.0, 51.7, 49.4, 41.6, 33.0, 27.5, 24.8, 19.8; EIMS m/z 270 (M^+), 255, 55; HRMS calcd for $C_{17}H_{18}O_3$ 270.1256, found 270.1252.

4-(2-Oxo-cycloheptyl)-2-butynoic Acid Methyl Ester (29a): IR (neat) 2930, 2236, 1714 cm^{-1}; ^1H NMR (500 MHz, $CDCl_3$) δ 1.35 (m, 1H), 1.42–1.60 (m, 2H), 1.68 (m, 1H), 1.80–1.95 (m, 3H), 2.00 (m, 1H), 2.40 (dd, $J = 17.6$, 8.7 Hz, 1H), 2.47 (m, 1H), 2.59 (m, 1H), 2.68 (dd, $J = 17.6$, 5.1 Hz, 1H), 2.82 (m, 1H), 3.75 (s, 3H); ^{13}C NMR (68 MHz, $CDCl_3$) δ 20.9, 23.6, 28.6, 29.2, 30.4, 43.1, 49.8, 52.4, 73.6, 87.9, 153.9, 217.7; LRMS m/z 208 (M^+); HRMS calcd for $C_{12}H_{16}O_3$ 208.1099, found 208.1087.

6-Oxo-2-heptynoic Acid Methyl Ester (29b): IR (neat) 2240, 1718 cm^{-1}; ^1H NMR (270 MHz, $CDCl_3$) δ 2.16 (s, 3H), 2.52–2.61 (m, 2H), 2.68–2.77 (m, 2H), 3.75 (s, 3H); ^{13}C NMR (68 MHz, $CDCl_3$) δ 12.8, 29.5, 40.8, 52.3, 72.8, 87.9, 153.8, 205.0; LRMS m/z 155 ($M^+ + H$), 139, 111; HRMS calcd for $C_8H_{11}O_3$ ($M^+ + H$) 155.0708, found 155.0698.

5-(2-Oxocyclohexyl)-2-pentynoic Acid Methyl Ester (29c): IR (neat) 1714 cm^{-1}; ^1H NMR (270 MHz, $CDCl_3$) δ 1.28–1.58 (m, 3H), 1.58–1.82 (m, 2H), 1.84–1.94 (m, 1H), 1.99–2.18 (m, 3H), 2.26–2.51 (m, 2H), 2.42 (t, $J = 7.1$ Hz, 2H), 3.75 (s, 3H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 16.0, 24.7, 27.1, 27.6, 33.6, 41.7, 48.6, 52.0, 72.7, 88.7, 153.5, 211.4; LRMS m/z 208 (M^+), 176, 111, 98; HRMS calcd for $C_{12}H_{16}O_3$ 208.1099, found 208.1105; Anal. Calcd for $C_{12}H_{16}O_3$: C, 69.21; H, 7.74%. Found: C, 69.20; H, 7.83%.

5-(2-Oxocyclopentyl)-2-pentynoic Acid Methyl Ester (29d): IR (neat) 1744, 1712 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$) δ 1.43–1.58 (m, 2H), 1.78 (m, 1H), 1.94–2.53 (m, 8H), 3.73 (s, 3H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 16.6, 20.3, 27.3, 29.2, 37.6, 47.6, 52.2, 73.0, 88.4, 153.7, 219.6; MS m/z 194 (M^+), 162, 111; HRMS calcd for $C_{11}H_{14}O_3$ 194.0943, found 194.0949; Anal. Calcd for $C_{11}H_{14}O_3$: C, 68.02; H, 7.27%. Found: C, 67.95; H, 7.27%.

5,5-Bis(benzyloxymethyl)-7-oxo-2-octynoic Acid Methyl Ester (29e): IR (neat) 2234, 1714 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$) δ 2.10 (s, 3H), 2.60 (s, 2H), 2.69 (s, 2H), 3.53 (s, 4H), 3.75 (s, 3H), 4.46 (s, 4H), 7.24–7.35 (m, 10H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 22.6, 31.7, 42.0, 43.7, 52.4, 71.3, 73.2, 74.8, 86.7, 127.4, 127.5, 128.2, 138.2, 153.9, 207.5; LRMS m/z 408 (M^+); HRMS calcd for $C_{25}H_{28}O_5$ 408.1947, found 408.1926; Anal. Calcd for $C_{25}H_{28}O_5$: C, 73.51; H, 6.91%. Found: C, 73.43; H, 7.11%.

