Methyltrioxorhenium-Catalyzed Oxidation of Secondary and Primary Amines with Hydrogen Peroxide

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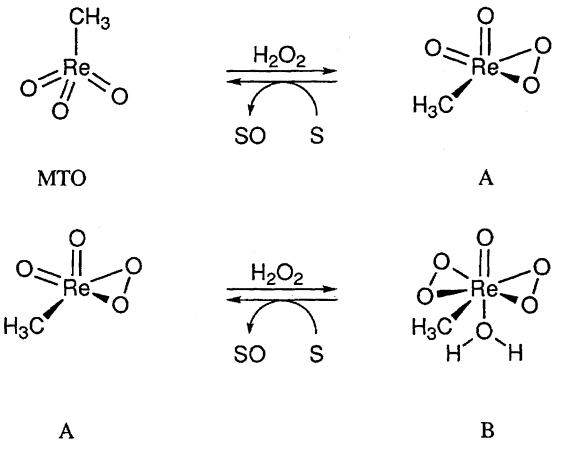
The methyltrioxorhenium-catalyzed oxidation of secondary amines and primary amines with hydrogen peroxide has been carried out. The oxidation of secondary amines afforded nitrones in good-to-excellent yield. Benzylamines were selectively oxidized to oximes, while general primary alkylamines possessing the α-C–H bond gave mixtures of oximes, nitroso dimers, and azoxy compounds.

Methyltrioxorhenium (MTO) as an oxidation catalyst was first reported by Herrmann and co-workers for the epoxidation of olefins with hydrogen peroxide as the terminal oxidant.[1a] Since then, MTO-catalyzed hydrogen peroxide oxidations have been explored with a variety substrates, such as alkynes,[2] arenes,[3] phenols,[4] cyclic ketones,[5] benzaldehydes,[6] sulfides,[7] amines,[8,9] and so on.[10—13] MTO reacts with hydrogen peroxide to form two η^2-peroxorhenium complexes, with 1 : 1 and 1 : 2 rhenium : peroxide ratios (A and B in Scheme 1).[14—16] These peroxocomplexes transfer oxygen to substrates and are catalytically active in the presence of hydrogen peroxide. The important features of MTO as a catalyst are its availability (ease of synthesis, now commercially available), its stability in air (dioxygen and humidity),and its solubility in various solvents, including water. Furthermore, hydrogen peroxide is an environmentally advantageous oxidizing agent, since its only waste by-product is water.

Recently the Espenson group has reported on the MTO-catalyzed oxidation of anilines and *N*,*N*-dimethylanilines to form nitrosobenzenes and *N*,*N*-dimethylaniline *N*-oxides, respectively.[8] More recently, the Murray group has published a short communication on the oxidation of nitrogen compounds by H_2O_2/MTO.[9] They have described the oxidation of anilines to nitrobenzenes, nitrosobenzene to nitrobenzene, primary amines having no α-hydrogen to nitroalkanes, azobenzene to azoxybenzene, pyridine to pyridine *N*-oxide, and pyrrolidine derivative having no hydrogen at the 2- and 5-positions to nitroxide. They have also demonstrated the oxidation of dibenzylamine to *N*,*N*-dibenzylhydroxylamine along with nitrone as a minor product.



Scheme 1.

The oxidation of amines is a fundamental reaction for the synthesis of oxygen-containing nitrogen compounds. Therefore, a variety of oxidation methods have been explored using not only traditional stoichiometric oxidants, but also hydrogen peroxide with various metal catalysts.[17] The oxygenation products of secondary amines are generally hydroxylamines, nitroxides and nitrones, while the general products of primary amine oxidation are azo compounds, azoxy compounds, nitro compounds, nitroso compounds, and oximes. The selective synthesis of specific oxygenated nitrogen compounds is obviously important. However, the product composition depends on the oxidants, catalysts, and reaction conditions employed, and it is generally difficult to control the selectivity of amine oxidation. Therefore, it is important to develop selective methods for the oxygenation of amines.

Here, we wish to repot on our results concerning the MTO-catalyzed hydrogen peroxide oxidation of secondary amines and primary amines possessing the α-C–H bond. The oxidation of secondary amines by H_2O_2/MTO resulted in the selective formation of nitrones in good-to-excellent yields.[18] Nitrones are valuable compounds as synthetic intermediates and spin-trapping reagents. The synthesis of nitrones from secondary amines by direct oxidation is an important synthetic procedure, because the starting amines are easily available and nitrones are obtained in a single step.[19] Several oxidations of secondary amines for nitrone synthesis have been reported.[19—25] The oxidation of benzylamines by H_2O_2/MTO afforded the corresponding benzaldehyde oximes in good yields. Primary alkylamines possessing the α-C–H bond afforded mixtures of oximes, nitroso dimers, and

azoxy compounds by this oxidation.

