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Synthesis of γ-Butyrolactams by Photoinduced PhSe Group Transfer Radical Cyclization and Formal Synthesis of (±)-Isocynometrine with Diphenyldiselenide as Promoter

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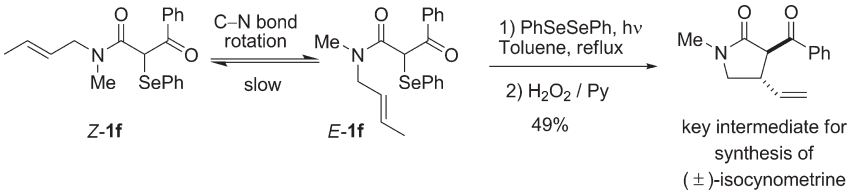
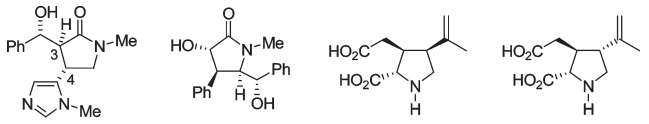


We have developed a strategy for constructing nitrogen heterocycles by photoinduced PhSe group transfer radical cyclization. *trans*-α,β-Disubstituted γ-butyrolactams (2-pyrrolidinones) were prepared in good yields (38−73%) with high regioselectivity and stereoselectivity from *N*-alkenyl α-PhSe β-keto amides. Reaction outcomes were modulated by the steric effect of the substituents on the nitrogen atom of the cyclization precursors and the stereoelectronic effect of the substrates. Diphenyldiselenide, as an additive, was found to promote ring closure. The advantage of this strategy in natural product synthesis is demonstrated by a formal synthesis of (±)-isocynometrine.

Introduction

γ-Butyrolactams (2-pyrrolidinones) are a class of versatile core structures found in many natural products (such as isocynometrine[1] and Clausenamide[2]) with interesting biological activities. They are also excellent precursors for the synthesis of biologically active pyrrolidine derivatives such as (+)-α-allokainic acid and its analogue (−)-α-kainic acid.[3] Therefore, they have stimulated great interest in the development of new ways of synthesizing pyrrolidinone skeletons with diverse structural features.[4]



Since the pioneering work of Curran, atom/group transfer radical cyclization has become an important method for synthesizing cyclic skeletons.[5] Previously, we reported Lewis acid-catalyzed atom/group transfer radical cyclization reactions of unsaturated α-bromo/phenylseleno β-keto esters[6] and amides[7,8] to yield five-membered-ring carbocycles with two substituents *trans* to each other. High enantiomeric excesses have been achieved by using chiral $Mg(ClO_4)_2$/bis(oxazoline) complexes as catalysts (up to 94% ee for unsaturated α-bromo β-keto esters,[6b] and up to 97% ee for α-PhSe β-keto esters[6c]). Here we report the PhSe group transfer radical cyclization of *N*-alkenyl α-PhSe β-keto amides and its application in the formal synthesis of (±)-isocynometrine.

Results and Discussion

PhSe Group Transfer Radical Cyclization of *N*-Alkenyl α-PhSe β-Keto Amides. In our previous work, stereoselective

(1) For the discovery of isocynometrine, see: (a) Khuong-Huu, F.; Monseur, X.; Ratle, G.; Lukacs, G.; Goutarel, R. *Tetrahedron Lett.* **1973**, *14*, 1757. For the structure determination of isocynometrine, see: (b) Chiaroni, A.; Riche, C.; Tchissambou, L.; Khuong-Huu, F. *J. Chem. Res., Synop.* **1981**, 182.

(2) Clausenamide was isolated from an aqueous extract of leaves of Chinese folk medicine *Clausena lansium* and exhibits potent hepatoprotective and antiamnesiac effects. For the discovery and characterization of Clausenamide, see: (a) Yang, M.-H.; Cao, Y.-H; Li, W.-X. *Yaoxue Xuebao* **1987**, *22*, 33. For examples of bioactivities, see: (b) Xu, L; Liu, S.-L; Zhang, J.-T. *Chirality* **2005**, *17*, 239. (c) Yu, L.; Liu, G. *Zhongguo Yaoxue Zazhi* **2000**, *35*, 446. (d) Liu, Y.; Shi, C. Z.; Zhang, J. T. *Yaoxue Xuebao* **1991**, *26*, 166.