Synthesis of Indole and Quinoline Derivatives Using Michael-Type Reaction. Typical Procedure for the Synthesis of Tetrahydroindole Derivative—Synthesis of Methoxycarbonylmethyl)-4,5,6,7-Tetrahydroindole (25a): To a solution of CsF (379 mg, 2.50 mmol) and **1a** (78.4.1mg, 0.404 mmol) in THF (3.0 mL) was added a THF solution of titanium–nitrogen complexes, prepared from $Ti(O^iPr)_4$ (0.15 mL, 0.504 mol), TMSCl (1.00 mL, 7.88 mmol), and Li (36.1 mg, 5.20 mmol) in THF (7.5 mL), and the solution was stirred at rt for 50 min. Water was added to the solution at 0 °C, and the solution was stirred at room temperature for 2 h. The aqueous layer was extracted with ethyl acetate. The organic layer was washed with brine, dried over Na_2SO_4, and concentrated. The residue was purified by column chromatgraphy on silica gel (hexane:EtOAc = 4:1 containing 1% Et_3N) to give **25a** (64.4 mg, 82%) as a pale-yellow oil: IR (neat) 3384, 2924, 2850, 1734, 1604 cm^{-1}; ^1H NMR (500 MHz, $CDCl_3$) δ 1.73 (tt, $J = 6.1$, 6.1 Hz, 2H), 1.81 (tt, $J = 6.1$, 6.1 Hz, 2H), 2.47 (t, $J = 6.1$ Hz, 2H), 2.56 (t, $J = 6.1$ Hz, 2H), 3.62 (s, 2H), 3.72 (s, 3H), 5.77 (brs, 1H), 8.09 (brs, 1H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 171.7, 127.1, 121.1, 116.9, 106.3, 52.1, 33.3, 23.8, 23.4, 22.8, 22.7; MS m/z 193 (M^+), 134; HRMS calcd for $C_{11}H_{15}NO_2$ 193.1102, found 193.1086.

5-Acetoxy-2-(methoxycarbonylmethyl)-4,5,6,7-tetrahydroindole (25b): IR (neat) 3378, 2950, 2850, 1732, 1606 cm^{-1}; ^1H NMR (500 MHz, $CDCl_3$) δ 1.90–2.10 (m, 2H), 2.04 (s, 3H), 2.57 (dd, $J = 15.5$, 6.7 Hz, 1H), 2.68 (m, 2H), 2.84 (dd, $J = 15.5$, 5.1 Hz, 1H), 3.61 (s, 2H), 3.75 (s, 3H), 5.16 (m, 1H), 5.76 (brs, 1H), 8.20 (brs, 1H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 171.7, 170.8, 125.5, 122.2, 113.8, 106.7, 70.6, 52.1, 33.2, 28.7, 27.9, 21.4, 20.0; MS m/z 251 (M^+), 191, 132; HRMS calced for $C_{13}H_{17}NO_4$ 251.1160, found 251.1174.

2-(Cyanomethyl)-4,5,6,7-tetrahydroindole (25c): IR (neat) 3366, 2254, 1604 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$) δ 1.67–1.74 (m, 2H), 1.74–1.82 (m, 2H), 2.43 (t, $J = 6.0$ Hz, 2H), 2.52 (t, $J = 6.0$ Hz, 2H), 3.69 (s, 2H), 5.84 (brs, 1H), 7.72 (brs, 1H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 16.9, 22.5, 22.7, 23.2, 23.6, 107.2, 116.4, 117.2, 117.5, 128.0; LRMS m/z 160 (M^+), 120; HRMS calcd for $C_{10}H_{12}N_2$ 160.1000, found 160.1028.

