Improved Conditions for Facile Overman Rearrangement[1]

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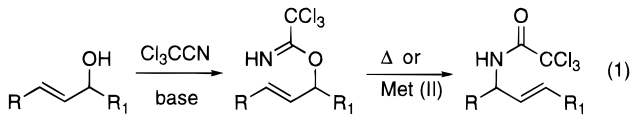
The rearrangement of allyl trichloroacetimidate into allyl trichloroacetamide (eq 1, the so-called Overman rearrangement),[2,3] has been widely used for the synthesis



of nitrogen-containing compounds, especially for amino acids,[4] amino sugars,[5] and other complex natural products.[6] The resulting trichloroacetamide has been directly transformed into acylurea[7] or guanidine derivative[8] and can be used as a precursor for radical cyclization.[9] Furthermore, the resulting olefin can be functionalized by neighboring group participation of the trichloroacetamide to afford amino alcohol.[10] Despite the usefulness of this rearrangement, low yields and unreproducible results have been reported in some cases (vide infra). To solve these problems, some modifications of the Overman rearrangement have been reported.[11,12] This paper describes our simple but useful solution for overcoming problems occasionally seen in Overman rearrangements.

In our previous studies on chiral tetrodotoxin synthesis, we developed a highly stereoselective introduction of a requisite amino group by using the Overman rearrangement as a key step (Scheme 1).[13,14] The *exo*-allyl alcohol **1** was transformed into an imidate **2** with DBU and trichloroacetonitrile in CH_2Cl_2 at 0 °C. The conformation of the imidate **2** should be as depicted in Scheme 1 (the acetonide group occupied the pseudoaxial position) due to A-strain between the *exo*-olefin and acetonide group. Consequently, imidate **2** underwent the rearrangement under xylene reflux in a highly stereoselective manner to afford the allyl trichloroacetamide **3** as a single stereoisomer in 74% yield (two steps). In attempted experiments to scale-up this reaction, however, we encountered decreasing yields (−50%), which prompted us to reexamine the reaction conditions in order to improve the yield and the reproducibility.

Extensive examination of reaction conditions[15] uncovered satisfactory conditions, i.e., xylene at reflux *in the presence of* K_2CO_3 *(2 mg/mL) as base.*[16] Addition of this base would trap acids generated during thermal rearrangement,[17] which might cause decomposition of the imidate. This modification increased the yield of **3** to over 90% (two steps from **1**), and the procedure was applicable to 10 g scale of **1** without decreasing the yield. Another important intermediate **4**[18] in our tetrodotoxin synthesis showed a similar improvement when the rearrangement was conducted under these optimized conditions. In the absence of K_2CO_3, Overman rearrangement (xylene, reflux) of **4** gave a mixture of desired rearranged product **6** and aromatized byproduct **7** in 37% and 32% yields, respectively. In contrast, addition of K_2CO_3 gave **6** in 62% yield (and recovered **5** in 10%) without giving any aromatic byproducts.

To determine the general utility of this procedure, we applied these improved conditions to other allylic alcohols. The results are summarized in the Table 1.[19] Some comments follow. Rearrangement of geraniol **8** in the absence K_2CO_3 gave **9** in good yield,[20] which could not be further improved by addition of the base (entry 1, 2).

(1) This study was presented at the annual meeting of Japan Society for Bioscience, Biotechnology and Agrochemistry, Abstract. p 119, Tokyo, Japan, April, 1997.

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(3) For a recent review, see: Ritter, K. In *Houben-Weyl. Stereoselective Synthesis.* E 21, Vol. 9; Helmechen, G., Hoffmann, R. W., Mulzer, J., Schaumann, E., Eds.; Thieme: Stuttgart, 1996; pp 5677−5699.

(4) For leading references, see: (a) Takano, S.; Akiyama, M.; Ogasawara, K. *J. Chem. Soc., Chem. Commun.* **1984**, 770−771. (b) Kakinuma, K.; Koudate, T.; Li, H.-Y.; Eguchi, T. *Tetrahedron Lett.* **1991**, *32*, 5801−5804. (c) Mehmandoust, M.; Petit, Y.; Larchevêque, M. *Tetrahedron Lett.* **1992**, *33*, 4313−4316. (d) Imogaï, H.; Petit, Y.; Larchevêque, M. *Tetrahedron Lett.* **1996**, *37*, 2573−2576.

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(6) For example, see: (a) Danishefsky, S.; Lee, J. Y. *J. Am. Chem. Soc.* **1989**, *111*, 4829−4837. (b) Chida, N.; Tsutsumi, N.; Ogawa, S. *J. Chem. Soc., Chem. Commun.* **1995**, 793−794.

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(8) Yamamoto, N.; Isobe, M. *Chem. Lett.* **1994**, 2299−2302.

