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# Mechanistic Studies on Nitrosation–Deaminocyclization of Mono-Carbamoylated Vicinal Amino Alcohols and Diols: A New Preparative In Situ Formation of Ethanediazo Hydroxide for the Ethylation of Carboxylates under Mild Conditions

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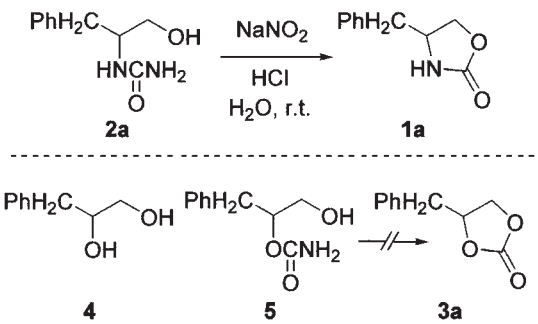
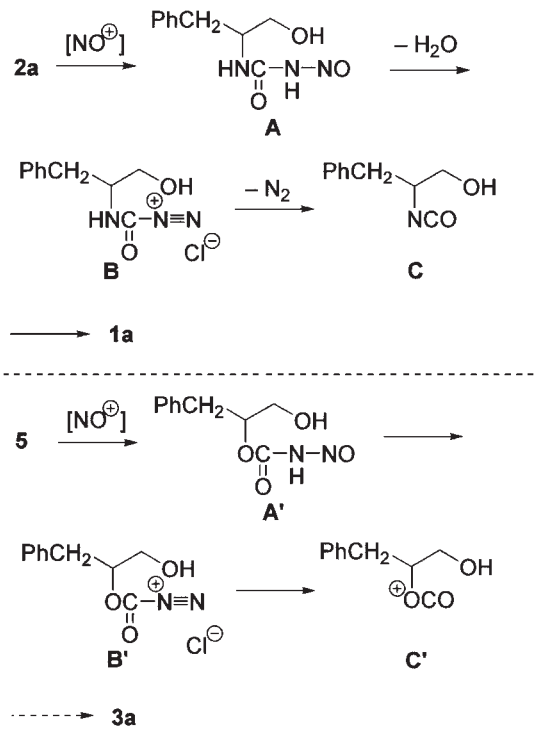
While the cyclization of *N*-carbamoylamino alcohols into oxazolidinones via the activation with $NO^+$ underwent smoothly, we found that similar reactions of vicinal diol monocarbamates were very slow. Mechanistic studies by means of time-resolved IR measurements of the former reaction suggested that the initial *O*-nitrosation was the rate-determining step. Indeed, the introduction of an ethyl group on the nitrogen terminus of diol monocarbamate promoted the desired cyclic carbonate formation. The concomitantly formed ethanediazo hydroxide, the precursor of the protonated form of diazoethane, was evidenced by trapping with *p*-nitrobenzoic acid as an ethyl ester. The formation of ethyl ester accelerates the reaction in an irreversible manner. Based on an elaboration of the substrates and reaction conditions, 2,3-dimethyl-2,3-butanediol mono-*N*-ethyl-*N*-nitrosocarbamate, which is easily prepared in situ from the corresponding ethylcarbamate and *t*-butyl nitrite, was developed as a new ethylation reagent of various carboxylic acids under mild conditions.

Recently, we proposed a new method for the preparation of oxazolidinone by the nitrosation–deaminocyclization of a readily available precursor, *N*-carbamoylated vicinal amino alcohol.[1,2] Upon treatment of substrate **2a** with $NaNO_2$ (1.0 eq.) in 2 M HCl, the reaction was completed within a couple of minutes at room temperature to give **1a** in 99% yield (Scheme 1).

By a simple analogy with the oxazolidinone formation, we extended the reaction conditions for a possible formation of cyclic carbonate **3a** from vicinal diols **4**[3] via the presumed intermediate, mono-carbamoylated form **5**. The reaction, however, was very slow, and only resulted in decomposition of **5** into the diol (**4**, Scheme 1). We therefore became interested in the contrasting reactions of **2a** and **5**. In the successful nitrosation–deaminocyclization of **2a**, the supposed reaction pathway would include the nitrosation on the terminal amino group of **A** and the subsequent dehydration to give an $\alpha$-oxo diazonium salt (**B**, Scheme 2). The release of a molecular nitrogen would provide an isocyanate **C**, which in turn would be intramolecularly attacked by the neighboring hydroxy group. The possible




Scheme 1.




Scheme 2.

intermediates from mono-carbamates **5** to **3a** corresponding to the above-mentioned path (**2a** to **1a** via **A**, **B**, and **C**) are **A′**, **B′**, and **C′**, respectively (Scheme 2). A mechanistic analysis of the pathway from **2a** to **1a** would help towards understanding the failure of the analogous **5**, and we embarked upon in situ detection of the intermediates by time-resolved IR measurements.

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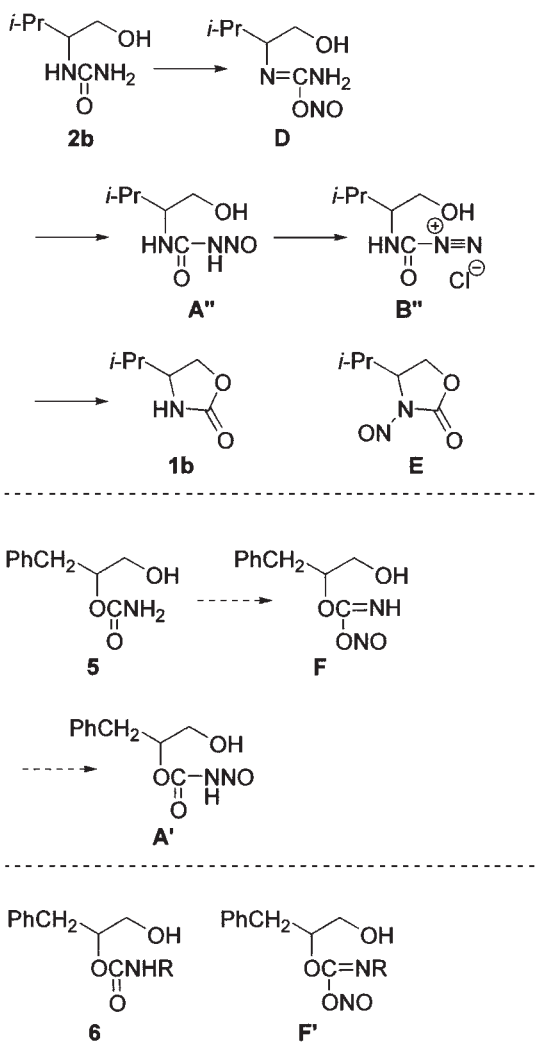
## Results and Discussion

The results of the above IR measurements can be explained as in Scheme 3 based on these observations of the intensity changes. For this purpose, we chose another good substrate, **2b**, (Scheme 3), whose increased solubility meets the criterion for the reaction to proceed in the aqueous homogeneous solution with a better S/N, without employing any organic co-solvents. Indeed, the spectrum (p, 0 s) is that of the starting material **2b** in aqueous HCl; N–H bending vibration bands (p-1, 1560; p-2, 1651 $cm^{-1}$) as well as a carbonyl stretching vibration band (p-3, 1683 $cm^{-1}$) are clearly shown in Fig. 1.

The first step from **2b** was the *O*-nitrosation to give **D**, as has been previously proposed.[4] In the IR spectrum, after the addition of $NaNO_2$, (q, 1.5 s), two strong absorption bands (q-1, 1597; q-2, 1629 $cm^{-1}$) were newly observed, and the former was attributed to *cis*-O–N=O.[5] The C=O stretching vibration band that is characteristic in *N*-nitrosourea (ca. 1700 $cm^{-1}$)[6] was not observed; instead, q-2 suggested the existence of the C=N double bond. Another high wavenumber band (q-3, 1908 $cm^{-1}$) was supposed to be attributed to the $\alpha$-oxo diazonium salt, whose carbonyl group was directly attached to a strongly electron-withdrawing group. The rate-determining




Scheme 3.