Results and Discussion

Oxidation of Secondary Amines. Several reaction conditions were examined using dibenzylamine as a substrate. Generally, dibenzylamine was dissolved in an "oxidation solution" (a solution of aqueous H_2O_2 in an appropriate solvent. The solution had been previously dried over anhydrous $MgSO_4$, ca. 1.0 M (M = mol dm^{-3}), see Experimental for detail); then, solid MTO was added to the stirred solution. An exothermic reaction occurred immediately along with a change in the colorless solution to yellow. The yellow color indicated the formation of peroxo complexes.[14,15] The exothermic reaction ceased within a few minutes, and the yellow color disappeared during oxidation. The results of the oxidations are summarized in Table 1. The nitrone (*N*-benzylidenebenzylamine *N*-oxide) and the hydroxylamine (*N*,*N*-dibenzylhydroxylamine) were generally isolated simultaneously. When an equal amount of H_2O_2 with the amine was used, the hydroxylamine was the main product (Entry 1). This result is in accord with Murray's result of dibenzylamine oxidation, which was carried out under the condition of a small ratio of the oxidant (amine/H_2O_2/MTO=166/33/1, hydroxylamine 80% and nitrone 10%).[9] The use of an excess amount of H_2O_2 produced the nitrone predominantly (Entries 5,6). In a separate experiment, the hydroxylamine was converted to nitrone quantitatively under the same catalytic conditions. These results indicated that this catalytic oxidation proceeded via the hydroxylamine as the intermediate.

When two or three molar amounts of H_2O_2 were used, the reaction stopped before the complete conversion of hydroxylamine to nitrone (Entries 2, 4). In these cases, the reaction was resumed by the addition of extra MTO to the reaction mixture. This was clearly confirmed by the reappearance of the yellow color of the solution, which indicated the formation of the peroxo complexes. This indicated that the catalyst initially added lost its activity at this stage. This was further confirmed by a following experiment. When extra H_2O_2 was added after the disappearance of the yellow color, the color of the solution was not changed (Entry 3). In this case, the yield of nitrone was somewhat higher than that of Entry 2. This was because the *N*,*N*-dibenzylhydroxylamine was slowly oxidized in the oxidation solution without a catalyst (36% conversion with 5 molar amounts of oxidation solution at 1 h). The use of excess oxidant (5 molar amounts) resulted in the exclusive formation of the nitrone (Entry 6). In this case, the yellow color of the peroxo complexes did not disappear, even after 1 h. The existence of a large excess H_2O_2 must stabilize the catalyst.

Alcohols and aprotic polar solvents were found to be effective as a solvent. Methanol was the best solvent among them for the synthesis of nitrone, because the reaction in other solvents stopped with a significant amount of the hydroxylamine (Entries 9—14). The catalyst deactivated within a shorter period in these solvents than in methanol. The use of aqueous 30% H_2O_2 in MeOH without a treatment over $MgSO_4$ resulted in a decrease in the selectivity of nitrone (Entry 7).

The application of this catalytic oxidation to other secondary amines was performed. The results are summarized in Table 2. Aliphatic secondary amines (Entries 1—3) were converted to the corresponding nitrones in good yields in isopropyl alcohol with a 0.05—0.1 molar amount catalyst.

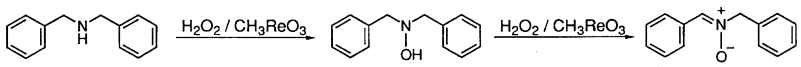
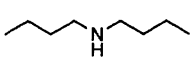
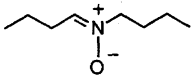
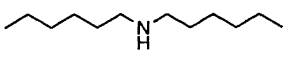
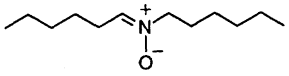
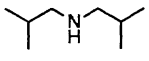
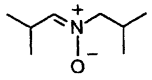
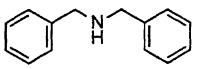
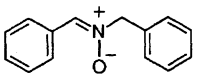
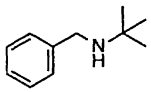
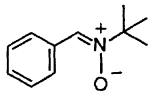
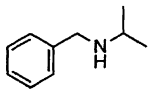
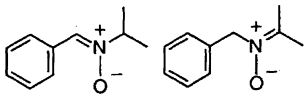
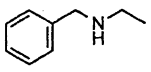
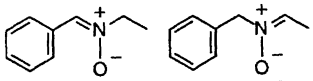