2-(*N*,*N*-Diethylcarbamoylmethyl)-4,5,6,7-tetrahydroindole (25d): IR (nujol) 3272, 1626 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$) δ 1.12 (t, $J = 6.8$ Hz, 3H), 1.20 (t, $J = 6.8$ Hz, 3H), 1.68–1.81 (m, 4H), 2.40–2.55 (m, 4H), 3.37 (q, $J = 6.8$ Hz, 4H), 3.62 (s, 2H), 5.68 (brs, 1H), 8.66 (brs, 1H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 170.0, 126.7, 122.7, 116.2, 105.4, 42.8, 40.7, 31.9, 23.9, 23.5, 22.9, 22.7, 14.6, 13.1; MS m/z 234 (M^+), 134; HRMS calcd for $C_{14}H_{22}N_2O$ 234.1732, found 234.1746.

2-(2-Oxypropyl)-4,5,6,7-tetrahydroindole (25e): IR (neat) 3372, 1706, 1604 cm^{-1}; ^1H NMR (500 MHz, $CDCl_3$) δ 1.70–1.82 (m, 4H), 2.21 (s, 3H), 2.45–2.58 (m, 4H), 3.67 (s, 2H), 5.74 (brs, 1H), 8.05 (brs, 1H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 206.6, 127.1, 121.6, 116.9, 106.6, 42.4, 29.6, 23.8, 23.4, 22.8, 22.7; MS m/z 177 (M^+), 134, 43; HRMS calcd for $C_{11}H_{15}NO$ 177.1154, found 177.1147.

2-Benzyl-4,5,6,7-tetrahydroindole (25g): IR (neat) 3424, 3364, 1602 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$) δ 1.68–1.82 (m, 4H), 2.45–2.52 (m, 4H), 3.91 (s, 2H), 5.70 (brs, 1H), 7.20–7.30 (m, 6H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 22.7, 22.8, 23.4, 23.8, 34.3, 105.4, 116.7, 126.0, 126.1, 128.4, 128.6, 128.7, 139.5; MS m/z 211 (M^+), 183, 134, 120; HRMS calcd for $C_{15}H_{17}N$ 211.1361, found 211.1375.

2-[(*p*-Methylphenyl)methyl]-4,5,6,7-tetrahydroindole (27a): IR (CCl_4) 3470, 1604 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$) δ 1.70–1.82 (m, 4H), 2.36 (s, 3H), 2.40–2.53 (m, 4H), 3.87 (s, 2H), 5.68 (brs, 1H), 7.05–7.35 (m, 5H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 136.5, 135.7, 129.2, 129.1, 129.0, 126.0, 116.8, 105.3, 33.9, 23.9, 23.5, 22.9, 22.7, 21.1; MS m/z 225 (M^+), 210, 197, 134, 120; HRMS calcd for $C_{16}H_{19}N$ 225.1518, found 225.1496.

2-[(*p*-Methoxycarbonylphenyl)methyl]-4,5,6,7-tetrahydroindole (27b): IR (CCl_4) 3470, 1726, 1610 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$) δ 1.68–1.82 (m, 4H), 2.45–2.53 (m, 4H), 3.91 (s, 2H), 3.96 (s, 3H), 5.70 (brs, 1H), 7.20–7.35 (m, 3H), 7.92–8.10 (m, 2H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 166.8, 145.0, 129.7, 128.6, 128.1, 127.6, 126.4, 116.8, 105.8, 52.0, 34.3, 23.8, 23.4, 22.8, 22.6; EIMS m/z 269 (M^+), 241, 210, 134, 120; HRMS calcd for $C_{17}H_{19}NO_2$ 269.1416, found 269.1408.

2-[(*p*-Cyanophenyl)methyl]-4,5,6,7-tetrahydroindole (27c): IR (CCl_4) 3474, 2230, 1606 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$) δ 1.68–1.83 (m, 4H), 2.42–2.53 (m, 4H), 3.96 (s, 2H), 5.68 (d, $J =$ 2.4 Hz, 1H), 7.27–7.38 (brs, 1H), 7.33 (d, $J = 8.1$ Hz, 2H), 7.59 (d, $J = 8.1$ Hz, 2H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 145.5, 132.2, 129.3, 126.8, 126.7, 118.9, 117.0, 110.0, 106.3, 34.4, 23.8, 23.4, 22.8, 22.7; MS m/z 236 (M^+), 208, 134; HRMS calcd for $C_{16}H_{16}N_2$ 236.1313, found 236.1314.