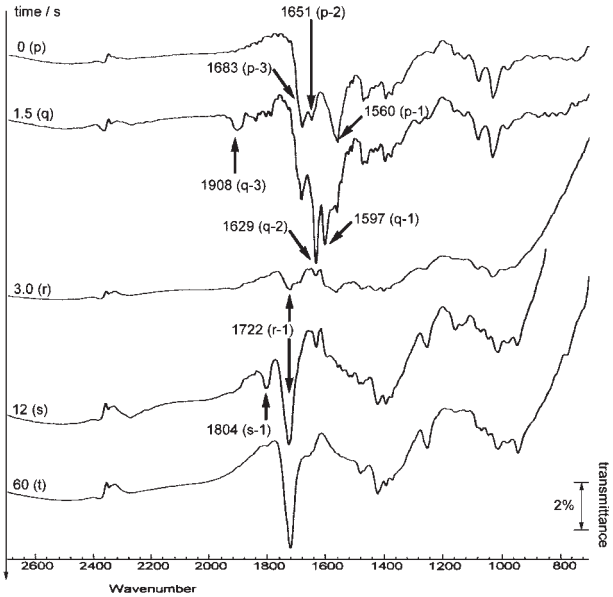


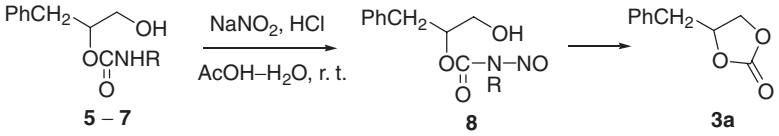

Fig. 1.

step was the migration of the nitroso group from oxygen to the terminal nitrogen atom **A″**, and the ensuing dehydration is very fast to give the $\alpha$-oxo diazonium salt **B″**. The intensities of these bands gradually decreased and the carbonyl C=O stretching band of the final product [r (3 s): r-1] started to appear at 1722 $cm^{-1}$. There was no positive evidence for the formation of the isocyanate (ca. 2250 $cm^{-1}$). Overnitrosation of the oxazolidinone was clearly observed by the action of $NaNO_2$, as shown in the spectrum [s (12 s): s-1, 1804 $cm^{-1}$; C=O]. An independent experiment revealed that *N*-nitrosyloxazolidinone **E** itself acted as the nitrosating reagent against **2b**, releasing $NO^+$ in a reversible manner.[7] When a 1:1 mixture of **E** and **2b** was incubated together, both were converged to **1b**. Finally, the observed intermediates were converged into the final product **1b** (t, 60 s). The above results suggested the importance of the nitrosation of the carbonyl oxygen atom of **2b** to **D**.

Accordingly, the reason for the very low reactivity of the mono-carbamoylated form **5** of the diol **4** was considered to be the lowered nucleophilicity of **5** (Scheme 3) as well as the very slow migration from **F** to **A′** as a result of the replacement of the internal nitrogen atom in **2a** with a more electron-withdrawing oxygen atom in **5**. The idea to overcome this situation was to introduce an alkyl group (**6**) to the terminal nitrogen atom of **5**, which would compensate the lowered nucleophilicity, and thus the desired intermediate **F′** would be provided. Another advantage is the increased stability of *N*-alkylated forms of *N*-nitroso carbamates.[8]

Toward this end, a variety of carbamoyl derivatives (**5**, **6a**, **7a–c**) was subjected to the nitrosation conditions with $NaNO_2$–HCl–$H_2O$–AcOH (Table 1). Gratifyingly, the introduction of a terminal alkyl group was turned out to be quite effective. The desired nitrosation followed by cyclization was observed when an ethyl group[9] was present (**6a**), giving the yield of 57% (entry 2). In the case of an isopropyl group (**7a**, entry 3) and a *t*-butyl group (**7b**, entry 4), the nitrosation itself proceeded as with the ethylcarbamate **6a** to give the corresponding *N*-nitroso compounds **8**, however, the subsequent cyclization was

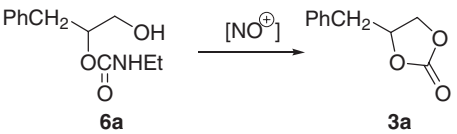
Table 1. The Attempts for the Nitrosation–Deaminocyclization Reactions on Diol Mono-carbamates




| Entry | Substrate | R | Product (**3a**/%) | Recovery /% | *N*-Nitroso compound (**8**/%) |
|---|---|---|---|---|---|
| 1 | **5** | H | 0[a)] | 48 | — |
| 2 | **6a** | Et | 57 | 24 | 0 |
| 3 | **7a** | *i*-Pr | 0 | 61[b)] | 37[b)] |
| 4 | **7b** | *t*-Bu | 0 | 51[b)] | 46[b)] |
| 5 | **7c** | Ph | 0 | quant. | 0 |

a) Decomposed to **4** (31%). b) See experimental.

Table 2. The Conditions for the Nitrosation–Deaminocyclization of Diol Mono-Ethyl-carbamate (**6a**)



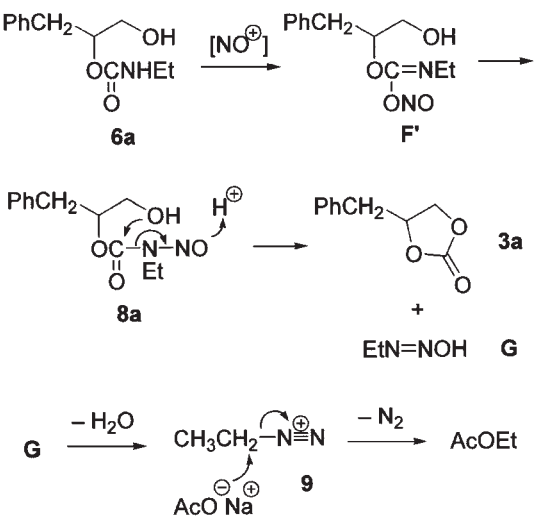

| Entry | Reagents | Proton source | Solvent | Temp. /°C | Time /h | Yield /% | Recovery (**6a**/%) |
|---|---|---|---|---|---|---|---|
| 1 | $NaNO_2$ | HCl | $AcOH/H_2O$ | r.t. | 0.5 | 57 | 24 |
| 2 | $NaNO_2$ | — | $AcOH/Ac_2O$ | r.t. | 1.5 | 4 | 0 |
| 3 | *t*-BuONO | — | DMF | r.t. → 50 | 15 | 42 | 25 |
| 4 | $HSO_3ONO$ | — | DMF | 0 → 50 | 5 | 35 | 18 |
| 5 | $NaNO_2$–MS3A | — | AcOH | r.t. → 50 | 15 | 84 | 0 |

slow. The reaction resulted in a mixture of the desired compounds and the starting materials. There is a report that the steric hindrance promoted the decomposition of *N*-nitroso compounds in a manner that gave the alkyl carbonate, $H_2O$, and $N_2$.[10] In our case, however, no such side reaction was the case, as judged from these results. Compared with the ethylcarbamate, the accumulation of nitrosated intermediates is consistent with those increased stability values, due to an increased electron-donating property.[8]

Phenylcarbamate, which had previously been reported as a readily cleavable protective group via nitrosation,[11] to our disappointment, showed no reactivity, presumably due to the lowered nucleophilicity being lowered by the delocalization of the lone pair electron into the aromatic ring.

We next further elaborated the cyclization condition on ethylcarbamate (**6a**, Table 2). Although acetic acid ($pK_a$ 4.76, in $H_2O$) itself worked as the proton source for the generation of nitrous acid ($pK_a$ ca. 3.2 in $H_2O$) as well as the promotor in the subsequent steps (entry 2), the yield turned extremely low. Non-aqueous conditions were also attempted. The use of *t*-BuONO/DMF (entry 3) or $HO_3SONO$/DMF[12] (entry 4) only gave a moderate yield (ca. 40%) of the desired products along with a substantial recovery of the unreacted starting material.

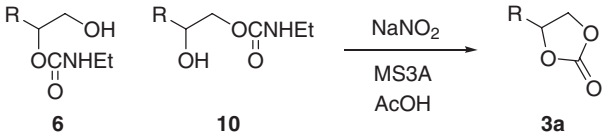
We carefully examined the reaction pathway as shown in Scheme 4. As we mentioned earlier, the initially formed *O*-nitroso derivative **F′** would rearrange to the *N*-nitroso compound **8a**. The desired cyclization reaction proceeds at the stage of **8a**

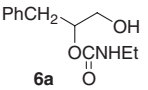
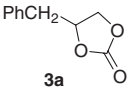
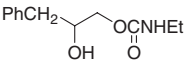
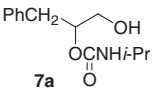
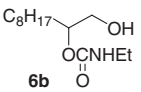
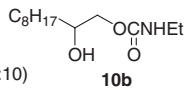
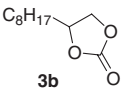
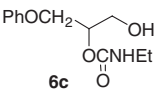
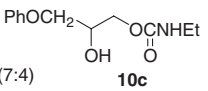
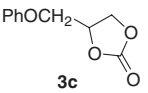
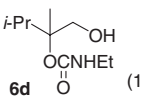
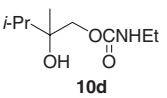
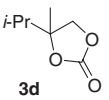
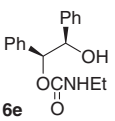
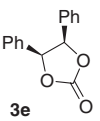
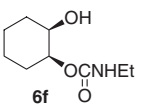
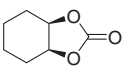
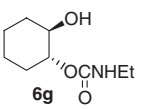
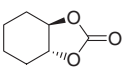
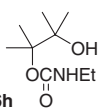
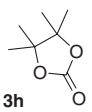
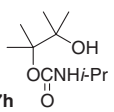