Table 1. Oxidation of Dibenzylamine with H_2O_2/MTO in Various Conditions[a]

Entry	Solvent	H_2O_2 [b] Mol amt.	MTO Mol amt.	Conv. %	Yield/% [c] Nitrone	Hydroxylamine
1	MeOH	1	0.02	77	6	66
2		2	0.02	100	53	43
3		2+2[d]	0.02	100	68	25
4		3	0.02	100	77	14
5		4	0.02	100	91	—
6		5	0.02	100	97	—
7		5[e]	0.02	100	11	73
8		5	0.01	100	74	22
9	EtOH	4	0.02	100	68	31
10	*i*-PrOH	4	0.02	100	64	31
11	*t*-BuOH	4	0.02	100	51	35
12	THF	4	0.02	100	26	59
13	AcOEt	4	0.02	100	45	53
14	CH_3CN	4	0.02	100	55	43

a) Room temperature, 1 h. b) Oxidation solution (H_2O_2/solvent mixed solution dried over anhydrous $MgSO_4$). See Experimental for detail. c) Isolated yield based on dibenzylamine used. d) Additional oxidation solution (2 molar amounts) was added at 10 min after the addition of MTO. e) Aqueous 30% H_2O_2 in MeOH was used instead of oxidation solution.

Table 2. Oxidation of Secondary Amines with H_2O_2/MTO[a)]

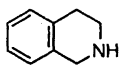
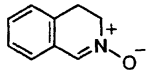
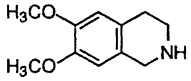
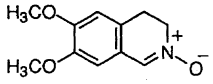
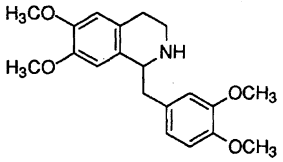
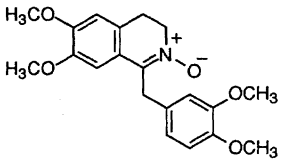
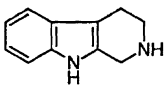
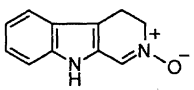
Entry	Amine	Solvent	MTO/Mol amt.	Nitrone	Yield/% [b)]
1		*i*-PrOH	0.05		87
2		*i*-PrOH	0.1		78
3		*i*-PrOH	0.07		83
4		MeOH	0.02		97
5		EtOH	0.1		88[c)]
6		MeOH	0.05		78,12
7		MeOH	0.05		31,26 [d)]

a) With 5 molar amounts of H_2O_2 at room temperature for 30 min (Entries 1—3) or for 1 h (Entries 4—7). b) Isolated yield by column chromatography. c) Recovered starting amine 4%. d) Benzaldehyde oxime (10%) was also isolated.

N-Alkylbenzylamines (Entries 4—7) were also converted to nitrones. The oxidation of *N*-(*t*-butyl)benzylamine afforded *N*-benzylidene-*t*-butylamine *N*-oxide, which is a useful spin trapping reagent. The oxidation of unsymmetrical secondary amines generally gives a mixture of regioisomeric nitrones. Regioisomers of nitrones were isolated by the oxiadation of *N*-isopropylbenzylamine and *N*-ethylbenzylamine (Entries 6, 7). These are typical examples of the disadvantage of the direct oxidation methods for the synthesis of nitrones.

1,2,3,4-Tetrahydroisoquinoline and its derivatives also gave nitrones (Table 3), which are useful precursors for the synthesis of isoquinoline alkaloids.[20,26)] The yields were somewhat lower than those of acyclic symmetrical secondary amines. The oxidation of 6,7-dimethoxy-1,2,3,4-tetrahydroisoquinoline gave a better nitrone yield (56%, Entry 2) than the result of H_2O_2/$NaWO_4$ oxidation reported previously

Table 3. Oxidation of 1,2,3,4-Tetrahydroisoquinolines and 1,2,3,4-Tetrahydro-9*H*-pyrido[3,4-*b*]inodole with H_2O_2/MTO [a)]

Entry	Amine	MTO/Mol amt.	Nitrone	Yield/% [b)]
1		0.02		66
2		0.04		56
3		0.05		36
4		0.04		33 [c)]

a) With 5 molar amounts of H_2O_2 in MeOH at room temperature for 1 h. b) Isolated yield by column chromatography. c) In CH_3CN.

(32.5% yield).[26]

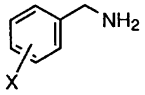
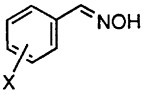
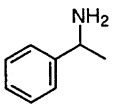
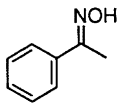
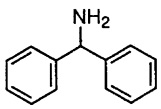
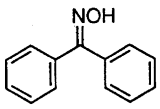
Oxidation of Primary Amines Possessing α-C–H Bond.