2-[(*p*-Trifluoromethylphenyl)methyl]-4,5,6,7-tetrahydroindole (27d): IR (CCl_4) 3470, 1618 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$) δ 1.69–1.82 (m, 4H), 2.44–2.51 (m, 4H), 3.96 (s, 2H), 5.69 (d, $J = 2.8$ Hz, 1H), 7.35 (d, $J = 8.2$ Hz, 2H), 7.35 (brs, 1H), 7.55 (d, $J = 8.2$ Hz, 2H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 143.9, 128.9, 128.3 (q, $J_{C-F} = 32$ Hz), 127.6, 126.5, 125.4 (q, $J_{C-F} = 4.1$ Hz), 124.2 (q, $J_{C-F} = 272$ Hz), 117.0, 106.0, 34.2, 23.8, 23.4, 22.9, 22.7; MS m/z 279 (M^+), 251; HRMS calcd for $C_{16}H_{16}F_3N$ 279.1235, found 279.1219.

2-[(*o*-Methoxycarbonylphenyl)methyl]-4,5,6,7-tetrahydroindole (27f): IR (neat) 3400, 1720, 1600 cm^{-1}; ^1H NMR (400 MHz, C_6D_6) δ 1.56–1.70 (m, 4H), 2.26 (dd, $J = 5.8$, 5.8 Hz, 2H), 2.61 (dd, $J = 5.7$, 5.7 Hz, 2H), 3.42 (s, 3H), 4.17 (s, 2H), 5.94 (d, $J = 2.4$ Hz, 1H), 6.88 (ddd, $J = 7.3$, 7.3, 1.5 Hz, 1H), 7.01 (ddd, $J = 7.3$, 7.3, 1.5 Hz, 1H), 7.13–7.21 (m, 1H), 7.77 (dd, $J = 7.3$, 1.5 Hz, 1H), 8.09 (brs, 1H); ^{13}C NMR (100 MHz, C_6D_6) δ 168.7, 143.4, 132.3, 131.7, 130.4, 129.5, 129.1, 126.0, 125.8, 116.7, 106.0, 51.9, 33.1, 24.8, 24.3, 23.9, 23.4; MS m/z 269 (M^+), 254, 241; HRMS calcd for $C_{17}H_{19}NO_2$ 269.1414, found 269.1416.

1,2,3,4,4a,6-Hexahydroindolo[1,2-*b*]isoquinolin-6-one (28): IR (CCl_4) 1734, 1660, 1636, 1622 cm^{-1}; ^1H NMR (500 MHz, $CDCl_3$) δ 1.05 (m, 1H), 1.33 (ddddd, $J = 13.6$, 13.6, 13.6, 4.1, 4.1 Hz, 1H), 1.59 (ddddd, $J = 13.6$, 13.6, 13.6, 3.4, 3.4 Hz, 1H), 1.90 (m, 1H), 2.20 (m, 1H), 2.36 (ddd, $J = 13.6$, 13.6, 5.5 Hz, 1H), 2.79 (ddd, $J = 13.6$, 2.2, 2.2 Hz, 1H), 3.36 (m, 1H), 4.45 (dd, $J = 11.1$, 5.6 Hz, 1H), 6.16 (s, 1H), 6.44 (s, 1H), 7.39 (dd, $J = 7.4$, 7.4 Hz, 1H), 7.49 (d, $J = 8.0$ Hz, 1H), 7.59 (m, 1H), 8.40 (d, $J = 7.4$ Hz, 1H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 161.1, 152.6, 145.6, 138.2, 131.8, 127.3, 125.7, 125.3, 123.8, 116.3, 98.0, 66.1, 32.0, 28.7, 27.5, 23.5; MS m/z 237 (M^+), 209; HRMS calcd for $C_{16}H_{15}NO$ 237.1154, found 237.1153.

