SYNTHESIS OF DIHYDROPYRROLES AND TETRAHYDROPYRIDINES BY THE CYCLIZATION OF *O*-METHYLSULFONYLOXIMES HAVING AN ACTIVE METHINE GROUP

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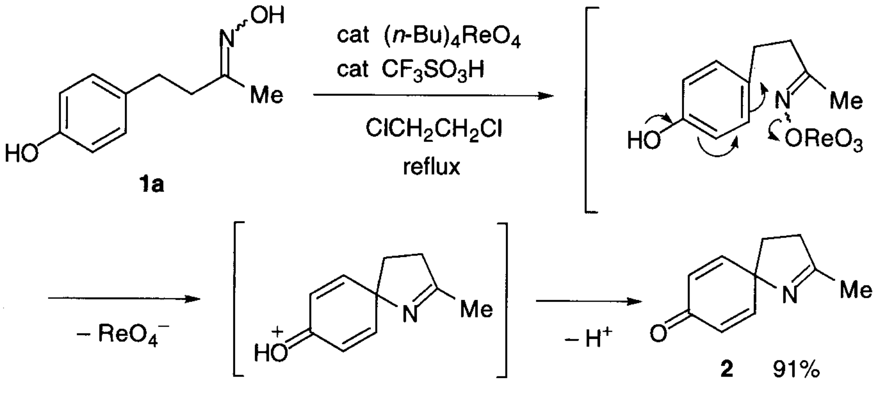
Abstract —— 3,4-Dihydro-2*H*-pyrroles and 2,3,4,5-tetrahydropyridines are prepared by treatment of (*E*)-*O*-methylsulfonyloximes having an active methine group at γ- or δ-position with 1,8-diazabicyclo[5.4.0]undec-7-ene *via* SN2-type substitution on sp^2 nitrogen atom of the oxime derivatives.

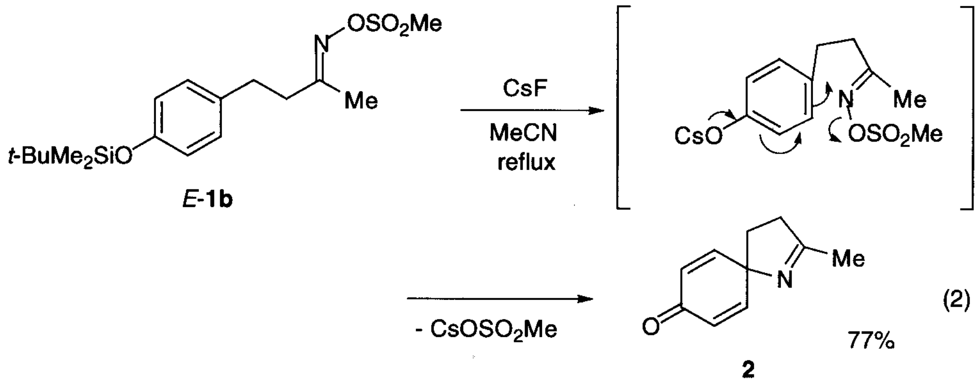
A wide variety of amino compounds are prepared by nucleophilic amination of carbon electrophiles, whereas electrophilic amination of carbon nucleophiles has not been generally employed as synthetic method.[1] We have found some electrophilic amination reactions by using oximes and their derivatives. For example, quinolines and azaspirotrienones are obtained by treating phenethyl ketone oximes with a catalytic amount of tetrabutylammonium perrhenate ($(n\text{-Bu})_4NReO_4$) and trifluoromethanesulfonic acid (CF_3SO_3H).[2a-c] *Ab initio* MP2 calculations revealed that such a cyclization of *O*-protonated 2-(4-hydroxyphenyl)ethyl ketone oxime (**1a**) to 1-azaspirotrienone (**2**) can proceed *via* SN2-type reaction on sp^2 nitrogen atom with a comparable activation energy to that of the Beckmann rearrangement.[2d]



(1)

Dedicated to Professor Teruaki Mukaiyama on the occasion of his 73rd birthday.

A similar cyclization also proceeds by employing *O*-methylsulfonyloxime as described in Eq. 2. That is, (*E*)-4-(4-*tert*-butyldimethylsiloxyphenyl)butan-2-one *O*-methylsulfonyloxime (*E*-**1b**) was converted to a spiro compound (**2**) by treating with cesium fluoride, whereas the *Z*-isomer did not give **2**.



(2)

Beckmann rearrangement and Neber reaction have been well known as typical reactions of oximes and their derivatives,[3] but there have been few examples of the substitution-type reaction with carbon nucleophiles on oxime nitrogen.[4,5] Accordingly we have investigated to develop similar substitution reactions of oxime derivatives, and have reported the cyclization reaction of (*E*)-*O*-methylsulfonyloximes having an active methine group at γ-position to 3,4-dihydro-2*H*-pyrroles.[6] This report describes a full account of this cyclization by SN2-type reaction on the *sp*^{2} nitrogen atom.

Result and Discussion

First, methyl (*E*)-2-methoxycarbonyl-5-methylsulfonyloxyimino-3-phenylhexanoate (*E*-**3a**) was chosen as a model compound to study the cyclization between the active methine group and the nitrogen atom. As listed in Table 1, when *E*-**3a** was treated with 1,8-diazabicyclo[5.4.0]undec-7-ene (DBU), 2,2-dimethoxycarbonyl-5-methyl-3-phenyl-3,4-dihydro-2*H*-pyrrole (**4a**) was obtained quantitatively, but the reaction with NaH, triethylamine, 4-dimethylaminopyridine (DMAP), or 1,4-diazabicyclo[2.2.2]octane (DABCO) gave **4a** in poorer yield.

