Available online at www.sciencedirect.com
SCIENCE DIRECT
Tetrahedron
Tetrahedron 62 (2006) 3629–3647

Efficient synthesis of indoles using [3,3]-sigmatropic rearrangement of *N*-trifluoroacetyl enehydrazines

Okiko Miyata,[a] Norihiko Takeda,[a] Yasuo Kimura,[a] Yoshiji Takemoto,[b] Norimitsu Tohnai,[c] Mikiji Miyata[c] and Takeaki Naito[a,*]

[a]*Kobe Pharmaceutical University, Motoyamakita, Higashinada, Kobe 658-8558, Japan*
[b]*Graduate School of Pharmaceutical Sciences, Kyoto University, Yoshida, Sakyo-ku, Kyoto 606-8501, Japan*
[c]*Graduate School of Engineering, Osaka University, Yamadaoka, Suita, Osaka 565-0871, Japan*

Received 28 June 2005; revised 23 January 2006; accepted 25 January 2006

Available online 28 February 2006

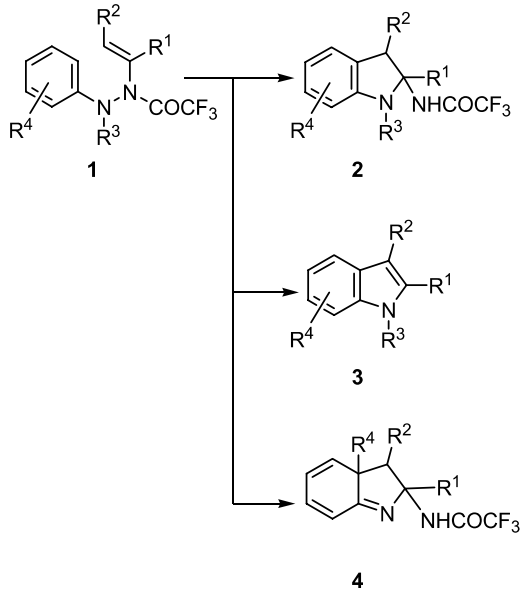
Abstract—[3,3]-Sigmatropic rearrangement of *N*-trifluoroacetyl enehydrazines provides a novel method for the construction of indoles. *N*-Trifluoroacetyl enehydrazine having a cyclopentene ring smoothly underwent [3,3]-sigmatropic rearrangement followed by cyclization to give indolines in excellent yield. On the other hand, both cyclohexenyl *N*-trifluoroacetyl enehydrazine and acyclic *N*-trifluoroacetyl enehydrazine gave indoles in good yield. Additionally, the substituent effect on the benzene ring was also studied. The rearrangement of *N*-trifluoroacetyl enehydrazines proceeded smoothly even under either aqueous or solvent-free conditions.

1. Introduction

Indole ring systems are the core structural elements in natural and synthetic organic compounds possessing a wide diversity of important biological activities. Therefore, there is continuously a need for developing concise and practical synthetic methods of indoles and the related compounds. Despite recently developed methodologies,[1] such as metal-catalyzed transformations and radical cyclization, the venerable Fischer indole synthesis has maintained its prominent role as a route to indoles. However, two major drawbacks to the Fischer indole synthesis are that yields are sometimes low[2–4] with numerous by products being formed. And the reactions involving unsymmetrical hydrazines or ketones often give products with low regioselectivity.[2,5–8] Particularly, the low yields are a persistent problem in the Fischer indole synthesis. Although the Fischer indolization is usually carried out in the presence of an acid catalyst, the acid may cause decomposition of the indole produced and, therefore, thermal cyclization in the absence of a catalyst appears to offer advantages over the acid-catalyzed procedure. However, high temperature (180–250 °C) is required for such cyclization.

Recently, we found that the [3,3]-sigmatropic rearrangement and subsequent cyclization of *N*-trifluoroacetyl enehydrazines **1** proceed smoothly under mild conditions (without acids and at below 90 °C) to give the indolines **2** and indoles **3**.[9,10a]

The [3,3]-sigmatropic rearrangement of *N*-trifluoroacetyl enehydrazines having either a methoxy or a methyl group on the benzene ring gave dienylimines **4** which correspond to the proposed intermediates of Fischer indolization.[10b]



Scheme 1.

Keywords: [3,3]-Sigmatropic rearrangement; *N*-Trifluoroacetyl enehydrazines; Indole; Indoline; Dienylimine.
* Corresponding author. Tel.: +81 78 441 7554; fax: +81 78 441 7556; e-mail: taknaito@kobepharma-u.ac.jp

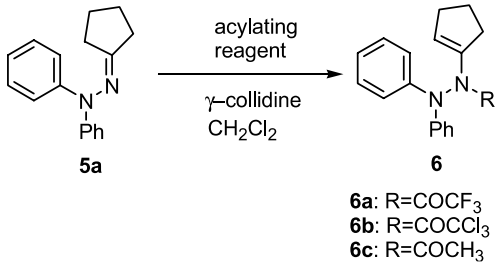
0040–4020/$ - see front matter © 2006 Elsevier Ltd. All rights reserved.
doi:10.1016/j.tet.2006.01.087

This reaction provides a new entry to the Fischer indole synthesis and was applied to not only one-pot synthesis of various types of indoles[11a] but also synthesis of natural indole products.[11b] We disclose herein the full details of the [3,3]-sigmatropic rearrangement of *N*-trifluoroacetyl enehydrazines which are indispensable in the synthesis of indoles (Scheme 1).[10]

2. Results and discussion

2.1. The substituent effects on the nitrogen atom in [3,3]-sigmatropic rearrangement of enehydrazines bearing a cyclopentene ring

At first, we investigated the substituent effects on the nitrogen atom. Three types of *N*-acyl enehydrazines **6a**, **6b**, and **6c** having a cyclopentene ring were employed as the substrate (Scheme 2, Table 1). The hydrazone **5a**,[12] prepared by condensation of cyclopentanone with *N*,*N*-diphenylhydrazine was subjected to acylation with trifluoroacetic anhydride (TFAA) in the presence of γ-collidine to give the corresponding *N*-trifluoroacetyl enehydrazines **6a** in excellent yield (entry 1). Similarly, *N*-trichloroacetyl enehydrazine **6b** and *N*-acetyl enehydrazine **6c** were prepared from **5a** (entries 2 and 3).

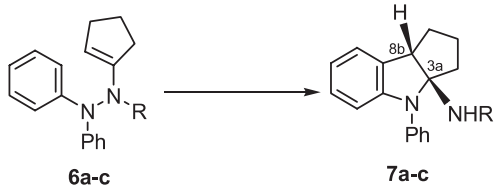


Scheme 2.

Table 1. The acylation of **5a** with various acylating agents

Entry	Acylating reagent	Temperature (°C)	Product	Yield (%)
1	TFAA	0	**6a**	99
2	$(CCl_3CO)_2O$	0	**6b**	99
3	AcCl, DMAP	25	**6c**	99

When a solution of **6a** in THF was heated at 65 °C for 5 h, indoline **7a** was obtained in 99% yield (Scheme 3, entry 1 in Table 2). Similarly, the reaction of *N*-trichloroacetyl enehydrazine **6b** at the same temperature gave indoline



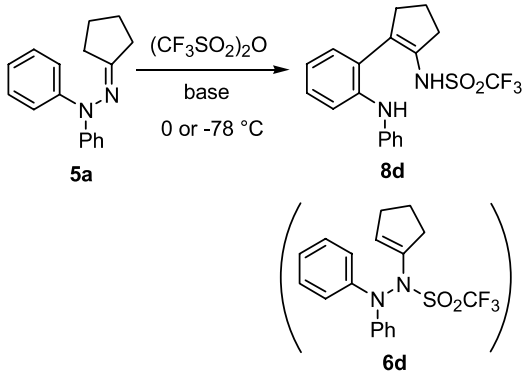
Scheme 3.

Table 2. The conversion of *N*-acyl enehydrazines **6a–c** into the indolines **7a–c**

Entry	Substrate	R	Conditions (°C)	Time (h)	Yield (%)
1	**6a**	$COCF_3$	THF (65)	5	99
2	**6b**	$COCCl_3$	THF (65)	5	56
3	**6c**	$COCH_3$	Xylene (140)	3	65

7b in 56% yield (entry 2). However, in the case of **6c**, higher reaction temperature (140 °C) was required for the successful rearrangement and cyclization (entry 3). These results suggest that strong electron-withdrawing group is suitable as the substituent on the nitrogen.

We next examined the rearrangement of the enehydrazine **6d** carrying a trifluoromethanesulfonyl group which has higher electron-withdrawing ability (Scheme 4, Table 3). The sulfonylation of hydrazone **5a** with trifluoromethanesulfonic anhydride was carefully carried out in the presence of γ-collidine at 0 °C. However, the reaction gave not the desired product **6d** but the rearranged product **8d** in low yield, along with the decomposition of **5a** (entry 1).



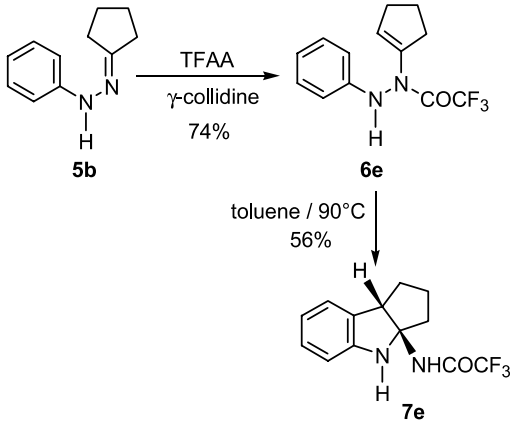
Scheme 4.

Table 3. The treatment of **5a** with $(CF_3SO_2)_2O$

Entry	Base	Temperature (°C)	Yield (%)
1	γ-Collidine	0	5
2	γ-Collidine	−78	25
3	Et_3N	−78	70

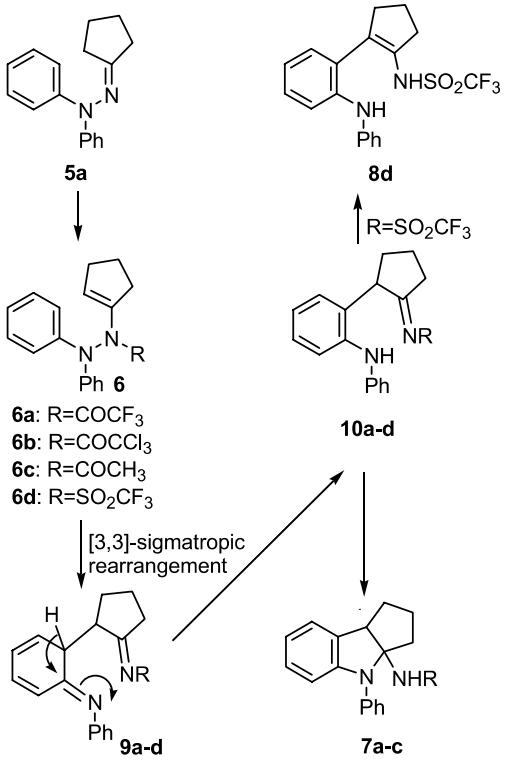
At lower reaction temperature of −78 °C, **8d** was obtained in 25% yield (entry 2). Replacement of γ-collidine to triethylamine as a base improved the yield to 70% (entry 3). Thus, this result suggests that the enehydrazine **6a** bearing a trifluoroacetyl group is the best substrate for our indole synthesis.

Similarly, the reaction of *N*-monophenylenehydrazine **6e**, prepared from **5b**,[13] proceeded smoothly in toluene at 90 °C to give the indoline **7e** along with the unreacted starting material **6e** (Scheme 5).



Scheme 5.

Considering our results obtained above and the related known Fischer indolization, we propose a plausible reaction pathway that is shown in Scheme 6. At first, [3,3]-sigmatropic rearrangement of the *N*-acyl enehydrazines **6a–c** followed by isomerization proceeds to form *N*-acylimines **10a–c** which then cyclized intramolecularly to give the indoline **7a–c**.

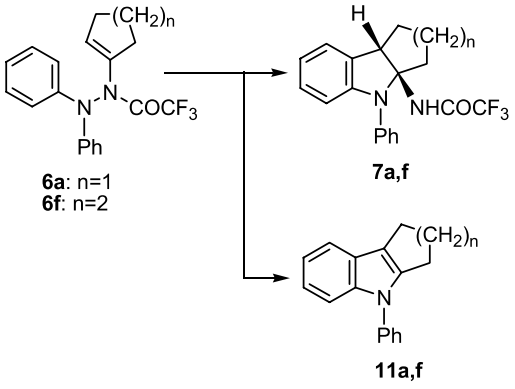


Scheme 6.

In sulfonylation of hydrazone **5a**, *N*-trifluoromethansulfonyl enehydrazine **6d** could not be isolated. Probably, the [3,3]-sigmatropic rearrangement of **6d** that would be transiently formed from hydrazone **5a** would take place easily even at −78 °C because a trifluoromethanesulfonyl group has a very strong electron-withdrawing property. The following cyclization of rearranged intermediate **10d** was prevented due to too low temperature (−78 °C). Therefore, **8d** was an isolable product in the reaction of **5a** with trifluoromethanesulfonic anhydride.

2.2. The substituent effect on the ene part in [3,3]-sigmatropic rearrangement of enehydrazines

We next investigated the substituent effects on the ene part. At first, *N*-trifluoroacetyl enehydrazines **6a** and **6f** having a cyclic enamine part was employed as substrate (Scheme 7, Table 4). As mentioned above, the reaction of enehydrazine **6a** having a cyclopentene ring gave the indoline **7a** in excellent yield (entry 1). Surprisingly, the reaction also proceeded at room temperature but required prolonged reaction time (entry 2). When the reaction of **6a** was carried out in toluene at 90 °C, a mixture of indoline **7a** and indole **11a**[14] was obtained (entry 3). The reaction of **6a** in xylene at 140 °C gave the indole **11a** as the sole product (entry 4). In the case of cyclohexenehydrazine **6f**,[15] the indole **11f**[16] was exclusively obtained without formation of the indoline **7f** (entry 5).



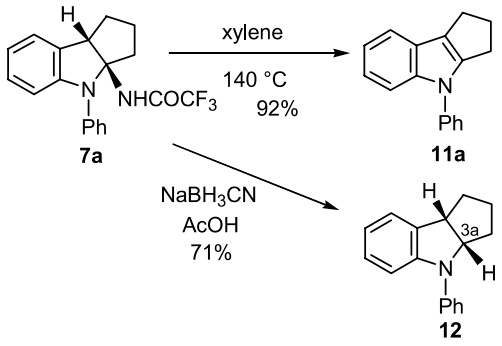
Scheme 7.

Table 4. The thermal reaction of enehydrazines **6a** and **6f** under various conditions

Entry	Substrate	Conditions (°C)	Time (h)	Yield (%)	
				7	**11**
1	**6a**	THF (65)	5	99	—
2	**6a**	$CDCl_3$ (25)	480	98	—
3	**6a**	Toluene (90)	3	61	30
4	**6a**	Xylene (140)	4	—	92
5	**6f**	THF (65)	11	—	53

Upon heating at 140 °C, the indoline **7a** was converted into the indole **11a** in quantitative yield as a result of the elimination of trifluoroacetamide (Scheme 8). Reductive deamination of **7a** with sodium cyanoborohydride proceeded smoothly to give the corresponding indoline **12**[17] in 71% yield that is unsubstituted at the 3a-position (Scheme 8).

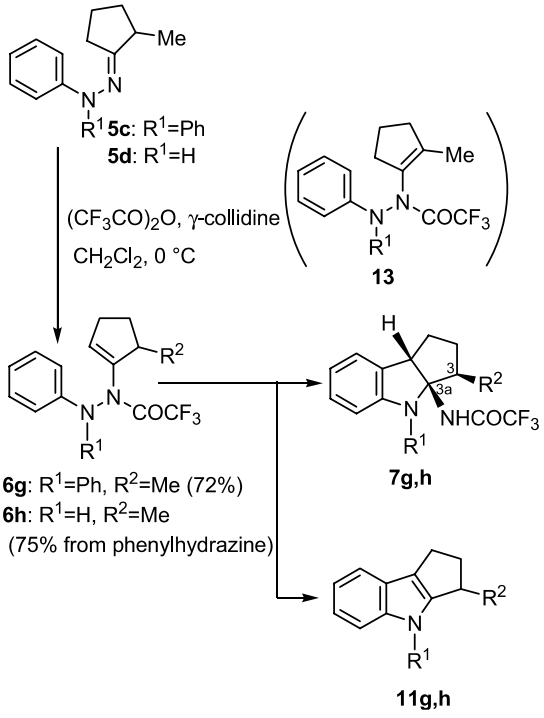
In general, it is difficult to isolate 2-aminoindolines which is proposed as an intermediate of Fischer indolization. To our knowledge, there has been only a few works[18–20] achieving the isolation of 2-aminoindoline derivatives.



Scheme 8.