1,2,3,6,12,12a-Hexahydroindolo[1,2-*b*]isoquinolin-6-one (28′): IR (CCl_4) 1692, 1672, 1634, 1604 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$) δ 1.41 (m, 1H), 1.61 (m, 1H), 1.92 (m, 1H), 2.14–2.28 (m, 2H), 2.42 (m, 1H), 2.62 (dddd, $J = 15.1$, 11.7, 1.7 Hz, 1H), 2.79 (m, 1H), 3.09 (dd, $J = 13.6$, 13.6, 13.6, 3.4, 3.4 Hz, 1H), 6.40 (d, $J = 1.7$ Hz, 1H), 6.89 (m, 1H), 7.38–7.45 (m, 2H), 7.58 (m, 1H), 8.41 (m, 1H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 21.6, 23.9, 28.5, 35.4, 37.1, 101.1, 112.6, 125.4, 125.8, 125.9, 127.8, 132.1, 136.8, 140.2, 142.5, 161.1; LRMS m/z 237 (M^+), 209; HRMS calcd for $C_{16}H_{15}NO$ 237.1154, found 237.1156.

(5,6,7,8-Tetrahydro-4*H*-cyclohepta[*b*]pyrrol-2-yl)acetic Acid Methyl Ester (30a): A crude product, which was synthesized from titanium–nitrogen complexes **7b**, prepared from $Ti(O^iPr)_4$ (0.15 mL, 0.504 mmol), TMSCl (1.00 mL, 7.88 mmol), and Li (36.4 mg, 5.24 mmol) in THF (7.5 mL) under nitrogen, **29a** (83.7 mg, 0.40 mmol), and CsF (382 mg, 2.51 mmol) in THF (3.0 mL), was purified by column chromatogrphy on silica gel (hexane–ethyl acetate containing 3% NEt_3, 5/1) to give **30a** (59.8 mg, 72%) as a colorless oil. IR (neat) 3384, 1732, 1436 cm^{-1}; ^1H NMR (270 MHz, $CDCl_3$) δ 1.58–1.81 (m, 6H), 2.94 (dd, $J = 5.9$, 5.9 Hz, 2H), 2.62 (dd, $J = 5.9$, 5.9 Hz, 2H), 3.56 (s, 2H), 3.69 (s, 3H), 5.73 (d, $J = 2.8$ Hz, 1H), 8.07 (brs, 1H); ^{13}C NMR (68 MHz, $CDCl_3$) δ 28.0, 28.3, 29.2, 29.3, 31.9, 33.0, 52.0, 109.5, 118.5, 121.4, 130.6, 171.8; MS m/z 207 (M^+), 148; HRMS calcd for $C_{12}H_{17}NO_2$ 207.1260, found 207.1277.

(5-Methylpyrrol-2-yl)acetic Acid Methyl Ester (30b): A crude product, which was synthesized from titanium–nitrogen complexes **7b**, prepared from $Ti(O^iPr)_4$ (0.15 mL, 0.504 mmol), TMSCl (1.00 mL, 7.88 mmol), Li (36.7 mg, 5.29 mmol) in THF (7.5 mL) under nitrogen, **29b** (61.9 mg, 0.402 mmol), and CsF (61.9 mg, 0.402 mmol) in THF (3.0 mL), was purified by column chromatography on silica gel (hexane–ether containing 3% NEt_3, 1/0 to 2/1) to give **30b** (24.0 mg, 39%) as a colorless oil. IR (neat) 3380, 1734 cm^{-1}; ^1H NMR (270 MHz, $CDCl_3$) δ 2.24 (s, 3H), 3.16 (s, 2H), 3.70 (s, 3H), 5.77 (m, 1H), 5.85 (m, 1H), 8.26 (brs, 1H); ^{13}C NMR (68 MHz, $CDCl_3$) δ 13.0, 33.2, 52.1, 105.8, 107.5, 121.6, 127.8, 171.8; LRMS m/z 153 (M^+), 94; HRMS calcd for $C_8H_{11}NO_2$ 153.0790, found 153.0794.