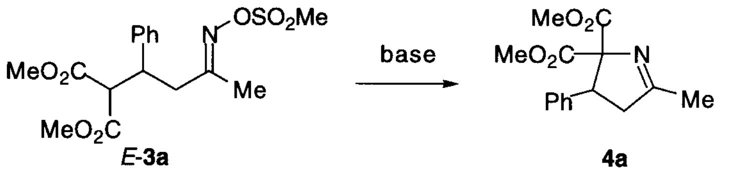
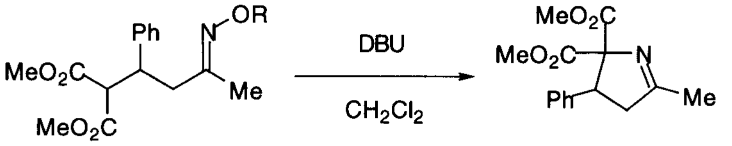


Table 1. The effect of base

Base	Solvent	Temp / °C	Time / h	Yield / %
NaH	THF	50	5	complex mixture
Et_3N	$ClCH_2CH_2Cl$	reflux	4	38
DMAP	$ClCH_2CH_2Cl$	50	13	69
DABCO	$ClCH_2CH_2Cl$	50	2.5	42
DBU	CH_2Cl_2	0	0.25	99

In contrast, the reaction of the corresponding *Z*-isomer of **3a** at 0 °C did not afford the cyclized product (**4a**), and the starting material was recovered. The prolonged reaction (3 h) at room temperature afforded several products including a Neber reaction product without forming **4a**. This stereospecificity of the cyclization is another evidence of SN2-type substitution on the nitrogen atom of oxime derivatives.[3c,5] In various solvents, such as dichloromethane, dichloroethane, acetonitrile, toluene, and THF, the cyclic imine formation proceeded smoothly and **4a** is obtained quantitatively.

The cyclization of *O*-acetyl and *O*-trifluoroacetyloximes was also attempted (Eq. 4). The cyclization of (*E*)-*O*-acetyloxime (*E*-**5**) did not proceed. (*E*)-*O*-Trifluoroacetyloxime (*E*-**6**) cyclized at 0 °C but much slower than (*E*)-*O*-methylsulfonyloximes did, yielding **4a** in 57% after 1.5 h. From these results, conversion of oxime hydroxyl group to a good leaving group like methylsulfonyloxy group is indispensable to promote the substitution smoothly.



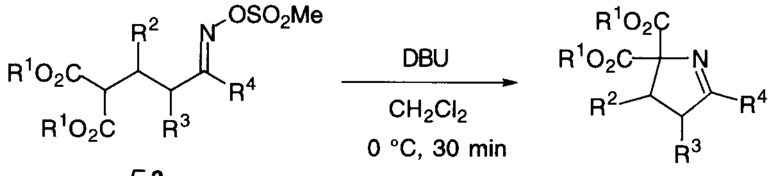
(4)

4a

R=Ac *E*-**5**
R=COCF$_3$ *E*-**6**

no reaction
57%

Various dihydro-2*H*-pyrrole derivatives (**4**) were prepared from (*E*)-*O*-methylsulfonyloximes (*E*-**3**), and the results are listed in Table 2. In all cases, the reaction was completed within 30 min to provide dihydro-2*H*-pyrrole derivatives (**4**) in high yield, and neither Beckmann rearrangement nor Neber reaction product was obtained. Oximes having substituent at *β*-position are converted to 3,4-dihydro-3-substituted 2*H*-pyrroles[4,7b] in good yield (Entries 1-3). Though it has been known that the Beckmann rearrangement readily proceeds in the reaction of *α*-substituted phenethyl ketone oxime,[2a,2c] 4-substituted dihydro-2*H*-pyrrole derivative (**4d**) was yielded from the α-substituted oxime (*E*-**3d**) in 87% yield without the Beckmann rearrangement (Entry 4). The oxime (*E*-**3e**) having no substituent on the ethylene tether (R^2 = R^3 = H) was cyclized to **4e** in 87% yield (Entry 5). *O*-Methylsulfonyloxime (*E*-**3f**) of *α*-keto ester also cyclized smoothly to 5-methoxycarbonyl-2*H*-pyrrole derivative (**4f**) (Entry 6).



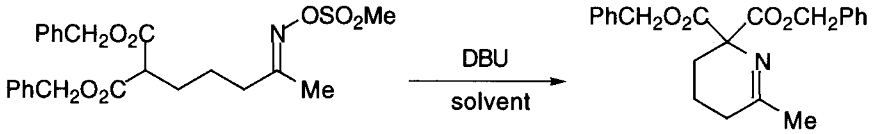
E-**3**

4

Table 2. Cyclization of *E*-**3**

Entry	R^1	R^2	R^3	R^4		Yield / %	
1	Me	Ph	H	Me	(**3a**)	99	(**4a**)
2	PhCH$_2$	*i*-Pr	H	Me	(**3b**)	96	(**4b**)
3	PhCH$_2$	*n*-C$_5$H$_{11}$	H	Me	(**3c**)	83	(**4c**)
4	PhCH$_2$	H	Me	Me	(**3d**)	87	(**4d**)
5	PhCH$_2$	H	H	Me	(**3e**)	87	(**4e**)
6	Me	Ph	H	CO$_2$Me	(**3f**)	83	(**4f**)

In addition to the synthesis of pyrrole derivatives (**4**), the present method was also applied to prepare tetrahydropyridine derivative from *O*-methylsulfonyloxime (*E*-**7**) of 6-oxoheptanoate. A marked solvent effect was observed in this cyclization. As shown in Table 3, the reaction in polar solvents such as DMF and acetonitrile gave the desired tetrahydropyridine (**8**) in good yield.