The MTO-catalyzed hydrogen peroxide oxidation of primary amines which have no α-C–H bond has been reported to give nitroso[8] or nitro[9] compounds, depending on the reaction conditions employed. We describe here our results in the oxidation of primary amines possessing the α-C–H bond with H_2O_2/MTO. At first, benzylamine was examined as a substrate. The oxidation of benzylamine in *t*-BuOH gave benzaldehyde oxime in 88% yield as the only important product (Table 4, Entry 1). The reaction proceeded smoothly at room temperature, and the reaction completed within 30 min. The oxidation of benzylamine in MeOH and EtOH resulted in the starting amine to remain in a significant amount under the same reaction conditions. The result of the oxidation in *i*-PrOH was almost the same as that in *t*-BuOH (100% conversion, 87% benzaldehyde oxime.) Benzylamines substituted by several groups at the 2, 3, and 4-positions also afforded the corresponding benzaldehyde oximes in 74—90% yields (Entries 2—9). 1-Phenylethylamine and benzhydrylamine gave acetophenone oxime and benzophenone oxime in 84 and 70%, respectively (Entries 10, 11).

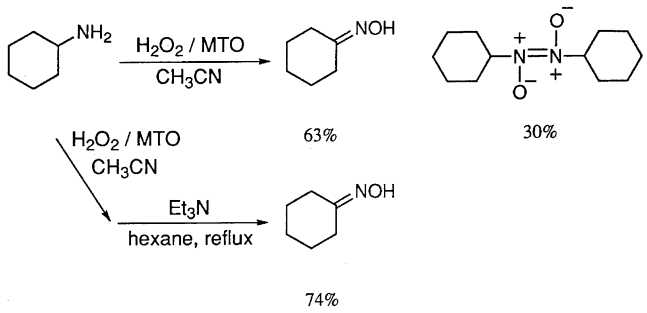
The oxidation of cyclohexylamine by H_2O_2/MTO gave cyclohexanone oxime and the nitrosocyclohexane dimer in 63 and 30% yields (Scheme 2). The nitroso dimers are easily converted to oximes by a treatment with a base.[27] When the crude product mixture was refluxed in hexane in the presence of triethylamine, cyclohexanone oxime was isolated in 74% yield (Scheme 2).

The oxidation of decylamine gave a mixture of oxime, nitroso dimer and azoxy compound (Table 5, Entry 1). 2-Phenylethylamine and 3-phenylpropylamine also gave a mixture of the three compounds (Entries 2, 3). Although the ratio of the products changed when a different solvent was used, no selectivity of the products was observed.

Table 4. Oxidation of Benzylamines with H_2O_2/MTO [a]

Entry	Amine	Oxime	Yield/% [b]
			
1	X=H		88
2	X=4-OCH_3		74
3	X=4-CH_3		81
4	X=3-CH_3		82
5	X=2-CH_3		77
6	X=4-Cl		85
7	X=3-Cl		85
8	X=2-Cl		86
9	X=4-NO_2		90
10			84
11			70

a) The reactions were carried out in *t*-BuOH at room temperature for 30 min with mol ratio of amine : H_2O_2 : MTO of 20 : 100 : 1.
b) Isolated yield by column chromatography.



Scheme 2.

The oxygenation of primary amines possessing an α-C–H bond generally produces hydroxylamines initially, which is subsequently oxidized to nitroso compounds. Further oxygenation produces nitro compounds with certain oxidants, such as dimethyldioxirane.[28] The unstable nitroso compounds transform to the nitroso dimer by dimerization or to oxime by tautomerization.[27] Some of nitroso compounds react with hydroxylamines to form azoxy compounds (Scheme 3).[29,30] In this MTO-catalyzed oxidation, no nitro compounds were isolated. The mixtures of oximes, nitroso dimers, and azoxy compounds were obtained in the MTO-catalyzed oxidation of primary alkylamines. On the other hand, oximes were the only significant products in the oxidation of benzylamines. The phenyl substituent at the α-carbon of the primary amines facilitates the formation of oximes from the intermediate nitrosoalkanes.[27,29] The $NaWO_4$-catalyzed hydrogen peroxide oxidation of primary amines was reported to give mixtures of oximes, nitroso dimers, and azoxy compounds.[31]

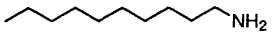
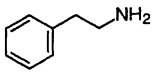
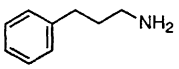
Mechanism of Oxidation. As reported by Espenson,[8] the oxidation must proceed via the oxygenation of amines by peroxorhenium complexes A and B of Scheme 1. In the oxidation of secondary amines, the primary product is hydroxylamine, which is oxygenated further to form nitrone (Scheme 4).