(9) (a) Nagashima, H.; Wakamatsu, H.; Itoh, K. *J. Chem. Soc., Chem. Commun.* **1984**, 652−653. (b) Nagashima, H.; Wakamatsu, H.; Ozaki, N.; Ishii, T.; Watanabe, M.; Tajima, T.; Itoh, K. *J. Org. Chem.* **1992**, *57*, 1682−1689, and references cited therein.

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(11) For review of Hg(II)- and Pd(II)-catalyzed rearrangement, see: Overman, L. E. *Angew. Chem., Int. Ed. Engl.* **1984**, *23*, 579−586.

(12) For trifluoroacetimidate version of Overman rearrangement, see: (a) Savage, I.; Thomas, E. J. *J. Chem. Soc., Chem. Commun.* **1989**, 717−719. (b) Chen, A.; Savage, I.; Thomas, E. J.; Wilson, P. D. *Tetrahedron Lett.* **1993**, *34*, 6769−6772.

(13) Isobe, M.; Nishikawa, T.; Fukami, N.; Goto, T. *Pure Appl. Chem.* **1987**, *59*, 399−406.

(14) (a) Isobe, M.; Fukuda, Y.; Nishikawa, T.; Chabert, P.; Kawai, T.; Goto, T. *Tetrahedron Lett.* **1990**, *31*, 3327−3330. (b) Yamamoto, N.; Nishikawa, T.; Isobe, M. *Synlett* **1995**, 505−506.

(15) For solvent effects in Overman rearrangement, see: (a) Vyas, D. M.; Chiang, Y.; Doyle, T. W. *J. Org. Chem.* **1984**, *49*, 2037−2039. (b) ref 5 (d).

(16) Addition of other bases such as pyridine, DBU and *n*-Bu_3N showed little improvement. Addition of radical inhibitors such as BHT and 5-*tert*-butyl-4-hydroxy-2-methylphenyl sulfide had no effect.

(17) In fact, *p*-toluic acid was detected (by ^1H NMR) in the crude mixture after xylene reflux overnight.

(18) Preparation of **4** will be published elsewhere.

(19) For preparation of substrates, see: **15**: Nicolaou, K. C.; Hwang, C.-K.; Marron, B. E.; DeFees, S. A.: Couladouros, E. A.; Abe, Y.; Carroll, P. J.; Snyder, J. P. *J. Am. Chem. Soc.* **1990**, *112*, 3040−3054. **17**: ref 5 (c).

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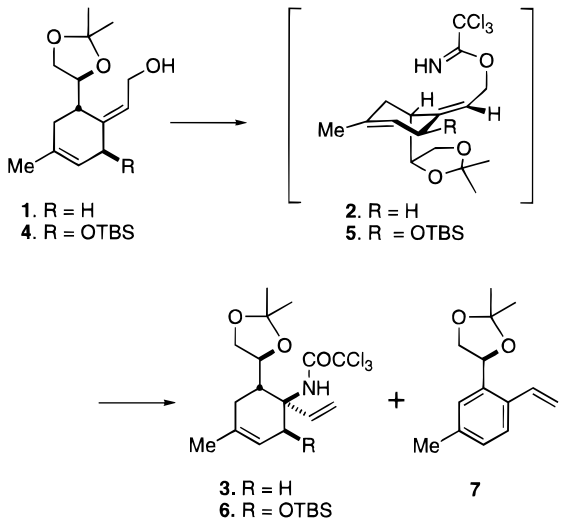
Scheme 1



Thermal rearrangement of the trifluoroacetimidate of 2,4-hexadien-1-ol **10** was reported to give the trifluoroacetamide **12** only in 35% yield, even though trifluoroacetimidate was considered more reactive than the corresponding trichloroacetimidate.[12] However, the trichloroacetimidate of **10** gave trichloroacetamide **11** in acceptable yield even in the absence of K_2CO_3 (entry 3). Rearrangement of (−)-myrtenol **13** was improved to yield **14**[21] in 95% under the new conditions (entry 5 vs 6).