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SCHEME 1

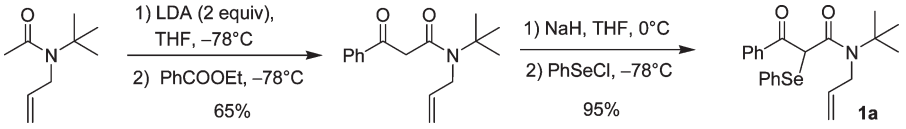
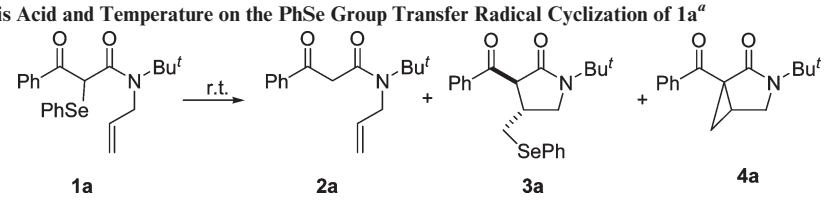


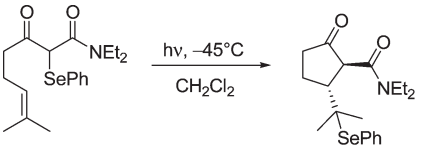
TABLE 1. Effects of Lewis Acid and Temperature on the PhSe Group Transfer Radical Cyclization of 1a[a]



					yield[b] (%)		
entry	$Yb(OTf)_3$ (equiv)	condition	solvent	time (h)	**2a**	**3a**	**4a**
1[c]	1	*hν*	Et_2O	3.5	40	21	11
2		*hν*	Et_2O	3.5		75	
3		*hν*	THF	6	10	81	
4	1		THF	55	28		44

[a]Unless otherwise indicated, all reactions were carried out with 0.4−0.5 mmol of substrate in 10 mL of solvent. [b]Isolated yield. [c]10% substrate recovered.

PhSe group transfer radical cyclization of *C*-alkenyl α-PhSe *β*-keto amides was achieved in 80% yield with 0.6 equiv of $Yb(OTf)_3$ as catalyst under photolysis condition at −45 °C in CH_2Cl_2 (eq 1).[8] We expected that the addition of $Yb(OTf)_3$ might be useful in the PhSe group transfer radical cyclization of *N*-alkenyl α-PhSe *β*-keto amides. Therefore, after the condensation of *N*-allyl-*N*-*tert*-butylacetamide with ethyl benzoate,[9] followed by the introduction of a phenylseleno group at the α-carbon (Scheme 1), *N*-alkenyl α-PhSe *β*-keto amide **1a** was prepared and subjected to photolysis condition. The results are summarized in Table 1.



Substrate **1a** is stable at room temperature without radical initiator. The reaction of **1a** in Et_2O was first irradiated with UV light at room temperature in the presence of 1 equiv of $Yb(OTf)_3$. After 3.5 h, 10% of the substrate was recovered, and reduced product **2a** (40%), cyclization product **3a** (21%), and cyclopropanation product **4a** (11%) were obtained (Table 1, entry 1). In contrast, in the control reaction without the addition of Lewis acid, **3a** was obtained in 75% yield (entry 2). When the solvent was changed to THF, the yield of **3a** was improved to 81% over an extended reaction time along with the formation of reduced product **2a** (10%; entry 3).[10] These results indicated that Lewis acid $Yb(OTf)_3$ had no positive effect on the cyclization of **1a** to yield **3a**. In contrast, when the reaction was carried out in the presence of 1 equiv of $Yb(OTf)_3$ without UV light irradiation, **4a** was obtained in 44% yield with the concomitant formation of reduced product **2a** (28%), and no compound **3a** was obtained (entry 4). Since there is no radical initiation, **4a** is believed to be formed by a Lewis acid-promoted ionic cyclization[11] followed by an intramolecular S_N2 substitution reaction to form the

(3) Parsons, A. F. *Tetrahedron* **1996**, *52*, 4149 and references cited therein.