The oxygenation of primary amines possessing the α-C–H bond must proceed in a way similar to aniline oxidation, as proposed by Espenson, to form nitroso compounds.[8] The 1-alkyl-1-nitrosoalkanes are generally unstable and tautomerize to oximes, dimerize to nitroso dimers, and react with intermediate hydroxylamines to form azoxy compounds under the reaction conditions (Scheme 3).

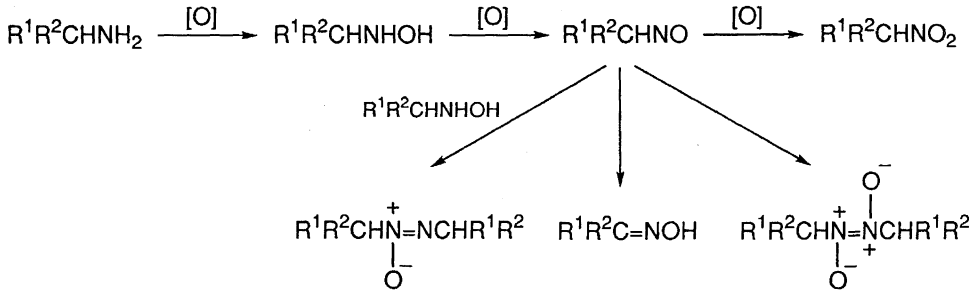
Conclusion

MTO/H_2O_2 broadened its versatility as an oxidation catalyst system due to this research. A variety of nitrones have been effectively prepared in good-to-excellent yields by the MTO-catalyzed oxidation of the secondary amines. The oxidation of benzylamines afforded oximes selectively by H_2O_2/MTO. Primary alklamines possessing the α-C–H

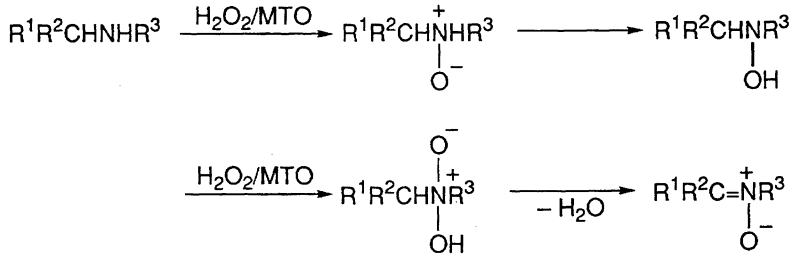
Table 5. Oxidation of Primary Amines with H_2O_2/MTO [a]

Entry	Amine	Solvent	MTO	Yield/% [b]		
			Mol amt.	Oxime	Nitroso dimer	Azoxy
1		*t*-BuOH	0.1	38	11	47
		CH_3CN	0.05	43	20	40
2		*i*-PrOH	0.05	59	trace	33
		t-BuOH	0.05	38	27	24
		CH_3CN	0.05	26	45	25
3		*t*-BuOH	0.05	53	10	24
		CH_3CN	0.05	26	36	26

a) With 5 molar amounts of H_2O_2 at room temperature for 30 min. b) Isolated yield by column chromatography.



Scheme 3.



Scheme 4.

bond were oxygenated to mixtures of oximes, nitroso dimers, and azoxy compounds under the same reaction conditions.

Experimental

General. The melting points are uncorrected. IR spectra were recorded on a JASCO FT/IR-3 spectrophotometer. ^1H and ^{13}C NMR were recorded on a JEOL EX-90 spectrometer at 90 and 22.5 MHz with tetramethylsilane as an internal standard. Elemental analyses were performed with a Yanaco MT-5 elemental analyzer. The progress of the reaction was monitored by a TLC analysis on silica-gel (Merck Silica Gel 60 F_{254}) or by a GC analysis on a Shimadzu GC-14A with a Hewlett Packard HP-1 (30 m×0.53 mm) wide bore capillary column. Column chromatography was performed using silica-gel (Wakogel C-200). MTO was prepared from Re_2O_7 and $Sn(CH_3)_4$ in the presence of perfluoroglutaric anhydride.[32] 1-(3, 4-Dimethoxybenzyl)-6,7-dimethoxy-1,2,3,4-tetrahydroisoquinoline (norlaudanosine) was prepared according reported procedure.[33] All of the other amines used in this research were commercially available, and used without further purification.