These conditions could be applied to unsaturated sugar derivatives. The trichloroacetimidate of pyran **15** rearranged to give **16** in good yield even in the absence of K_2CO_3 (entry 7), while the corresponding ethoxy glycoside **17** was reported not to rearrange under xylene reflux.[5c] Surprisingly, at elevated temperature (165 °C in *o*-dichlorobenzene (DCB)) in the presence of K_2CO_3, the latter rearrangement took place to afford the desired product **18**[22] in 56% yield (entry 10). The higher temperature might be required to invert the ground state conformation (imidate equatorial) into the necessary conformation (imidate group occupying axial position) for rearrangement. In the absence of the base, the imidate rapidly decomposed at this elevated temperature to give **18** only in low yield (entry 9).[23]

Rearrangements of cyclic γ-substituted allylic secondary alcohols were reported to take place in low yields and to be unreproducible due to instability of the imidates,[2b,24] which tended to eliminate trichloroacetamide.[25] In fact, rearrangements of trichloroacetimidate derivative of 3-methyl-2-cyclohexen-1-ol **19** gave **20** in low yield, even in the presence of K_2CO_3 (entry 11). We found that lower temperature (at −20 °C) during preparation of the imidate was indispensable to avoid the elimination, and this low temperature resulted in remarkable improvement of the yield of **20** (entry 12). In this particular case, addition of K_2CO_3 had only a small effect (entry 13). On the other hand, these modifications did not improve the rearrangement of **21** having a *gem*-dimethyl group (in entry 15). The reason might be the severe 1,3-diaxal interactions between the imidate and methyl group in transition state, which cannot be avoided.

This study expands the range of substrates that undergo the Overman rearrangement effectively,[26] which makes this reaction even more useful for syntheses of complex nitrogen-containing natural products.

Experimental Section

General: Melting points were recorded on a Yanaco MP−S3 melting point apparatus and are not corrected. Infrared spectra were recorded on a JASCO FT/IR-8300 spectrophotometer and are reported in wave number (cm^{-1}). Proton nuclear magnetic resonance (^1H NMR) spectra were recorded on Brucker ARX-400 (400 MHz) and Varian Gemini-2000 (300 MHz) spectrometers. Carbon nuclear magnetic resonance (^{13}C NMR) spectra were recorded on JEOL EX-270 (67.9 MHz) and Varian Gemini-2000 (75 MHz) spectrometers. Optical rotations were measured on a JASCO DIP-370 digital polarimeter. Low resolution mass spectra (EI) were recorded on JEOL JMS-D 100 and JEOL JMS-700 spectrometers. High-resolution mass spectra (HRMS) were recorded on a JEOL DX-705L spectrometer and reported in *m*/*z*. Elemental analyses were performed by the Analytical Laboratory of the School of Bioagricultural Sciences, Nagoya University. Unless otherwise noted, nonaqueous reactions were carried out under nitrogen or argon atmospheres. Dry CH_2Cl_2 was distilled from CaH_2 under a nitrogen atmosphere. All other commercially available reagents were used as received.

Overman Rearrangement of 1 into Trichloroacetimidate 3 via Trichloroacetimidate 2 *in the presence of K_2CO_3*. To a solution of allylic alcohol **1** (701 mg, 2.94 mmol) in dry CH_2Cl_2 (20 mL) was added DBU (0.53 mL, 3.52 mmol), and the solution was cooled to 0 °C. To this solution was added CCl_3CN (0.44 mL, 4.41 mmol) over 15 min. After stirring at 0 °C for 1 h, the reaction mixture was quenched with sat. NH_4Cl solution. The organic layer was washed with sat. NH_4Cl solution (×2), passed through a column packed with anhydrous Na_2SO_4 and silica gel (to remove polymeric products), and evaporated under reduced pressure to give crude trichloroacetimidate **2**, which was used for the following step without any purifications: ^1H NMR (300 MHz, $CDCl_3$) δ 1.33 (3H, s), 1.41 (3H, s), 1.64 (3H, br s), 1.72 (1H, br d, J = 18 Hz), 2.33 (1H, br d), 2.67 (1H, br d, J = 19 Hz), 2.94−3.10 (2H, m), 3.71 (1H, dd, J = 8, 6.5 Hz), 4.10 (1H, dd, J = 8, 6 Hz), 4.23 (1H, dt, J = 10, 6.5 Hz), 4.77 (1H, ddd, J = 12, 6, 2 Hz), 5.00 (1H, ddd, J = 12, 8, 2 Hz), 5.38 (1H, br s), 5.71 (1H, ddd, J = 8, 6, 2 Hz), 8.25 (1H, br s). To a solution of the crude imidate **2** in *p*-xylene (50 mL) was added powdered anhydrous K_2CO_3 (100 mg), and the mixture was heated at reflux for 13 h with vigorous stirring. After cooling to rt, the mixture was filtered through a pad of Super-Cel, and the precipitate was washed with toluene. The combined filtrate was evaporated in vacuo. The residue was purified by column chromatography (silica 50 g, ether/hexane = 1:10 → 1:5) to give **3** (1.02 g, 91%).