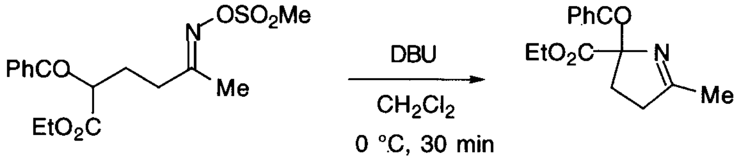
E-**7** **8**

Table 3. Cyclization of *O*-methylsulfonyloxime (*E*-**7**)

Entry	Solvent	Temp / °C	Time / h	Yield / %
1	CH_2Cl_2	reflux	9	31[a)]
2	THF	reflux	9	31[a)]
3	MeCN	rt	27	72[a)]
4	DMF	rt	24	70[a)]
5	DMF	rt	120	83[b)]

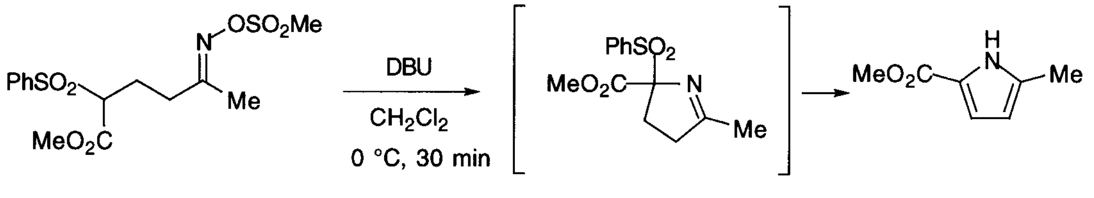
a) 3 Molar amounts of DBU were used.
b) 1.5 Molar amounts of DBU were used.

Other active methine groups can be utilized as nucleophilic groups. That is, *E*-**9** having a *β*-keto ester moiety could be transformed to a cyclic imine (**10**) in 80% yield (Eq. 5). *O*-Methylsulfonyloxime (*E*-**11**) which has α-sulfonyl ester moiety gave 2,5-disubstituted pyrrole (**12**), by the elimination of the sulfonyl group from initially formed cyclic imine (Eq. 6).



(5)

E-**9** **10** 80 %

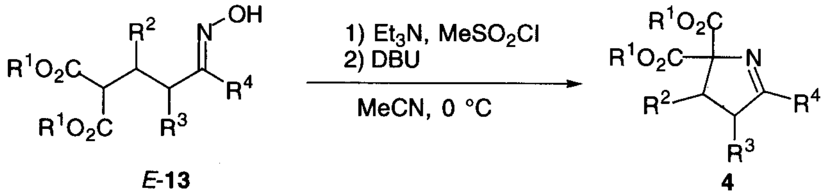


(6)

E-**11** **12** 48 %

In the above reaction, dihydro-2*H*-pyrroles were synthesized from oximes in two-step procedure, preparation of *O*-methylsulfonyloximes from *E*-oximes and the successive cyclization. Though *O*-methylsulfonyloximes (*E*-**3**) are readily prepared from the corresponding oximes in 80-90% yield with methanesulfonyl chloride, they are generally labile and decompose gradually. Therefore, one-pot synthesis of dihydro-2*H*-pyrroles from oximes was examined without the isolation of *O*-methylsulfonyloximes. (*E*)-Oximes (*E*-**13**) were treated with triethylamine and methanesulfonyl chloride in acetonitrile and then with

2.2-3.0 molar amounts of DBU, and dihydro-2*H*-pyrroles (**4**) were resulted in good yield as shown in Table 4. In all cases, the yield of one-pot synthesis is equal or higher than the total yield of two-step procedure *via* the isolation of *O*-methylsulfonyloximes.

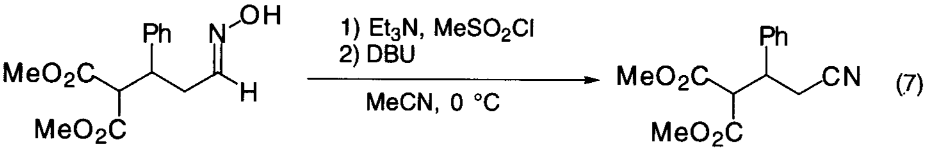


E-**13** **4**

Table 4. One-pot synthesis of **4**

Entry	R^1	R^2	R^3	R^4		Yield / %
1	$PhCH_2$	*i*-Pr	H	Me	(**13b**)	79 (**4b**)
2	$PhCH_2$	H	Me	Me	(**13d**)	79 (**4d**)
3	$PhCH_2$	H	H	Me	(**13e**)	96 (**4e**)
4	Me	Ph	H	CO_2Me	(**13f**)	80 (**4f**)

Even by this one-pot procedure, aldoxime (*E*-**13g**) could not be employed for the cyclic imine formation, but nitrile (**14**) was obtained as a result of Beckmann fragmentation (Eq. 7).



(*E*)-**13g** **14**

Summary

Pyrrole derivatives are generally prepared by Knorr method,[8] Hantzsch method,[9] Beckmann rearrangement,[10] and the condensation of conjugated enones with aminomalonate.[11] As mentioned above, a new preparative method is thus developed by the SN2-type substitution on the sp^2 nitrogen atom of the oxime derivatives.