(4) For selected examples of the synthesis of *γ*-butyrolactams and pyrrolidines, see: (a) Lei, A.; Waldkirch, J. P.; He, M.; Zhang, X. *Angew. Chem., Int. Ed.* **2002**, *41*, 4526. (b) Jahn, U.; Müller, M.; Aussieker, S. *J. Am. Chem. Soc.* **2000**, *122*, 5212. (c) Trost, B. M.; Pinkerton, A. B.; Kremzow, D. *J. Am. Chem. Soc.* **2000**, *122*, 12007. (d) Duncan, D.; Livinghouse, T. *J. Org. Chem.* **2001**, *66*, 5237. (e) Marino, J. P.; Zou, N. *Org. Lett.* **2005**, *7*, 1915. (f) Iwamoto, K.; Kojima, M.; Chatani, N.; Murai, S. *J. Org. Chem.* **2001**, *66*, 169. (g) Nagashima, H.; Isono, Y.; Iwamatsu, S.-I. *J. Org. Chem.* **2001**, *66*, 315. (h) Yoon, C. H.; Flanigan, D. L.; Chong, B.-D.; Jung, K. W. *J. Org. Chem.* **2002**, *67*, 6582. (i) Schobert, R.; Bieser, A.; Mullen, G.; Gordon, G. *Tetrahedron Lett.* **2005**, *46*, 5459. (j) Paderes, M. C.; Chemler, S. R. *Org. Lett.* **2009**, *11*, 1915. (k) Portela-Cubillo, F.; Scott, J. S.; Walton, J. C. *J. Org. Chem.* **2008**, *73*, 5558. (l) Clark, A. J.; Wilson, P. *Tetrahedron Lett.* **2008**, *49*, 4848. (m) Jiang, C.; Frontier, A. J. *Org. Lett.* **2007**, *9*, 4939. (n) Young, I. S.; Williams, J. L.; Kerr, M. A. *Org. Lett.* **2005**, *7*, 953.

(5) For reviews, see: (a) Jasperse, C. P.; Curran, D. P.; Fevig, T. L. *Chem. Rev.* **1991**, *91*, 1237. (b) Curran, D. P. *Synthesis* **1988**, 489. (c) Byers, J. In *Radicals in Organic Synthesis*; Renaud, P., Sibi, M. P., Eds.; Wiley-VCH: Weinheim, Germany; 2001; Vol. 1, Chapter 1.5. (d) Curran, D. P. In *Comprehensive Organic Synthesis*; Trost, B. M., Flemming, I., Eds.; Pergamon: Oxford, UK, 1991; Vol. 4, Chapter 4.2. (e) Majumdar, K. C.; Basu, P. K.; Mukhopadhyay, P. P. *Tetrahedron* **2005**, *61*, 10603.

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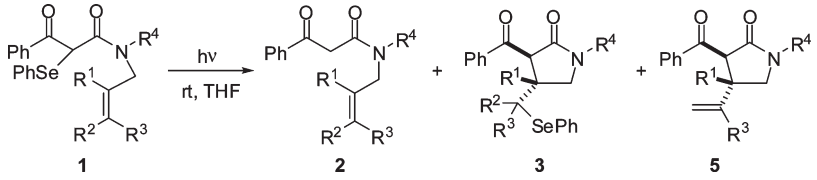
(8) Yang, D.; Gao, Q.; Lee, O.-Y. *Org. Lett.* **2002**, *4*, 1239.

(9) Christoffers, J.; Werner, T.; Unger, S.; Frey, W. *Eur. J. Org. Chem.* **2003**, 425.

(10) Here **2a** may come from the abstraction of hydrogen atom from the solvent. See: (a) Chung, S. K. *J. Org. Chem.* **1980**, *45*, 3513. (b) Ashby, E. C.; Welder, C. O. *Tetrahedron Lett.* **1995**, *36*, 7171.

(11) Jackson, W. P.; Ley, S. V.; Morton, J. A. *Tetrahedron Lett.* **1981**, *22*, 2601.

TABLE 2. PhSe Group Transfer Radical Cyclization of *N*-Alkenyl α-PhSe *β*-Keto Amides[a]



							yield (%)[b]		
entry	substrate	R^1	R^2	R^3	R^4	time (h)	**2**	**3**	**5**
1	**1a**	H	H	H	*t*-Bu	6	10	81	
2	**1b**	H	CH_3	H	*t*-Bu	6	20	65	8
3	**1c**	H	CH_3	CH_3	*t*-Bu	6	31	41	27
4	**1d**	CH_3	H	H	*t*-Bu	7	31	64 (1.8:1)[c]	
5[d]	**1e**	H	CH_3	H	Bn	6	30	45[e]	
6	**1f**	H	CH_3	H	Me	20	46	16[e]	
7[f]	**1f**	H	CH_3	H	Me	36	48	37[e]	