Preparation of Oxidation Solution (Hydrogen Peroxide–Methanol Solution). MeOH (290 mL) was mixed with 30% H_2O_2 (30 mL). The solution was stirred with anhydrous $MgSO_4$ (25 g) for 3 h, and then filtered. The obtained oxidation solution was titrated (1.0 M = 1.0 mol dm^{-3}) and stored in a refrigerator (5 °C). The concentration did not change for months. Oxidation solutions in other solvents (Table 1) were prepared in a same manner.

General Procedure for Oxidation of Secondary Amines. A typical reaction procedure (Table 1, Entry 6) is as follows: Dibenzylamine (400 mg, 2.03 mmol) was dissolved in oxidation solution (1.0 M H_2O_2/CH_3OH, 10 mL, 10 mmol). Crystalline MTO (10 mg, 0.040 mmol) was added to the solution. MTO dissolved immediately along with a change in the color of the solution to yellow, which indicated the formation of peroxo complexes.[14,15] The temperature of the solution first rose, and then fell within 5 min. The reaction mixture was stirred at room temperature for 1 h. The resulting mixture was poured into brine, and the products were extracted with dichloromethane (10 mL×3). After the combined extracts were dried over anhydrous $Na_2SO_4/MgSO_4$ (1 : 1 mixture), the solvent was distilled out by an evaporator. *N*-Benzylidenebenzylamine *N*-oxide[20b] (414 mg, 97%) was isolated by silica-gel column chromatography (10 : 1 dichloromethane/ethyl acetate as the eluent).

Some of the obtained products were identified by comparing physical data with literature results (*N*-butylidenebutylamine *N*-oxide,[21b] *N*-benzylidene-*t*-butylamine *N*-oxide,[19a,21b] *N*-benzylideneisopropylamine *N*-oxide,[34] *N*-isopropylidenebenzylamine *N*-oxide,[35] *N*-benzylideneethylamine *N*-oxide,[34] *N*-ethylideneben-

zylamine *N*-oxide,[34] 3,4-dihydroisoquinoline *N*-oxide,[19a,21b] 6,7-dimethoxy-3,4-dihydroisoquinoline *N*-oxide,[26] and *N*,*N*-dibenzylhydroxylamine[36]).

***N*-Hexylidenehexylamine *N*-Oxide:**[20] IR (KBr) 2970, 2940, 2870, 1595, 1467, 1420, 1175, 1120 cm^{-1}; ^1H NMR ($CDCl_3$) δ = 0.6—1.0 (m, 6H), 1.0—1.7 (m, 12H), 1.7—2.1 (m, 2H), 2.3—2.7 (m, 2H), 3.75 (t, J = 7.0 Hz, 2H), 6.71 (t, J = 5.9 Hz, 1H); ^{13}C NMR ($CDCl_3$) δ = 13.93, 22.38, 22.53, 25.30, 26.14, 26.61, 27.45, 31.33, 31.69, 31.86, 65.37, 139.54.

***N*-(Isobutylidene)isobutylamine *N*-Oxide:**[20,21a] IR (neat) 2960, 2875, 1595, 1470, 1420, 1390, 1370, 1292, 1238, 1200, 1172, 1170, 1119, 985, 898 cm^{-1}; ^1H NMR ($CDCl_3$) δ = 0.95 (d, J = 6.8 Hz, 6H), 1.11 (d, J = 6.8 Hz, 6H), 2.2—2.7 (m, 1H), 3.0—3.4 (m, 1H), 3.51 (d, J = 7.3 Hz, 2H), 6.50 (d, J = 7.3 Hz, 1H); ^{13}C NMR ($CDCl_3$) δ = 18.98, 19.57, 25.87, 26.11, 72.77, 145.12.

1-(3,4-Dimethoxybenzyl)-6,7-dimethoxy-3,4-dihydroisoquinoline *N*-Oxide: Mp 152—154 °C; IR (KBr) 1605, 1590, 1517, 1465, 1452, 1375, 1332, 1297, 1278, 1260, 1232, 1217, 1190, 1155, 1140, 1022, 955, 890 cm^{-1}; ^1H NMR ($CDCl_3$) δ = 3.07 (t, J = 7.5 Hz, 2H), 3.78 (s, 3H), 3.38 (s, 6H), 3.88 (s, 3H), 4.19 (t, J = 7.5 Hz, 2H), 4.28 (s, 2H), 6.6—7.0 (m, 5H); ^{13}C NMR ($CDCl_3$) δ = 27.54, 31.77, 55.88, 56.06, 56.12, 58.36, 108.42, 110.66, 111.46, 112.09, 120.38, 122.35, 124.86, 129.69, 143.69, 147.86, 148.10, 149.29, 149.38. Found: C, 67.01; H, 6.49; N, 3.65%. Calcd for $C_{20}H_{23}NO_5$: C, 67.21; H, 6.49; N, 3.92%.