The difference between the structures of products (indolines **7a** from cyclopentenehydrazine **6a** and indoles **11f** from cyclohexenehydrazines **6f**) could be explained as follows. The indole double bond is not readily accommodated in a fused system such as 1,2,3,3a,4,8b-hexahydrocyclopent-[*b*]indoles in which the two rings are five-membered and rather rigid. On the other hand, it is clear that no comparable difficulty exists in the elimination of trifluoroacetamide when the more flexible six-membered cyclohexane ring is present.

Next, the reaction of enehydrazines **6g** and **6h** having a methyl group on the cyclopentene ring was examined (Scheme 9, Table 5). The enehydrazines **6g** and **6h** were prepared by the treatment of hydrazones **5c** and **5d**[21] with TFAA without formation of the regioisomer **13**. The enehydrazine **6g** was subjected to the heating at 65 °C to give the indoline **7g** in 76% yield (entry 1) while the indoline **7h** could not be isolated from **6h** under the same conditions probably because of its instability. On the other hand, the reaction of **6h** in toluene at 90 °C gave the indole **11h**[22] in excellent yield (entry 2).



Scheme 9.

Table 5. The thermal reaction of enehydrazines **6g** and **6h**

Entry	Substrate	Conditions (°C)	Time (h)	Yield (%)	
				7	**11**
1	**6g**	THF (65)	5	76	—
2	**6h**	Toluene (90)	7	—	99

It is known[5] that the classical Fischer indolization of hydrazone prepared from unsymmetrical ketone gives a mixture of substituted indoles with no regioselectivity. Therefore, this regioselective formation of indolines and indoles from unsymmetrical hydrazones **5c**,**d** would be useful for the synthesis of variously substituted polycyclic indole alkaloids.

The stereostructures of indolines **7a**, **7g**, and **12** were established by NOESY of ^{1}H NMR spectra. The assignment of those configurations is based on the observed NOE correlations as shown in Figure 1. In the case of **7a**, NOE was observed between 8b-H and NH. NOE in **7g** was observed between 3-Me and 8b-H, 3-Me and NH, and NH and 8b-H. The stereostructures of **7b**,**c**,**e** were deduced from comparison of the ^{1}H NMR spectra with those of **7a**. In the case of **12**, NOE was observed between 8b-H and 3a-H.[23]

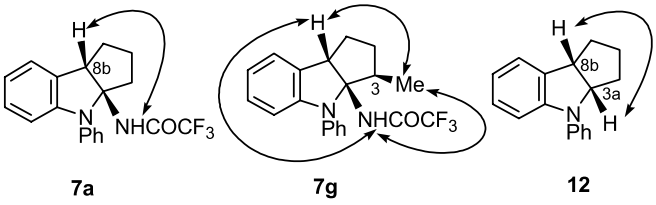
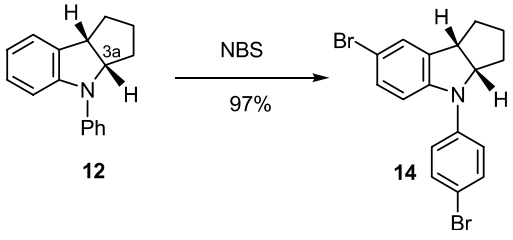


Figure 1. NOE correlations of compounds **7a**, **7g** and **12**.

Furthermore, the stereostructure of **12** was firmly established by the single-crystal X-ray analysis of the dibromide **14** which was prepared by bromination of **12** with NBS (Scheme 10, Fig. 2).



Scheme 10.

We propose the possible reaction pathway for the formation of **7g** as shown in Scheme 11. The rearrangement of **6g** would proceed via a stable conformation **A** of **6g** to give the intermediate **B** which was converted into the stable product **7g**.

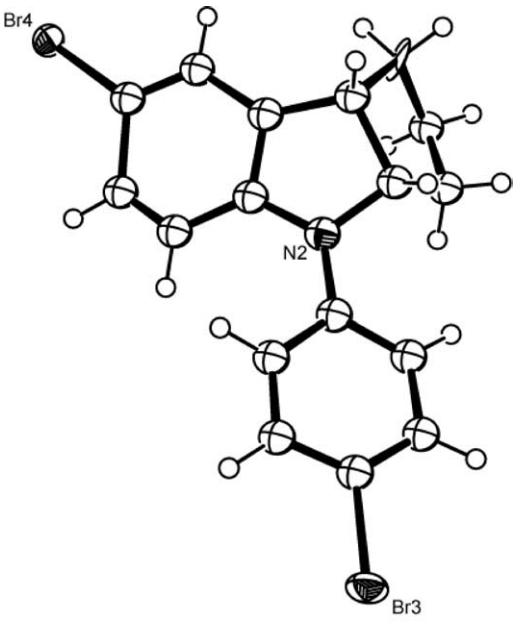
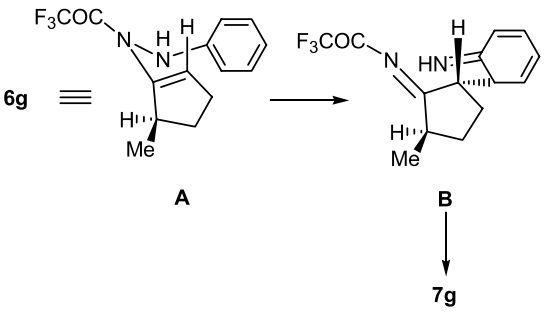
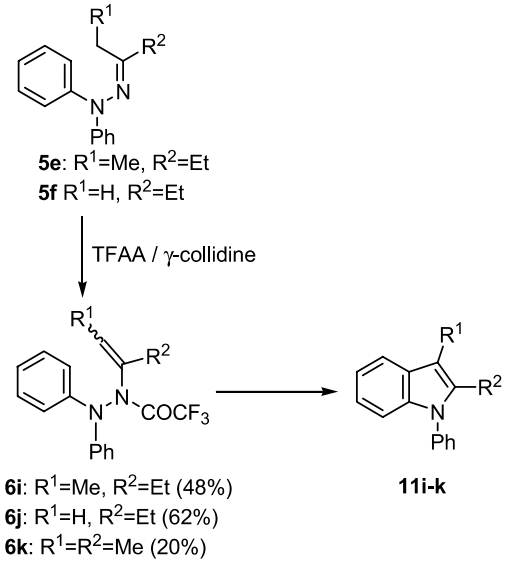


Figure 2. The single-crystal X-ray analysis of **14**.



Scheme 11.

We then investigated the reaction of enehydrazine with an acyclic chain on the ene part (Scheme 12, Table 6). The enehydrazine **6i** was prepared by the acylation of hydrazone **5e** with TFAA. The acylation of hydrazone **5f**[24] with TFAA



Scheme 12.

Table 6. The thermal reaction of enehydrazines **6i–k**

Entry	Substrate	Conditions (°C)	Time (h)	Yield (%)[a]
1	**6i**	THF (65)	4	69
2	**6i**	$CDCl_3$ (25)	480	50
3	**6j**	THF (65)	10	24 (38)
4	**6j**	Toluene (90)	6	77
5	**6k**	THF (65)	10	79

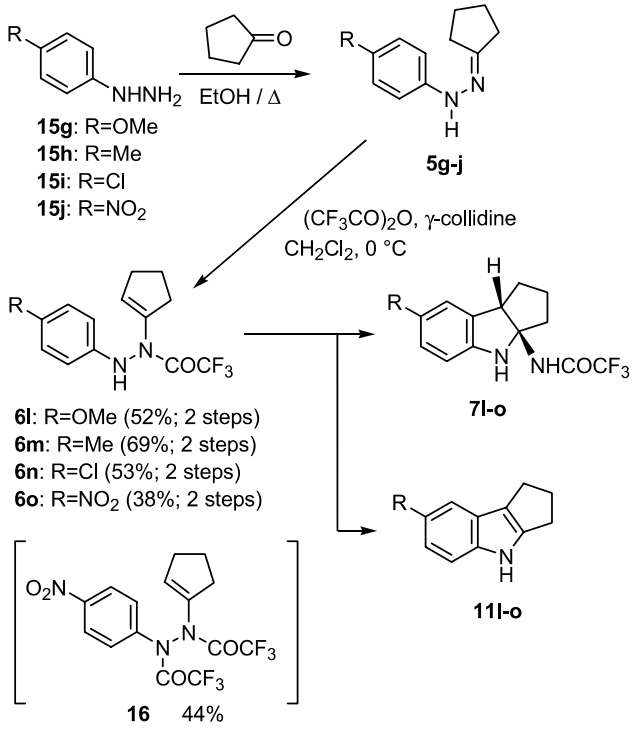
[a] Yield in parenthesis is for recovered starting material.

gave a 3:1 mixture of enehydrazines **6j** and **6k**. The stereostructures of **6i**,**k** have not been established. The enehydrazine **6i** was heated at 65 °C to afford the corresponding indoles **11i** as the sole product (entry 1).

The thermal reaction of **6j** at 90 °C gave indole **11j** in 77% yield (entry 4). Similarly, **11k**[25] was obtained from **6k** (entry 5). Since the rearrangement and cyclization of **6i–k** occurred with no isomerization of the olefin part under mild conditions, the substituted indoles such as 2-mono- and 2,3-disubstituted indoles would be selectively obtained as the sole product.

2.3. The substituent effects on benzene ring in [3,3]-sigmatropic rearrangement of enehydrazines bearing cycloalkene ring

To demonstrate the generality of the rearrangement and cyclization of *N*-trifluoroacetyl enehydrazines, we next investigated the substituent effects on the benzene ring. We chose methoxyl, methyl, nitro, and chloro groups as a substituent. At first, the reaction of enehydrazine having a substituent at the *p*-position on the benzene ring was examined (Scheme 13, Table 7).



Scheme 13.

Table 7. The thermal reaction of enehydrazines **6l–o**

Entry	Substrate	Conditions (°C)	Time (h)	Yield (%)	
				7	**11**
1	**6l**	THF (65)	5	99	—
2	**6m**	THF (65)	12	—	—
3	**6m**	Toluene (90)	8	68	—
4	**6n**	Toluene (90)	15	25	20
5	**6o**	Toluene (90)	15	—	—
6	**6o**	Toluene (110)	29	48	25
7	**6o**	Xylene (140)	6	54	19

The condensation of hydrazines **15g–i** with cyclopentanone gave the corresponding unstable hydrazones **5g–i**, which without isolation were acylated to give enehydrazines **6l–n** in 52–69% yield. On the other hand, in the case of **6o** having a nitro group, the hydrazone **5j**[26] could be isolated and then acylated to give the desired product **6o** and diacylated product **16** in 38 and 44% yields, respectively. The substrate **6l** having a methoxy group underwent cyclization at lower temperature (65 °C) than the reaction of unsubstituted enehydrazine **6e** at 90 °C (see Scheme 5). The indoline **7l** was produced in excellent yield (entry 1). Similarly, the substrate **6m** with a methyl group gave the indoline **7m** at 90 °C (entry 3). On the other hand, in the case of the enehydrazines **6n** and **6o** having an electron-withdrawing group, prolonged reaction time and high reaction temperature were required (entries 4–7). These substituent effects are almost in agreement with those obtained in the classical Fischer indolization.[2] The existence of an electron-donating group on a benzene ring makes the thermal reaction relatively easy to occur while in the case of an electron-withdrawing group, harsh conditions were required for successful reaction.

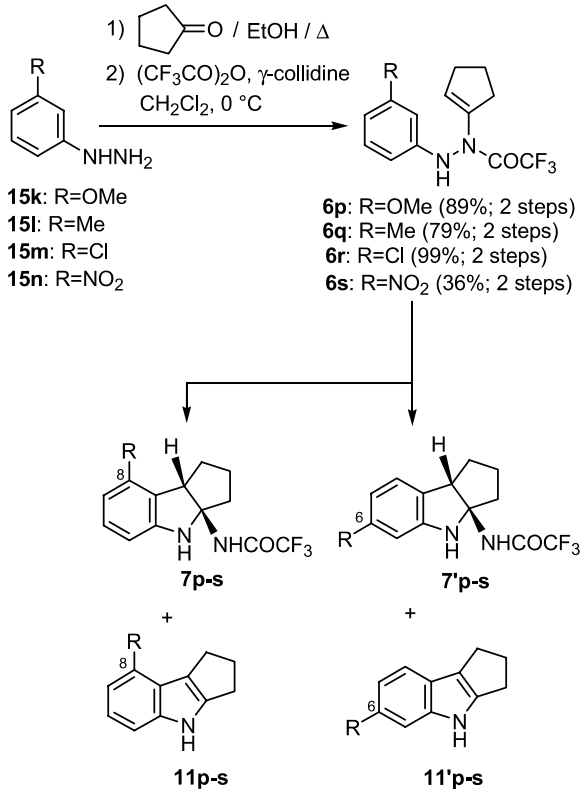
We next investigated the thermal reaction of *m*-substituted enehydrazines **6p–s**, prepared from *m*-substituted phenylhydrazines **15k–n** (Scheme 14, Table 8). The reaction of **6p** bearing an *m*-methoxy group proceeded in toluene at 90 °C to give the 8-substituted indoline **7p** and indole **11p**, and 6-substituted indoline **7′p** and indole **11′p** (entry 2).

Table 8. The thermal reaction of enehydrazines **6p–s**

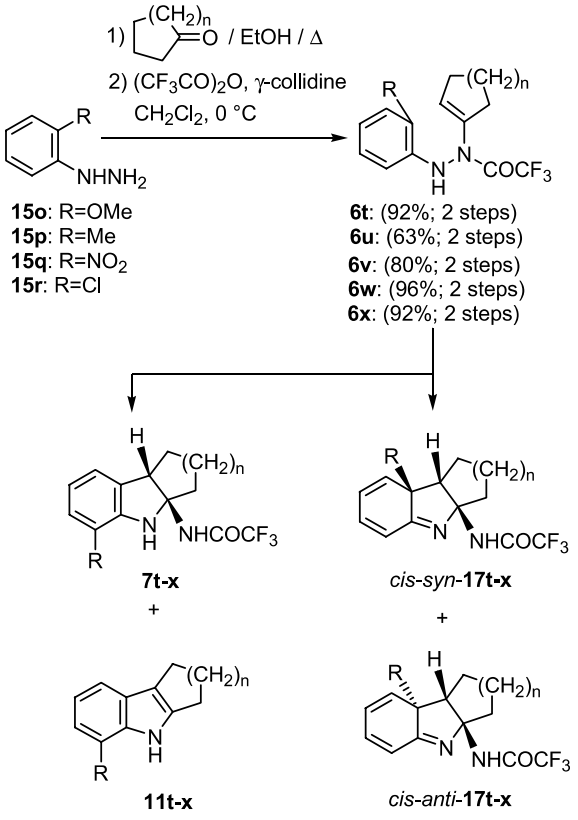
Entry	Substrate	Conditions (°C)	Time (h)	Yield (%)			
				7	**11**	**7′**	**11′**
1	**6p**	THF (65)	5	—	—	—	—
2	**6p**	Toluene (90)	11	11	24	6	20
3	**6q**	Toluene (90)	8	15	6	15	6
4	**6r**	Toluene (90)	15	17	8	12	—
5	**6s**	Toluene (90)	15	—	—	—	—
6	**6s**	Toluene (110)	29	14	66	14	5

Similarly, *m*-methyl enehydrazine **6q** gave the 8-substituted products **7q** and **11q**, and 6-substituted products **7′q** and **11′q** (entry 3). In the case of enehydrazine **6s** with a nitro group, four products **7s**, **11s**,[27] **7′s**, and **11′s**[27] were obtained after prolonged reaction time (entry 6). Thus, the [3,3]-sigmatropic rearrangement of *m*-substituted enehydrazines proceeded with low regioselectivity.

We next investigated the reaction of *o*-substituted enehydrazines (Scheme 15, Table 9). At first, [3,3]-sigmatropic rearrangement of **6t** having an *o*-methoxy group was



Scheme 14.



Scheme 15.

Table 9. The thermal reaction of enehydrazines **6t–x**

Entry	Substrate	R	*n*	Conditions (°C)	Time (h)	Yield (%)		
						7	**11**	**17** (*cis-syn*:*cis-anti*)
1	**6t**	OMe	1	THF (65)	10	63	—	36 (5:1)
2	**6t**	OMe	1	MeCN (80)	5	51	—	48 (5:1)
3	**6t**	OMe	1	Toluene (90)	7	69	—	29 (4:1)
4	**6t**	OMe	1	Hexane (70)	22	75	—	24 (4:1)
5	**6t**	OMe	1	MeOH (65)	6	—	24	15 (7:1)
6	**6u**	OMe	2	THF (65)	10	—	34	3 (2:1)
7	**6u**	OMe	2	MeCN (80)	10	—	52	17 (2:1)
8	**6u**	OMe	2	Toluene (90)	10	—	75	9 (2:1)
9	**6v**	Me	1	MeCN (80)	8	30	37	32 (7:1)
10	**6v**	Me	1	Toluene (90)	8	14	42	18 (14:1)
11	**6w**	Cl	1	Toluene (90)	15	66	—	—
12	**6x**	NO_2	1	Toluene (110)	29	31	—	—

examined. **6t** was heated in THF at 65 °C to give a mixture of indoline **7t** and two dienylimines **17t** in 63 and 36% yields, respectively (entry 1). The dienylimines **17t** were obtained as the result of the rearrangement at the root of a methoxy group. Furthermore, **17t** was easily separated into two diastereomers, *cis-syn*-**17t** and *cis-anti*-**17t**, in a 5:1 ratio. Interestingly, the polarity of the organic solvent used influences both the product ratio of the indoline and dienylimine and the reaction time. In MeCN, the reaction proceeded smoothly to give a 1:1 mixture of **7t** and **17t** in 99% yield (entry 2). On the other hand, in a less polar solvent, such as toluene and hexane, **7t** was obtained as a major product in 69–75% yield, although prolonged reaction time was required for complete consumption of **6t** (entries 3 and 4). In methanol, the indole **11t** and the dienylimines **17t** were obtained with no formation of indoline **7t** (entry 5). The reaction of cyclohexenyl hydrazine **6u** proceeded slowly under similar mild conditions to give 7-methoxyindole **11u**[28] and dienylimines **17u** (entries 6–8).