[a]Unless otherwise indicated, all reactions were carried out at room temperature with 0.4−0.5 mmol of substrate in 10 mL of THF. [b]Isolated yield. [c]Ratio of *trans*:*cis* isomers. Stereochemistry was determined by NOESY experiment. [d]11% substrate recovered. [e]Diastereomer ratio could not be determined because of signal overlap in ^{1}H NMR. [f]Reacted at the THF refluxing temperature.

cyclopropyl ring.[6] These results clearly indicated that **3a** was produced via radical cyclization induced by UV light, whereas Lewis acid $Yb(OTf)_3$ made the cyclization reaction complicated.

The 3,4-*trans* relationship of products **3a** was determined by NOESY experiments (Figure 1). The methylene group of CH_2SePh has strong NOE with both H_a and H_d, but no NOE with H_c, which suggested that the CH_2SePh group, H_a, and H_d are on one face of the pyrrolidine ring, while the benzoyl group, H_b, and H_c are on the other face. Thus the *trans* relationship of the substituents benzoyl group and CH_2SePh group is ascertained. The weak NOE observed between H_a and H_b is accorded with the above stereochemistry assignment.

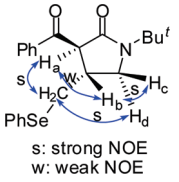


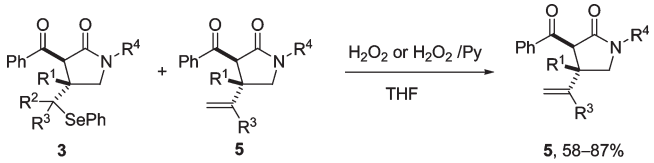
FIGURE 1. NOE correlations of compound **3a**.

To explore the substrate scope, several *N*-alkenyl α-PhSe *β*-keto amides (**1b**−**f**) were prepared as cyclization precursors following the synthetic strategy of **1a**[12] and subjected to the optimized radical cyclization conditions (Table 2). *trans*-*γ*-Butyrolactam products (**3a**−**c**, **3e**, **3f**, **5b**, and **5c**) were obtained from **1a**−**c** and **1e**−**f** (entries 1−3 and 5−7) through 5-*exo* cyclization mode. A mixture of *trans*-**3d** and *cis*-**3d** with a ratio of 1.8:1 was produced from substrate **1d** (entry 4). Cyclization yield in the range of 68−81% was achieved for *N*-*tert*-butyl α-PhSe *β*-keto amides **1a**−**d** (entries 1−4), as compared to 45% for benzyl-substituted substrate **1e** (entry 5). Only 16% yield was attained for the methyl-substituted substrate **1f** (entry 6), but the yield can be increased to 37% when the reaction temperature was raised to that of refluxing THF (entry 7).

(12) For details, see the Supporting Information.

To determine the structures and stereochemistries of cyclized products **3b**, **3c**, **3e**, and **3f** with three stereogenic centers, oxidative elimination of the PhSe group by hydrogen peroxide was performed (Scheme 2).[13] Only one regioisomer of the elimination product with a *γ*-lactam structure was observed in the ^{1}H NMR spectrum of each reaction mixture. The 3,4-*trans* relationship of products **5b**, **5c**, **5e**, and **5f** was assigned by the coupling constants (J = 6−8 Hz) of the α-protons according to the literature reports.[6] The stereochemistries of **3d**, **5b**, and **5e** were further confirmed by NOESY experiments, and that of **5f** was further confirmed by comparing with the literature report.[14]

SCHEME 2

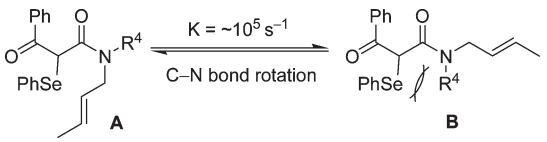


b R^1 = H, R^2 = CH_3, R^3 = H, R^4 = *t*-Bu **c** R^1 = H, R^2 = R^3 = CH_3, R^4 = *t*-Bu
e R^1 = H, R^2 = CH_3, R^3 = H, R^4 = Bn **f** R^1 = H, R^2 = CH_3, R^3 = H, R^4 = Me