Scheme 4.

concomitantly to afford ethanediazo hydroxide (**G**). This unstable intermediate loses one $H_2O$ molecule to the protonated form of diazoethane (**9**). The competing reaction is the attack of an $H_2O$ molecule, which is formed as above even under the initial anhydrous condition, onto the nitroso group to provide the starting material **6a**. This prompted us to add molecular sieves 3A to remove $H_2O$ from the reaction system. Gratifyingly, the yield rose to as high as 84% when the reaction was

Table 3. Nitrosation–Deminocyclization of Diol Mono-Ethylcarbamates




| Entry | Substrates | Product | Time[a)]/h | Yield/% |
|---|---|---|---|---|
| 1 |  **6a** |  **3a** | 15[b)] | 84 |
| 2 |  **10a** | **3a** | 15 | 77 |
| 3 | **6a** + **10a** (5:4) | **3a** | 15 | 80 |
| 4 |  **7a** | **3a** | 15 | 59 |
| 5 |  **6b** (9:10)  **10b** |  **3b** | 15 | 90 |
| 6 |  **6c** (7:4)  **10c** |  **3c** | 15 | 90 |
| 7 |  **6d** (1:3)  **10d** |  **3d** | 15 | 72 |
| 8 |  **6e** |  **3e** | 15 | 72 |
| 9 |  **6f** |  **3f** | 15 | 65 |
| 10 |  **6g** |  **3g** | 15 | 60 |
| 11 |  **6h** |  **3h** | 15[c)] | 88 |
| 12 |  **7h** | **3h** | 20[c)] | 89 |

a) The reaction was carried out at 80 °C. b) At 50 °C. c) At r.t.

performed at a higher temperature of 50 °C. We could not recover any trace of the starting material or specific by-products such as ethyl carbonate[10] of the parent diol; the loss of such material is probably due to the formation of some unknown strongly polar material.

Encouraged by these results, we submitted a number of diol mono-ethylcarbamates to the reaction conditions (Table 3). From the regioisomeric starting material **10a**, with a liberated secondary alcohol, the cyclic carbonate **3a** was obtained in a similar yield (77%, entry 2). There was no significant difference between the reactions of the primary (**6a**, entry 1) alcohols and those of the secondary (**10a**, entry 2) alcohols. Accordingly, a mixture of monocarbamates **6a** and **10a** (5:4), which was non-selectively prepared from diol **4**, was effectively transformed to cyclic carbonate (entry 3). The corresponding *N*-isopropyl derivative **7a** also underwent the cyclization, with a lower yield (59%, entry 4). Aliphatic (**6b** + **10b**) and aryloxy-substituted (**6c** + **10c**) ethylcarbamates were very good substrates (entries 5 and 6). A carbamate mixture with one tertiary hydroxy derivative (**6d** + **10d**, 1:3) also cyclized to give carbonate **3d** in 72%.

A series of mono-ethylcarbamoylated diols with symmetric substituents (**6e**–**6h**, entries 8–11) were then submitted to the reaction, and their cyclization successfully proceeded. No difference was observed between the rates of cyclization in the two conformationally fixed cyclohexane-1,2-diol mono-ethylcarbamates **6f** (*cis*) and **6g** (*trans*) and the reaction temperature as high as 80 °C was required. To our surprise, mono-ethylcarbamate **6h** of 2,3-dimethyl-2,3-butanediol (pinacol), a structurally very hindered tertiary alcohol, promptly cyclized even at room temperature (entry 11) in 88% yield. Also, the reaction of the corresponding isopropylcarbamate (**7h**, entry 12) was very fast. The unexpectedly high reactivity is supposed to be due to the beneficial effect of the electron-donating property of tertiary alcohol, as well as the preferred conformation in the precursor **6h**, of which an intramolecular hydrogen bonding

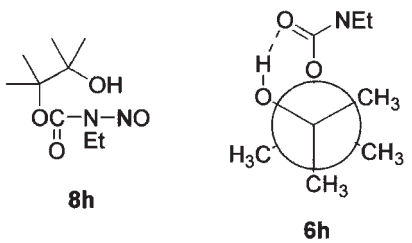



Fig. 2.

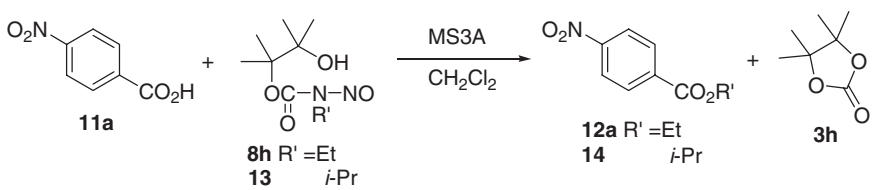
was observed by $^1$H NMR as shown in Fig. 2.

Again we return to Scheme 4. The cyclization proceeds with an equimolar formation of ethanediazo hydroxide **G**. The resulting protonated form of diazoethane (**9**) was trapped by the reaction with acetic acid, which was added as the solvent, and this final irreversible step is one of the promoters of this total reaction. As this reaction seems to be a new approach of diazoethane,[13] then the trap of this species was attempted by the replacement of acetic acid by *p*-nitrobenzoic acid (Table 4). As expected, the cyclization reaction by the combined use of *p*-nitrobenzoic acid (**11a**) and the isolated form of *N*-ethyl-*N*-nitrosocarbamate **8h** proceeded and the ethyl ester **12a** was obtained (entry 1); as this material is the evidence of the formation of ethanediazo hydroxide (**G**). The yield of ester **12a** was further enhanced by increasing the equivalent of the nitrosocarbamate (3.0) to as high as 93%. As suggested from the fact that the cyclization of the corresponding *N*-isopropyl-*N*-nitrorocarbamate also worked well (Table 3, entry 12), 1-methylethanediazo hydroxide, as the protonated form of 2-diazopropane,[14] would be an intermediate. Indeed, the reaction proceeded; however, it was slow and the yield was low (32%, entry 3). This result is in accordance with the previously reported, low reactivity of 2-diazopropane and its unstable nature, to which makes it easily undergo dimerization into 2,3-dimethyl-2-butene.[15]

The ethyl ester is enzymatically cleavable in our body, but there is a large difference from the corresponding methyl ester. The ethyl ester is substantially resistant to chemical and enzyme-catalyzed hydrolysis,[16] and there are some successful examples of its use as a drug precursor such as oseltamivir phosphate.[17] The ethylation under mild conditions is, accordingly, a very important method for derivatization of carboxylic acids. The so-far developed reaction conditions prompted us to apply in situ formed *N*-ethyl-*N*-nitrosocarbamate **8h**, by a combination of carbamate **6h** and *t*-BuONO in 1,2-dichloroethane in the presence of MS3A, for the ethylation of carboxylates and related substances as summarized in Table 5.

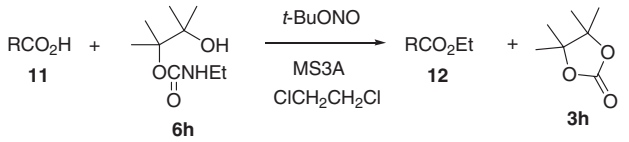
A heteroaromatic substrate (**11b**, entry 2) worked well (99%). The ethylation of an $\alpha$-heteroatom-substituted carboxylic acid (**11c**, entry 3), which is prone to racemization under either acidic or basic conditions,[18] proceeded smoothly (98%) without any loss of the enantiomeric purity. The reaction was also successful on the Boc-protected amino acid derivative **11d** (entry 4, quantitative). Even in the case that the protected form retains a liberated NH such as NHAc group (**11e**, entry 5), there was decomposition of neither the starting material nor the product via the nitorosation on the nitrogen atom by the action