Oxidation of 1,2,3,4-Tetrahydro-9*H*-pyrido[3,4-*b*]indole. 1,2,3,4-Tetrahydro-9*H*-pyrido[3,4-*b*]indole (344 mg, 2.00 mmol) and oxidation solution (1.0 M H_2O_2/CH_3CN, 10 mL, 10 mmol) was placed in a round-bottom flask. Acetonitrile (40 mL) was added to the mixture in order to dissolve the amine. Crystalline MTO (20 mg, 0.080 mmol) was added to the solution. After stirring magnetically at room temperature for 1 h, the mixture was poured into brine. The organic layer was separated, and the remaining aqueous layer was extracted with CH_2Cl_2 (10 mL×2). After the organic layer and combined extracts were dried over anhydrous Na_2SO_4, the solvent was removed out by an evaporator. 3,4-Dihydro-9-pyrido[3,4-*b*]indole *N*-oxide[26] (122 mg, 33%) was obtained by silica-gel column chromatography (10 : 1 ethyl acetate/methanol) as yellow crystals.

Oxidation of *N*,*N*-Dibenzylhydroxylamine. *N*,*N*-Dibenzylhydroxylamine (400 mg, 1.88 mmol) was added to the oxidation solution (1.0 M H_2O_2/MeOH, 9.4 mL, 9.4 mmol), and MeOH (9.4 mL) was added to dissolve the hydroxylamine. Crystalline MTO (9.3 mg, 0.038 mmol) was added to the solution. After stirring for 30 min at room temperature, the resulting mixture was poured into brine, and then extracted with dichloromethane (10 mL×3). The combined extracts were dried over anhydrous $Na_2SO_4/MgSO_4$ (1 : 1 mixture); the solvent was then distilled out by an evaporator. The obtained white solid residue was almost pure *N*-benzylidenebenzylamine *N*-oxide (391 mg, 99%).

The oxidation of *N*,*N*-dibenzylhydroxylamine without MTO was also examine in the same oxidation solution (0.50 M H_2O_2/MeOH, 5 molar amounts). The ^1H NMR of the reaction mixture showed the formation of nitrone in 36% yield along with 64% unreacted hydroxylamine by a 1 h reaction.

General Procedure for Oxidation of Benzylamines. A typical reaction procedure (Table 4, Entry 1) is as follows: Benzylamine (193 mg, 1.80 mmol) was dissolved in the oxidation solution (1.0 M H_2O_2/*t*-BuOH, 10 mL, 10 mmol). Crystalline MTO (22 mg, 0.090 mmol) was added to the solution with stirring. MTO dissolved immediately along with a change in the color of the solution to yellow. The temperature of the solution first rose, and then fell within 5 min. The reaction mixture was stirred at room temperature for 30 min. The resulting mixture was poured into brine, and the products were extracted with dichloromethane (10 mL×3). Benzaldehyde oxime (192 mg, 88%) was isolated by silica-gel column chromatography (dichloromethane as the eluent).

The obtained oximes (Table 4) were known compounds, and were identified by a comparison of the physical data with authentic samples that were prepared separately by a condensation of the corresponding aldehydes or ketones with hydroxylamine.

Oxidation of Cyclohexylamine. Cyclohexylamine (190 mg, 1.92 mmol) was dissolved in the oxidation solution (1.0 M H_2O_2/CH_3CN, 9.6 mL, 9.6 mmol), and crystalline MTO (24 mg, 0.096 mmol) was added to the solution with stirring. MTO dissolved immediately along with a change in the color of the solution to yellow, which disappeared within one minute. After the reaction mixture was stirred at room temperature for 15 min, extra MTO (0.024 g, 0.096 mmol) was added to the mixture. After stirring for an additional 15 min, the resulting mixture was poured into brine, and the products were extracted with dichloromethane (10 mL×3). After the combined extracts were dried over anhydrous $Na_2SO_4/MgSO_4$ (1 : 1 mixture), the solvent was distilled out by an evaporator. Column chromatography (silica-gel, dichloromethane as the eluent) of the white solid residue afforded nitrosocyclohexane dimer[36] (66 mg, 30%) first, and then cyclohexanone oxime[27] (148 mg, 63%).