(*Z*)-(1,2,3,4,5,6,7,8-Octahydroquinolin-2-ylidene)acetic Acid Methyl Ester (30c): A crude product, which was synthesized

from titanium–nitrogen complexes **7b**, prepared from $Ti(O^iPr)_4$ (0.15 mL, 0.504 mmol), TMSCl (1.00 mL, 7.88 mmol), Li (35.9 mg, 5.17 mmol) in THF (7.5 mL) under nitrogen, **29c** (83.9 mg, 0.403 mmol), and CsF (383 mg, 2.52 mmol) in THF (3.0 mL), was purified by column chromatography on silica gel (hexane containing 3% NEt_3) to give **30c** (55.1 mg, 66%) as a colorless oil. IR (neat) 3284, 1660, 1612 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$) δ 1.54–1.70 (m, 4H), 1.91–2.05 (m, 6H), 2.44 (dd, $J = 7.3$, 7.3 Hz, 2H), 3.61 (s, 3H), 4.47 (s, 1H), 9.25 (brs, 1H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 22.6, 22.9, 24.7, 26.6, 28.4, 28.8, 50.2, 82.3, 109.3, 127.9, 156.6, 170.5; LRMS m/z 207 (M^+), 175, 147; HRMS calcd for $C_{12}H_{17}NO_2$ 207.1260, found 207.1257.

(*Z*)-(2,3,4,5,6,7-Hexahydro-1*H*-cyclopenta[*b*]pyridin-5-ylidene)acetic Acid Methyl Ester (30d): A crude product, which was synthesized from titanium–nitrogen complexes **7b**, prepared from $Ti(O^iPr)_4$ (0.15 mL, 0.504 mmol), TMSCl (1.00 mL, 7.88 mmol), Li (36.2 mg, 5.22 mmol) in THF (7.5 mL) under nitrogen, **29d** (78.5 mg, 0.404 mmol), and CsF (78.5 mg, 0.404 mmol) in THF (3.0 mL), was purified by column chromatography on silica gel (hexane containing 3% NEt_3) to give **30d** (33.8 mg, 34%) as a colorless oil. IR (neat) 3926, 1666, 1614 cm^{-1}; ^1H NMR (500 MHz, $CDCl_3$) δ 1.88–1.93 (m, 2H), 2.08–2.14 (m, 2H), 2.26–2.31 (m, 2H), 2.33–2.39 (m, 2H), 2.52 (dd, $J = 7.4$, 7.4 Hz, 2H), 3.63 (s, 3H), 4.60 (s, 1H), 9.46 (brs, 1H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 21.0, 21.3, 29.2, 31.0, 32.9, 50.2, 84.2, 112.6, 133.5, 156.9, 170.5; MS m/z 193 (M^+), 161, 133; HRMS calcd for $C_{11}H_{15}NO_2$ 193.1103, found 193.1115.

(*Z*)-[4,4-Bis(benzyloxymethyl)-6-methyl-1,2,3,4-tetrahydropyridin-2-ylidene]acetic Acid Methyl Ester (30e): A crude product, which was synthesized from titanium–nitrogen complexes **7b**, prepared from $Ti(O^iPr)_4$ (0.075 mL, 0.252 mmol), TMSCl (0.50 mL, 3.94 mmol), Li (17.4 mg, 2.51 mmol) in THF (3.8 mL) under nitrogen, **29e** (82.3 mg, 0.201 mmol), and CsF (187 mg, 1.23 mmol) in THF (1.5 mL), was purified by column chromatography on silica gel (hexane–ethyl acetate containing 3% NEt_3, 1/0 to 5/1) to give **30e** (55.1 mg, 66%) as a colorless oil. IR (neat) 3308, 1662, 1610 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$) δ 1.80 (s, 3H), 2.42 (s, 2H), 3.25 (d, $J = 9.0$ Hz, 2H), 3.34 (d, $J = 9.0$ Hz, 2H), 3.64 (s, 3H), 4.47 (s, 4H), 4.58 (s, 1H), 4.61 (s, 1H), 7.21–7.35 (m, 10H), 9.36 (brs, 1H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 19.5, 33.5, 38.9, 50.3, 72.3, 73.3, 85.9, 102.7, 127.4, 127.4, 128.3, 133.2, 138.5, 155.6, 170.3; MS m/z 407 (M^+); HRMS calcd for $C_{25}H_{29}NO_4$ 407.2096, found 407.2085.