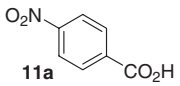
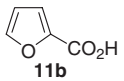
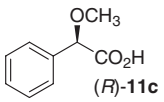
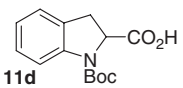
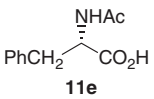
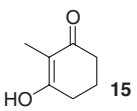
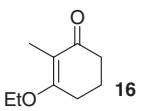
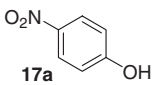
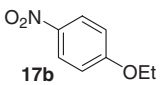
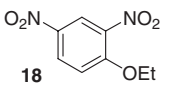
Table 4. The Reaction Conditions of Esterification with Nitrosocarbamates




| Entry | Reagent (eq.) | Temp. | Time/h | Product | Yield/% |
|---|---|---|---|---|---|
| 1 | **8h** (1.1) | r.t. | 15 | **12a** | 42 |
| 2 | **8h** (3.0) | r.t. | 15 | **12a** | 93 |
| 3 | **13** (3.0) | r.t. → reflux | 36 | **14** | 32 |

Table 5. Ethyl Ester Formation with Ethylcarbamate and *t*-BuONO and Related Reactions




| Entry | Substrates[a)] | *t*-BuONO/eq. | Temp/°C | Time/h | Product | Yield/% |
|---|---|---|---|---|---|---|
| 1[b)] |  | 3.3 | 45 | 12 | **12a** | 95 |
| 2 |  | 3.3 | 60 | 12 | **12b** | 99 |
| 3 |  | 3.3 | 60 | 12 | **12c** | 98 |
| 4 |  | 3.3 | 60 | 12 | **12d** | quant. |
| 5 |  | 3.3 | 60 | 12 | **12e** | quant. |
| 6 | $CH_3(CH_2)_{16}CO_2H$ **11f** | 4.5 | 105 | 12 | **12f** | quant. |
| 7 |  | 4.5 | 80 | 36 |  | 42 |
| 8 |  | 4.5 | 95 | 48 |  | 58 |
| | | | | |  | 21 |

a) Three molar equivalents of **6a** were applied throughout the experiments. b) $CH_2Cl_2$ was used as the solvent.

of excessively used *t*-BuONO. The reaction of aliphatic fatty acid **11f** (entry 6) was slow, but elevated reaction temperature (105 °C) overcame the low reactivity to obtain a good yield (quantitative). As we experienced in the case of **11f**, we became interested in the relationship between the Brønsted acidity and the reactivity. Then two different types of compounds other than carboxylic acid, 2-methylcyclohexane-1,3-dione (mostly enol form **15**, entry 7) and *p*-nitrophenol (**17a**, entry 8), both of them weakly acidic, were submitted to the reaction. Although the yield of the ethylation products was not so high (**16**: 42%; **17b**: 58%), we could prove that those compounds worked as the proton donors and that the conjugated Brønsted base reacted as the nucleophile towards the protonated form of diazoethane (**9**). In the case of the nitrophenol, *ortho*-nitrosation and oxidation increased the reactivity to provide a by-product **18** in 21% yield, prior to the ethylation of the starting material.

## Conclusion

We were inspired by the initial formation of *O*-nitroso compounds from the *N*-carbamoylamino alcohol observed in the time-resolved IR measurement. Our elaboration of the intermediates and reaction conditions enabled a cyclic carbonate formation from 1,2-diols via nitrosation as the key step. From

the mono-ethylcarbamate of 2,3-dimethyl-2,3-butanediol, the cyclization was very fast, and the concomitantly in situ-formed ethanediazo hydroxide worked well as the ethylation reagent of carboxylic acids.

## Experimental

Analytical and preparative thin-layer chromatography (TLC) were developed on Silica-gel 60 $F_{254}$ plates (E. Merck No. 5715; 0.25 mm and 5744; 0.50 mm, respectively). Column chromatography was performed on Silica-Gel 60 (Kanto Chemical Co., Inc., spherical; 100–210 μm, 37558-79). NMR spectra were measured on a JEOL EX-270, GX-400 spectrometer ($^1$H at 270, 400 MHz and $^{13}$C at 100 MHz). $^1$H chemical shifts are referenced at 7.26 ppm and $^{13}$C chemical shifts at 77.0 ppm with $CDCl_3$. IR spectra except for time-resolved measurements were carried out on a Jasco FT/IR-410 spectrometer. Optical rotations were measured on a Jasco DIP 360 polarimeter. HRMS were recorded on Hitachi M-80B spectrometer at 70 eV. HPLC data were recorded on Jasco PU-2080Plus and FP-920 liquid chromatographs. All melting points were measured with a Yanaco MP-S3 and are uncorrected.

**Cyclization of 2-Ureido-3-methyl-1-butanol (2b) to 4-Isopropyl-1,3-oxazolidin-2-one (1b): Time-Resolved IR Measurements.** All of the time-resolved infrared spectroscopic measurements were performed using a Fourier transform infrared spectrometer, BIO-RAD FTS-60A/896, which was equipped with a liquid $N_2$-cooled MCT detector and an attenuated total reflection (ATR) attachment (circle) in the sample position. The time resolution in these IR measurements (rapid scanning method) was 0.11 second per spectrum and the wavenumber resolution was 8 $cm^{-1}$. The background spectrum was measured by filling the sample circle cell with 2 M HCl solution.

To a 0.41 M *N*-carbamoylamino alcohol (**2b**) in 2 M HCl solution in the circle cell was added saturated aqueous $NaNO_2$ solution; this moment was defined as time zero. The results are shown in Fig. 1. Spectra (p) to (t) correspond to those after the exposure time of zero to 60 seconds, respectively.

**Overnitrosation of 4-Isopropyl-1,3-oxazolidin-2-one (1b) and the Reaction with 2-Ureido-3-methyl-1-butanol (2b).** To a solution of oxazolidinone (**1b**, 349 mg, 2.70 mmol) in 2 M HCl (6.0 mL) was added $NaNO_2$ (374 mg, 5.41 mmol) at 0 °C. After the reaction mixture was stirred at 0 °C for 5 min, it was extracted with $CHCl_3$ four times. The combined organic layer was dried over $Na_2SO_4$ and concentrated in vacuo to give the nitroso compound (**E**, 383 mg, 90% yield). $^1$H NMR (400 MHz, $CDCl_3$) $\delta$ 4.44–4.30 (m, 3H), 2.22 (m, 1H), 0.88 (d, 3H, $J = 6.8$ Hz), 0.82 (d, 3H, $J = 6.8$ Hz); IR (film) 3021, 2971, 1805, 1521, 1485, 1383, 1216, 1149, 754, 668 $cm^{-1}$; MS $m/z = 159$ ($M^+ + H$); HRMS $m/z = 159.0778$ ($M^+ + H$, Calcd for $C_6H_{11}N_2O_3$: 159.0769).

To a suspension of nitroso compound as above (**E**, 116 mg, 0.74 mmol) in 2 M HCl (5.0 mL) was added *N*-carbamoylamino alcohol (**2b**, 108 mg, 0.74 mmol). After being stirred at room temperature for 5 min, the reaction mixture was saturated with NaCl and extracted with AcOEt three times. The combined organic layer was dried over $Na_2SO_4$ and concentrated in vacuo to give **1b** (176 mg, 93% yield based on **E** + **2b**). $^1$H NMR (400 MHz, $CDCl_3$) $\delta$ 6.77 (br s, 1H), 4.45 (t, 1H, $J = 8.8$ Hz), 4.10 (dd, 1H, $J = 6.3$, 8.8 Hz), 3.62 (m, 1H), 1.73 (m, 1H), 0.97 (d, 3H, $J = 6.8$ Hz), 0.90 (d, 3H, $J = 6.3$ Hz); IR (KBr) 3270, 2961, 1750, 1726, 1472, 1406, 1362, 1247, 1091, 1050, 1010 $cm^{-1}$. $^1$H NMR and IR spectra were identical with those previously reported.[1]

**Preparation of *N*-Substituted Carbamates. 1-Hydroxymethyl-2-phenylethyl Ethylcarbamate (6a) and 2-Hydroxy-3-phenylpropyl Ethylcarbamate (10a):** To a solution of 3-phenylpropane-1,2-diol (207 mg, 1.30 mmol) in $CH_2Cl_2$ (4.0 mL) was added ethyl isocyanate (0.16 mL, 1.98 mmol); then the mixture was refluxed overnight. After cooling to room temperature, the reaction mixture was concentrated in vacuo. The residue was purified by silica-gel column chromatography [hexane–AcOEt (1:1) to AcOEt only]. Preparative TLC [hexane–AcOEt (2:3)] afforded **6a** (34 mg, 12%) and **10a** (93 mg, 32%). **6a**: $R_f = 0.33$ [hexane–AcOEt (2:3)]; $^1$H NMR (400 MHz, $CDCl_3$) $\delta$ 7.26 (m, 5H), 4.98 (m, 1H), 4.73 (br s, 1H), 3.74 (dd, 1H, $J = 2.0$, 12.0 Hz), 3.60 (dd, 1H, $J = 5.9$, 12.0 Hz), 3.20 (m, 2H), 2.95 (dd, 1H, $J = 6.8$, 13.9 Hz), 2.88 (dd, 1H, $J = 7.3$, 13.9 Hz), 2.20 (br s, 1H), 1.12 (t, 1H, $J = 7.3$ Hz); IR (film) 3339, 2925, 1694, 1528, 1454, 1256, 1082, 1051, 701 $cm^{-1}$. HRMS $m/z = 224.1294$ ($M^+ + H$, Calcd for $C_{12}H_{18}NO_3$: 224.1286).