Next, we turned our attention to the corresponding *o*-methyl-*N*-trifluoroacetyl enehydrazine. The reaction of **6v** proceeded smoothly in MeCN and toluene at 80–90 °C to give the indoline **7v**, indole **11v**,[29] *cis-syn*-**17v**, and *cis-anti*-**17v** (entries 9 and 10). When an electron-withdrawing group such as a chlorine or nitro group was present in the *o*-position, the indolization occurred regioselectively at the unsubstituted position to give 5-substituted products (entries 11 and 12).

The stereostructures of *cis-syn*-**17t–v** and *cis-anti*-**17t–v** were firmly established by NOESY of the ^{1}H NMR spectra (Fig. 3). Taking *cis-syn*-**17t** and *cis-anti*-**17t** as a typical example, the assignment of those configurations is based on the observed NOE correlations as shown in Figure 3. In the case of *cis-syn*-**17t**, NOE was observed between MeO and 8b-H, 8b-H and NH, NH and MeO. On the other hand, NOE in *cis-anti*-**17t** was observed only between 8b-H and NH.

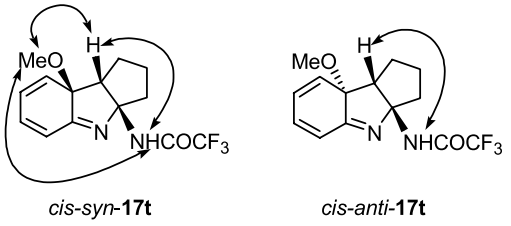
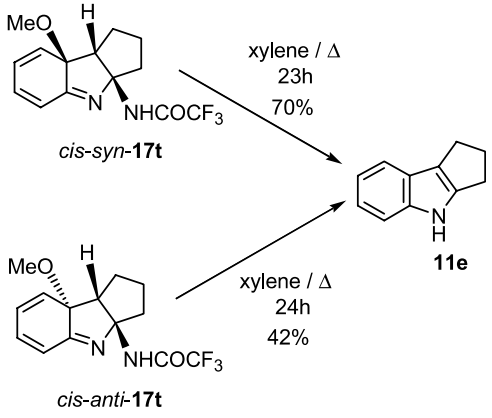


Figure 3. NOE correlations of compounds *cis-syn*-**17t** and *cis-anti*-**17t**.

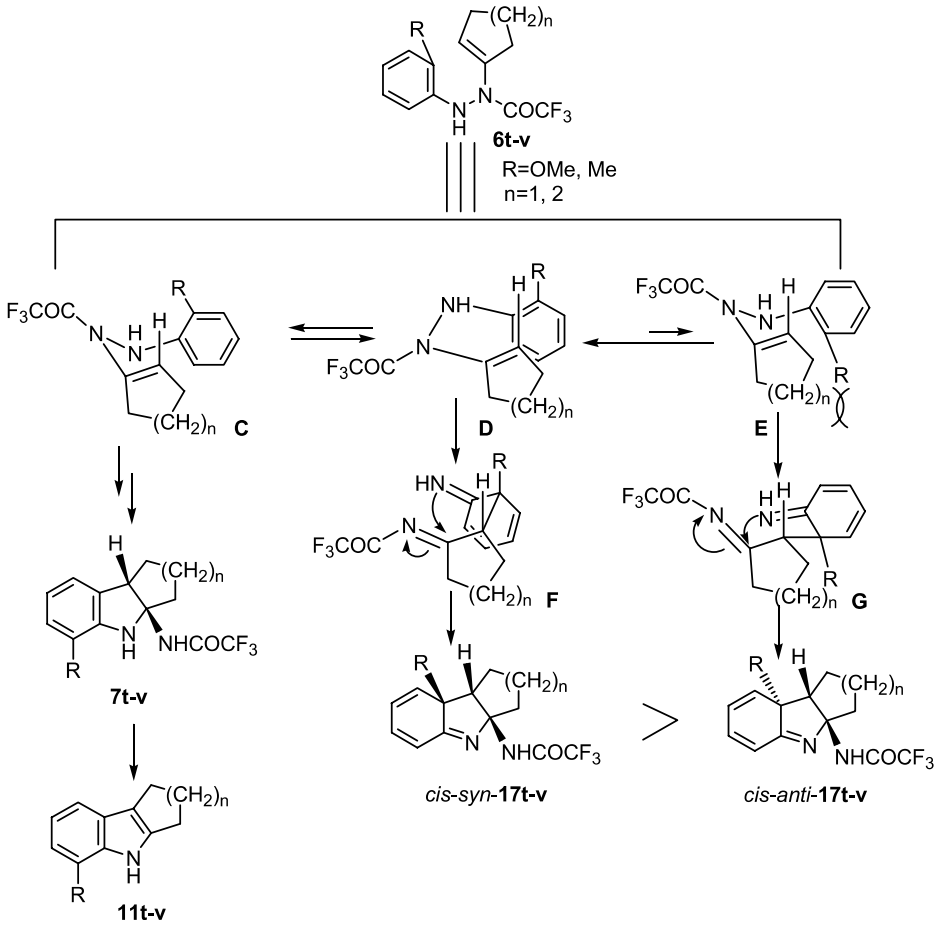
The stereostructure of *cis-syn*-**17t** was established unambiguously by single-crystal X-ray analysis.[30] Furthermore, heating the dienylimines, *cis-syn*-**17t** and *cis-anti*-**17t**, in xylene at 140 °C afforded exclusively indole **11e**[31] (Scheme 16). This reaction pathway is ambiguous at the moment.



Scheme 16.

We have now succeeded in the isolation and structure determination of the dienylimine intermediate in the thermal reaction of the *o*-methoxyenehydrazine. Additionally, the *cis-syn*-isomer was obtained as the major product among dienylimines.

It is well-known[2–4,32,33] that Fischer indolization of (2-methoxyphenyl)hydrazone gives 7-methoxyindole as a minor product and the abnormal 6-substituted indole as a major product without the isolation of dienylimine. The isolation and determination of the dienylimine intermediates in the Fischer indolization of *o*-methoxy and *o*-methyl enehydrazines provides good evidence for the postulated reaction mechanism, including a stereochemical rationalization, particularly for the [3,3]-sigmatropic rearrangement

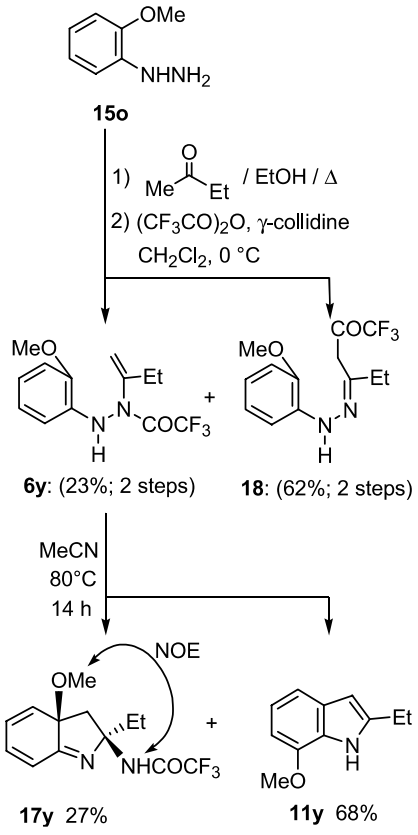


Scheme 17.

step. To the best of our knowledge, there has been only one paper[34] pertaining to the isolation of a pure dienylimine having a methyl group at the 3a-position in which the relative configurations at the 2-, 3- and 3a-position remain to be established. Additionally, Brown[35] has reported that attempts to isolate a tricyclic dienylimine having a methyl group were unsuccessful. Therefore, our result is the first example of isolation and structure determination of the tricyclic dienylimine with a methyl group.

The thermal reaction of *o*-substituted enehydrazine can be summarized as follows. The reaction of enehydrazines having an electron-donating group proceeded to give indolines, indoles, and dienylimines. The *cis-syn*-dienylimines were formed in preference to *cis-anti*-isomers. The degree of regioselectivity on [3,3]-sigmatropic rearrangement was shown to be dependent on the reaction solvent. Thus, in a polar solvent, ca. 1:1 mixture of indolines or indoles and dienylimines was obtained, while the reaction employing a less polar solvent gave the indole or indoline as a major product. In the case of enehydrazine bearing an electron-withdrawing group, prolonged reaction time and higher reaction temperature were required and no formation of dienylimines was observed.

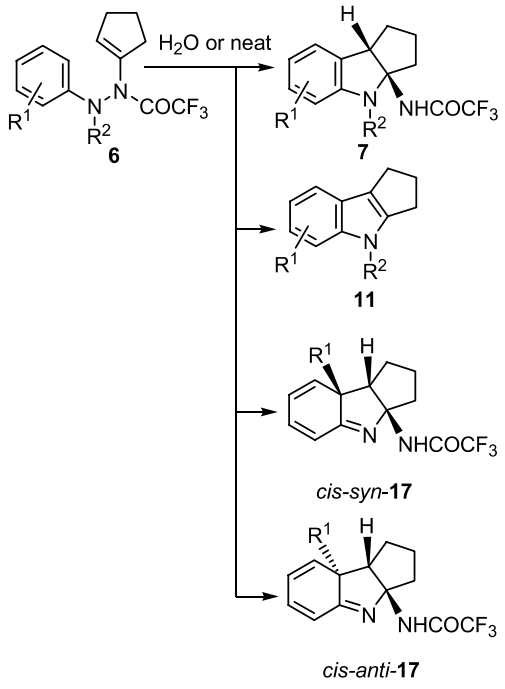
We next propose the possible reaction pathway for the formation of dienylimines **17t–v** (Scheme 17). The enehydrazines **6t–v** would exist in three different conformations **C**, **D**, and **E**. The indolines **7t–v** were obtained via



Scheme 18.

[3.3]-sigmatropic rearrangement of **C**. In the case of **7u**,**v**, they were converted into the indoles **11u**,**v** by the elimination of the trifluoroacetamido group. On the other hand, the rearrangement of **D** and **E** followed by the cyclization of the resulting imines **F** and **G** gave *cis-syn*-**17t–v** and *cis-anti*-**17t–v**, respectively. The conversion of **D** into *cis-syn*-**17t–v** proceeded more readily than that into *cis-anti*-**17t–v** because conformation **E** is less stable than conformation **D** due to the steric hindrance between a methoxy group and methylene on a cyclopentene or cyclohexene ring in **E**. The rearrangement of **6w**,**x** gave the indolines **7w**,**x** as the sole product. We are unable at this time to offer an explanation of the difference in regioselectivity between enehydrazine having an electron-donating group and enehydrazine having an electron-withdrawing group.

We next examined the reaction of acyclic enehydrazine **6y** having the *o*-methoxy group (Scheme 18). The condensation of **15o** with 2-butanone followed by acylation of the resulting hydrazone gave the enehydrazine **6y** and *C*-acylated product **18**. The isolated enehydrazine **6y** was heated at 80 °C to give *cis*-dienylimines **17y** and indole **11y**[36] in 27% and 68% yields, respectively.



Scheme 19.

2.4. [3,3]-Sigmatropic rearrangement of enehydrazines under both aqueous and solvent-free conditions

Due to the natural abundance of water as well as the inherent advantages of using water as a solvent, much interest has been recently growing in developing organic synthetic reactions in water.[37] We next investigated the [3,3]-sigmatropic rearrangement of enehydrazines **6a**,**l**,**o**,**t**,**x** in aqueous media (Scheme 19, Table 10). Suspension of enehydrazine **6a** in water was heated at 65 °C. Extraction and purification of the product by chromatography gave the indoline **7a** and indole **11a** in 61 and 33% yield, respectively (entry 1). The reaction of enehydrazine **6l** having a *p*-methoxy group gave the indole **11l** as the sole product. When a methoxy group exists at the *o*-position on the benzene ring, the dienylimines **17t** were obtained in addition to indoline **7t** and indole **11t**. The reaction of enehydrazines **6o** and **6x** bearing a nitro group on the benzene ring did not occur even at 100 °C.

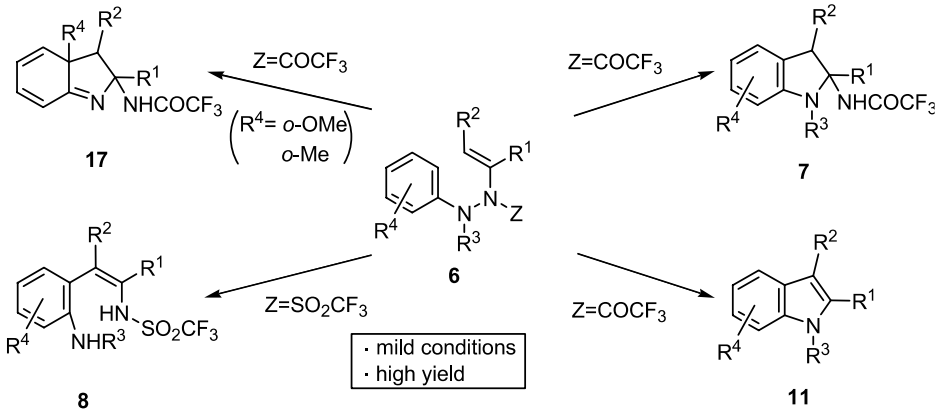
Finally, the rearrangement of enehydrazines was examined under solvent-free conditions (Scheme 19, Table 10). The reaction of enehydrazine **6a** at 65 °C afforded the indoline **7a** as a major product while the enehydrazine **6l** having a *p*-methoxy group gave the indole **11l** as the sole product (entries 6 and 7). In the case of enehydrazine **6o** and **6x** having a nitro group which did not undergo the reaction at 100 °C, heating at from 120 to 160 °C allowed the reaction to proceed but inefficiently (entries 8 and 10). The reaction of *o*-methoxy substituted enehydrazine **6t** gave **7t**, **11t**, and **17t** in favor of **7t** (entry 9). It is worth mentioning that the indoles **11** are predominantly obtained under both aqueous and solvent-free conditions except the case of *o*-methoxy substituted enehydrazine **6t**. Particularly, the enehydrazine **6l** having a *p*-methoxy group gave the indole **11l** even at 65 °C under these conditions while the reaction of **6l** proceeded at 65 °C in a solvent to give the indoline **7l** as the sole product (entry 1 in Table 7, Scheme 13).

3. Conclusion

We have established a novel [3,3]-sigmatropic rearrangement of *N*-trifluoroacetyl enehydrazines for synthesis of indolines and indoles. At below 100 °C, *N*-trifluoroacetyl enehydrazine having a cyclopentene ring smoothly underwent [3,3]-sigmatropic rearrangement followed by cyclization to give indolines in excellent yield. On the other hand, both cyclohexenyl *N*-trifluoroacetyl enehydrazine and

Table 10. The thermal reaction of enehydrazines **6** under aqueous and solvent-free conditions

Entry	Substrate	R^1	R^2	Solvent	Temperature (°C)	Time (h)	Yield (%)		
							7	**11**	**17** (*cis-syn*:*cis-anti*)
1	**6a**	H	Ph	H_2O	65	5	61	33	—
2	**6l**	*p*-OMe	H	H_2O	65	0.5	—	60	—
3	**6o**	*p*-NO_2	H	H_2O	100	7	—	—	—
4	**6t**	*o*-OMe	H	H_2O	65	7	8	39	29 (14:1)
5	**6x**	*o*-NO_2	H	H_2O	100	7	—	—	—
6	**6a**	H	Ph	Neat	65	4	83	4	—
7	**6l**	*p*-OMe	H	Neat	65	5	—	89	—
8	**6o**	*p*-NO_2	H	Neat	160	5	—	41	—
9	**6t**	*o*-OMe	H	Neat	65	5	51	10	25 (4:1)
10	**6x**	*o*-NO_2	H	Neat	120	10	5	17	—



Scheme 20.

acyclic *N*-trifluoroacetyl enehydrazine gave indoles in good yield under the almost same conditions. The rearrangement of enehydrazine having an *o*-methoxy or an *o*-methyl group on the benzene ring gave dienylimines that were clearly characterized for the first time. The *N*-trifluoromethanesulfonyl enehydrazine was converted into the rearranged product at low temperature (Scheme 20).