The above results reveal that the substituents on the nitrogen atom of the tertiary amides and reaction temperature significantly affect the reaction results.[15a] Tertiary amides generally have two rotamers around the C−N bonds. Among the three substrates **1b** (R^4 = *t*-Bu), **1e** (R^4 = Bn), and **1f** (R^4 = Me), which differ only in the substituent on the amide nitrogen atom, only one rotamer was detected for substrate **1b**, whereas two rotamers were observed with a ratio of about 5:3 for substrate **1e** and a 1:1 ratio for substrate **1f** (determined by ^{1}H NMR). This was possibly caused by the moderate rate for the rotation of the amide C−N bond (about 10^5 s^{-1} at 20 °C)[15] and the steric effect of the

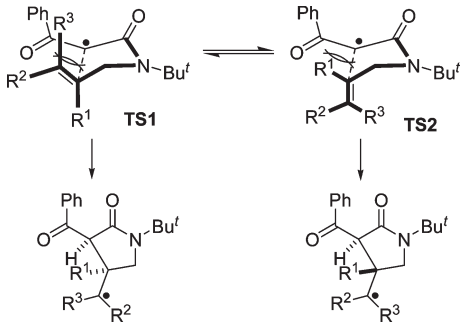
(13) Beach, J. W.; Kim, H. O.; Jeong, L. S.; Nampalli, S.; Islam, Q.; Ahn, S. K.; Babu, R.; Chu, C. K. *J. Org. Chem.* **1992**, *57*, 3887.
(14) Xie, X.; Lu, X.; Liu, Y.; Xu, W. *J. Org. Chem.* **2001**, *66*, 6545.
(15) (a) Curran, D. P.; Tamine, J. *J. Org. Chem.* **1991**, *56*, 2746. (b) Musa, O. M.; Horner, J. H.; Newcomb, M. *J. Org. Chem.* **1999**, *64*, 1022.

SCHEME 3



substituents on the amide group. As shown in Scheme 3, both rotamers **A** and **B** are in equilibrium for **1e** and **1f**. In the case of **1b**, rotamer **A** is strongly favored over **B** due to the large size of the *tert*-butyl group. While the radical intermediate generated from rotamer **A** can cyclize to give product **3**, the radical intermediate generated from rotamer **B** cannot cyclize directly. As a result, substrate **1b** gave the highest yield of the desired product (**3b**) (Table 2, cf. entry 2 versus entries 5 and 6). However, raising the reaction temperature will accelerate the rotation of the amide bond and disturb the equilibrium between rotamers **A** and **B**, thus consequently increase the cyclization yield (Table 2, cf. entry 7 versus entry 6).

SCHEME 4. Proposed Transition States for Radical Cyclization



The outcome of regio- and stereocontrol is rationalized in Scheme 4. Because of dipole repulsion, the two carbonyl groups of the substrates prefer to be *trans* to each other. Two possible transition states (TS1 and TS2) are involved in this reaction. The steric interaction between the benzoyl group and the olefinic group will decrease the stability of TS1, whereas that between the R^1 substituent and the benzoyl group disfavors TS2. The reactions of substrates **3a**−**c** (where R^1 = H) preferentially proceed through TS2 because of less steric repulsion,[16−18] and give *trans*-disubstituted 5-*exo* ring closure products. For **1d**, where R^1 = Me, the similar size of the methyl group and the methylene group yielded two diastereomers with a ratio of 1.8:1 through TS2 and TS1, respectively (Table 2, entry 4).

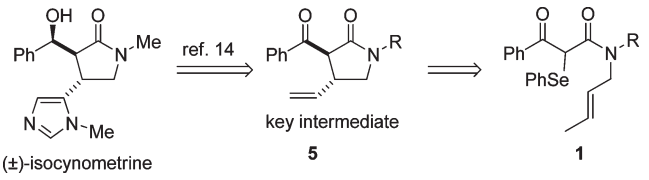


FIGURE 2. Retro-synthetic analysis for (±)-isocynometrine.

Synthesis of the Key Intermediate for (±)-Isocynometrine. Isocynometrine is an imidazole alkaloid isolated from the *Cynometra* species, which has been used in Africa as a traditional folk medicine with antitussive and analgesic activities. Several total syntheses of this alkaloid have been reported.[14,19] In the retro-synthetic analysis, the cyclized products **5b**, **5e**, and **5f** are possible intermediates (Figure 2). As suggested by the above results, the cyclization of *tert*-butyl protected amides **1b** gave the highest yield, but unexpectedly, the *tert*-butyl group of **3b** or **5b** could not be removed under acidic condition.[20] Thus we decided to optimize the reaction conditions to improve the yield for the radical cyclization of *N*-methyl α-phenylseleno *β*-keto amide **5f**.