EXPERIMENTAL

General All melting points are uncorrected. ^1H NMR (500 MHz) and ^{13}C NMR (125 MHz) spectra were recorded on Bruker AM500, Bruker DRX500, and JEOL A500 spectrometers with $CHCl_3$ (δ=7.24 and 77.0) as an internal standard. IR spectra were measured with a Horiba FT-300S spectrophotometer. High resolution mass (HRMS) spectra were recorded on a JEOL JMS-SX102A mass spectrometer operating at 70 eV. Elemental analyses were carried out at the Elemental Analysis Laboratory, Department of Chemistry, Faculty of Science, the University of Tokyo. Flash column chromatography was performed on silica gel (Merck Silica gel 60) and preparative thinlayer chromatography was carried out using Wakogel

B-5F. Methanesulfonyl chloride was purchased from Tokyo Kasei Kogyo Co., Ltd. and distilled from CaH_2. DBU was purchased from Tokyo Kasei Kogyo Co., Ltd. and was distilled from CaH_2 under reduced pressure. Et_3N was distilled from CaH_2 and dried over KOH. DMAP and DABCO were recrystallized. 60% NaH was purchased in condition of including parafin liquid from Kanto Chemical Co., Inc. and was washed with distilled petroleum ether under argon, followed by drying under reduced pressure. Acetonitrile and CH_2Cl_2 was distilled from P_2O_5 and then from CaH_2. DMF was distilled from CaH_2.

Preparation of Oximes Experimental procedures for the preparation of oximes were shown below as a typical example for the synthesis of benzyl (*E*)-2-benzyloxycarbonyl-5-hydroxyiminohexanoate (*E*-**13e**). To a solution of dibenzyl malonate (1.70 g, 5.98 mmol) and *tert*-BuOK (0.167 g, 1.48 mmol) in THF (4 mL) was added a solution of 3-buten-2-one (210 mg, 3.00 mmol) in THF (3 mL) dropwise for 1 h at rt. Then it was stirred for 3 h and quenched with 2 mol dm^{-3} hydrochloric acid. The organic materials were extracted with ethyl acetate, and organic layer was washed with brine and dried over $MgSO_4$. After the solvent was removed *in vacuo*, the crude materials were purified by flash column chromatography (hexane:ethyl acetate=5:1) to give benzyl 2-benzyloxycarbonyl-5-oxohexanoate as an oil (0.966 g, 90%). A methanol (5 mL) solution of benzyl 2-benzyloxycarbonyl-5-oxohexanoate (0.966 g, 2.73 mmol) was added into a H_2O (20 mL) solution of hydroxylamine hydrochloride (415 mg, 5.97 mmol) and Na_2CO_3 (318 mg, 2.99 mmol). After stirring for 4 h at rt, the mixture was extracted with ethyl acetate and organic layer was washed with brine and dried over $MgSO_4$. After the solvent was removed *in vacuo*, the crude materials were purified by flash column chromatography (hexane:ethyl acetate=2:1) to give benzyl (*E*)-2-benzyloxycarbonyl-5-hydroxyiminohexanoate (*E*-**13e**) (0.712 g, 71%) and benzyl (*Z*)-2-benzyloxycarbonyl-5-hydroxyiminohexanoate (*Z*-**13e**) (0.211 g, 21%).

Spectral Data for Oximes.

Benzyl (*E*)-2-benzyloxycarbonyl-5-hydroxyimino-3-isopropylhexanoate (13b): Colorless oil; IR (neat) 2954, 1734, 1217, 1151, 742, 698 cm^{-1}; ^1H NMR ($CDCl_3$) $\delta = 0.81$ (3H, d, $J = 6.9$ Hz), 0.88 (3H, d, $J = 6.9$ Hz), 1.70-1.75 (1H, m), 1.81 (3H, s), 2.19 (1H, dd, $J = 7.0$, 14.7 Hz), 2.28 (1H, dd, $J = 6.3$, 14.7 Hz), 2.48-2.53 (1H, m), 3.55 (1H, d, $J = 7.9$ Hz), 5.03-5.14 (4H, m), 7.23-7.31 (10H, m), 8.56 (1H, br s); ^{13}C NMR ($CDCl_3$) $\delta = 13.3$, 18.0, 20.1, 29.4, 34.9, 40.5, 54.4, 67.1, 128.2, 128.4, 128.5, 135.3, 157.5, 168.7. Anal. Calcd for $C_{24}H_{29}NO_5$: C, 70.05; H, 7.10; N, 3.40. Found: C, 69.78; H, 7.07; N, 3.32.

Benzyl (*E*)-2-benzyloxycarbonyl-5-hydroxyimino-4-methylhexanoate (13d): Colorless oil; IR (neat) 2964, 2933, 1735, 1226, 1153, 744, 698 cm^{-1}; ^1H NMR ($CDCl_3$) $\delta = 1.06$ (3H, d, $J = 6.9$ Hz), 1.74 (3H, s), 2.0 (1H, ddd, $J = 5.7$, 8.3, 14.0 Hz), 2.14 (1H, ddd, $J = 6.5$, 9.2, 14.0 Hz), 2.35 (1H, ddt, $J = 6.5$, 9.2, 6.9 Hz), 3.49 (1H, dd, $J = 6.5$, 8.3 Hz), 5.07-5.15 (4H, m), 7.22-7.30 (10H, m); ^{13}C NMR ($CDCl_3$) $\delta = 10.7$, 18.0, 32.4, 37.7, 50.1, 67.1, 128.1, 128.2, 128.5, 135.2, 159.8, 168.7. HRMS Found m/z 383.1735. Calcd for $C_{22}H_{25}NO_5$, M 383.1733.

Benzyl (*E*)-2-benzyloxycarbonyl-5-hydroxyiminohexanoate (13e): Colorless needles, mp 79 °C (ethyl acetate-hexane); IR (KBr) 2952, 1736, 1219, 1151, 744, 698 cm^{-1}; ^{1}H NMR (CDCl$_3$) $\delta = 1.81$ (3H, s), 2.14 (2H, q, J = 7.0 Hz), 2.20 (2H, t, J = 7.0 Hz), 3.49 (1H, t, J = 7.0 Hz), 5.10-5.16 (4H, m), 7.24-7.32 (10H, m), 8.21 (1H, br s); ^{13}C NMR (CDCl$_3$) $\delta = 13.4$, 25.1, 33.3, 51.1, 67.2, 128.1, 128.3, 128.5, 135.3, 156.9, 168.8. Anal. Calcd for $C_{21}H_{23}NO_5$: C, 68.28; H, 6.28; N, 3.79. Found: C, 68.42; H, 6.31; N, 3.87.