4. Experimental

4.1. General

Melting points are uncorrected. ^{1}H and ^{13}C NMR spectra were recorded at 200, 300, or 500 MHz and at 125 MHz, respectively. IR spectra were recorded using FTIR apparatus. Mass spectra were obtained by EI method. Flash column chromatography (FCC) was preformed using E. Merck Kieselgel 60 (230–400 mesh). Medium-pressure column chromatography (MCC) was performed using Lober Größe B (E. Merck 310-25, Lichroprep Si60).

4.2. General procedure (A) for preparation of *N*-acyl enehydrazines 6

To a solution of hydrazone (10 mmol) in CH_2Cl_2 (100 mL) were added γ-collidine (30 mmol) and the corresponding acid anhydride (20 mmol) at 0 °C. After being stirred at the same temperature for 1.5–5.5 h, the reaction mixture was concentrated under reduced pressure. Purification of the residue by FCC (hexane/AcOEt 20:1–7:1) gave the *N*-acyl enehydrazine **6**.

4.2.1. Trifluoroacetic acid 1-(1-cyclopenten-1-yl)-2,2-diphenylhydrazide (6a). According to the general procedure (A) given for preparation of *N*-acyl enehydrazine, the treatment of hydrazone **5a**[12] (2.5 g, 10 mmol) with TFAA (2.8 mL, 20 mmol) in the presence of γ-collidine (3.8 mL, 30 mmol) gave the enehydrazine **6a** (3.43 g, 99%) as a yellow oil; IR ($CHCl_3$) 1711 cm^{-1}; ^{1}H NMR (300 MHz, $CDCl_3$) δ 1.85 (2H, br quint, $J=8$ Hz), 2.28 and 2.58 (each 2H, m), 5.80 (1H, br s), 7.01–7.39 (10H, m); HRMS (EI, *m/z*) calcd for $C_{19}H_{17}F_3N_2O$ (M^+) 346.1292, found 346.1273.

4.2.2. Trichloroacetic acid 1-(1-cyclopenten-1-yl)-2,2-diphenylhydrazide (6b). According to the general procedure (A) given for preparation of *N*-acyl enehydrazine, the treatment of hydrazone **5a**[12] (2.5 g, 10 mmol) with trichloroacetic anhydride (4.1 mL, 20 mmol) in the presence of γ-collidine (3.8 mL, 30 mmol) gave the enehydrazine **6b** (3.90 g, 99%) as a yellow oil; IR ($CHCl_3$) 1699 cm^{-1}; ^{1}H NMR (300 MHz, $CDCl_3$) δ 1.85 (2H, br quint, $J=8$ Hz), 2.28 and 2.58 (each 2H, m), 5.81 (1H, br s), 7.01–7.39 (10H, m); HRMS (EI, *m/z*) calcd for $C_{19}H_{17}^{35}Cl_3N_2O$ (M^+) 394.0406, found 394.0406.

4.2.3. Acetic acid 1-(1-cyclopenten-1-yl)-2,2-diphenylhydrazide (6c). To a solution of hydrazone **5a**[12] (500 mg, 2.0 mmol) and γ-collidine (727 mg, 6.0 mmol) in CH_2Cl_2 (15 mL) was added acetyl chloride (314 mg, 4.0 mmol) and dimethylaminopyridine (DMAP) (12.2 mg, 0.1 mmol) under a nitrogen atmosphere at room temperature. After being stirred at the same temperature for 24 h, the reaction mixture was concentrated under reduced pressure. Purification of the residue by FCC (*n*-hexane/ethyl acetate 10:1) gave the *N*-acetyl enehydrazine **6c** (548 mg, 99%) as a yellow oil; IR ($CHCl_3$) 1680 cm^{-1}; ^{1}H NMR (300 MHz, $CDCl_3$) δ 1.82 (2H, br quint, $J=7.5$ Hz), 2.04 (3H, s), 2.29 and 2.66 (each 2H, m), 5.70 (1H, br s), 6.99–7.33 (10H, m); HRMS (EI, *m/z*) calcd for $C_{19}H_{20}N_2O$ (M^+) 292.1575, found 292.1576.

4.3. General procedure for thermal reaction of *N*-acyl enehydrazines 6

A solution of enehydrazines **6** (0.12–0.50 mmol) in solvent (5–15 mL) was heated while monitoring the reaction by TLC. The reaction mixture was concentrated under reduced pressure. Purification of the residue by MCC (hexane/AcOEt 20:1–5:1) gave the products.

4.4. Thermal reaction of 6a–c (Table 2)

According to the general procedure given for the reaction of **6**, the enehydrazines **6a–c** were heated under the conditions shown in Table 2 to give the indoline **7a–c** in the yield shown in Table 2.

4.4.1. *cis*-3a-[(Trifluoroacetyl)amino]-1,2,3,3a,4,8b-hexahydro-4-phenylcyclopent[*b*]indole (7a). Colorless crystals, mp 137–140 °C (hexane/AcOEt); IR ($CHCl_3$) 3425, 1725 cm^{-1}; ^1H NMR (300 MHz, $CDCl_3$) δ 1.59–1.65 (1H, m), 1.79–1.86 (2H, m), 2.14–2.27 (2H, m), 2.35–2.42 (1H, m), 3.96 (1H, br dd, J=9.5, 3 Hz), 6.58 (1H, br d, J=8 Hz), 6.74 (1H, br s), 6.81 (1H, br t, J=8 Hz), 7.06 (1H, br t, J=8 Hz), 7.15 (1H, br d, J=8 Hz), 7.23 (1H, br t, J=8 Hz), 7.26 (2H, br d, J=8 Hz), 7.40 (2H, br t, J=8 Hz). NOE was observed between 8b-H (δ 3.96) and NH (δ 6.74) in NOESY spectroscopy. ^{13}C NMR (125 MHz, $CDCl_3$) δ 24.6, 34.9, 36.4, 52.9, 90.9, 108.7, 115.4 (q, CF_3), 119.7, 124.5, 125.1, 125.8, 127.5, 129.7, 132.1, 140.2, 148.1, 155.7 (q, $COCF_3$); HRMS (EI, m/z) calcd for $C_{19}H_{17}F_3N_2O$ (M^+) 346.1292, found 346.1277. Anal. Calcd for $C_{19}H_{17}F_3N_2O$: C, 65.89; H, 4.95; N, 8.09, found: C, 65.93; H, 5.13; N, 8.14.

4.4.2. *cis*-3a-[(Trichloroacetyl)amino]-1,2,3,3a,4,8b-hexahydro-4-phenylcyclopent[*b*]indole (7b). A yellow oil; IR ($CHCl_3$) 3424, 1714 cm^{-1}; ^1H NMR (300 MHz, $CDCl_3$) δ 1.56 (1H, br s), 1.63 (2H, m), 1.83 (1H, m), 2.16–2.42 (3H, m), 4.00 (1H, dd, J=9.5, 3 Hz), 6.60 (1H, d, J=8 Hz), 6.80 (1H, br t, J=8 Hz), 6.93 (1H, br t, J=8 Hz), 7.06 (1H, m), 7.15–7.42 (5H, m); HRMS (EI, m/z) calcd for $C_{19}H_{17}^{35}Cl_3N_2O$ (M^+) 394.0406, found 394.0406.

4.4.3. *cis*-3a-Acetylamino-1,2,3,3a,4,8b-hexahydro-4-phenylcyclopent[*b*]indole (7c). Colorless crystals, mp 218–221 °C (AcOEt); IR ($CHCl_3$) 3436, 1678 cm^{-1}; ^1H NMR (300 MHz, $CDCl_3$) δ 1.55 (1H, m), 1.70–1.81 (2H, m), 1.90 (3H, s), 2.08 (1H, m), 2.20–2.38 (2H, m), 3.96 (1H, dd, J=9.5, 3 Hz), 6.02 (1H, br s), 6.62 (1H, d, J=8 Hz), 6.76 (1H, br t, J=8 Hz), 7.02 (1H, br t, J=8 Hz), 7.13 (1H, m), 7.16–7.49 (5H, m); HRMS (EI, m/z) calcd for $C_{19}H_{20}N_2O$ (M^+) 292.1575, found 292.1576. Anal. Calcd for $C_{19}H_{20}N_2O\cdot 1/100H_2O$: C, 77.45; H, 6.77; N, 9.47, found: C, 77.28; H, 6.93; N, 9.49.

4.4.4. Reaction of hydrazone 5a with triflic anhydride (Table 3). (entry 1) According to the general procedure (A) given for the preparation of enehydrazine **6**, the hydrazone **5a** (2.50 g, 10 mmol) was treated with Tf_2O (5.64 g, 20 mmol) in the presence of γ-collidine (3.46 g, 30 mmol) at 0 °C. After being stirred at the same temperature for 3 h, the reaction mixture was concentrated under reduced pressure. Purification of the residue by FCC (hexane/ethyl acetate 20:1) gave *N*-[2-[2-(phenylamino)phenyl]cyclopenten-1-yl]trifluoromethanesulfonamide (**8d**) (191 mg, 5%) as a yellow oil; IR ($CHCl_3$) 3327, 1603 cm^{-1}; ^1H NMR (300 MHz, $CDCl_3$) δ 1.92 (2H, br quint, J=8 Hz), 2.26 (1H, br s), 2.79 (4H, m), 7.05–7.38 (9H, m), 8.56 (1H, br s); HRMS (EI, m/z) calcd for $C_{18}H_{17}F_3N_2O_2S$ (M^+) 382.0962, found 382.0959.

(entry 2) To a solution of hydrazone **5a** (52.8 mg, 0.21 mmol) in CH_2Cl_2 (7 mL) was added γ-collidine (38.8 mg, 0.32 mmol) and Tf_2O (59.2 mg, 0.21 mmol) at −78 °C. The reaction mixture was stirred at the same temperature for 1.5 h, monitoring the reaction by TLC. The reaction mixture was purified without concentration by FCC (*n*-hexane/ethyl acetate 20:1) to give **8d** (20.1 mg, 25%) as a yellow oil.

(entry 3) To a solution of hydrazone **5a** (35.0 mg, 0.14 mmol) in CH_2Cl_2 (4 mL) was added triethylamine (14.2 mg, 0.14 mmol) and Tf_2O (39.5 mg, 0.14 mmol) at −78 °C. The reaction mixture was stirred at the same temperature for 1.5 h, monitoring the reaction by TLC. The reaction mixture was purified without concentration by FCC (*n*-hexane/ethyl acetate 20:1) to give **8d** (37.5 mg, 70%) as a yellow oil.

4.4.5. Trifluoroacetic acid 1-(1-cyclopenten-1-yl)-2-phenylhydrazide (6e). According to the general procedure (A) given for the preparation of enehydrazine **6**, the acylation of hydrazone **5b**[13] (348 mg, 2 mmol) with TFAA (0.6 mL, 4 mmol) gave enehydrazine **6e** (400 mg, 74%) as a yellow oil; IR ($CHCl_3$) 3421, 1721 cm^{-1}; ^1H NMR (300 MHz, $CDCl_3$) δ 1.89 (2H, br quint, J=8 Hz), 2.36 and 2.69 (each 2H, m), 5.72 (1H, br s), 6.17 (1H, br s), 6.75 (2H, br d, J=8.5 Hz), 6.88 (1H, br t, J=8.5 Hz), 7.28 (2H, br d, J=8.5 Hz); HRMS (EI, m/z) calcd for $C_{13}H_{13}F_3N_2O$ (M^+) 270.0980, found 270.0994.

4.4.6. *cis*-3a-[(Trifluoroacetyl)amino]-1,2,3,3a,4,8b-hexahydrocyclopent[*b*]indole (7e). According to the general procedure given for the thermal reaction of **6**, **6e** (30 mg, 0.11 mmol) was heated in toluene (15 mL) at 90 °C to give the indoline **7e** (17 mg, 56%) as a colorless oil; IR ($CHCl_3$) 3424, 1720 cm^{-1}; ^1H NMR (300 MHz, $CDCl_3$) δ 1.66 (1H, m), 1.74–1.88 (2H, m), 2.20 (1H, m), 2.31–2.42 (2H, m), 3.69 (1H, dd, J=8.5, 2 Hz), 4.67 (1H, br s), 6.57 (1H, dd, J=7, 1 Hz), 6.78 (1H, td, J=7, 1 Hz), 6.79 (1H, br s), 7.07 (2H, m); HRMS (EI, m/z) calcd for $C_{13}H_{13}F_3N_2O$ (M^+) 270.0980, found 270.0962.

4.4.7. Thermal reaction of 6a at 140 °C (entry 4, Table 4). According to the general procedure given for the thermal reaction of **6**, **6a** was heated in xylene at 140 °C to give 1,2,3,4-tetrahydro-4-phenylcyclopent[*b*]indole **11a**[14] (165 mg, 92%) as a yellow oil; ^1H NMR (300 MHz, $CDCl_3$) δ 2.55 (2H, br quint, J=7 Hz), 2.91 (4H, t-like, J=7 Hz), 7.10–7.52 (9H, m); HRMS (EI, m/z) calcd for $C_{17}H_{15}N$ (M^+) 233.1203, found 233.1177.

4.4.8. Trifluoroacetic acid 1-(1-cyclohexen-1-yl)-2,2-diphenylhydrazide (6f). According to the general procedure (A) given for the preparation of enehydrazine **6**, the acylation of diphenylhydrazone[15] (2.64 g, 10 mmol) of cyclohexanone with TFAA (2.8 mL, 20 mmol) gave enehydrazine **6f** (3.38 g, 94%) as a yellow oil; IR ($CHCl_3$) 1711 cm^{-1}; ^1H NMR (300 MHz, $CDCl_3$) δ 1.44–1.80 (4H, m), 2.04 and 2.35 (each 2H, m), 5.55 (1H, br s), 7.00–7.24 (10H, m); HRMS (EI, m/z) calcd for $C_{20}H_{19}F_3N_2O$ (M^+) 360.1448, found 360.1423.

4.4.9. 1,2,3,4-Tetrahydro-9-phenyl-9*H*-carbazole (11f) (entry 5, Table 4). According to the general procedure given for the thermal reaction of **6**, **6f** (75 mg, 0.21 mmol) was heated in THF (10 mL) at 65 °C to give the indole **11f**[16] (27.5 mg, 53%) as a yellow oil; ^1H NMR (200 MHz, $CDCl_3$) δ 1.89 (4H, br quint, J=3 Hz), 2.60 and 2.80 (each 2H, m), 7.02–7.54 (9H, m); HRMS (EI, m/z) calcd for $C_{18}H_{17}N$ (M^+) 247.1360, found 247.1357.

4.4.10. Conversion of indoline 7a into indole 11a. A solution of indoline **7a** (82.3 mg, 0.24 mmol) in xylene (4 mL) was refluxed, monitoring the reaction by TLC. After being refluxed at the same temperature for 4 h, the reaction mixture was concentrated under reduced pressure. Purification of the residue by MCC (hexane/ethyl acetate 9:1) gave **11a** (35.4 mg, 92%).

4.4.11. *cis*-1,2,3,3a,4,8b-Hexahydro-4-phenylcyclopent-[*b*]indole (12).[17] To a stirred solution of indoline **7a** (187 mg, 0.54 mmol) in AcOH (3 mL) was added $NaBH_3$-CN (67.9 mg, 1.08 mmol) at 0 °C. After being stirred at room temperature for 19 h, the reaction mixture was neutralized with 4 M-NaOH and extracted with $CHCl_3$. The organic phase was washed with H_2O, dried over $MgSO_4$, and concentrated under reduced pressure. Purification of the residue by MCC (hexane/AcOEt 9:1) afforded indoline **12** (129 mg, 71%) as a yellow oil; ^{1}H NMR (500 MHz, $CDCl_3$) δ 1.53 and 1.64 (each 1H, m), 1.80–1.96 (3H, m), 2.03 (1H, dddd, J=12.5, 11, 8.5, 6.5 Hz), 3.83 (1H, td, J=8.5, 3 Hz), 4.73 (1H, ddd, J=8.5, 6.5, 3 Hz), 6.73–7.31 (9H, m); NOE was observed between 8b-H (δ 3.83) and 3a-H (δ 4.75) in NOESY spectroscopy. ^{13}C NMR (125 MHz, $CDCl_3$) δ 24.5, 34.0, 34.8, 45.5, 68.7, 108.2, 118.7, 119.0, 121.1, 124.7, 127.1, 129.1, 135.0, 143.4, 147.3; HRMS (EI, *m*/*z*) calcd for $C_{17}H_{17}N$ (M^+) 235.1360, found 235.1361.