Synthesis of Cyclohexanone Oxime. Cyclohexylamine (335 mg, 3.38 mmol) was dissolved in the oxidation solution (1.0 M H_2O_2/CH_3CN, 17 mL, 17 mmol), and crystalline MTO (42 mg, 0.17 mmol) was added. After 15 min of stirring at room temperature, MTO (42 mg, 0.17 mmol) was added to the mixture again. After stirring for an additional 15 min, the resulting mixture was treated as described above. A white-solid residue obtained was dissolved in 100 mL of hexane; then triethylamine (0.56 mL, 4.1 mmol) was added. The mixture was refluxed for 10 h. The solvent was distilled out by an evaporator, and the obtained white-solid residue was dried under a vacuum. A ^1H NMR analysis of the solid indicated the presence of no nitroso dimer. Column chromatography on silica-gel with dichloromethane as the eluent afforded cyclohexanone oxime (284 mg, 74%).

Oxidation of Decylamine. Decylamine (229 mg, 1.46 mmol) was dissolved in the oxidation solution (1.0 M H_2O_2/*t*-BuOH, 7.3 mL, 7.3 mmol). Crystalline MTO (18 mg, 0.073 mmol) was added to the solution with stirring. MTO dissolved immediately along with a change in the color of the solution to yellow, which disappeared within 5 min. After the reaction mixture was stirred at room temperature for 15 min, extra MTO (18 mg, 0.073 mmol) was added to the mixture. After stirring for an additional 15 min, the resulting mixture was poured into brine, and the products were extracted with dichloromethane (10 mL×3). The combined extracts were dried over anhydrous $Na_2SO_4/MgSO_4$ (1 : 1 mixture), and then the solvent was distilled out by an evaporator. Column chromatography (silica-gel, dichloromethane as the eluent) of the reddish oil afforded 1,1′-azoxydecane (112 mg, 47%) first, then 1-nitrosodecane dimer[27] (27 mg, 11%), and finally *n*-decanal oxime[27] (69 mg, 38%).

Azoxy-1,1′-decane: Oil; IR (neat) 2960, 2930, 2850, 1508, 1465, 1320, 720 cm^{-1}; ^1H NMR ($CDCl_3$) δ = 0.7—1.0 (m, 6H), 1.0—2.2 (m, 32H), 3.40 (t, J = 6.8 Hz, 2H), 4.15 (t, J = 7.0 Hz, 2H); ^{13}C NMR ($CDCl_3$) δ = 14.11, 22.71, 26.40, 27.15, 27.87, 29.03, 29.30, 29.36, 29.42, 29.51, 29.63, 31.95, 52.12, 69.73. Found: C, 73.39; H, 12.70; N, 8.28%. Calcd for $C_{20}H_{42}N_2O$: C, 73.56; H, 12.96; N, 8.58%.

Oxidations of 2-phenylethylamine and 3-phenylpropylamine

were performed in a same manner, except that MTO was added all at once. 1-Nitroso-2-phenylethane dimer,[34] 1,1′-azoxybis(2-phenylethane),[34] 2-phenylacetaldehyde oxime,[37] and 3-phenylpropanal oxime[38] were identified by a comparison of the physical data with the literature results.

1-Nitroso-3-phenylpropane Dimer: Mp 54—56 °C; IR (KBr) 1605, 1497, 1455, 1385, 1342, 1275, 1220, 1210, 1030, 910, 752, 702 cm^{-1}; ^1H NMR ($CDCl_3$) δ = 1.9—2.4 (m, 4H), 2.67 (t, J = 6.8 Hz, 4H), 4.22 (t, J = 7.1 Hz, 4H), 6.9—7.4 (m, 10H); ^{13}C NMR ($CDCl_3$) δ = 26.46, 32.76, 58.27, 126.32, 128.41, 128.56, 140.17. Found: C, 75.50; H, 7.51; N, 9.10%. Calcd for $C_{18}H_{22}N_2O_2$: C, 72.46; H, 7.43; N, 9.39%.

1,1′-Azoxybis(3-phenylpropane): Oil; IR (neat) 3050, 3030, 2930, 2860, 1605, 1500, 1456, 1438, 1320, 1170, 1030, 745, 700 cm^{-1}; ^1H NMR ($CDCl_3$) δ = 1.8—2.5 (m, 4H), 2.5—2.9 (m, 4H), 3.44 (t, J = 6.8 Hz, 2H), 4.17 (t, J = 6.8 Hz, 2H), 7.0—7.5 (m, 10H); ^{13}C NMR ($CDCl_3$) δ = 28.70, 29.30, 32.55, 33.92, 51.44, 68.80, 125.90, 126.26, 128.38, 128.47, 128.53, 140.40, 141.60. Found: C, 76.55; H, 7.91; N, 9.76%. Calcd for $C_{18}H_{22}N_2O$: C, 76.56; H, 7.85; N, 9.92%.

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