Dimethyl (Z)-5-hydroxyimino-2-methoxycarbonyl-3-phenyladipate (13f): Colorless oil; IR (neat) 2956, 1733, 1440, 1207, 702 cm^{-1}; ^{1}H NMR (CDCl$_3$) $\delta = 3.00$-3.06 (2H, m), 3.40 (3H, s), 3.63 (3H, s), 3.74 (3H, s), 3.81 (1H, d, J = 10.8 Hz), 3.95 (1H, dt, J = 10.8, 7.3 Hz), 7.14-7.24 (5H, m); ^{13}C NMR (CDCl$_3$) $\delta = 29.5$, 42.1, 52.3, 52.4, 52.6, 57.7, 127.3, 128.0, 128.3, 139.4, 150.5, 163.5, 167.8, 168.4. Anal. Calcd for $C_{16}H_{19}NO_7$: C, 56.97; H, 5.68; N, 4.15. Found: C, 56.75; H, 5.58; N, 3.94.

Preparation of *O*-Methylsulfonyloximes Experimental procedures for the preparation of *O*-methylsulfonyloximes were shown below as a typical example for the synthesis of benzyl (*E*)-2-benzyloxycarbonyl-5-(methylsulfonyloxyimino)hexanoate (*E*-**3e**).

To a dichloromethane (2 mL) solution of (*E*)-2-benzyloxycarbonyl-5-hydroxyiminohexanoate (122 mg, 0.331 mmol) were added triethylamine (67.0 mg, 0.662 mmol) and a dichloromethane (1.5 mL) solution of methanesulfonyl chloride (56.9 mg, 0.497 mmol) at 0 °C. After the mixture was stirred for 30 min at 0 °C, a buffer (pH 7) was added to the mixture. The mixture was extracted with ethyl acetate and organic layer was washed with brine and dried over MgSO$_4$. After the solvent was removed *in vacuo*, (*E*)-2-benzyloxycarbonyl-5-(methylsulfonyloxyimino)hexanoate (*E*-**3e**) (141 mg) was obtained in 95% yield, which was pure enough for next cyclization reaction. Several *O*-methylsulfonyloximes (*E*-**3a**, *E*-**3e**) were recrystallized.

Spectral Data for *O*-Methylsulfonyloximes.

Methyl (*E*)-2-methoxycarbonyl-5-methylsulfonyloxyimino-3-phenylhexanoate (3a): Colorless needles, mp 92 °C (hexane-dichloromethane); IR (neat) 1747, 1720, 1360, 1269, 1180, 793 cm^{-1}; ^{1}H NMR (CDCl$_3$) $\delta = 1.92$ (3H, s), 2.68 (3H, s), 2.69-2.80 (2H, m), 3.43 (3H, s), 3.70-3.74 (2H, m), 3.76 (3H, s), 7.14-7.28 (5H, m); ^{13}C NMR (CDCl$_3$) $\delta = 15.6$, 36.0, 39.5, 42.3, 52.4, 52.8, 57.5, 127.6, 128.1, 128.6, 138.7, 165.2, 167.6, 168.2. Anal. Calcd for $C_{16}H_{21}NO_7S$: C, 51.74; H, 5.70; N, 3.77; S, 8.63. Found: C, 51.52; H, 5.62; N, 3.85; S, 8.92.

Benzyl (*E*)-2-benzyloxycarbonyl-3-isopropyl-5-(methylsulfonyloxyimino)hexanoate (3b): Colorless oil; IR (neat) 1732, 1365, 1180, 791, 752 cm^{-1}; ^{1}H NMR (CDCl$_3$) $\delta = 0.85$ (3H, d, J = 6.9 Hz), 0.89 (3H, d, J = 6.9 Hz), 1.71-1.78 (1H, m), 1.95 (3H, s), 2.36 (1H, dd, J = 6.2, 15.1 Hz), 2.45 (1H, dd, J = 6.6, 15.1 Hz), 2.52-2.58 (1H, m), 3.03 (3H, s), 3.59 (1H, d, J = 7.3 Hz), 5.06-5.14 (4H, m), 7.23-7.32 (10H, m); ^{13}C NMR (CDCl$_3$) $\delta = 15.5$, 18.1, 20.1, 29.7, 34.9, 36.3, 40.1, 54.0, 67.4, 128.1, 128.3, 128.5, 135.1, 167.7, 168.4.

Benzyl (*E*)-2-benzyloxycarbonyl-5-methylsulfonyloxyimino-3-pentylhexanoate (3c): Colorless oil; IR (neat) 1736, 1367, 1182, 793, 746 cm^{-1}; ^{1}H NMR (CDCl$_3$) $\delta = 0.83$ (3H, t, $J = 7.1$ Hz), 1.09-1.25 (8H, m), 1.94 (3H, s), 2.35 (1H, dd, $J = 8.2$, 14.6 Hz), 2.41-2.51 (2H, m), 3.03 (3H, s), 3.61 (1H, d, $J = 5.9$ Hz), 5.08-5.12 (4H, m), 7.25-7.35 (10H, m); ^{13}C NMR (CDCl$_3$) $\delta = 13.9$, 15.7, 22.4, 26.1, 31.1, 31.6, 35.1, 36.3, 37.7, 54.2, 67.2, 128.3, 128.5, 128.7, 135.0, 166.9, 168.2.