4.4.12. *cis*-7-Bromo-4-(4-bromophenyl)-1,2,3,3a,4,8b-hexahydrocyclopent[*b*]indole (14). To a solution of 1,2,3,3a,4,8b-hexahydro-4-phenylcyclopent[*b*]indole **12** (105.2 mg, 0.45 mmol) in acetone (4.5 mL) was added *N*-bromosuccinimide (NBS) (159.4 mg, 0.90 mmol) at 0 °C under a nitrogen atmosphere in the dark. After being stirred at the same temperature for 2 h, the reaction mixture was quenched with H_2O and extracted with $CHCl_3$. The organic phase was washed with brine, dried over $MgSO_4$ and concentrated at reduced pressure. The crude solid obtained was recrystallized from *n*-hexane to afford **14** (169.8 mg, 97%) as colorless crystals, mp 151–153 °C (hexane): ^{1}H NMR (500 MHz, $CDCl_3$) δ 1.56–1.69 (2H, m), 1.81–1.88 (3H, m), 1.97–2.10 (1H, m), 3.80 (1H, br td, J=8.5, 3 Hz), 4.71 (1H, ddd, J=8.5, 6.5, 3 Hz), 6.80 (1H, d, J=8 Hz), 7.11 (2H, br d, J=8 Hz), 7.12 (1H, dd, J=8, 2.5 Hz), 7.19 (1H, dd, J=2.5, 1.5 Hz), 7.41 (2H, br d, J=8 Hz); HRMS (EI, *m*/*z*) calcd for $C_{17}H_{15}Br_2N$ (M^+) 390.9574, found 390.9570. NOE was observed between 8b-H (δ 3.80) and 3a-H (δ 4.71) in NOESY spectroscopy.

Determination of single-crystal structures by X-ray crystallography: the dibromide **14** was recrystallized from acetone to give single crystals suitable for X-ray single crystallographic analysis. X-ray diffraction data was collected on a Rigaku RAPID imaging plate with two-dimensional area detector and graphite-monochromatized Cu Kα radiation (λ=1054186Å). The crystallographic calculation was performed with the TEXSAN software package from the Molecular Structure Corporation. The crystal structure was solved by direct methods (SIR-92), and refined by the full-matrix least-squares method. All non-hydrogen atoms were anisotropically refined. Hydrogen atoms were located in idealized positions and were not subjected to further refinement. X-ray diffraction study was performed at 93 K. The independent four molecules are in a unit cell. Crystallographic data of: C_{68} H_{60} Br_8 N_4; space group *P*1; *a*=8.371(1) Å, *b*=12.564(2) Å, *c*=13.862(2) Å, α=86.99(1)°, β=81.07(1)°, γ=89.91(1)°; *V*=1438.2(4) Å^3 *Z*=1; *T*=93.2 K; μ=7.044 mm^{-1}; reflection total: 14240, unique: 4774, observed: 4774($I > -10.0\sigma(I)$); parameters refined:721; *R*1=0.067, *Rw*=0.181; GOF=1.81. Crystallographic data for the structure in this paper have been deposited with the Cambridge Crystallographic Data Centre as supplementary publication number CCDC-292640. These data can be obtained free of charge via www.ccdc.cam.ac.uk/conts/retrieving.html (or from the Cambridge Crystallographic Data Centre, 12 Union Road, Cambridge CB2 1EZ, UK; fax: +44 1223 336 033; or deposit@ccdc.cam.uk).

4.4.13. Trifluoroacetic acid 2,2-diphenyl-1-[1-(5-methylcyclopenten-1-yl)]hydrazide (6g). According to the general procedure (A) given for the preparation of enehydrazine **6**, the acylation of hydrazone **5c** (528 mg, 2 mmol) with TFAA (0.6 mL, 4 mmol) gave enehydrazine **6g** (520 mg, 72%) as a yellow oil; IR ($CHCl_3$) 1709 cm^{-1}; ^{1}H NMR (300 MHz, $CDCl_3$) δ 0.86 (3H, d, J=8.5 Hz), 2.20 (4H, m), 3.56 (1H, m), 5.49 (1H, br s), 6.98–7.38 (10H, m); HRMS (EI, *m*/*z*) calcd for $C_{20}H_{19}F_3N_2O$ (M^+) 360.1448, found 360.1458.

4.5. General procedure (B) for preparation of *N*-acyl enehydrazines 6

To a solution of hydrazine (10 mmol) in EtOH (50 mL) was added ketone (20 mmol) at room temperature. After being stirred at the same temperature for 3–5 h, the reaction mixture was concentrated under reduced pressure to give the crude hydrazone. To a stirred solution of crude hydrazone in CH_2Cl_2 (100 mL) was added γ-collidine (30 mmol) and TFAA (20 mmol) at 0 °C. After being stirred at the same temperature for 1–5 h, the reaction mixture was concentrated under the reduced pressure. Purification of the residue by FCC (hexane/AcOEt 20:1–5:1) gave the enehydrazine **6**.

4.5.1. Trifluoroacetic acid 1-[1-(5-methylcyclopenten-1-yl)]-2-phenylhydrazide (6h). According to the general procedure (B) given for the preparation of **6**, the condensation of phenylhydrazine with 2-methylcyclopentanone (1.02 g, 10.4 mmol) followed by acylation of the resulting hydrazone with TFAA (2.9 mL, 20.8 mmol) gave enehydrazine **6h** (2.20 g, 75%) as a yellow oil; IR ($CHCl_3$) 3354, 1720 cm^{-1}; ^{1}H NMR (300 MHz, $CDCl_3$) δ 1.09 (3H, d, J=8.5 Hz), 2.19 (4H, m), 3.30 (1H, m), 5.53 (1H, br s), 6.05 (1H, br s), 6.71–7.32 (5H, m); HRMS (EI, *m*/*z*) calcd for $C_{14}H_{15}F_3N_2O$ (M^+) 284.1136, found 284.1142.

4.5.2. (3α,3aα,8bα)-3a-[(Trifluoroacetyl)amino]-1,2,3,3a,4,8b-hexahydro-3-methyl-4-phenyl-cyclopent-[*b*]indole (7g). According to the general procedure given for the thermal reaction of **6**, **6g** (75.6 mg, 0.21 mmol) was heated in THF (10 mL) at 65 °C to give the indoline **7g** (57.5 mg, 76%) as colorless crystals, mp 92–94 °C (hexane/AcOEt); IR ($CHCl_3$) 1740 cm^{-1}; ^{1}H NMR (500 MHz, $CDCl_3$) δ 0.95 (3H, d, J=7.5 Hz), 1.62–1.67 (2H, m), 1.91–1.96 (1H, m), 2.41–2.51 (2H, m), 4.13 (1H, br dd, J=9.5, 6 Hz), 6.40 (1H, br d, J=8 Hz), 6.71 (1H, br s), 6.78 (1H, br

t, J=8 Hz), 7.02 (1H, br t, J=8 Hz), 7.14 (1H, br d, J=8 Hz), 7.24 (2H, br d, J=8 Hz), 7.28 (1H, br t, J=8 Hz), 7.41 (2H, br t, J=8 Hz). NOE were observed between 3-Me (δ 0.95) and 8b-H (δ 4.13), 3-Me (δ 0.95) and NH (δ 6.71), NH (δ 6.71) and 8b-H (δ 4.13) in NOESY spectroscopy. ^{13}C NMR (125 MHz, $CDCl_3$) δ 15.0, 32.6, 33.3, 43.9, 52.6, 91.3, 108.0, 115.7 (q, *C*F_3), 119.2, 123.8, 126.6, 127.1, 127.5, 129.8, 131.8, 140.3, 148.5, 156.1 (q, *C*OCF$_3$); HRMS (EI, *m*/*z*) calcd for $C_{20}H_{19}F_3N_2O$ (M^+) 360.1448, found 360.1455. Anal. Calcd for $C_{20}H_{19}F_3N_2O$: C, 66.66; H, 5.31; N, 7.77, found: C, 66.71; H, 5.42; N, 7.79.

4.5.3. 1,2,3,4-Tetrahydro-3-methylcyclopent[*b*]indole (11h). According to the general procedure given for the thermal reaction of **6**, **6h** (59.6 mg, 0.21 mmol) was heated in toluene(10 mL) at 90 °C to give the indole **11h** (35.5 mg, 99%) as a yellow oil; IR ($CHCl_3$) 3475 cm^{-1}; ^{1}H NMR (300 MHz, $CDCl_3$) δ 1.29 (3H, d, J=7 Hz), 2.05 (2H, m), 2.64–2.90 (3H, m), 6.95–7.48 (4H, m), 7.78 (1H, br s); HRMS (EI, *m*/*z*) calcd for $C_{12}H_{13}N$ (M^+) 171.1047, found 171.1065.

4.5.4. Trifluoroacetic acid 2,2-diphenyl-1-(1-ethyl-1-propenyl)hydrazide (6i). According to the general procedure (A) given for the preparation of **6**, the acylation of hydrazone **5e** (2.52 g, 10 mmol) with TFAA (2.8 mL, 20 mmol) gave the enehydrazine **6i** (1.67 g, 48%) as a yellow oil; IR ($CHCl_3$) 1709 cm^{-1}; ^{1}H NMR (300 MHz, $CDCl_3$) δ 1.17 (3H, t, J=8 Hz), 1.64 (3H, d, J=6 Hz), 2.37 (2H, br q, J=8 Hz), 5.28 (1H, br q, J=6 Hz), 7.02 and 7.32 (each 5H, m); HRMS (EI, *m*/*z*) calcd for $C_{19}H_{19}F_3N_2O$ (M^+) 348.1449, found 348.1451.

4.5.5. Acylation of hydrazone 5f with TFAA. According to the general procedure given for the preparation of enehydrazine **6**, acylation of **5f**[24] (2.38 g, 10 mmol) with TFAA (2.8 mL, 20 mmol) gave **6j** (2.07 g, 62%) and **6k** (668 mg, 20%).

4.5.6. Trifluoroacetic acid 1-(1-methylenepropyl)-2,2-diphenylhydrazide (6j). A yellow oil; IR ($CHCl_3$) 1713 cm^{-1}; ^{1}H NMR (300 MHz, $CDCl_3$) δ 1.12 (3H, m), 2.24 (2H, br q, J=8 Hz), 4.09 and 5.07 (each 1H, br s), 7.04 and 7.32 (each 5H, m); HRMS (EI, *m*/*z*) calcd for $C_{18}H_{17}F_3N_2O$ (M^+) 334.1292, found 334.1285.

4.5.7. Trifluoroacetic acid 1-(1-methyl-2-propenyl)-2,2-diphenylhydrazide (6k). A yellow oil; IR ($CHCl_3$) 1712 cm^{-1}; ^{1}H NMR (300 MHz, $CDCl_3$) δ 1.61 (3H, br d, J=7 Hz), 1.98 (3H, s), 5.33 (1H, br q, J=7 Hz), 7.07 and 7.35 (each 5H, m); HRMS (EI, *m*/*z*) calcd for $C_{18}H_{17}F_3N_2O$ (M^+) 334.1292, found 334.1291.

4.6. Thermal reaction of enehydrazines 6i–k

According to the general procedure for thermal reaction of enehydrazine **6**, **6i–k** was heated at temperature shown in Table 6 to afford **11i–k** in the yield shown in Table 6.

4.6.1. 2-Ethyl-3-methyl-1-phenyl-1*H*-indole (11i). A yellow oil; ^{1}H NMR (200 MHz, $CDCl_3$) δ 0.98 (3H, t, J=8 Hz), 2.34 (3H, s), 2.68 (2H, q, J=8 Hz), 7.07 (3H, m), 7.32 (2H, m), 7.49 (4H, m); HRMS (EI, *m*/*z*) calcd for $C_{17}H_{17}N$ (M^+) 235.1360, found 235.1374.

4.6.2. 2-Ethyl-1-phenyl-1*H*-indole (11j). A yellow oil; ^{1}H NMR (200 MHz, $CDCl_3$) δ 1.22 (3H, t, J=8 Hz), 2.63 (2H, q, J=8 Hz), 6.42 (1H, br s), 7.08 (3H, m), 7.35 (2H, m), 7.43–7.61 (4H, m); HRMS (EI, *m*/*z*) calcd for $C_{16}H_{15}N$ (M^+) 221.1203, found 221.1226.

4.6.3. 2,3-Dimethyl-1-phenyl-1*H*-indole (11k).[25] A yellow oil; ^{1}H NMR (200 MHz, $CDCl_3$) δ 2.24 and 2.32 (each 3H, s), 7.10 (3H, m), 7.32 (2H, m), 7.41–7.59 (4H, m); HRMS (EI, *m*/*z*) calcd for $C_{16}H_{15}N$ (M^+) 221.1203, found 221.1208.

4.7. Preparation of *N*-trifluoroacetyl enehydrazines 6l–n

According to the general procedure (B) given for the preparation of enehydrazine **6**, the condensation of corresponding hydrazines **15g–i** with cyclopentanone followed by acylation of hydrazones **5g–i** gave **6l–n** in the yield shown in Table 7.

4.7.1. Trifluoroacetic acid 1-(1-cyclopenten-1-yl)-2-(4-methoxyphenyl)hydrazide (6l). A yellow oil; IR ($CHCl_3$) 3478, 1720 cm^{-1}; ^{1}H NMR (300 MHz, $CDCl_3$) δ 1.90 (2H, br q, J=8 Hz), 2.34 and 2.66 (each 2H, m), 3.77 (3H, s), 5.71 (1H, br s), 5.92 (1H, br s), 6.72 (2H, br d, J=8.5 Hz), 6.84 (2H, br d, J=8.5 Hz); HRMS (EI, *m*/*z*) calcd for $C_{14}H_{15}F_3N_2O_2$ (M^+) 300.1085, found 300.1101.

4.7.2. Trifluoroacetic acid 1-(1-cyclopenten-1-yl)-2-(4-methylphenyl)hydrazide (6m). A yellow oil; IR ($CHCl_3$) 3354, 1717 cm^{-1}; ^{1}H NMR (300 MHz, $CDCl_3$) δ 1.88 (2H, br quint, J=7.5 Hz), 2.28 (3H, s), 2.34 and 2.68 (each 2H, m), 5.70 (1H, br s), 5.94 (1H, br s), 6.64 and 7.07 (each 2H, br d, J=8 Hz); HRMS (EI, *m*/*z*) calcd for $C_{14}H_{15}F_3N_2O$ (M^+) 284.1135, found 284.1113.

4.7.3. Trifluoroacetic acid 2-(4-chlorophenyl)-1-(1-cyclopenten-1-yl)hydrazide (6n). A yellow oil; IR ($CHCl_3$) 3353, 1721 cm^{-1}; ^{1}H NMR (300 MHz, $CDCl_3$) δ 1.90 (2H, br quint, J=7.5 Hz), 2.35 and 2.67 (each 2H, m), 5.64 (1H, br s), 6.13 (1H, br s), 6.69 (2H, br d, J=8.5 Hz), 7.24 (2H, br d, J=8.5 Hz); HRMS (EI, *m*/*z*) calcd for $C_{13}H_{12}^{35}ClF_3N_2O$ (M^+) 304.0590, found 304.0602.

4.7.4. Conversion of hydrazine 15j into 6o. According to the general procedure (B) given for the preparation of **6**, the condensation of hydrazine **15j** (3.06 g, 20 mmol) with cyclopentanone (1.68 g, 40 mmol) followed by acylation of the resulting hydrazone **5j** with TFAA (5.6 mL, 40 mmol) gave the enehydrazine **6o** (315 mg, 10%) and **5j** (3.9 g, 89%). According to the general procedure (A) given for preparation of **6**, the acylation of **5j** (3.9 g, 17.8 mmol) with TFAA (5 mL, 35.6 mmol) gave the enehydrazine **6o** (1.74 g, 31% from **15j**) and diacylated enehydrazine **16** (3.58 g, 49% from **15j**).

4.7.5. Trifluoroacetic acid 1-(1-cyclopenten-1-yl)-2-(4-nitrophenyl)hydrazide (6o). A yellow oil; IR ($CHCl_3$) 3310, 1727, 1525, 1342 cm^{-1}; ^{1}H NMR (300 MHz, $CDCl_3$) δ 1.94 (2H, br quint, J=7 Hz), 2.38 and 2.71 (each 2H, m),

5.71 (1H, br s), 6.62 (1H, br d, J=8.5 Hz), 6.82 (1H, d, J=8.5 Hz), 6.83 (1H, br s), 8.20 (2H, d, J=8.5 Hz); HRMS (EI, *m/z*) calcd for $C_{13}H_{12}F_3N_3O_3$ (M^+) 315.0830, found 315.0828.

4.7.6. Cyclopentanone 4-nitrophenylhydrazone (5j).[26] A yellow oil; IR ($CHCl_3$) 3602, 1521, 1211 cm^{-1}; ^1H NMR (300 MHz, $CDCl_3$) δ 1.80 and 1.93 (each 2H, quint, J=7 Hz), 2.31 and 2.51 (each 2H, br td, J=7, 2 Hz), 7.01 (2H, br d, J=9 Hz,), 7.30 (1H, br s), 8.13 (2H, br d, J=9 Hz); HRMS (EI, *m/z*) calcd for $C_{11}H_{13}N_3O_2$ (M^+) 219.1007, found 219.1014.

4.7.7. Trifluoroacetic acid 1-(1-cyclopenten-1-yl)-2-trifluoroacetyl-2-(4-nitrophenyl) hydrazide (16). A yellow oil; IR ($CHCl_3$) 1725, 1752, 1535, 1348 cm^{-1}; ^1H NMR (300 MHz, $CDCl_3$) δ 2.10 (2H, m), 2.46 (4H, m), 5.85 (1H, br s), 7.63 (2H, br d, J=8.5 Hz), 8.34 (2H, br d, J=8.5 Hz); HRMS (EI, *m/z*) calcd for $C_{15}H_{11}F_6N_3O_4$ (M^+) 411.0652, found 411.0654.