It is known that diphenyldiselenide can be used as an accelerant in many radical pathways.[21] Homolytic cleavage of the Se−Se bond of diphenyldiselenide under UV or visible light irradiation is a common method to produce phenylseleno radical (PhSe$^\bullet$), which can initiate radical chain reaction or be involved in radical propagation steps to accelerate the reaction process. Kinetic study of phenylseleno radical addition reaction to vinyl monomers indicated that the addition reaction is reversible. In addition, the recombination of PhSe$^\bullet$ radical is faster (rate constant 7×10^9 M^{-1} s^{-1}) than radical addition of PhSe$^\bullet$ to a C=C double bond (rate constants in the range of 1.4×10^4 to 2.9×10^6 M^{-1} s^{-1}).[22] Thus we supposed that a high concentration of diphenyldiselenide may build up a persistent phenylseleno radical concentration to benefit both the initiation of α-centered radical and the subsequent radical cylization step.

As shown in Table 2, the yield of cyclized product **3f** can be improved by raising the reaction temperature to that of the reflux THF and moderately extending the reaction time (Table 2, cf. entry 7 versus entry 6). Further raising the reaction temperature to that of refluxing toluene did accelerate the reaction but gave no improvement to the cyclization yield of **3f** (38% in 12 h; Table 3, entry 1). However, in the presence of 4 equiv of diphenyldiselenide, the total yield of cyclized products **3f** and **5f** was increased to 53% along with

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(18) For examples of controlled radical cyclization, see: (a) Belvisi, L.; Gennari, C.; Poli, G.; Scolastico, C.; Salom, B. *Tetrahedron: Asymmetry* **1993**, *4*, 273. (b) Myers, A. G.; Condroski, K. R. *J. Am. Chem. Soc.* **1995**, *117*, 3057. (c) Takahashi, T.; Tomida, S.; Sakamoto, Y.; Yamada, H. *J. Org. Chem.* **1997**, *62*, 1912.

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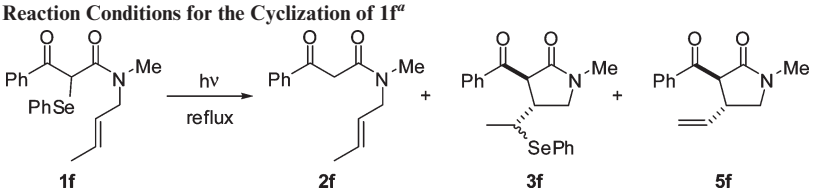
(22) Ito, O. *J. Am. Chem. Soc.* **1983**, *105*, 850.

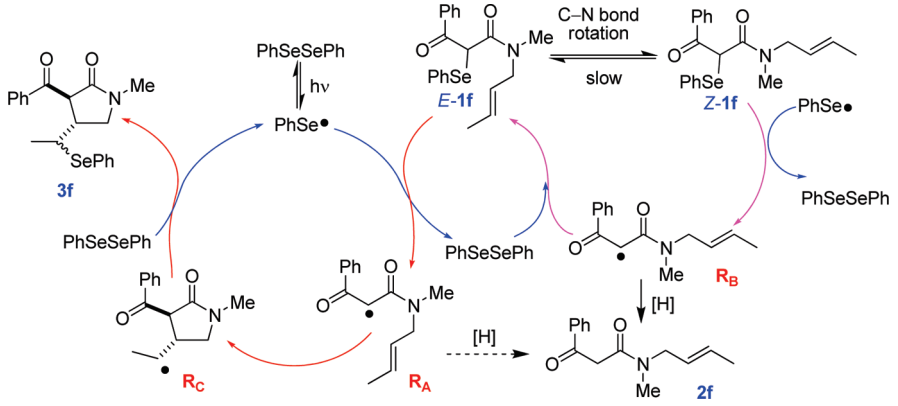
TABLE 3. Optimization of Reaction Conditions for the Cyclization of 1f[a]



					yield (%)[b]		
entry	solvent	temp (°C)	PhSeSePh (equiv)	time (h)	**2f**	**3f**	**5f**
1	toluene	110		12	40[c]	38[c]	<1%
2	THF	66	4	6	13	44	9
3	toluene	110	4	6	44[c]	53[c]	<1%
4	xylene	143	4	6	51	47	<1%
5[d]	toluene	110	4	6	33	66	<1%

[a]Unless otherwise indicated, all reactions were carried out with 0.5 mmol of substrate in 10 mL of solvent. [b]Yield determined by ^{1}H NMR. [c]Isolated yield. [d]0.5 mmol of substrate in 1 mL of solvent.