**10a**: $R_f = 0.36$ [hexane–AcOEt (2:3)]; $^1$H NMR (400 MHz, $CDCl_3$) $\delta$ 7.31 (m, 2H), 7.24 (m, 3H), 4.80 (br s, 1H), 4.19 (dd, 1H, $J = 2.2$, 11.0 Hz), 4.06 (m, 1H), 4.00 (dd, 1H, $J = 6.6$, 11.0 Hz), 3.23 (m, 2H), 2.83 (m, 2H), 2.29 (br s, 1H), 1.15 (t, 3H, $J = 7.3$ Hz); IR (film) 3339, 2975, 2936, 1698, 1537, 1454, 1258, 1086, 1027, 701 $cm^{-1}$. HRMS $m/z = 223.1221$ ($M^+$, Calcd for $C_{12}H_{17}NO_3$: 223.1207).

**1-Hydroxymethyl-2-phenylethyl Isopropylcarbamate (7a):** A silica-gel column chromatographic separation [hexane–AcOEt (1:1)] followed by a preparative TLC [hexane–AcOEt (1:1)] afforded **7a** as colorless oil. $R_f = 0.49$ [hexane–AcOEt (2:3)]; $^1$H NMR (400 MHz, $CDCl_3$) $\delta$ 7.25 (m, 5H), 4.97 (m, 1H), 4.68 (br s, 1H), 3.76 (m, 1H), 3.72 (m, 1H), 3.60 (m, 1H), 2.91 (m, 2H), 2.70 (br s, 1H), 1.11 (d, 6H, $J = 6.3$ Hz); IR (film) 3327, 2972, 1691, 1531, 1454, 1248, 1078, 700 $cm^{-1}$. HRMS $m/z = 238.1409$ ($M^+$, Calcd for $C_{13}H_{19}NO_3$: 238.1397).

**(*S*)-1-Hydroxymethyl-2-phenylethyl *t*-Butylcarbamate (7b):** A silica-gel column chromatographic separation [hexane–AcOEt (7:3) to hexane–AcOEt–MeOH (7:3:1)] afforded **7b** as colorless oil. $R_f = 0.21$ [hexane–AcOEt (7:3)]; $^1$H NMR (400 MHz, $CDCl_3$) $\delta$ 7.25 (m, 5H), 4.95 (m, 1H), 4.69 (br s, 1H), 3.72 (m, 1H), 3.58 (dd, 1H, $J = 5.6$, 12.0 Hz), 2.94 (dd, 1H, $J = 6.3$, 13.7 Hz), 2.87 (dd, 1H, $J = 7.3$, 13.7 Hz), 2.32 (br s, 1H), 1.29 (s, 9H); IR (film) 3342, 2966, 1699, 1537, 1506, 1456, 1269, 1211, 1090, 700 $cm^{-1}$. HRMS $m/z = 251.1498$ ($M^+$, Calcd for $C_{14}H_{21}NO_3$: 251.1520).

**1-Hydroxymethyl-2-phenylethyl Phenylcarbamate (7c):** A preparative TLC separation [hexane–AcOEt (7:8)] afforded **7c** as colorless oil. $R_f = 0.23$ [hexane–AcOEt (7:3)]; $^1$H NMR (400 MHz, $CDCl_3$) $\delta$ 7.35–7.20 (m, 9H), 7.06 (m, 1H), 6.80 (br s, 1H), 5.10 (m, 1H), 3.79 (dd, 1H, $J = 2.9$, 12.2 Hz), 3.65 (dd, 1H, $J = 5.9$, 12.2 Hz), 3.02 (dd, 1H, $J = 6.8$, 13.9 Hz), 2.95 (dd, 1H, $J = 7.3$, 13.9 Hz), 2.34 (br s, 1H); IR (film) 3313, 2927, 1705, 1601, 1541, 1444, 1225, 1063, 750, 698 $cm^{-1}$. HRMS $m/z = 273.1280$ ($M^+$, Calcd for $C_{16}H_{17}NO_3$: 273.1275).

**1-(Hydroxymethyl)nonyl Ethylcarbamate (6b) and 2-Hydroxydecyl Ethylcarbamate (10b):** A silica-gel column chromatographic separation [hexane–AcOEt (2:3)] afforded a mixture of **6b** and **10b**. $R_f = 0.38$ and 0.46 [hexane–AcOEt (2:3)]; $^1$H NMR (400 MHz, $CDCl_3$) $\delta$ 4.88 (br s, 0.47H), 4.81 (br s, 0.53H), 4.68 (m, 0.53H), 4.07 (dd, 0.47H, $J = 2.4$, 11.5 Hz), 3.86 (dd, 0.47H, $J = 7.3$, 11.5 Hz), 3.73 (m, 0.47H), 3.64 (dd, 0.53H, $J = 2.7$, 12.0 Hz), 3.52 (dd, 0.53H, $J = 6.6$, 12.0 Hz), 3.15 (m, 2H), 2.74 (br s, 1H), 1.47–1.19 (m, 14H), 1.08 (t, 3H, $J = 7.1$ Hz), 0.81 (t, 3H, $J = 6.8$ Hz). The ratio between **6b** and **10b** was estimated to be 10:9 by comparing the signals of **6b** (H-1 and H′-1: $\delta$ 3.64

and 3.52) with those of **10b** (H-1 and H′-1: $\delta$ 4.07 and 3.86). IR (film) 3334, 2925, 2856, 1695, 1539 $cm^{-1}$.

**1-Hydroxymethyl-2-phenoxyethyl Ethylcarbamate (6c) and 2-Hydroxy-3-phenoxypropyl Ethylcarbamate (10c):** A silica-gel column chromatographic separation [hexane–AcOEt (2:3) afforded a mixture of **6c** and **10c**. $R_f = 0.26$ and 0.35 [hexane–AcOEt (2:3)]; $^1$H NMR (400 MHz, $CDCl_3$) $\delta$ 7.28 (m, 2H), 6.94 (m, 3H), 5.09 (m, 0.64H), 4.88 (br s, 1H), 4.32 (dd, 0.36H, $J = 3.4$, 11.7 Hz), 4.25 (m, 0.36H), 4.20 (m, 0.36H), 4.15 (m, 0.64H), 4.01 (m, 1.64H), 3.91 (m, 1H), 3.23 (m, 2H), 2.60 (br s, 1H), 1.14 (t, 3H, $J = 7.3$ Hz). The ratio between **6c** and **10c** was estimated to be 7:4 by comparing the signal of **6c** (H-1: $\delta$ 5.09) with that of **10c** (H-2: $\delta$ 4.20). IR (film) 3344, 1699, 1599, 1531 $cm^{-1}$.

**1-Hydroxymethyl-1,2-dimethylpropyl Ethylcarbamate (6d) and 2-Hydroxy-2,3-dimethylbutyl Ethylcarbamate (10d):** A silica-gel column chromatographic separation [$CHCl_3$–MeOH (24:1)] afforded the mixture of **6d** and **10d**. $R_f = 0.22$ and 0.31 [$CHCl_3$–MeOH (24:1)]; $^1$H NMR (270 MHz, $CDCl_3$) $\delta$ 4.82 (br s, 1H), 4.07 (d, 0.75H, $J = 11.4$ Hz), 4.00 (d, 0.75H, $J = 11.4$ Hz), 3.71 (m, 0.5H), 3.31–3.14 (m, 2H), 2.33 (m, 1.25H), 1.82 (m, 0.75H), 1.26–1.09 (m, 6H), 0.97 (d, 3H, $J = 6.9$ Hz), 0.91 (d, 3H, $J = 6.8$ Hz). The ratio between **6d** and **10d** was estimated to be 1:3, by comparing the signal of **6d** (H-1′ and H′-1′: $\delta$ 3.71) with those of **10d** (H-1 and H′-1: $\delta$ 4.07 and 4.00). IR (film) 3338, 2974, 1697, 1537 $cm^{-1}$.