4.8. Thermal reaction of *N*-trifluoroacetyl enehydrazines 6l–o

According to the general procedure given for the thermal reaction of **6**, enehydrazines **6l–o** were heated at the temperature shown in Table 7 to give indoline **7l–o** and indole **11l–o** in the yield shown in Table 7.

4.8.1. *cis*-3a-[(Trifluoroacetyl)amino]-1,2,3,3a,4,8b-hexahydro-7-methoxycyclopent[*b*]indole (7l). A yellow oil; IR ($CHCl_3$) 3478, 1750 cm^{-1}; ^1H NMR (300 MHz, $CDCl_3$) δ 1.66 (1H, m), 1.82 (2H, m), 2.08 (1H, m), 2.40 (2H, m), 3.72 (1H, br d, J=8 Hz), 3.75 (3H, s), 4.31 (1H, br s), 6.52 (1H, br d, J=8 Hz), 6.65 (1H, dd, J=8, 2 Hz), 6.67 (1H, d, J=2 Hz), 6.78 (1H, br s); HRMS (EI, *m/z*) calcd for $C_{14}H_{15}F_3N_2O_2$ (M^+) 300.1085, found 300.1095.

4.8.2. *cis*-3a-[(Trifluoroacetyl)amino]-1,2,3,3a,4,8b-hexahydro-7-methylcyclopent[*b*]indole (7m). A yellow oil; IR ($CHCl_3$) 3423, 1721 cm^{-1}; ^1H NMR (300 MHz, $CDCl_3$) δ 1.66 (1H, m), 1.81 (2H, m), 2.13 (1H, m), 2.26 (3H, s), 2.38 (2H, m), 3.68 (1H, dd, J=10, 1 Hz), 4.49 (1H, br s), 6.49 (1H, br d, J=8.5 Hz), 6.74 (1H, br s), 6.86–6.91 (2H, m); HRMS (EI, *m/z*) calcd for $C_{14}H_{15}F_3N_2O$ (M^+) 284.1135, found 284.1153.

4.8.3. *cis*-7-Chloro-3a-[(trifluoroacetyl)amino]-1,2,3,3a,4,8b-hexahydrocyclopent[*b*]indole (7n). A yellow oil; IR ($CHCl_3$) 3424, 1720 cm^{-1}; ^1H NMR (300 MHz, $CDCl_3$) δ 1.66 (1H, m), 1.72–1.90 (2H, m), 2.20 (1H, m), 2.28–2.38 (2H, m), 3.67 (1H, dd, J=10.5, 2.5 Hz), 4.66 (1H, br s), 6.47 (1H, br d, J=8.5 Hz), 6.81 (1H, br s), 7.00–7.04 (2H, m); HRMS (EI, *m/z*) calcd for $C_{13}H_{12}^{35}ClF_3N_2O$ (M^+) 304.0590, found 304.0595.

4.8.4. 7-Chloro-1,2,3,4-tetrahydrocyclopent[*b*]indole (11n).[38] A yellow oil; IR ($CHCl_3$) 3475 cm^{-1}; ^1H NMR (300 MHz, $CDCl_3$) δ 2.53 (2H, br quint, J=8 Hz), 2.76–2.88 (4H, t-like, J=8 Hz), 7.03 (1H, dd, J=8.5, 2 Hz), 7.18 (1H, br d, J=8.5 Hz), 7.39 (1H, br d, J=2 Hz), 7.84 (1H, br s); HRMS (EI, *m/z*) calcd for $C_{11}H_{10}^{35}ClN$ (M^+) 191.0501, found 191.0516.

4.8.5. *cis*-3a-[(Trifluoroacetyl)amino]-1,2,3,3a,4,8b-hexahydro-7-nitrocyclopent[*b*]indole (7o). A yellow oil; IR ($CHCl_3$) 3439, 1725, 1518, 1330 cm^{-1}; ^1H NMR (300 MHz, $CDCl_3$) δ 1.68 (1H, m), 1.78–1.94 (2H, m), 2.18 and 2.32 (each 1H, m), 2.44 (1H, m), 3.68 (1H, dd, J=9, 2 Hz), 5.59 (1H, br s,), 6.49 (1H, d, J=8.5 Hz), 6.99 (1H, br s), 7.95 (1H, br s), 8.19 (1H, dd, J=8.5, 2 Hz); HRMS (EI, *m/z*) calcd for $C_{13}H_{12}F_3N_3O_3$ (M^+) 315.0830, found 315.0848.

4.8.6. 1,2,3,4-Tetrahydro-7-nitrocyclopent[*b*]indole (11o). A yellow oil; IR ($CHCl_3$) 3468, 1519, 1334 cm^{-1}; ^1H NMR (300 MHz, $CDCl_3$) δ 2.59 (2H, br quint, J=8 Hz), 2.88 (4H, t-like, J=8 Hz), 7.31 (1H, dd, J=8.5, 1 Hz), 8.05 (1H, dd, J=8.5, 2.5 Hz), 8.28 (1H, br s), 8.39 (1H, br d, J=2.5 Hz); HRMS (EI, *m/z*) calcd for $C_{11}H_{10}N_2O_2$ (M^+) 202.0742, found 202.0748.

4.9. Preparation of *N*-trifluoroacetyl enehydrazines 6p–s

According to the general procedure (B) given for the preparation of enehydrazine **6**, the condensation of corresponding hydrazines **15k–n** with cyclopentanone followed by acylation of the corresponding hydrazones gave **6p–s** in 36–99% yields.

4.9.1. Trifluoroacetic acid 1-(1-cyclopenten-1-yl)-2-(3-methoxyphenyl)hydrazide (6p). A yellow oil; IR ($CHCl_3$) 3355, 1721 cm^{-1}; ^1H NMR (300 MHz, $CDCl_3$) δ 1.89 (2H, br quint, J=7.5 Hz), 2.35 and 2.68 (each 2H, m), 3.77 (3H, s), 5.73 (1H, br s), 6.09 (1H, br s), 6.29 (1H, br s), 6.34 (1H, br d, J=8.5 Hz), 6.51 (1H, ddd, J=8.5, 2.5, 1 Hz), 7.17 (1H, t, J=8.5 Hz); HRMS (EI, *m/z*) calcd for $C_{14}H_{15}F_3N_2O_2$ (M^+) 300.1085, found 300.1079.

4.9.2. Trifluoroacetic acid 1-(1-cyclopenten-1-yl)-2-(3-methylphenyl)hydrazide (6q). A yellow oil; IR ($CHCl_3$) 3455, 1718 cm^{-1}; ^1H NMR (300 MHz, $CDCl_3$) δ 1.88 (2H, br quint, J=7.5 Hz), 2.31 (3H, s), 2.35 and 2.68 (each 2H, m), 5.70 (1H, br s), 6.02 (1H, br s), 6.52 (1H, br d, J=8 Hz), 6.56 (1H, br s), 6.78 (1H, br d, J=8 Hz), 7.16 (1H, br t, J=8 Hz); HRMS (EI, *m/z*) calcd for $C_{14}H_{15}F_3N_2O$ (M^+) 284.1135, found 284.1154.

4.9.3. Trifluoroacetic acid 2-(3-chlorophenyl)-1-(1-cyclopenten-1-yl)hydrazide (6r). A yellow oil; IR ($CHCl_3$) 3408, 1728 cm^{-1}; ^1H NMR (300 MHz, $CDCl_3$) δ 1.90 (2H, br quint, J=7.5 Hz), 2.36 and 2.69 (each 2H, m), 5.74 (1H, br s), 6.47 (1H, br s), 6.63 and 6.93 (each 1H, m), 6.76 (1H, br s), 7.19 (1H, br dd, J=8.5, 8 Hz); HRMS (EI, *m/z*) calcd for $C_{13}H_{12}^{35}ClF_3N_2O$ (M^+) 304.0590, found 304.0589.

4.9.4. Trifluoroacetic acid 1-(1-cyclopenten-1-yl)-2-(3-nitrophenyl)hydrazide (6s). A yellow oil; IR ($CHCl_3$) 3315, 1725, 1515, 1340 cm^{-1}; ^1H NMR (300 MHz, $CDCl_3$) δ 1.94 (2H, br quint, J=7.0 Hz), 2.37 and 2.72 (each 2H, m), 5.68 (1H, br s), 6.37 (1H, br s), 7.06 (1H, br dd, J=8, 2 Hz), 7.46 (1H, br t, J=8 Hz), 7.61 (1H, br s), 7.84 (1H, dd, J=8, 2 Hz); HRMS (EI, *m/z*) calcd for $C_{13}H_{12}F_3N_3O_3$ (M^+) 315.0830, found 315.0841.

4.10. Thermal reaction of *N*-trifluoroacetyl enehydrazines 6p–s

According to the general procedure given for the thermal reaction of **6**, enehydrazines **6p–s** were heated at the temperature shown in Table 8 to give indoline **7p–s**, **7′p–s** and indole **11p–s**, **11′p–s** in the yield shown in Table 8.

4.10.1. *cis*-3a-[(Trifluoroacetyl)amino]-1,2,3,3a,4,8b-hexahydro-8-methoxycyclopent[*b*]indole (7p). A yellow oil; IR ($CHCl_3$) 3425, 1721 cm^{-1}; ^1H NMR (300 MHz, $CDCl_3$) δ 1.67 (1H, m), 1.84 (2H, m), 2.14–2.35 (3H, m), 3.68 (1H, dd, $J=8$, 2 Hz), 3.81 (3H, s), 4.72 (1H, br s), 6.23 and 6.32 (each 1H, d, $J=8$ Hz), 6.76 (1H, br s), 7.05 (1H, t, $J=8$ Hz); HRMS (EI, *m/z*) calcd for $C_{14}H_{15}F_3N_2O_2$ (M^+) 300.1085, found 300.1073.

4.10.2. 1,2,3,4-Tetrahydro-8-methoxycyclopent[*b*]indole (11p). A yellow oil; IR ($CHCl_3$) 3479 cm^{-1}; ^1H NMR (300 MHz, $CDCl_3$) δ 2.51 (2H, m), 2.83 and 2.96 (each 2H, t-like, $J=7$ Hz), 3.90 (3H, s), 6.49 (1H, dd, $J=8$, 1 Hz), 6.92 (1H, dd, $J=8$, 1 Hz), 6.99 (1H, t, $J=8$ Hz), 7.81 (1H, br s); HRMS (EI, *m/z*) calcd for $C_{12}H_{13}NO$ (M^+) 187.0996, found 187.1001.

4.10.3. *cis*-3a-[(Trifluoroacetyl)amino]-1,2,3,3a,4,8b-hexahydro-6-methoxycyclopent[*b*]indole (7′p). A yellow oil; IR ($CHCl_3$) 3424, 1720 cm^{-1}; ^1H NMR (300 MHz, $CDCl_3$) δ 1.60–1.88 (3H, m), 2.15–2.46 (3H, m), 3.61 (1H, br d, $J=8$ Hz), 3.75 (3H, s), 5.72 (1H, br s), 6.15 (1H, d, $J=3$ Hz), 6.31 (1H, dd, $J=8$, 3 Hz), 6.78 (1H, br s), 6.94 (1H, d, $J=8$ Hz); HRMS (EI, *m/z*) calcd for $C_{14}H_{15}F_3N_2O_2$ (M^+) 300.1085, found 300.1094.

4.10.4. 1,2,3,4-Tetrahydro-6-methoxycyclopent[*b*]indole (11′p). A yellow oil; IR ($CHCl_3$) 3477 cm^{-1}; ^1H NMR (300 MHz, $CDCl_3$) δ 2.51 (2H, m), 2.80 (4H, br m), 3.82 (3H, s), 6.74 (1H, dd, $J=8.5$, 2.5 Hz), 6.83 (1H, d, $J=2.5$ Hz), 7.30 (1H, d, $J=8.5$ Hz), 7.70 (1H, br s); HRMS (EI, *m/z*) calcd for $C_{12}H_{13}NO$ (M^+) 187.0996, found 187.1011.

4.10.5. *cis*-3a-[(Trifluoroacetyl)amino]-1,2,3,3a,4,8b-hexahydro-8-methylcyclopent[*b*]indole (7q) and *cis*-3a-[(trifluoroacetyl)amino]-1,2,3,3a,4,8b-hexahydro-6-methylcyclopent[*b*]indole (7′q). The indolines **7q** and **7′q** are inseparable: a yellow oil; ^1H NMR (300 MHz, $CDCl_3$) δ 1.61–1.86 and 2.13–2.45 (6H, m), 2.23 and 2.27 (each 3/2H, s), 3.63 and 3.66 (each 1/2H, dd, $J=8$, 2 Hz), 4.63 and 4.66 (each 1/2H, br s), 6.41 (1/2H, br s), 6.43 (1/2H, br d, $J=8$ Hz), 6.59 (1H, br d, $J=8$ Hz), 6.94 (1/2H, br d, $J=8$ Hz), 6.99 (1/2H, t, $J=8$ Hz).

4.10.6. 1,2,3,4-Tetrahydro-8-methylcyclopent[*b*]indole (11q) and 1,2,3,4-tetrahydro-6-methylcyclopent[*b*]indole (11′q). The indoles **11q** and **11′q** are inseparable: a yellow oil; ^1H NMR (300 MHz, $CDCl_3$) δ 2.43 and 2.57 (each 3/2H, s), 2.82 (4H, m), 3.04 (2H, m), 6.82, 6.89 and 7.09 (each 1/2H, br d, $J=8$ Hz), 6.97 (1/2H, t, $J=7.5$ Hz), 7.10 (1/2H, br s), 7.32 (1/2H, br d, $J=8$ Hz).

4.10.7. *cis*-8-Chloro-3a-[(trifluoroacetyl)amino]-1,2,3,3a,4,8b-hexahydrocyclopent[*b*]indole (7r). A yellow oil; IR ($CHCl_3$) 3425, 1721 cm^{-1}; ^1H NMR (300 MHz, $CDCl_3$) δ 1.70 (1H, m), 1.82–1.88 (2H, m), 2.27–2.40 (3H, m), 3.72 (1H, dd, $J=10$, 2.5 Hz), 4.81 (1H, br s), 6.44 and 6.71 (each 1H, br d, $J=8$ Hz), 6.82 (1H, br s, NH), 7.00 (1H, t, $J=8$ Hz); HRMS (EI, *m/z*) calcd for $C_{13}H_{12}^{35}ClF_3N_2O$ (M^+) 304.0590, found 304.0569.

4.10.8. *cis*-6-Chloro-3a-[(trifluoroacetyl)amino]-1,2,3,3a,4,8b-hexahydrocyclopent[*b*]indole (7′r). A yellow oil; IR ($CHCl_3$) 3426, 1721 cm^{-1}; ^1H NMR (300 MHz, $CDCl_3$) δ 1.66 (1H, m), 1.71–1.89 (2H, m), 2.23–2.36 (3H, m), 3.62 (1H, br dd, $J=9.5$, 2 Hz), 4.78 (1H, br s), 6.53 (1H, d, $J=2$ Hz), 6.72 (1H, dd, $J=8$, 2 Hz), 6.78 (1H, br s, NH), 6.95 (1H, dd, $J=8$, 1 Hz); HRMS (EI, *m/z*) calcd for $C_{13}H_{12}^{35}ClF_3N_2O$ (M^+) 304.0590, found 304.0604.

4.10.9. 8-Chloro-1,2,3,4-tetrahydrocyclopent[*b*]indole (11r).[39] A yellow oil; IR ($CHCl_3$) 3686 cm^{-1}; ^1H NMR (300 MHz, $CDCl_3$) δ 2.53 (2H, br quint, $J=7$ Hz), 2.85 and 3.04 (each 2H, t-like, $J=7$ Hz), 6.96 (1H, t, $J=8$ Hz), 7.03 and 7.17 (each 1H, dd, $J=8$, 1 Hz), 7.92 (1H, br s); HRMS (EI, *m/z*) calcd for $C_{11}H_{10}^{35}ClN$ (M^+) 191.0501, found 191.0504.

4.10.10. *cis*-3a-[(Trifluoroacetyl)amino]-1,2,3,3a,4,8b-hexahydro-8-nitrocyclopent[*b*]indole (7s). A yellow oil; IR ($CHCl_3$) 3424, 1724, 1532, 1346 cm^{-1}; ^1H NMR (300 MHz, $CDCl_3$) δ 1.76–1.89 (3H, m), 2.22 (1H, ddd, $J=13.5$, 10, 7.5 Hz), 2.48 (2H, m),4.21 (1H, dd, $J=12$, 2 Hz), 5.30 (1H, br s), 6.80 and 7.55 (each 1H, dd, $J=8.5$, 1 Hz), 6.91 (1H, br s), 7.22 (1H, t, $J=8.5$ Hz); HRMS (EI, *m/z*) calcd for $C_{13}H_{12}F_3N_3O_3$ (M^+) 315.0830, found 315.0847.