Synthesis of Lactams from Keto–Carboxylic Acid. 2-Ethoxycarbonyl-5-oxohexanoate (39, R = H): A solution of ethyl 2-ethoxycarbonyl-5-oxohexanate (2.47 g, 10.7 mmmol) in an EtOH (80 mL) and 10% NaOH solution (7.0 mL, 10.6 mmol) was stirred at room temperature for 2.5 h. The solvent was evaporated and the residue was dissolved in water. The aqueous layer was extracted with Et_2O and acidified with 10% HCl. The aqueous layer was extracted with ethyl acetate. The organic layer was washed with brine, dried over Na_2SO_4, and concentrated to give a colorless oil of **39** (1.72 g, 80%). IR (neat) 3200, 1718, 1448 cm^{-1}; ^1H NMR (270 MHz, $CDCl_3$) δ 1.28 (t, $J = 7.2$ Hz, 3H), 2.15 (s, 3H), 2.16 (q, $J = 7.2$ Hz, 2H), 2.58 (t, $J = 7.2$ Hz, 2H), 3.44 (t, $J = 7.2$ Hz, 1H), 4.21 (q, $J = 7.2$ Hz, 2H), 7.64 (brs, 1H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 13.9, 22.4, 29.8, 40.3, 50.2, 61.8, 169.0, 174.1, 207.8; MS m/z 202 (M^+), 184, 157, 132, 86, 43; HRMS calcd for $C_9H_{14}O_5$ 202.0855, found 202.0837.

3,3-Bis(*t*-butoxycarbonyl)-5-oxohexanoic Acid (43, R = H): mp 91–92 °C; IR (nujol) 3286, 1742, 1700 cm^{-1}; ^1H NMR (270 MHz, $CDCl_3$) δ 1.43 (s, 18H), 2.16 (s, 3H), 3.11 (s, 2H), 3.26 (s, 2H); ^{13}C NMR (67.5 MHz, $CDCl_3$) δ 27.6, 30.2, 37.1, 45.9, 54.3, 82.4, 168.2, 176.7, 205.6; MS m/z 274 ($M^+ - CH_3C(CH_3)=CH_2$), 259, 218, 201, 156, 113, 57; HRMS m/z calcd for $C_{12}H_{18}O_7$ ($M^+ - CH_3C(CH_3)=CH_2$) 274.1052, found 274.1036.

Synthesis of Lactams. Methyl 6-Methyl-1,2,3,4-tetrahydro-2-oxo-3-pyridinecarboxylate (40): A compound **39** was prepared from carboxylic acid (74.6 mg, 0.37 mmol), $ClPO(OEt)_2$ (0.068 mL, 0.47 mmol), and NEt_3 (0.07 mL, 0.50 mmol). A crude product, which was synthesized from titanium–nitrogen complexes **7b**, prepared from Li (34.7 mg, 5.0 mmol), $Ti(O^iPr)_4$ (0.15 mL, 0.55 mmol), TMSCl (0.65 mL, 5.1 mmol) under nitrogen, crude **40**, and CsF (383 mg, 2.52 mmol) in THF (7.5 mL), was purified by column chromatography on silica gel (hexane/ethyl acetate, 2/1) to give **40** (13.0 mg, 19%) as a colorless crystal. mp 87–88 °C; IR (nujol) 3226, 1742, 1700, 1676 cm^{-1}; ^1H NMR (270 MHz, $CDCl_3$) δ 1.28 (t, $J = 7.3$ Hz, 3H), 1.80 (d, $J = 1.5$ Hz, 3H), 2.47 (m, 1H), 2.71 (m, 1H), 3.40 (dd, $J = 8.6$, 7.3 Hz, 1H), 4.12–4.31 (m, 2H), 4.82 (m, 1H), 7.08 (brs, 1H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 14.1, 18.8, 23.9, 47.1, 61.4, 99.2, 133.0, 167.6, 169.8; MS m/z 183 (M^+), 138, 110, 92, 80, 67, 42; HRMS calcd for $C_9H_{13}NO_3$ 183.0896, found 183.0899.