**(1*R**,2*S**)-2-Hydroxy-1,2-diphenylethyl Ethylcarbamate (6e):** Recrystallization from hexane–AcOEt twice afforded **6e** as colorless needles. $R_f = 0.51$ [hexane–AcOEt (2:3)]; mp 89.6–90.2 °C; $^1$H NMR (400 MHz, $CDCl_3$) $\delta$ 7.28 (m, 6H), 7.18 (m, 4H), 5.89 (d, 1H, $J = 4.9$ Hz), 5.03 (d, 1H, $J = 4.9$ Hz), 4.74 (br s, 1H), 3.17 (m, 2H), 2.52 (br s, 1H), 1.09 (t, 3H, $J = 7.1$ Hz); IR (KBr) 3357, 3276, 2974, 1691, 1545, 1454, 1271, 1024, 698, 586 $cm^{-1}$. HRMS $m/z$ = 286.1446 ($M^+$ + H, Calcd for $C_{17}H_{20}NO_3$: 286.1442).

**(1*R**,2*S**)-2-Hydroxycyclohexyl Ethylcarbamate (6f):** A silica-gel column chromatographic separation [hexane–AcOEt (2:3) to hexane–AcOEt–EtOH (4:6:1)] afforded **6f** as colorless oil. $R_f = 0.29$ [hexane–AcOEt (2:3)]; $^1$H NMR (400 MHz, $CDCl_3$) $\delta$ 4.84 (m, 2H), 3.87 (m, 1H), 3.23 (m, 2H), 2.39 (br s, 1H), 1.84 (m, 1H), 1.74–1.58 (m, 5H), 1.36 (m, 2H), 1.15 (t, 3H, $J = 7.3$ Hz); IR (film) 3342, 2937, 2866, 1695, 1537, 1448, 1259, 1082, 1009 $cm^{-1}$. HRMS $m/z$ = 188.1212 ($M^+$, Calcd for $C_9H_{17}NO_3$: 188.1178).

**(1*R**,2*R**)-2-Hydroxycyclohexyl Ethylcarbamate (6g):** A silica-gel column chromatographic separation [hexane–AcOEt–EtOH (50:50:3)] afforded **6g** as colorless oil. $R_f = 0.26$ [hexane–AcOEt (2:3)]; $^1$H NMR (400 MHz, $CDCl_3$) $\delta$ 4.75 (br s, 1H), 4.44 (m, 1H), 3.49 (m, 1H), 3.23 (m, 2H), 2.85 (br s, 1H), 2.05 (m, 2H), 1.70 (m, 2H), 1.39–1.21 (m, 4H), 1.15 (t, 3H, $J = 7.1$ Hz); IR (film) 3334, 2937, 2862, 1693, 1537, 1452, 1257, 1080, 1032 $cm^{-1}$. HRMS $m/z$ = 187.1200 ($M^+$, Calcd for $C_9H_{17}NO_3$: 187.1207).

**2-Hydroxy-1,1,2-trimethylpropyl Ethylcarbamate (6h):** To a solution of pinacol (3.00 g, 25.1 mmol) in DMF (10.0 mL) was added ethyl isocyanate (2.00 mL, 25.1 mmol). After stirring at room temperature overnight, $H_2O$ (5.0 mL) followed by $NaIO_4$ (5.98 g, 28.0 mmol) were added at 0 °C. The mixture was stirred at room temperature overnight and then extracted with AcOEt three times. The combined organic layer was washed with $H_2O$ and brine, dried over $Na_2SO_4$, and concentrated in vacuo to give crude product. Kugelrohr distillation (122 °C/2.4 mmHg) afforded **6h** as colorless oil (3.47 g, 73% yield). $^1$H NMR (400 MHz, $CDCl_3$) $\delta$ 5.63 (br s, 1H), 5.04 (br s, 1H), 4.43 (m, 2H), 1.20 (s, 6H), 0.96 (s, 6H), 0.90 (t, 3H, $J = 7.3$ Hz); $^{13}$C NMR (100 MHz, $CDCl_3$) $\delta$ 156.5, 87.4, 74.1, 35.3, 25.0, 22.3, 14.7; IR (film) 3327, 2983, 2939, 1682, 1537, 1377, 1275, 1163, 1115, 995, 957 $cm^{-1}$. Anal. Calcd for $C_9H_{19}NO_3$: C, 57.12; H, 10.12; N, 7.40%. Found: C, 56.89; H, 9.93; N, 7.69%.

When the above $NaIO_4$-mediated degradation of the unreacted starting material omitted and the reaction mixture was extracted with ether three times, an alternative preparative method was provided. In this case, the major product **6h** was distilled (105 °C/2.4 mmHg) in the yield of 45–50%, however, the distillate contained pinacol (ca. 10%) and the corresponding biscarbamate (8–10%). Due to the very close $R_f$ values [**6h**: $R_f = 0.60$, biscarbamate: $R_f = 0.64$, hexane–AcOEt (2:3)] and the very viscose nature of **6h** at room temperature; the authors recommend the following procedure: the remaining pinacol should be removed by pre-treatment with $NaIO_4$ and the subsequent fractional distillation of the desired product from the biscarbamate.

**2-Hydroxy-1,1,2-trimethylpropyl Isopropylcarbamate (7h):** The reaction between pinacol and isopropyl isocyanate in the same manner as described for **6h**, and subsequent silica-gel column chromatographic separation [hexane–AcOEt (7:3) to hexane–AcOEt–EtOH (70:30:3)], afforded **7h** (70% yield). Kugelrohr distillation (115 °C/1.7 mmHg) provided a colorless solid. Mp 41.6–41.8 °C; $^1$H NMR (400 MHz, $CDCl_3$) $\delta$ 5.02 (br s, 1H), 4.63 (br s), 3.78 (m, 1H), 1.43 (s, 6H), 1.19 (s, 6H), 1.15 (d, 6H, $J = 6.3$ Hz); IR (KBr) 3302, 3267, 2979, 1670, 1537, 1275, 1159, 1074, 958, 706 $cm^{-1}$. Anal. Calcd for $C_{10}H_{21}NO_3$: C, 59.08; H, 10.41; N, 6.89%. Found: C, 59.07; H, 10.41; N, 6.86%.

**Partial Purification of Nitroso Compounds.** The experimental procedure is exemplified as in the formation of **8h**. Due to the unstable nature, the partially purified products were applied in the next steps.

**2-Hydroxy-1,1,2-trimethylpropyl *N*-Ethyl-*N*-nitrosocarbamate (8h):** To a suspension of ethylcarbamate (**2h**, 68 mg, 0.36 mmol) in 2 M HCl (1.0 mL, 2.00 mmol) was added $NaNO_2$ (83 mg, 1.20 mmol), followed by addition of $Et_2O$ (1.0 mL) immediately to avoid the decomposition of the product into the substrate. After stirring at room temperature for 10 min, the reaction mixture was extracted with $Et_2O$ twice. The combined organic layer was washed with brine, dried over $Na_2SO_4$, and concentrated in vacuo. The residue was purified by silica-gel column chromatography (11 g). Elution with hexane–AcOEt (7:3) afforded **8h** as yellow oil (58 mg, 74% yield) with the recovery of **2h** (8 mg, 12%). $^1$H NMR (400 MHz, $CDCl_3$) $\delta$ 3.72 (q, 2H, $J = 7.1$ Hz), 2.54 (br s, 1H), 1.66 (s, 6H), 1.25 (s, 6H), 0.96 (t, 3H, $J = 7.1$ Hz). Due to its rather unstable nature, neither the correct elemental analysis nor the high resolution mass spectrum was obtained.

**2-Hydroxy-1,1,2-trimethylpropyl *N*-Isopropyl-*N*-nitrosocarbamate (13):** Nitrosation of isopropylcarbamate (**7h**) in the same manner as described above; subsequent silica-gel column chromatographic separation [hexane–AcOEt (7:3 to 1:1)] afforded **13** as yellow oil (16% yield, 76% recovery). $^1$H NMR (400 MHz, $CDCl_3$) $\delta$ 4.85 (qq, 1H, $J = 6.8$, 6.8 Hz), 2.76 (br s, 1H), 1.63 (s, 6H), 1.22 (s, 6H), 1.19 (d, 6H, $J = 6.8$ Hz); $^{13}$C NMR (100 MHz, $CDCl_3$) $\delta$ 151.9, 92.3, 75.2, 43.6, 24.7, 21.1, 19.0; IR (film) 3413, 2983, 1747, 1516, 1460, 1383, 1317, 1082, 995, 723 $cm^{-1}$.