Benzyl (*E*)-2-benzyloxycarbonyl-4-methyl-5-(methylsulfonyloxyimino)hexanoate (3d): Colorless oil; IR (neat) 1736, 1365, 1182 cm^{-1}; ^{1}H NMR (CDCl$_3$) $\delta = 1.14$ (3H, d, $J = 6.9$ Hz), 1.90 (3H, s), 2.07 (1H, ddd, $J = 5.7$, 8.1, 14.2 Hz), 2.19 (1H, ddd, $J = 6.5$, 9.1, 14.2 Hz), 2.52 (1H, ddq, $J = 5.7$, 9.1, 6.9 Hz), 2.99 (3H, s), 3.46 (1H, dd, $J = 6.5$, 8.1 Hz), 5.07-5.15 (4H, m), 7.24-7.32 (10H, m); ^{13}C NMR (CDCl$_3$) $\delta = 13.0$, 17.7, 32.0, 36.3, 38.0, 49.9, 67.4, 128.2, 128.4, 128.6, 135.1, 168.5, 169.9.

Benzyl (*E*)-2-benzyloxycarbonyl-5-(methylsulfonyloxyimino)hexanoate (3e): Colorless needles, mp 47 °C (benzene-hexane); IR (KBr) 1733, 1365, 1182, 797 cm^{-1}; ^{1}H NMR (CDCl$_3$) $\delta = 1.95$ (3H, s), 2.20 (2H, dt, $J = 7.4$, 7.4 Hz), 2.36 (2H, t, $J = 7.4$ Hz), 3.04 (3H, s), 3.49 (1H, t, $J = 7.4$ Hz), 5.11-5.16 (4H, m), 7.25-7.34 (10H, m); ^{13}C NMR (CDCl$_3$) $\delta = 15.8$, 24.4, 33.2, 36.3, 50.8, 67.4, 128.2, 128.5, 128.6, 135.1, 166.7, 168.4. Anal. Calcd for $C_{22}H_{25}NO_7S$: C, 59.05; H, 5.63; N, 3.13; S, 7.17. Found: C, 58.91; H, 5.59; N, 3.13; S, 7.24.

Dimethyl (*Z*)-2-methoxycarbonyl-5-methylsulfonyloxyimino-3-phenyladipate (3f): Colorless oil; IR (neat) 2956, 1733, 1440, 1207, 702 cm^{-1}; ^{1}H NMR (CDCl$_3$) $\delta = 2.93$ (3H, s), 3.04-3.13 (2H, m), 3.42 (3H, s), 3.70 (3H, s), 3.76-3.82 (1H, m), 3.78 (3H, s), 3.91-3.94 (1H, m), 7.15-7.37 (5H, m); ^{13}C NMR (CDCl$_3$) $\delta = 31.5$, 36.5, 42.5, 52.4, 52.9, 53.2, 57.4, 127.8, 128.1, 128.6, 138.4, 161.8, 165.8, 167.3, 167.9.

Benzyl (*E*)-2-benzyloxycarbonyl-6-(methylsulfonyloxyimino)heptanoate (7): Colorless oil; IR (neat) 1734, 1365, 1182, 793 cm^{-1}; ^{1}H NMR (CDCl$_3$) $\delta = 1.50$-1.61 (2H, m), 1.90-1.96 (2H, m), 1.91 (3H, s), 2.23 (2H, t, $J = 7.4$ Hz), 3.05 (3H, s), 3.45 (1H, t, $J = 7.4$ Hz), 5.10-5.16 (4H, m), 7.25-7.35 (10H, m); ^{13}C NMR (CDCl$_3$) $\delta = 15.4$, 23.1, 27.9, 35.0, 36.3, 51.4, 67.2, 128.2, 128.4, 128.6, 135.3, 167.3, 168.7.

Ethyl (*E*)-2-benzoyl-5-(methylsulfonyloxyimino)hexanoate (9): Colorless oil; IR (neat) 2981, 1736, 1685, 1365, 1180, 793 cm^{-1}; ^{1}H NMR (CDCl$_3$) $\delta = 1.09$ (3H, t, $J = 7.0$ Hz), 1.97 (3H, s), 2.19-2.28 (2H, m), 2.37-2.40 (2H, m), 2.98 (3H, s), 4.07 (2H, q, $J = 7.0$ Hz), 4.39 (1H, t, $J = 6.9$ Hz), 7.42 (2H, t, $J = 7.6$ Hz), 7.54 (1H, t, $J = 7.6$ Hz), 7.94 (2H, d, $J = 7.6$ Hz); ^{13}C NMR (CDCl$_3$) $\delta = 13.7$, 15.7, 24.4, 33.3, 36.2, 52.5, 61.4, 128.5, 128.7, 133.6, 135.9, 167.1, 169.2, 194.5.

Methyl (*E*)-5-methylsulfonyloxyimino-2-phenylsulfonylhexanoate (11): Colorless oil; IR (neat) 2948, 1741, 1365, 1325, 1180, 1151 cm^{-1}; ^{1}H NMR (CDCl$_3$) $\delta = 1.95$ (3H, s), 2.23-2.30 (1H, m), 2.36-2.47 (3H, m), 3.08 (3H, s), 3.58 (3H, s), 4.08 (1H, dd, *J* = 3.2, 10.1 Hz), 7.55 (2H, t, *J* = 7.4 Hz), 7.66 (1H, t, *J* = 7.4 Hz), 7.84 (2H, d, *J* = 7.4 Hz); ^{13}C NMR ($CDCl_3$) δ = 15.8, 22.0, 32.7, 36.3, 52.9, 69.1, 128.2, 129.0, 129.1, 134.4, 137.1, 165.8.