4.10.11. *cis*-3a-[(Trifluoroacetyl)amino]-1,2,3,3a,4,8b-hexahydro-6-nitrocyclopent[*b*]indole (7′s). A yellow oil; IR ($CHCl_3$) 3426, 1724, 1527, 1339 cm^{-1}; ^1H NMR (300 MHz, $CDCl_3$) δ 1.65 (1H, m), 1.76–1.92 (2H, m), 2.30 (2H, m), 2.38 (1H, m), 3.74 (1H, dd, $J=9.5$, 2 Hz), 4.99 (1H, br s), 6.82 (1H, br s), 7.16 (1H, d, $J=8$ Hz), 7.32 (1H, d, $J=2$ Hz), 7.65 (1H, dd, $J=8$, 2 Hz); HRMS (EI, *m/z*) calcd for $C_{13}H_{12}F_3N_3O_3$ (M^+) 315.0830, found 315.0850.

4.10.12. 1,2,3,4-Tetrahydro-8-nitrocyclopent[*b*]indole (11s).[27] A yellow oil; IR ($CHCl_3$) 3471, 1514, 1327 cm^{-1}; ^1H NMR (300 MHz, $CDCl_3$) δ 2.53 (2H, quint, $J=7$ Hz), 2.94 and 3.22 (each 2H, t-like, $J=7$ Hz), 7.11 (1H, t, $J=8$ Hz), 7.55 and 8.02 (each 1H, dd, $J=8$, 1 Hz), 8.28 (1H, br s); HRMS (EI, *m/z*) calcd for $C_{11}H_{10}N_2O_2$ (M^+) 202.0742, found 202.0768.

4.10.13. 1,2,3,4-Tetrahydro-6-nitrocyclopent[*b*]indole (11′s).[27] A yellow oil; IR ($CHCl_3$) 3468, 1513, 1323 cm^{-1}; ^1H NMR (300 MHz, $CDCl_3$) δ 2.59 (2H, quint, $J=7$ Hz), 2.86 and 2.94 (each 2H, t-like, $J=7$ Hz), 7.43 (1H, d, $J=8.5$ Hz), 8.01 (1H, dd, $J=8.5$, 2 Hz), 8.26 (1H, d, $J=2$ Hz), 8.30 (1H, br s); HRMS (EI, *m/z*) calcd for $C_{11}H_{10}N_2O_2$ (M^+) 202.0742, found 202.0760.

4.11. Preparation of *N*-trifluoroacetyl enehydrazines 6t–x

According to the general procedure (B) given for the preparation of enehydrazine **6**, the condensation of

corresponding hydrazines **15o–r** with cyclopentanone or cyclohexanone followed by acylation of the corresponding hydrazones gave **6t–x** in 63–96% yields.

4.11.1. Trifluoroacetic acid 1-(1-cyclopenten-1-yl)-2-(2-methoxyphenyl)hydrazide (6t). A yellow oil; IR ($CHCl_3$) 3418, 1720 cm^{-1}; ^1H NMR (300 MHz, $CDCl_3$) δ 1.86 (2H, br quint, $J=7.5$ Hz), 2.32 and 2.64 (each 2H, m), 3.89 (3H, s), 5.67 (1H, br s), 6.65–6.94 (5H, m); HRMS (EI, *m/z*) calcd for $C_{14}H_{15}F_3N_2O_2$ (M^+) 300.1085, found 300.1101.

4.11.2. Trifluoroacetic acid 1-(1-cyclohexen-1-yl)-2-(2-methoxyphenyl)hydrazide (6u). A yellow oil; IR ($CHCl_3$) 3421, 1710 cm^{-1}; ^1H NMR (300 MHz, $CDCl_3$) δ 1.50–1.63 (4H, m), 2.07–2.17 (4H, m), 3.81 (3H, s), 5.88 (1H, br s), 6.78 (1H, br s), 6.77–6.92 (4H, m); HRMS (EI, *m/z*) calcd for $C_{15}H_{17}F_3N_2O_2$ (M^+) 314.1241, found 314.1252.

4.11.3. Trifluoroacetic acid 1-(1-cyclopenten-1-yl)-2-(2-methylphenyl)hydrazide (6v). A yellow oil; IR ($CHCl_3$) 3455, 1718 cm^{-1}; ^1H NMR (300 MHz, $CDCl_3$) δ 1.89 (2H, br quint, $J=7.5$ Hz), 2.35 and 2.67 (each 2H, m), 2.23 (3H, s), 5.68 (1H, br s), 5.96 (1H, br s), 6.65 (1H, br d, $J=8$ Hz), 6.89 (1H, td, $J=7.5$, 1 Hz), 7.10–7.17 (2H, m); HRMS (EI, *m/z*) calcd for $C_{14}H_{15}F_3N_2O$ (M^+) 284.1135, found 284.1154.

4.11.4. Trifluoroacetic acid 2-(2-chlorophenyl)-1-(1-cyclopenten-1-yl)hydrazide (6w). A yellow oil; IR ($CHCl_3$) 3402, 1719 cm^{-1}; ^1H NMR (300 MHz, $CDCl_3$) δ 1.89 (2H, br quint, $J=7.5$ Hz), 2.34 and 2.67 (each 2H, m), 5.68 (1H, br s), 6.71 (1H, br s), 6.75 (1H, br dd, $J=8$, 0.5 Hz), 6.91 (1H, ddd, $J=8$, 7.5, 1.5 Hz), 7.20 (1H, dddd, $J=8.5$, 8, 1.5, 0.5 Hz), 7.32 (1H, dd, $J=8$, 1.5 Hz); HRMS (EI, *m/z*) calcd for $C_{13}H_{12}^{35}ClF_3N_2O$ (M^+) 304.0590, found 304.0588.

4.11.5. Trifluoroacetic acid 1-(1-cyclopenten-1-yl)-2-(2-nitrophenyl)hydrazide (6x). A yellow oil; IR ($CHCl_3$) 3259, 1728, 1533, 1337 cm^{-1}; ^1H NMR (300 MHz, $CDCl_3$) δ 1.93 (2H, br quint, $J=7.5$ Hz), 2.39 and 2.71 (each 2H, m), 5.78 (1H, br s), 6.93 (1H, br d, $J=8.5$ Hz), 7.03 and 7.58 (each 1H, td, $J=8.5$, 1 Hz), 8.25 (1H, dd, $J=8.5$, 1 Hz), 9.24 (1H, br s); HRMS (EI, *m/z*) calcd for $C_{13}H_{12}F_3N_3O_3$ (M^+) 315.0830, found 315.0836.

4.12. Thermal reaction of *N*-trifluoroacetyl enehydrazines 6t–x

According to the general procedure given for the thermal reaction of **6**, enehydrazines **6t–x** were heated at the temperature shown in Table 9 to give indoline **7t–x**, indole **11t–x**, and dienylimine **17t–v** in the yield shown in Table 9.

4.12.1. *cis*-3a-[(Trifluoroacetyl)amino]-1,2,3,3a,4,8b-hexahydro-5-methoxycyclopent[*b*]indole (7t). A yellow oil; IR ($CHCl_3$) 3490, 1625 cm^{-1}; ^1H NMR (300 MHz, $CDCl_3$) δ 1.65 (1H, m), 1.83 (2H, m), 2.10 (1H, m), 2.33–2.53 (2H, m), 3.80 (1H, br d, $J=9.5$ Hz), 3.84 (3H, s), 4.48 (1H, br s), 6.69 (1H, br d, $J=8$ Hz), 6.72 (1H, br d, $J=8$ Hz), 6.79 (1H, br s), 6.80 (1H, t, $J=8$ Hz); HRMS (EI, *m/z*) calcd for $C_{14}H_{15}F_3N_2O_2$ (M^+) 300.1085, found 300.1086.

4.12.2. (3aα,8aα,8bα)-3a-[(Trifluoroacetyl)amino]-1,2,3,3a,8a,8b-hexahydro-8a-methoxycyclopent[*b*]-indole (*cis-syn*-17t). Colorless crystals, mp 140–141 °C (hexane); IR ($CHCl_3$) 1732 cm^{-1}; ^1H NMR (500 MHz, $CDCl_3$) δ 1.28–1.36 (2H, m), 1.75 (1H, m, 2-H), 1.90 (1H, m), 2.38 (1H, ddd, $J=17$, 9.5, 7.5 Hz), 2.47 (1H, m, 3-H), 2.82 (1H, dd, $J=10.5$, 5 Hz), 3.18 (3H, s), 6.12 (1H, dt, $J=9.5$, 1 Hz), 6.45 (1H, dt, $J=9.5$, 3.5 Hz), 6.53 (2H, dd, $J=3.5$, 1 Hz), 7.24 (1H, br s); NOE was observed between NH (δ 7.24) and 8a-OMe (δ 3.18), NH (δ 7.24) and 8b-H (δ 2.82), and 8a-OMe (δ 3.18) and 8b-H (δ 2.82) in NOESY spectroscopy. HRMS (EI, *m/z*) calcd for $C_{14}H_{15}F_3N_2O_2$ (M^+) 300.1085, found 300.1110. The crystal data of *cis-syn*-**17t** was shown in previous communication.[30]

4.12.3. (3aα,8aβ,8bα)-3a-[(Trifluoroacetyl)amino]-1,2,3,3a,8a,8b-hexahydro-8a-methoxycyclopent[*b*]indole (*cis-anti*-17t). Colorless crystals, mp 140–141 °C (hexane); IR ($CHCl_3$) 1731 cm^{-1}; ^1H NMR (500 MHz, $CDCl_3$) δ 1.94–2.21 (6H, m), 3.06 (1H, br dd, $J=9$, 2 Hz), 3.16 (3H, s), 6.03 (1H, dt, $J=9.5$, 1 Hz), 6.41 (1H, ddd, $J=9.5$, 5.5, 1 Hz), 6.52 (1H, ddd, $J=9.5$, 5.5, 1 Hz), 6.61 (1H, br dt, $J=9.5$, 1 Hz), 6.71 (1H, br s); NOE was observed between NH (δ 6.71) and 8b-H (δ 3.06) in NOESY spectroscopy. HRMS (EI, *m/z*) calcd for $C_{14}H_{15}F_3N_2O_2$ (M^+) 300.1085, found 300.1098.

4.12.4. 1,2,3,4-Tetrahydro-5-methoxycyclopent[*b*]indole (11t). A yellow oil; IR ($CHCl_3$) 3479 cm^{-1}; ^1H NMR (300 MHz, $CDCl_3$) δ 2.53 (2H, br quint, $J=7.5$ Hz), 2.83 (4H, t-like, $J=7.5$ Hz), 3.94 (3H, s), 6.60 (1H, br dd, $J=9$, 1 Hz), 7.12 (2H, m), 8.05 (1H, br s); HRMS (EI, *m/z*) calcd for $C_{12}H_{13}NO$ (M^+) 187.0996, found 187.0997.

4.12.5. 1,2,3,4-Tetrahydro-8-methoxy-9*H*-carbazole (11u).[28] A yellow oil; IR ($CHCl_3$) 3422 cm^{-1}; ^1H NMR (300 MHz, $CDCl_3$) δ 1.87 (4H, m), 2.70 (4H, m), 3.93 (3H, s), 6.59 (1H, dd, $J=8$, 1 Hz, 7-H), 6.98 (1H, t, $J=8$ Hz), 7.07 (1H, dd, $J=8$, 1 Hz), 7.92 (1H, br s); HRMS (EI, *m/z*) calcd for $C_{13}H_{15}NO$ (M^+) 201.1153, found 201.1160.

4.12.6. (4aα,4bα,9aα)-9a-[(Trifluoroacetyl)amino]-1,2,3,4,4a,9a-hexahydro-4b-methoxy-4b*H*-carbazole (*cis-syn*-17u). Colorless crystals, mp 139–140 °C (hexane/AcOEt); IR ($CHCl_3$) 1732 cm^{-1}; ^1H NMR (500 MHz, $CDCl_3$) δ 0.65 (1H, dtd, $J=13.5$, 12, 4 Hz), 1.12 (1H, qt, $J=13.5$, 3.5 Hz), 1.22–1.33 (1H, qt, $J=13.5$, 3.5 Hz), 1.57 (1H, m), 1.63–1.71 (2H, m), 2.16 (1H, td, $J=13.5$, 4.5 Hz), 2.63 (1H, dd, $J=12$, 7 Hz), 3.15 (1H, dtd, $J=13.5$, 3.5, 2 Hz), 3.17 (3H, s), 6.08 (1H, dt, $J=9.5$, 1 Hz), 6.43 (1H, ddd, $J=9.5$, 5.5, 1 Hz), 6.56 (1H, ddd, $J=9.5$, 5.5, 1 Hz), 6.63 (1H, br d, $J=9.5$ Hz), 7.41 (1H, br s); NOE was observed between NH (δ 7.41) and 4b-OMe (δ 3.17), and NH (δ 7.41) and 4a-H (δ 2.63) in NOESY spectroscopy. HRMS (EI, *m/z*) calcd for $C_{15}H_{17}F_3N_2O_2$ (M^+) 314.1241, found 314.1252.

4.12.7. (4aα,4bβ,9aα)-9a-[(Trifluoroacetyl)amino]-1,2,3,4,4a,9a-hexahydro-4b-methoxy-4b*H*-carbazole (*cis-anti*-17u). Colorless crystals, mp 138–140 °C (hexane/AcOEt); IR ($CHCl_3$) 1720 cm^{-1}; ^1H NMR (500 MHz,

$CDCl_3$) δ 1.44 (1H, qt, J=13.5, 3 Hz), 1.60 (1H, m), 1.65–1.87 (4H, m), 2.10 (1H, dm, J=13.5 Hz), 2.35 (1H, dm, J=13.5 Hz), 2.78 (1H, br dt, J=8, 1 Hz), 3.07 (3H, s), 6.11 (1H, dt, J=9.5, 1 Hz), 6.41 (1H, br s), 6.44 (1H, ddd, J=9.5, 5.5, 1 Hz), 6.54 (1H, ddd, J=9.5, 5.5, 1 Hz), 6.66 (1H, dt, J=9.5, 1 Hz); NOE was observed between NH (δ 6.41) and 4a-H (δ 2.78) in NOESY spectroscopy. HRMS (EI, *m/z*) calcd for $C_{15}H_{17}F_3N_2O_2$ (M^+) 314.1241, found 314.1260.

4.12.8. *cis*-3a-[(Trifluoroacetyl)amino]-1,2,3,3a,4,8b-hexahydro-5-methylcyclopent[*b*]indole (7v). A yellow oil; IR ($CHCl_3$) 3423, 1721 cm^{-1}; ^1H NMR (300 MHz, $CDCl_3$) δ 1.66 (1H, m), 1.74–1.89 (2H, m), 2.13 (3H, s), 2.18 (1H, m), 2.30–2.48 (2H, m), 3.72 (1H, dd, J=10, 1 Hz), 4.43 (1H, br s), 6.73 (1H, t, J=8 Hz), 6.78 (1H, br s), 6.90–6.94 (2H, m); HRMS (EI, *m/z*) calcd for $C_{14}H_{15}F_3N_2O$ (M^+) 284.1135, found 284.1142.

4.12.9. (3aα,8aα,8bα)-3a-[(Trifluoroacetyl)amino]-1,2,3,3a,8a,8b-hexahydro-8a-methylcyclopent[*b*]indole (*cis-syn*-17v). Colorless crystals, mp 139–140 °C (hexane/AcOEt); IR ($CHCl_3$) 1721 cm^{-1}; ^1H NMR (500 MHz, $CDCl_3$) δ 1.24 (3H, s), 1.29 (1H, m), 1.51 (1H, m), 1.78 (1H, m), 1.99 (1H, br ddd, J=13, 7, 4 Hz), 2.07 (1H, dtd, J=13, 9.5, 6.5 Hz), 2.42 (1H, ddd, J=13, 9.5, 7 Hz), 2.90 (1H, dd, J=9.5, 5 Hz), 6.06 (1H, ddd, J=9.5, 5.5, 1 Hz), 6.23 (1H, br d, J=9.5 Hz), 6.27 (1H, dt, J=9.5, 1 Hz), 6.51 (1H, ddd, J=9.5, 5.5, 1 Hz), 8.11 (1H, br s); NOE was observed between NH (δ 8.11) and 8a-Me (δ 1.24), NH (δ 8.11) and 8b-H (δ 2.90), and 8a-Me (δ 1.24) and 8b-H (δ 2.90) in NOESY spectroscopy. HRMS (EI, *m/z*) calcd for $C_{14}H_{15}F_3N_2O$ (M^+) 284.1135, found 284.1125. Anal. Calcd for $C_{14}H_{15}F_3N_2O$: C, 59.15; H, 5.32; N, 9.85, found: C, 59.03; H, 5.31; N, 9.85.

4.12.10. (3aα,8aβ,8bα)-3a-[(Trifluoroacetyl)amino]-1,2,3,3a,8a,8b-hexahydro-8a-methylcyclopent[*b*]indole (*cis-anti*-17v). Colorless crystals, mp 138–139 °C (hexane/AcOEt); IR ($CHCl_3$) 1724 cm^{-1}; ^1H NMR (500 MHz, $CDCl_3$) δ 1.18 (3H, s), 1.78 (1H, br dquint, J=13, 8 Hz), 1.89 (1H, m), 1.97 (1H, ddd, J=13, 8, 5.5 Hz), 2.05 (1H, m), 2.21–2.29 (2H, m), 3.04 (1H, br dd, J=9, 2 Hz), 5.99 (1H, ddd, J=9.5, 5.5, 1 Hz), 6.26 (1H, dt, J=9.5, 1 Hz), 6.41 (1H, br dt, J=9.5, 1 Hz), 6.48 (1H, ddd, J=9.5, 5.5, 1.5 Hz), 6.73 (1H, br s); NOE was observed between NH (δ 6.73) and 8b-H (δ 3.04) in NOESY spectroscopy. HRMS (EI, *m/z*) calcd for $C_{14}H_{15}F_3N_2O$ (M^+) 284.1135, found 284.1151. Anal. Calcd for $C_{14}H_{15}F_3N_2O$: C, 59.15; H, 5.32; N, 9.85, found: C, 59.13; H, 5.31; N, 9.83.