**Attempts for Optimization of the Precursor of Cyclic Carbonate via Nitrosation–Deaminocyclization.** To a solution of ethylcarbamate (**6a**, 26 mg, 0.12 mmol) in 2 M HCl (0.4 mL) and AcOH (0.4 mL) was added $NaNO_2$ (130 mg, 1.88 mmol). After be-

ing stirred at room temperature for 30 min, the reaction mixture was extracted with AcOEt three times. The combined organic layer was washed with pH 7.4 phosphate buffer and brine, dried over $Na_2SO_4$, and concentrated in vacuo to give the crude product. The residue was purified by silica-gel column chromatography (12 g). Elution with hexane–AcOEt (2:3) afforded **3a** (12 mg, 57% yield), with the recovery of **6a** (6 mg, 24%). $^1$H NMR (400 MHz, $CDCl_3$) $\delta$ 7.30 (m, 5H), 4.94 (m, 1H), 4.45 (dd, 1H, $J = 7.8$, 8.8 Hz), 4.18 (dd, 1H, $J = 6.8$, 8.8 Hz), 3.17 (dd, 1H, $J = 6.3$, 14.2 Hz), 3.00 (dd, 1H, $J = 6.8$, 14.2 Hz); $^{13}$C NMR (100 MHz, $CDCl_3$) $\delta$ 154.6, 133.8, 129.2, 128.7, 127.3, 76.8, 68.4, 39.4; IR (film) 3030, 2920, 1799, 1498, 1481, 1454, 1396, 1371, 1169, 1080, 1061, 702 cm$^{-1}$. Kugelrohr distillation (176–178 °C/2.4 mmHg) afforded an elemental analytical sample as a colorless oil. Anal. Calcd for $C_{10}H_{10}O_3$: C, 67.41; H, 5.66%. Found: C, 67.49; H, 5.71%.

Both from the corresponding isopropylcarbamate (**6b**) and from the corresponding *t*-butylcarbamate (**6c**), a mixture of an *N*-nitrosocarbamate and the recovery (3:5 and 9:10, respectively) was obtained. The ratios were estimated by $^1$H NMR of the crude products dissolved in $CDCl_3$, by comparing the signals of the *N*-nitrosocarbamates (H-1: $\delta$ 5.16 for the product from **6b** derivative and $\delta$ 5.14 for the product from **6c**) with those of the recoveries (H-1: $\delta$ 4.97 for **6b** and $\delta$ 4.95 for **6c**). The yields of the *N*-nitroso compounds were estimated to be 37% with 61% recovery (**6b**), and 46% with 51% recovery (**6c**) respectively, based on these $^1$H NMR analyses. From the corresponding phenylcarbamate (**6d**), the starting material was quantitatively recovered.

**Successful Cyclization: Typical Cyclization Procedure. 4-Benzyl-1,3-dioxolan-2-one (3a):** To a mixture of ethylcarbamate (**6a**, 17 mg, 0.07 mmol) and MS3A (ca. 200 mg) in AcOH 0.5 mL was added $NaNO_2$ (41 mg, 0.60 mmol). The reaction mixture was heated to 50 °C and stirred overnight. After cooling to room temperature, the reaction mixture was filtered to remove insoluble materials and the filtrate was extracted with $Et_2O$ three times. The combined organic layer was washed with aqueous $NaHCO_3$ and brine, dried over $Na_2SO_4$, and concentrated in vacuo. The residue was purified by preparative TLC [hexane–AcOEt (2:3)] to give **3a** (11 mg, 84% yield). The spectral data were identical with those described above.

**4-Octyl-1,3-dioxolan-2-one (3b):** $^1$H NMR (400 MHz, $CDCl_3$) $\delta$ 4.64 (m, 1H), 4.46 (m, 1H), 4.00 (m, 1H), 1.74 (m, 1H), 1.61 (m, 1H), 1.40 (m, 1H), 1.35–1.20 (m, 11H), 0.81 (t, 3H, $J = 6.8$ Hz); IR (film) 2927, 2856, 1801, 1466, 1385, 1169, 1065, 775 cm$^{-1}$. $^1$H NMR and IR spectra were identical with those previously reported.[19]

**4-Phenoxymethyl-1,3-dioxolan-2-one (3c):** Mp 96.2–97.2 °C; $^1$H NMR (400 MHz, $CDCl_3$) $\delta$ 7.32 (m, 2H), 7.02 (t, 1H, $J = 7.6$ Hz), 6.91 (d, 2H, $J = 7.8$ Hz), 5.03 (m, 1H), 4.62 (dd, 1H, $J = 8.3$, 8.3 Hz), 4.54 (dd, 1H, $J = 5.9$, 8.3 Hz), 4.24 (dd, 1H, $J = 4.4$, 10.5 Hz), 4.15 (dd, 1H, $J = 3.4$, 10.5 Hz); IR (KBr) 2925, 1805, 1603, 1495, 1396, 1250, 1167, 1092, 760 cm$^{-1}$. $^1$H NMR and IR spectra were identical with those previously reported.[19]

**4-Isopropyl-4-methyl-1,3-dioxolan-2-one (3d):** $^1$H NMR (400 MHz, $CDCl_3$) $\delta$ 4.18 (d, 1H, $J = 8.3$ Hz), 3.99 (d, 1H, $J = 8.3$ Hz), 1.94 (qq, 1H, $J = 6.8$, 6.8 Hz), 1.37 (s, 3H), 0.95 (d, 3H, $J = 6.8$ Hz), 0.89 (d, 3H, $J = 6.8$ Hz); $^{13}$C NMR (100 MHz, $CDCl_3$) $\delta$ 154.5, 86.2, 72.8, 35.5, 20.9, 16.3, 16.3; IR (film) 2974, 2883, 1797, 1469, 1387, 1246, 1126, 1061, 773 cm$^{-1}$. Kugelrohr distillation (110 °C/2.0 mmHg) afforded an elemental analytical sample as colorless oil. Anal. Calcd for $C_7H_{12}O_3$: C, 58.32; H, 8.39%. Found: C, 58.15; H, 8.34%.

**(4*R**,5*S**)-4,5-Diphenyl-1,3-dioxolan-2-one (3e):** Mp 125.1–126.2 °C; $^1$H NMR (400 MHz, $CDCl_3$) $\delta$ 7.08 (m, 6H), 6.87 (m, 4H), 5.92 (s, 2H); IR (KBr) 1790, 1452, 1338, 1173, 1047, 769, 746, 725, 696 cm$^{-1}$. $^1$H NMR and IR spectra were identical with those previously reported.[20]

**(4*R**,5*S**)-Hexahydro-1,3-benzodioxol-2-one (3f):** A semisolid. $^1$H NMR (400 MHz, $CDCl_3$) $\delta$ 4.69 (m, 2H), 1.91 (m, 4H), 1.63 (m, 2H), 1.43 (m, 2H); IR (film) 2943, 2868, 1799, 1720, 1452, 1352, 1252, 1167, 1138, 1030, 783, 731 cm$^{-1}$. $^1$H NMR and IR spectra were identical with those previously reported.[21]

**(4*R**,5*R**)-Hexahydro-1,3-benzodioxol-2-one (3g):** Mp 54.5–55.3 °C; $^1$H NMR (400 MHz, $CDCl_3$) $\delta$ 4.69 (m, 2H), 1.91 (m, 4H), 1.63 (m, 2H), 1.43 (m, 2H); IR (KBr) 2964, 1792, 1373, 1321, 1196, 1153, 1103, 1043, 1009, 935, 785 cm$^{-1}$. $^1$H NMR and IR spectra were identical with those previously reported.[21]

**4,4,5,5-Tetramethyl-1,3-dioxolan-2-one (3h):** To a mixture of ethylcarbamate (**6h**, 112 mg, 0.59 mmol) and MS3A (ca. 400 mg) in AcOH (5.0 mL) was added $NaNO_2$ (122 mg, 1.78 mmol). After being stirred at room temperature overnight, the reaction mixture was filtered to remove insoluble materials, and the filtrate was extracted with $Et_2O$ three times. The combined organic layer was washed with aqueous $NaHCO_3$ and brine, dried over $Na_2SO_4$, and concentrated in vacuo to give **3h** (75 mg, 88% yield). Recrystallization from $CHCl_3$ afforded colorless prisms. Mp 171.0–172.0 °C; $^1$H NMR (400 MHz, $CDCl_3$) $\delta$ 1.41 (s, 12H); IR (KBr) 2991, 1780, 1379, 1286, 1151, 1092, 1034, 1009, 783, 629 cm$^{-1}$. $^1$H NMR and IR spectra were identical with those previously reported.[20]

To a mixture of isopropylcarbamate (**7b**, 106 mg, 0.52 mmol) and MS3A (ca. 400 mg) in AcOH (5.0 mL), was added $NaNO_2$ (166 mg, 2.40 mmol). After being stirred at room temperature for 20 h, the reaction mixture was filtered to remove insoluble materials. Conventional workup as mentioned above and chromatographic separation [hexane–AcOEt (3:2)] afforded **3h** (89% yield).