General Procedure for the Synthesis of 3,4-Dihydro-*2H*-pyrroles and 2,3,4,5-Tetrahydropyridines (Table 1, Entry 5): To a dichloromethane (2 mL) solution of methyl (*E*)-2-methoxycarbonyl-5-methylsulfonyloxyimino-3-phenylhexanoate (*E*-**3a**) (100 mg, 0.270 mmol) was added a dichloromethane (1.5 mL) solution of DBU (61.7 mg, 0.405 mmol) at 0 °C. After the mixture was stirred for 15 min at 0 °C, solvent was removed *in vacuo*. The crude products were purified by thinlayer chromatography (silica gel, ethyl acetate) to afford 3,4-dihydro-2,2-dimethoxycarbonyl-5-methyl-3-phenyl-*2H*-pyrrole (**4a**) (74.0 mg) in 99% yield.

General Procedure for the Synthesis of 3,4-Dihydro-*2H*-pyrroles from Oximes (Table 4, Entry 3): To an acetonitrile (2 mL) solution of benzyl (*E*)-2-benzyloxycarbonyl-5-hydroxyimino-4-methylhexanoate (*E*-**13e**) (177 mg, 0.479 mmol) were added triethylamine (58.1 mg, 0.574 mmol) and an acetonitrile (1.5 mL) solution of methanesulfonyl chloride (60.3 mg, 0.526 mmol) at 0 °C. After being stirred for 30 min at 0 °C, an acetonitrile (1.5 mL) solution of DBU (160 mg, 1.05 mmol) was added. After the mixture was stirred for 30 min at 0 °C, acetonitrile was removed *in vacuo*. The crude products were purified by thinlayer chromatography (silica gel, ethyl acetate) to afford 2,2-dibenzyloxycarbonyl-5-methyl-3,4-dihydro-*2H*-pyrrole (**4e**) (163 mg) in 96% yield.

Spectral Data for 3,4-Dihydro-*2H*-pyrroles and 2,3,4,5-Tetrahydropyridines.

2,2-Dimethoxycarbonyl-5-methyl-3-phenyl-3,4-dihydro-*2H*-pyrrole (4a): Colorless needles, mp 84 °C (ethyl acetate-hexane); IR (neat) 1736, 1273, 1223 cm^{-1}; ^{1}H NMR ($CDCl_3$) δ = 2.22 (3H, s), 2.93 (1H, dd, *J* = 6.7, 17.8 Hz), 3.14 (1H, dd, *J* = 9.1, 17.8 Hz), 3.17 (3H, s), 3.77 (3H, s), 4.35 (1H, dd, *J* = 6.7, 9.1 Hz), 7.15-7.24 (5H, m); ^{13}C NMR ($CDCl_3$) δ = 20.0, 46.9, 48.9, 51.9, 53.1, 91.5, 127.3, 128.1, 128.2, 139.0, 167.9, 169.6, 181.0. Anal. Calcd for $C_{15}H_{17}NO_4$: C, 65.44; H, 6.22; N, 5.09 Found: C, 65.18; H, 6.21; N, 4.96.

2,2-Dibenzyloxycarbonyl-3-isopropyl-5-methyl-3,4-dihydro-*2H*-pyrrole (4b): Colorless oil; IR (neat) 1734, 1267, 1213, 744, 698 cm^{-1}; ^{1}H NMR ($CDCl_3$) δ = 0.71 (3H, d, *J* = 6.6 Hz), 0.86 (3H, d, *J* = 6.6 Hz), 1.51-1.61 (1H, m), 2.09 (3H, s), 2.40 (1H, dd, *J* = 8.4, 17.2 Hz), 2.66 (1H, dd, *J* = 8.5, 17.2 Hz), 2.85-2.90 (1H, m), 5.08 (1H, d, *J* = 12.5 Hz), 5.09-5.11 (2H, m), 5.30 (1H, d, *J* = 12.5 Hz), 7.21-7.33 (10H, m); ^{13}C NMR ($CDCl_3$) δ = 19.9, 20.4, 22.2, 28.8, 43.0, 50.8, 67.1, 67.3, 88.2, 127.9, 128.0, 128.22, 128.25, 128.3, 128.4, 134.9, 135.5, 168.0, 168.3, 181.0. Anal. Calcd for $C_{24}H_{27}NO_4$: C, 73.26; H, 6.92; N, 3.56. Found: C, 72.98; H, 7.02; N, 3.61.

2,2-Dibenzyloxycarbonyl-5-methyl-3-pentyl-3,4-dihydro-*2H*-pyrrole (4c): Colorless oil; IR (neat) 1736, 1265, 1211, 746 cm^{-1}; ^{1}H NMR ($CDCl_3$) δ = 0.81 (3H, t, *J* = 7.1 Hz), 0.91-1.00 (1H, m), 1.05-1.24 (6H, m), 1.49-1.56 (1H, m), 2.11 (3H, s), 2.30 (1H, dd, *J* = 8.8, 17.1 Hz), 2.72 (1H, dd, *J* =

8.5, 17.1 Hz), 2.84-2.91 (1H, m), 5.01 (1H, d, *J* = 12.2 Hz), 5.09 (1H, d, *J* = 12.4 Hz), 5.12 (1H, d, *J* = 12.2 Hz), 5.33 (1H, d, *J* = 12.4 Hz), 7.21-7.31 (10H, m); ^{13}C NMR ($CDCl_3$) δ = 13.9, 20.2, 22.3, 28.3, 30.4, 31.5, 44.6, 45.0, 67.1, 67.3, 88.6, 128.0, 128.19, 128.25, 128.29, 128.38, 128.41, 135.1, 135.5, 167.9, 169.4, 181.2. Anal. Calcd for $C_{26}H_{31}NO_4$: C, 74.08; H, 7.41; N, 3.32. Found: C, 73.85; H, 7.44; N, 3.33.