4.12.11. 1,2,3,4-Tetrahydro-5-methylcyclopent[*b*]indole (11v).[29] A yellow oil; IR ($CHCl_3$) 3480 cm^{-1}; ^1H NMR (300 MHz, $CDCl_3$) δ 2.46 (3H, s, Me), 2.55 (2H, br quint, J=7.5 Hz), 2.79–2.90 (4H, t-like, J=7.5 Hz), 6.90 (1H, br d, J=8 Hz), 7.00 (1H, t, J=8 Hz), 7.29 (1H, br d, J=8 Hz), 7.66 (1H, br s); HRMS (EI, *m/z*) calcd for $C_{12}H_{13}N$ (M^+) 171.1048, found 171.1069.

4.12.12. *cis*-5-Chloro-3a-[(trifluoroacetyl)amino]-1,2,3,3a,4,8b-hexahydrocyclopent[*b*]indole (7w). A yellow oil; IR ($CHCl_3$) 3424, 1720 cm^{-1}; ^1H NMR (300 MHz, $CDCl_3$) δ 1.64 (1H, m), 1.73–1.90 (2H, m), 2.22 (1H, m), 2.29–2.43 (2H, m), 3.80 (1H, dd, J=8, 1 Hz), 4.83 (1H, br s), 6.70 (1H, t, J=8 Hz), 6.88 (1H, br s), 6.94 and 7.06 (each 1H, br d, J=8 Hz); HRMS (EI, *m/z*) calcd for $C_{13}H_{12}^{35}ClF_3N_2O$ (M^+) 304.0590, found 304.0571.

4.12.13. *cis*-3a-[(Trifluoroacetyl)amino]-1,2,3,3a,4,8b-hexahydro-5-nitrocyclopent[*b*]indole (7x). A yellow oil; IR ($CHCl_3$) 3436, 1729, 1518, 1331 cm^{-1}; ^1H NMR (300 MHz, $CDCl_3$) δ 1.65 (1H, m), 1.81–1.91 (2H, m), 2.24–2.44 (3H, m), 3.83 (1H, br d, J=9.5 Hz), 6.72 (1H, t, J=8 Hz), 6.86 (1H, br s), 7.16 (1H, br s), 7.25 and 7.87 (each 1H, br d, J=8 Hz); HRMS (EI, *m/z*) calcd for $C_{13}H_{12}F_3N_3O_3$ (M^+) 315.0830, found 315.0842.

4.12.14. 1,2,3,4-Tetrahydrocyclopent[*b*]indole (11e) (conversion of dienylimines *cis-syn*-17t and *cis-anti*-17t into indole 11e). A solution of *cis-syn*-**17t** (27 mg, 0.09 mmol) in xylene (5 mL) was heated at 140 °C for 23 h. After the reaction mixture was concentrated under the reduced pressure, purification of the residue by MCC (*n*-hexane/ethyl acetate 2:1) gave the indole **11e**[31] (9.9 mg, 70%). Similarly, *cis-anti*-**17t** (27 mg, 0.09 mmol) was converted into indole **11e**[31] (5.9 mg, 42%) as a yellow oil, IR ($CHCl_3$) 3477 (NH) cm^{-1}; ^1H NMR (300 MHz, $CDCl_3$) δ 2.52 (2H, br quint, J=8 Hz), 2.84 (4H, t-like, J=8 Hz), 7.07 (2H, m), 7.28 and 7.42 (1H, m,), 7.76 (1H, br s); HRMS (EI, *m/z*) calcd for $C_{11}H_{11}N$ (M^+) 157.0891, found 157.0891.

4.13. Condensation of hydrazine 15o followed by acylation

According to the general procedure (B) given for the preparation of enehydrazine **6**, the condensation of corresponding hydrazine **15o** (2.76 g, 20 mmol) with 2-butanone (1.79 mL, 20 mmol) followed by acylation of the corresponding hydrazone gave **6y** (1.29 g, 23%) and *C*-acylated product **18** (3.44 g, 62%).

4.13.1. Trifluoroacetic acid (*Z*)-2-(2-methoxyphenyl)-1-(1-ethyl-1-propenyl)hydrazide (6y). A yellow oil; IR ($CHCl_3$) 3357, 1720 cm^{-1}; ^1H NMR (500 MHz, $CDCl_3$) δ 1.07 (3H, t, J=7.5 Hz), 2.32 (2H, br q, J=7.5 Hz), 3.89 (3H, s), 5.09 (2H, br d, J=15 Hz), 6.68 (1H, br s), 6.77–6.95 (4H, m); HRMS (EI, *m/z*) calcd for $C_{13}H_{15}F_3N_2O_2$ (M^+) 288.1087, found 288.1079.

4.13.2. 1,1,1-Trifluoro-2,4-hexanedione 4-(2-methoxyphenyl)hydrazone (18). A yellow oil; IR ($CHCl_3$) 3372, 1711 cm^{-1}; ^1H NMR (200 MHz, $CDCl_3$) δ 1.15 (3H, t, J=7.5 Hz), 2.04 (2H, br s), 2.41 (2H, br q, J=7.5 Hz), 3.85 (3H, s), 6.95–7.02 (2H, m), 7.29–7.42 (2H, m); HRMS (EI, *m/z*) calcd for $C_{13}H_{15}F_3N_2O_2$ (M^+) 288.1085, found 288.1079.

4.14. Thermal reaction of *N*-trifluoroacetyl enehydrazine 6y

According to the general procedure given for the thermal reaction of **6**, the enehydrazine **6y** (51.2 mg, 0.18 mmol) was heated at 80 °C in MeCN. After the reaction mixture was concentrated under reduced pressure, the residue was purified by MCC (hexane/AcOEt 10:1) to give the

dienylimine **17y** (13.7 mg, 27%) and indole **11y**[36] (21.2 mg, 68%).

4.14.1. *cis*-2-Ethyl-2-[(trifluoroacetyl)amino]-2,3-dihydro-3a-methoxy-3a*H*-indole (17y). Colorless crystals, mp 117–118 °C (hexane/Et_2O); IR ($CHCl_3$) 3416, 1725 cm^{-1}; ^1H NMR (500 MHz, $CDCl_3$) δ 1.06 (3H, t, J=7.5 Hz), 1.98 (1H, dq, J=15, 7.5 Hz), 2.23 and 2.86 (each 1H, AB q, J=13.5 Hz), 2.47 (1H, dq, J=15, 7.5 Hz), 3.14 (3H, s), 6.19 (1H, br d, J=9.5 Hz), 6.41 (1H, br ddd, J=9.5, 5.5, 1 Hz), 6.57 (1H, br ddd, J=9.5, 5.5, 1 Hz), 6.61 (1H, br d, J=9.5 Hz), 6.96 (1H, br s); ^{13}C NMR (125 MHz, $CDCl_3$) δ 9.0, 32.5, 49.9, 51.9, 82.3, 88.1, 115.6 (q, CF_3), 123.1, 126.5, 132.2, 134.5, 155.6 (q, $COCF_3$), 174.9; HRMS (EI, *m*/*z*) calcd for $C_{13}H_{15}F_3N_2O_2$ (M^+) 288.1084, found 288.1091. Anal. Calcd for $C_{13}H_{15}F_3N_2O_2$: C, 54.17; H, 5.24; N, 9.72, found: C, 54.37; H, 5.33; N, 9.68; NOE was observed between 3a-OMe (δ 3.14) and NH (δ 6.96) in NOESY spectroscopy.

4.14.2. 2-Ethyl-7-methoxyindole (11y). Colorless oil; IR ($CHCl_3$) 3372 cm^{-1}; ^1H NMR (200 MHz, $CDCl_3$) δ 1.32 (3H, t, J=7.5 Hz), 2.76 (2H, q, J=7.5 Hz), 3.94 (3H, s), 6.21 (1H, br s), 6.58 (1H, br d, J=8 Hz), 6.97 (1H, br t, J=8 Hz), 7.14 (1H, br d, J=8 Hz), 8.11 (1H, br s); HRMS (EI, *m*/*z*) calcd for $C_{11}H_{13}NO$ (M^+) 175.0997, found 175.0984.

4.15. Thermal reaction of *N*-trifluoroacetyl enehydrazines 6a,l,o,t,x in water

A suspended solution of enehydrazines **6a**,**l**,**o**,**t**,**x** (0.18–0.25 mmol) in H_2O (10–15 mL) was heated under the conditions shown in Table 10. The reaction mixture was extracted with $CHCl_3$ and the organic phase was washed with H_2O, dried over Na_2SO_4, and concentrated under the reduced pressure. Purification of the residue by MCC (hexane/AcOEt 20:1–5:1) afforded the indoline **7**, indole **11**, dienylimine **17** in the yield shown in Table 10.

4.16. Thermal reaction of *N*-trifluoroacetyl enehydrazines 6a,l,o,t,x under solvent-free conditions

The enehydrazines **6a**,**l**,**o**,**t**,**x** (0.18–0.25 mmol) was heated directly under the conditions shown in Table 10. Purification of the residue by MCC (hexane/AcOEt 20:1–5:1) afforded the indoline **7**, indole **11**, dienylimine **17** in the yield shown in Table 10.

Acknowledgements

We acknowledge Grants-in Aid for Scientific Research (B) (T.N.) and Scientific Research (C) (O.M.) from Japan Society for the Promotion of Science. Our thanks are also directed to the Science Research Promotion Fund of the Japan Private School Promotion Foundation for a research grant.

References and notes

1. Reviews of indole synthesis: (a) Gribble, G. W. *Contemp. Org. Synth.* **1994**, 145. (b) Moody, C. J. *Synlett* **1994**, 681. (c) Gilchrist, T. L. *J. Chem. Soc., Perkin Trans. 1* **1999**, 2848. (d) Gribble, G. W. *J. Chem. Soc., Perkin Trans. 1* **2000**, 1045.
2. Reviews of Fischer indole synthesis: (a) Robinson, B. *Chem. Rev.* **1963**, *63*, 373. (b) Robinson, B. *Chem. Rev.* **1969**, *69*, 227. (c) Robinson, B. *The Fischer Indole Synthesis*; Wiley: New York, 1982. (d) Hughes, D. L. *Org. Prep. Proced. Int.* **1993**, *25*, 609.
3. Kelly, A. H.; McLeod, D. H.; Parrick, J. *J. Chem. Soc.* **1965**, 296.
4. Kidwai, M. M.; AhLuwalia, V. K. *Indian J. Chem.* **1988**, *27B*, 962.
5. Miller, F. M.; Schinske, W. N. *J. Org. Chem.* **1978**, *43*, 3384.
6. Hughes, D. L.; Zhao, D. *J. Org. Chem.* **1993**, *58*, 228.
7. Zhao, D.; Hughes, D. L.; Bender, D. R.; DeMarco, A. M.; Reider, P. J. *J. Org. Chem.* **1991**, *56*, 3001.
8. Maruoka, K.; Oishi, M.; Yamamoto, H. *J. Org. Chem.* **1993**, *58*, 7638.
9. Although the Fischer indolization of *N*-acetyl enehydrazine has previously been reported, it required either an elevated temperature (170 °C) or an acid catalysis (dichloroacetic acid) to achieve successful cyclization. Schiess, P.; Sendi, E. *Helv. Chim. Acta* **1978**, *61*, 1364.
10. (a) Miyata, O.; Kimura, Y.; Muroya, K.; Hiramatsu, H.; Naito, T. *Tetrahedron Lett.* **1999**, *40*, 3601. (b) Miyata, O.; Kimura, Y.; Naito, T. *Chem. Commun.* **1999**, 2429.
11. (a) Miyata, O.; Kimura, Y.; Naito, T. *Synthesis* **2001**, 1635. (b) Miyata, O.; Takeda, N.; Naito, T. *Heterocycles* **2002**, *57*, 1101.
12. Goerdeler, J.; Bischoff, M. *Chem. Ber.* **1972**, *105*, 3566.
13. (a) Okimoto, M.; Takahashi, Y.; Kakuchi, T. *Synthesis* **2003**, 2057. (b) Liljebris, C.; Martinsson, J.; Tedenborg, L.; Williams, M.; Barker, E.; Duffy, J. E. S.; Nygren, A.; James, S. *Bioorg. Med. Chem.* **2002**, *10*, 3197. (c) Duncan, D. C.; Trumbo, T. A.; Almquist, C. D.; Lentz, T. A.; Beam, C. F. *J. Heterocycl. Chem.* **1987**, *24*, 555.
14. Odera, T.; Sato, M. Patent JP 2000169446, 2000; *Chem. Abstr.* **2000**, *133*, 17376.
15. Sharma, S. D.; Pandhi, S. B. *J. Org. Chem.* **1990**, *55*, 2196.
16. Moran, R. J.; Cramer, C.; Falvey, D. E. *J. Org. Chem.* **1997**, *62*, 2742.
17. Torizuka, K. Patent JP 2001175012; *Chem. Abstr.* **2001**, *135*, 68523.
18. Southwick, P. L.; McGrew, B.; Engel, R. R.; Milliman, G. E.; Owellen, R. J. *J. Org. Chem.* **1963**, *28*, 3058.
19. Eberle, M. K.; Brzechffa, L. *J. Org. Chem.* **1976**, *41*, 3775.
20. Bast, K.; Durst, T.; Huisgen, R.; Lindner, K.; Temme, R. *Tetrahedron* **1998**, *54*, 3745.
21. Rodriguez, J. G.; San Andres, A. *J. Heterocycl. Chem.* **1991**, *28*, 1293.
22. Iwama, T.; Birman, V. B.; Kozmin, S. A.; Rawal, V. H. *Org. Lett.* **1999**, *1*, 673.
23. Ney, J. E.; Wolfe, J. P. *J. Am. Chem. Soc.* **2005**, *127*, 8644.
24. Sharma, S. D.; Pandhi, S. B. *J. Org. Chem.* **1990**, *55*, 2196.
25. Antilla, J. C.; Klapars, A.; Suchwald, S. L. *J. Am. Chem. Soc.* **2002**, *124*, 11684.
26. (a) Zhang, G.-S.; Chai, B. *Synth. Commun.* **2000**, *30*, 1849. (b) Linstead, R. P. *J. Chem. Soc.* **1929**, 2493.
27. Moskalev, N.; Barbasiewicz, M.; Makosza, M. *Tetrahedron* **2004**, *60*, 347.
28. Caubere, C.; Caubere, P.; Ianelli, S.; Nardelli, M.; Jamart-Gregoire, B. *Tetrahedron* **1994**, *50*, 11903.
29. Dobbs, A. P.; Voyle, M.; Whittall, N. *Synlett* **1999**, 1594.
30. The crystal data and figure of *cis*-*syn*-**17t** were shown in a previous communication.[10b]

31. (a) Lachance, N.; Chan, W. Y. *J. Heterocycl. Chem.* **2003**, *40*, 289. (b) Robinson, B. *J. Heterocycl. Chem.* **1987**, *24*, 1321.
32. Ishii, H. *Acc. Chem. Res.* **1981**, *14*, 275.
33. Murakami, Y.; Yokoo, H.; Yokoyama, Y.; Watanabe, T. *Chem. Pharm. Bull.* **1999**, *47*, 791.
34. Bajwa, G. S.; Brown, R. K. *Can. J. Chem.* **1969**, *47*, 785.
35. Bajwa, G. S.; Brown, R. K. *Can. J. Chem.* **1970**, *48*, 2293.
36. Chen, B.-C.; Hynes, J., Jr.; Pandit, C. R.; Zhao, R.; Skoumbourdis, A. P.; Wu, H.; Sundeen, J. E.; Leftheris, K. *Heterocycles* **2001**, *55*, 951.
37. Garner, P. P.; Parker, D. T.; Gajewski, J. J.; Lubineau, A.; Ange, J.; Queneau, Y.; Beletskaya, I. P.; Cheprakov, A.; Fringuelli, F.; Piermatti, O.; Pizzo, F.; Kobayashi, S. In *Organic Synthesis in Water*; Grieco, P. A., Ed.; Blackie Academic and Professional: London, 1998.
38. (a) Massey, J. P.; Plant, S. G. P. *J. Chem. Soc.* **1931**, 1990. (b) Lachance, N.; Chan, W. Y. *J. Heterocycl. Chem.* **2003**, *40*, 289.
39. Bently, J. M.; Roffey, J. R. A.; Davidson, J. E. P.; Mansell, H. L.; Hamlyn, R. J.; Cliffe, I. A.; Adams, D. R.; Monck, N. J. Patent WO 2001012603, 2001; *Chem. Abstr.* **2001**, *134*, 193339.