**Esterification of *p*-Nitrobenzoic Acid (11a) by *N*-Alkyl-*N*-nitrosocarbamates.** To the mixture of *N*-ethyl-*N*-nitrosocarbamate (**8h**, 104 mg, 0.48 mmol) and MS3A (ca. 200 mg) in $CH_2Cl_2$ (3.0 mL) was added *p*-nitrobenzoic acid (**11a**, 27 mg, 0.16 mmol). After being stirred at room temperature overnight, the reaction mixture was filtered; the filtrate was concentrated in vacuo to give the crude product. The residue was purified by silica-gel column chromatography (39 g). Elution with hexane–AcOEt (7:3) to AcOEt afforded the ethyl ester (**12a**, 29 mg, 93%), cyclic carbonate (**3h**, 54 mg, 78%) and ethylcarbamate (**8h**, 12 mg, 14%). **12a**: Mp 54.9–55.1 °C; $^1$H NMR (400 MHz, $CDCl_3$) $\delta$ 8.29 (m, 2H), 8.22 (m, 2H), 4,44 (q, 2H, $J = 7.1$ Hz), 1.43 (t, 3H, $J = 7.1$ Hz); IR (KBr) 3120, 2991, 1716, 1606, 1525, 1321, 1279, 1103, 1011, 872, 843, 715 cm$^{-1}$. $^1$H NMR and IR spectra were identical with those previously reported.[22] From the corresponding isopropylcarbamate (**13**), an ester **14** was obtained (32%). **14**: Mp 104.2–104.7 °C; $^1$H NMR (400 MHz, $CDCl_3$) $\delta$ 8.29 (d, 2H, $J = 8.8$ Hz), 8.21 (d, 2H, $J = 8.8$ Hz), 5.29 (m, 1H), 1.41 (d, 6H, $J = 6.1$ Hz). The $^1$H NMR spectrum was identical with that previously reported.[23]

**Ethyl Ester Formation of Various Acids with Ethylcarbamate (6h), *t*-Butyl Nitrite, and MS3A in $ClCH_2CH_2Cl$: Typical Procedure. Ethyl 2-Furoate (12b):** To a mixture of ethylcarbamate (**6h**, 199 mg, 1.05 mmol) and MS3A (ca. 200 mg) in $ClCH_2CH_2Cl$ (4.0 mL) was added *t*-butyl nitrite (139 µL, 1.17 mmol). The mixture was stirred at room temperature for 30 min, followed by an addition of 2-furoic acid (39 mg, 0.35 mmol). After

stirring at 60 °C overnight, the reaction mixture was cooled to room temperature and filtered to remove insoluble materials. The filtrate was concentrated in vacuo. The residue was purified by silica-gel column chromatography (10 g). Elution with hexane–AcOEt (7:3) afforded **12b** (49 mg, 99%). Mp 35.1–35.3 °C; $^1$H NMR (400 MHz, $CDCl_3$) $\delta$ 7.58 (m, 1H), 7.18 (dd, 1H, $J = 1.0$, 3.4 Hz), 6.51 (dd, 1H, $J = 2.0$, 3.4 Hz), 4.37 (q, 2H, $J = 7.1$ Hz), 1.38 (t, 3H, $J = 7.1$ Hz). The spectral data were identical with those of the commercially available sample (TCI, F0098).

**Ethyl (*R*)-2-Methoxy-2-phenylacetate (12c):** $^1$H NMR (400 MHz, $CDCl_3$) $\delta$ 7.45 (m, 2H), 7.36 (m, 3H), 4.76 (s, 1H), 4.19 (m, 2H), 3.41 (s, 3H), 1.22 (t, 3H, $J = 7.1$ Hz); IR (film) 2983, 2937, 2827, 1749, 1454, 1257, 1180, 1107, 1028, 731, 698 $cm^{-1}$; $[\alpha]_D^{24}$ −97.7 (*c* 1.01, $CHCl_3$). On the basis of HPLC analysis, the ee was estimated to be >99.9%. HPLC [column, Chiralcel OJ; 0.46 cm × 25 cm; hexane-2-propanol (9:1); flow rate 0.5 mL/min]: $t_R = 24.7$ min for (*R*)-**12c**, 27.8 min for (*S*)-**12c**. $^1$H NMR and IR spectra were identical with those of racemate previously reported.[24]

**Ethyl (*S*)-*N*-Boc-indoline-2-carboxylate (12d):** Mp 62.0–62.3 °C; $^1$H NMR (400 MHz, $CDCl_3$) $\delta$ 7.90 (br s, 0.7H), 7.49 (br s, 0.3H), 7.20 (dd, 1H, $J = 7.3$, 7.3 Hz), 7.11 (d, 1H, $J = 7.3$ Hz), 6.94 (dd, 1H, $J = 7.3$, 7.3 Hz), 4.90 (br s, 0.3H), 4.85 (br s, 0.7H), 4.21 (m, 2H), 3.51 (m, 1H), 3.10 (dd, 1H, $J = 3.9$, 16.6 Hz), 1.59 (s, 3H), 1.50 (s, 6H), 1.27 (t, 3H, $J = 7.1$ Hz); IR (KBr) 2987, 1747, 1703, 1603, 1487, 1390, 1321, 1201, 1167, 750 $cm^{-1}$. The spectral data were identical with those of an authentic sample, prepared from indolin-2-carboxylic acid via the *t*-butoxycarbonylation and esterification with $K_2CO_3$–EtI. Elemental analysis of the authentic specimen: Anal. Calcd for $C_{16}H_{21}NO_4$: C, 65.96; H, 7.27; N, 4.81%. Found: C, 65.88; H, 7.22; N, 4.84%.

***N*-Acetyl-L-phenylalanine Ethyl Ester (12e):** Mp 87.4–87.9 °C; $^1$H NMR (400 MHz, $CDCl_3$) $\delta$ 7.27 (m, 3H), 7.10 (m, 2H), 5.95 (d, 1H, $J = 6.3$ Hz), 4.87 (m, 1H), 4.17 (q, 2H, $J = 7.3$ Hz), 3.12 (m, 2H), 1.99 (s, 3H), 1.25 (t, 3H, $J = 7.3$ Hz); IR (KBr) 3317, 2972, 2933, 1732, 1645, 1533, 1377, 1346, 1223, 1200, 698 $cm^{-1}$. The spectral data were identical with those of the commercially available sample (Sigma, A-4251).

**Ethyl Octadecanoate (12f):** Mp 30.9–31.2 °C; $^1$H NMR (400 MHz, $CDCl_3$) $\delta$ 4.12 (q, 2H, $J = 7.1$ Hz), 2.28 (t, 2H, $J = 7.6$ Hz), 1.61 (m, 2H), 1.32–1.23 (m, 31H), 0.88 (t, 3H, $J = 6.8$ Hz); IR (KBr) 2918, 2850, 1739, 1468, 1379, 1176, 721 $cm^{-1}$. The spectral data were identical with those of the commercially available sample (Aldrich, 22317-4).

**3-Ethoxy-2-methyl-2-cyclohexenone (15):** $^1$H NMR (400 MHz, $CDCl_3$) $\delta$ 4.07 (q, 2H, $J = 6.8$ Hz), 2.56 (t, 2H, $J = 6.3$ Hz), 2.35 (t, 2H, $J = 6.3$ Hz), 1.98 (tt, 2H, $J = 6.3$, 6.3 Hz), 1.70 (s, 3H), 1.36 (t, 3H, $J = 6.8$ Hz); IR (film) 2945, 1643, 1614, 1381, 1354, 1236, 1124, 1095 $cm^{-1}$. The IR spectrum was identical with that previously reported.[25]

***p*-Nitrophenetole (17b):** Mp 58.0–58.2 °C; $^1$H NMR (400 MHz, $CDCl_3$) $\delta$ 8.20 (m, 2H), 6.95 (m, 2H), 4.13 (q, 2H, $J = 7.0$ Hz), 1.47 (t, 3H, $J = 7.0$ Hz); IR (KBr) 2987, 1595, 1496, 1473, 1327, 1259, 1109, 1039, 850, 654 $cm^{-1}$. The spectral data were identical with those of the commercially available sample (TCI, N0216).

**2,4-Dinitrophenetole (18):** Mp 85.0–85.2 °C; $^1$H NMR (400 MHz, $CDCl_3$) $\delta$ 8.66 (m, 1H), 8.35 (m, 1H), 7.13 (m, 1H), 4.25 (q, 2H, $J = 7.0$ Hz), 1.47 (t, 3H, $J = 7.0$ Hz); IR (KBr) 3120, 2989, 1614, 1525, 1352, 1290, 1155, 1024, 742 $cm^{-1}$; MS $m/z = 212$ ($M^+$). The spectral data were identical with those of the commercially available sample (TCI, D2621).

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