6-Methyl-1,2,3,4-tetrahydro-2-pyridone (42): A compound **41** was prepared from carboxylic acid (100.8 mg, 0.775 mmol), $ClPO(OEt)_2$ (0.14 mL, 0.969 mmol) and NEt_3 (0.13 mL, 0.933 mmol). A crude product, which was synthesized from titanium–nitrogen complexes **7b**, prepared from Li (69.5 mg, 10.0 mmol), $Ti(O^iPr)_4$ (0.30 mL, 1.01 mmol), TMSCl (1.3 mL, 10.2 mmol) under nitrogen, crude **41**, and CsF (782 mg, 5.15 mmol) in THF (15 mL), was purified by column chromatography on silica gel (hexane/ethyl acetate, 2/1) to give **42** (26.2 mg, 29%) as a colorless crystal. mp 112–114 °C; IR (nujol) 3198, 3104, 1696, 1674 cm^{-1}; ^1H NMR (270 MHz, $CDCl_3$) δ 1.79 (d, $J = 1.5$ Hz, 3H), 2.20–2.31 (m, 2H), 2.41 (ddd, $J = 8.1$, 8.1, 1.5 Hz, 2H), 4.77 (m, 1H), 7.89 (brs, 1H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 18.8, 20.1, 30.2, 100.2, 132.9, 172.3; MS m/z 111 (M^+), 96, 83, 68, 54, 42; HRMS calcd for C_6H_9NO 111.0685, found 111.0684.

Di-*t*-butyl 6-Methyl-1,2,3,4-tetrahydro-2-oxo-4,4-pyridinedicarboxylate (44) and Di-*t*-butyl 6-Methylene-2-oxo-2,3,4,5-tetrahydro-1*H*-4,4-piperidinedicarboxylate (44′): A compound **43** was prepared from carboxylic acid (100 mg, 0.303 mmol), $ClPO(OEt)_2$ (0.052 mL, 0.360 mmol), and NEt_3 (0.050 mL, 0.359 mmol). A crude product, which was synthesized from titanium–nitrogen complexes **7b**, prepared from Li (25.3 mg, 3.64 mmol), $Ti(O^iPr)_4$ (0.11 mL, 0.370 mmol), TMSCl (0.47 mL, 3.70 mmol) under nitrogen, crude **43**, and CsF (277 mg, 1.82 mmol) in THF (6 mL), was purified by column chromatography on silica gel (hexane/ethyl acetate, 2/1) to give **44** (50.6 mg, 51%) as a colorless crystal. **44**: mp 146–149 °C; IR (nujol) 3216, 3162, 3112, 1732, 1698, 1676 cm^{-1}; ^1H NMR (270 MHz, $CDCl_3$) δ 1.45 (s, 18H), 1.86 (d, $J = 1.1$ Hz, 3H), 2.84 (s, 2H), 5.03 (brt, 1H), 6.74 (brs, 1H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 19.1, 36.8, 55.0, 82.2, 98.2, 135.4, 168.6, 169.3, 277.7; MS m/z 311 (M^+), 256, 210, 154, 126, 57; HRMS calcd for $C_{16}H_{25}O_5N$ 311.1733, found 311.1710. **44′**: mp 126–129 °C; IR (nujol) 3198, 1726, 1682, 1654 cm^{-1}; ^1H NMR (270 MHz, $CDCl_3$) δ 1.44 (s, 18H), 2.75 (s, 2H), 2.82 (s, 2H), 4.17 (s, 1H), 4.29 (s, 1H), 7.58 (brs, 1H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 27.7, 35.5, 36.7, 53.1, 82.5, 92.9, 137.7, 168.3, 168.4; MS m/z 311 (M^+), 210, 199, 182, 154, 126, 110, 57; HRMS calcd for $C_{16}H_{25}NO_5$ 311.1733, found 311.1726.

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