SCHEME 5. Plausible Mechanism of Radical Cyclization Promoted by PhSeSePh



13% yield of reduced product **2f** after refluxing in THF for 6 h (entry 2). Under refluxing condition in toluene, a similar yield of the cyclized product **3f** (53%) was obtained (entry 3). Upon increasing the reaction temperature to that of refluxing xylene, the yield was slightly decreased (47%, entry 4). On the basis of these results, we concluded that excessively high reaction temperatures are ineffective for improving the yield of cyclization. On the other hand, more reduced product **2f** was obtained from the reaction in toluene (44%) than that in THF (13%; cf. entry 3 versus entry 2). Upon increasing the concentration of the reaction mixture by a factor of 10, the yield of cyclized product **3f** was increased to 66% (entry 5).

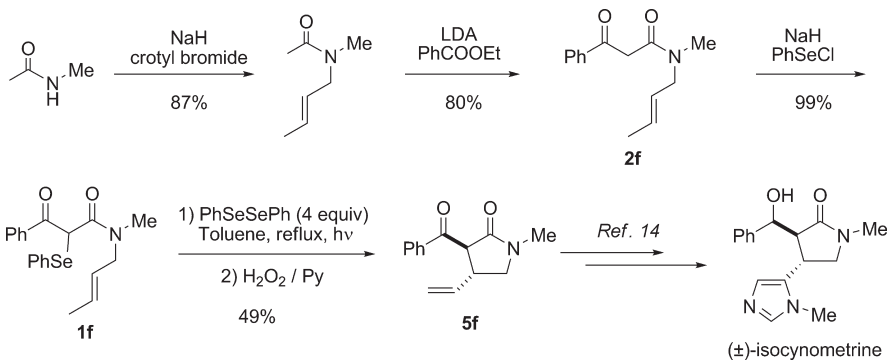
A plausible mechanism of the radical cyclization reactions is shown in Scheme 5. Under UV irradiation, diphenyldiselenide is homolytically cleaved into phenylseleno radicals. Then the radical intermediates **A** and **B** ($\mathbf{R_A}$ and $\mathbf{R_B}$) are generated from conformers ***E*-1f** and ***Z*-1f**, respectively. Radical **A** ($\mathbf{R_A}$) can cyclize smoothly whereas $\mathbf{R_B}$ cannot. In the presence of diphenyldiselenide, $\mathbf{R_B}$ can transform and regenerate substrate **1f**. But under the radical reaction condition, both $\mathbf{R_A}$ and $\mathbf{R_B}$ can abstract the hydrogen atom from the solvent to produce reduced product **2f**.[10] The better hydrogen donor the solvent is (for example, toluene over THF), the more reduced product **2f** is formed (Table 3, cf. entry 3 versus entry 2). On the other hand, diphenyldiselenide also plays the role of a radical trap to the cyclized radical $\mathbf{R_C}$ to give the product **3f** and regenerate PhSe$^\bullet$, which promotes the chain propagation of radical ring closure.

We then applied this method to the formal synthesis of the key intermediate of (±)-isocynometrine (Scheme 6). The key intermediate **5f** was prepared from *N*-methylacetamide in 40% yield in 5 steps. The key step was the PhSe group transfer radical cyclization promoted by PhSeSePh. A mixture of **3f** and the oxidative elimination product **5f** was obtained; after oxidative elimination of the mixture by H_2O_2/pyridine, the key intermediate of (±)-isocynometrine was generated.

Conclusion

In summary, *trans*-α,*β*-disubstituted *γ*-butyrolactams have been efficiently constructed through a PhSe group transfer radical cyclization reaction, which is characterized by high stereoselectivity and moderate to good yields. The size of the substituent on the nitrogen atom (R^4 group) of tertiary amides is positively correlated with the yield of this reaction, presumably because of the steric effect on substrates' conformation. The key intermediate for the total synthesis of nature product (±)-isocynometrine was obtained in 40% overall yield from *N*-methylacetamide. The key step is a photoinduced PhSe group transfer radical cyclization promoted by diphenyldiselenide.