2,2-Dibenzyloxycarbonyl-4,5-dimethyl-3,4-dihydro-*2H*-pyrrole (4d): Colorless oil; IR (neat) 1738, 1267, 1120, 698 cm^{-1}; ^{1}H NMR ($CDCl_3$) δ = 1.13 (3H, d, *J* = 7.3 Hz), 1.99 (1H, dd, *J* = 7.3, 13.6 Hz), 2.07 (3H, s), 2.72 (1H, dd, *J* = 8.8, 13.6 Hz), 2.80-2.94 (1H, m), 5.05 (1H, d, *J* = 12.3 Hz), 5.10 (1H, d, *J* = 12.3 Hz), 5.18 (1H, d, *J* = 12.3 Hz), 5.23 (1H, d, *J* = 12.3 Hz), 7.22-7.27 (10H, m); ^{13}C NMR ($CDCl_3$) δ = 17.3, 17.7, 38.6, 46.1, 67.4, 84.5, 128.0, 128.2, 128.4, 135.3, 169.3, 169.8, 184.5. HRMS Found m/z 365.1599. Calcd for $C_{22}H_{23}NO_4$, M 365.1627.

2,2-Dibenzyloxycarbonyl-5-methyl-3,4-dihydro-*2H*-pyrrole (4e): Colorless oil; IR (neat) 1763, 1267, 1157, 1086 cm^{-1}; ^{1}H NMR ($CDCl_3$) δ = 2.13 (3H, s), 2.44 (2H, t, *J* = 7.8 Hz), 2.65 (2H, t, *J* = 7.8 Hz), 5.08 (2H, d, *J* = 12.4 Hz), 5.21 (2H, d, *J* = 12.4 Hz), 7.21-7.28 (10H, m); ^{13}C NMR ($CDCl_3$) δ = 19.8, 30.6, 39.6, 67.3, 86.6, 128.1, 128.4, 128.5, 135.3, 169.4, 181.3. Anal. Calcd for $C_{21}H_{21}NO_4$: C, 71.79; H, 6.02; N, 3.99. Found: C, 71.57; H, 6.06; N, 3.98.

3-Phenyl-2,2,5-trimethoxycarbonyl-3,4-dihydro-*2H*-pyrrole (4f): Colorless oil; IR (neat) 1743, 1276, 1232 cm^{-1}; ^{1}H NMR ($CDCl_3$) δ = 3.10-3.14 (2H, m), 3.69 (9H, s), 3.92 (1H, dd, *J* = 5.4, 9.7 Hz), 7.25-7.38 (5H, m); ^{13}C NMR ($CDCl_3$) δ = 21.9, 46.1, 53.3, 68.4, 117.8, 128.5, 128.9, 129.4, 136.4, 165.8. Anal. Calcd for $C_{16}H_{17}NO_6$: C, 60.18; H, 5.37; N, 4.39. Found: C, 60.39; H, 5.45; N, 4.32.

2,2-Dibenzyloxycarbonyl-6-methyl-2,3,4,5-tetrahydropyridine (8): Colorless oil; IR (neat) 1739, 1658, 1257, 1178, 744, 700 cm^{-1}; ^{1}H NMR ($CDCl_3$) δ = 1.62 (2H, tt, *J* = 6.4, 6.4 Hz), 2.05 (3H, s), 2.06 (2H, t, *J* = 6.4 Hz), 2.13 (2H, t, *J* = 6.4 Hz), 5.07 (2H, d, *J* = 12.3 Hz), 5.21 (2H, d, *J* = 12.3 Hz), 7.23-7.29 (10H, m); ^{13}C NMR ($CDCl_3$) δ = 16.0, 26.5, 27.8, 29.8, 67.3, 70.7, 128.09, 128.12, 128.4, 135.5, 169.5, 173.5. HRMS Found m/z 365.1627. Calcd for $C_{22}H_{23}NO_4$, M 365.1627.

2-Benzoyl-2-ethoxycarbonyl-5-methyl-3,4-dihydro-*2H*-pyrrole (10): Colorless oil; IR (neat) 2981, 1743, 1689, 1263, 696 cm^{-1}; ^{1}H NMR ($CDCl_3$) δ = 0.98 (3H, t, *J* = 7.1 Hz), 2.11 (3H, s), 2.18 (1H, ddd, *J* = 7.3, 9.2, 13.3 Hz), 2.62-2.67 (2H, m), 2.95 (1H, ddd, *J* = 5.9, 8.6, 13.3 Hz), 4.05-4.12 (2H, m), 7.42 (2H, t, *J* = 7.4 Hz), 7.49 (1H, t, *J* = 7.4 Hz), 8.16 (2H, d, *J* = 7.4 Hz); ^{13}C NMR ($CDCl_3$) δ = 13.7, 20.0, 30.3, 39.4, 61.6, 90.1, 128.3, 129.8, 132.9, 135.2, 171.8, 180.4, 192.8. HRMS Found m/z 259.1217. Calcd for $C_{15}H_{17}NO_3$, M 259.1208.

2-Methoxycarbonyl-5-methyl-*1H*-pyrrole (12): Colorless needles, mp 100 °C (ethyl acetate-hexane); IR (neat) 3307, 1682, 1228, 793, 769 cm^{-1}; ^{1}H NMR ($CDCl_3$) δ = 2.29 (3H, s), 3.82 (3H, s), 5.93 (1H, dd, $J = 2.8, 2.8$ Hz), 6.79 (1H, dd, $J = 2.8, 2.8$ Hz), 9.43 (1H, br s); ^{13}C NMR ($CDCl_3$) $\delta =$ 13.0, 51.2, 108.9, 116.2, 121.0, 134.1, 161.8. HRMS Found m/z 139.0646. Calcd for $C_7H_9NO_2$, M 139.0633.

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