SCHEME 6. Preparation of the Key Intermediate of (±)-Isocynometrine



Experimental Section

A 320 nm, 125W high-pressure mercury lamp was used as the UV source. The reactions were carried out in Pyrex glass flasks.

Typical Procedure for Diphenyldiselenide-Promoted PhSe Group-Transfer Radical Cyclization Reaction. *trans*-3-Benzoyl-1-methyl-4-(1-(phenylseleno)ethyl)pyrrolidin-2-one (3f). Compound **1f** (294 mg, 0.76 mmol) and PhSeSePh (948 mg, 3.04 mmol) were dissolved in toluene (1.8 mL). The solution was degassed with N_2 for 30 min, warmed up to reflux, and irradiated with a 125 W high-pressure mercury lamp for 6 h. The reaction was monitored by TLC. After concentration and filtration through a short plug of silica gel, **3f** was obtained in 66% yield (determined by ^{1}H NMR). The crude product was further purified by flash column chromatography to give a mixture of **3f** and **5f** as a light yellow oil. **3f** (diastereoisomer ratio = 3:2): Analytical TLC (silica gel 60), EtOAc:*n*-hexane = 1:2, R_f = 0.45; ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.09 (d, J = 6.8 Hz, 0.4 × 2H), 8.01 (d, J = 6.8 Hz, 0.6 × 2H), 7.65−7.24 (m, 8H), 4.49−4.48 (m, 1H), 3.65−3.60 (m, 1H), 3.38−3.27 (m, 3H), 2.87 (s, 0.6 × 3H), 2.84 (s, 0.4 × 3H), 1.40−1.38 (m, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 196.1, 196.0, 169.4, 169.2, 136.7, 136.6, 135.1(2), 133.6, 133.5, 129.7, 129.6, 129.4, 129.3, 128.6, 128.2(2), 128.1(2), 55.8, 55.3, 52.3, 51.8, 43.5, 43.2, 40.9, 40.8, 30.0, 20.6, 19.9; IR (neat) 2922, 1696, 1676 cm^{-1}; LRMS for $C_{20}H_{21}NO_2Se$ (EI, 20 eV) m/z 387 (M^+, 3), 105 (100); HRMS (EI) for $C_{20}H_{21}NO_2Se$ (M^+): calcd 387.0738, found 387.0735.

Typical Procedure for Oxidative Elimination of the PhSe Group. *trans*-3-Benzoyl-1-methyl-4-vinylpyrrolidin-2-one (5f).[14] To the mixture of **3f** and **5f** (66 mg, 0.18 mmol) in THF (5 mL) was added a drop of pyridine. Hydrogen peroxide (30% solution, 40 μL, 0.36 mmol) was then added dropwise to the above mixture at 0 °C. After stirring overnight, the reaction mixture was concentrated on a rotavap to remove the solvent. The residue was dissolved in dichloromethane, washed with saturated $NaHCO_3$ solution, water, brine and then dried over anhydrous $MgSO_4$. The crude product was purified by flash chromatography to give **5f** (34 mg, 49% yield in two steps) as a light yellow oil. Analytical TLC (silica gel 60), EtOAc:*n*-hexane = 1:2, R_f = 0.36; ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.09 (d, J = 7.8 Hz, 2H), 7.59 (t, J = 7.8 Hz, 1H), 7.49 (t, J = 7.8 Hz, 2H), 5.86 (ddd, J = 17.4, 11.2, 2.3 Hz, 1H), 5.15 (d, J = 17.0 Hz, 1H), 5.10 (d, J = 11.2 Hz, 1H), 4.30 (d, J = 6.4 Hz, 1H), 3.71 (t, J = 8.2 Hz, 1H), 3.69−3.61 (m, 1H), 3.23 (dd, J = 8.2, 6.0 Hz, 1H), 2.89 (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 195.5, 169.6, 137.6, 136.6, 133.7, 129.6, 128.6, 116.9, 56.6, 53.2, 39.3, 30.1.

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Supporting Information Available: Synthetic schemes, characterization data, and NMR spectra of compounds **1a**−**f**, **2a**−**f**, **3a**−**f**, **4a**, **5b**, **5c**, **5e**, and **5f**. This material is available free of charge via the Internet at http://pubs.acs.org.