(1*S*,6*S*,1′*S*)-Trichloro-*N*-[1-vinyl-4-methyl-6-(3′,3′-dimethyl-2′,4′-dioxolanyl)-cyclohex-3-enyl]acetamide (3): mp 100−102 °C. $[\alpha]^{27}_D$ +70.2 (*c* 0.97, $CHCl_3$). IR (KBr) 3313, 2987, 2924, 1727, 1542, 1261, 1067 cm^{-1}. ^1H NMR (400 MHz, $CDCl_3$) δ 1.39

(21) The product **14** was a single isomer, and its stereochemistry was determined by NOE observed between Ha and Hb as shown in Table 1.

(22) The stereochemistry of **18** was confirmed as follows. Reduction of **18** with Zn−Cu gave the corresponding acetamide, which was identical in ^1H NMR and ^{13}C NMR spectra to authentic sample given by Dr. Y. Ichikawa. For Ichikawa's approach, see: (a) Ichikawa, Y.; Kobayashi, C.; Isobe, M. *Synlett* **1994**, 919−921. (b) Ichikawa, Y.; Kobayashi, C.; Isobe, M. *J. Chem. Soc., Perkin Trans 1* **1996**, 377−382.

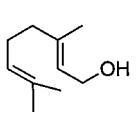
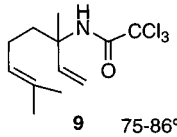
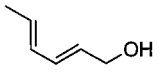
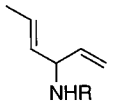
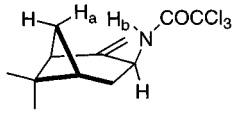
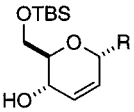
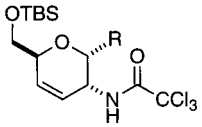
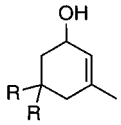
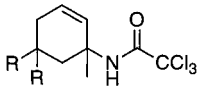
(23) During preparation of this manuscript, the Overman rearrangement of a substrate similar to **17** was reported to proceed under 210 °C (in diphenyl ether) for short time to give a corresponding trichloroacetamide. We thank Dr. Sugai for exchanging the information prior to the publication. Okazaki, H.; Kuboki, A.; Sugai, T.; Ohta, H. The 72th Annual Meeting of the Chemical Society of Japan, Abstract p 1017, Tokyo, Japan, March, 1997.

(24) Overman, L. E. *Tetrahedron Lett.* **1975**, 1149−1152.

(25) In fact, the imidates of **19** and **21** could not be detected on silica gel TLC, but observed by ^1H-NMR (see Experimental Section). In contrast, all other imidates depicted in Table 1 could be monitored by silica gel TLC.

(26) Recently, enantioselective Overman rearrangement by using chiral catalyst was reported, see: Calter, M.; Hollis, T. K.; Overman, L. E.; Ziller, J.; Zipp, G. G. *J. Org. Chem.* **1997**, *62*, 1449−1456.

Table 1. Overman Rearrangement of Allylic Alcohol

entry	substrate	conditions[a] temp. of prep. of imidate	conditions[a] thermal rearrangement	product	yield[b, c] (2 steps)
1	 **8**	0 °C	xylene, reflux	 **9**	75-86% (67-74%)[2]
2		0 °C	K_2CO_3, xylene, reflux		84%
3	 **10**	0 °C	xylene, reflux	 **11** R = $COCCl_3$	63%
4		0 °C	K_2CO_3, xylene, reflux	**11** **12** R = $COCF_3$	73% (35%)[12b]
5	 **13**	0 °C	xylene, reflux	 **14**	72%
6		0 °C	K_2CO_3, xylene, reflux		95%
7	 **15** R = H	0 °C	xylene, reflux	 **16** R = H	85%
8		0 °C	K_2CO_3, xylene, reflux	**16**	88%
9	**17** R = OEt	0 °C	DCB,165°C	**18** R = OEt	7%(0%)[5b]
10		0 °C	K_2CO_3, DCB,165°C	**18**	56%
11	 **19** R = H	0 °C	K_2CO_3, toluene, reflux	 **20** R = H	29%
12		-20 °C	toluene, reflux		72%
13		-20 °C	K_2CO_3, toluene, reflux		80%
14	**21** R = Me	--	toluene, reflux	**22** R = Me	(10-43%)[2b]
15		-20 °C	K_2CO_3, toluene, reflux		19%

[a] All reactions were carried out using 1.00 or 2.00 mmol of starting material. [b] Values in parentheses are yields from the literatures as indicated. [c] Isolated yield.

(3H, s), 1.42 (3H, s), 1.64−1.71 (5H, m), 2.08 (1H, td, J = 9, 7.5 Hz), 2.27 (1H, d quintet, J = 17.5, 2.5 Hz), 3.37 (1H, ddd, J = 17.5, 6, 1.5 Hz), 3.63 (1H, dd, J = 9, 7.5 Hz), 4.03 (1H, td, J = 9, 5.5 Hz), 4.10 (1H, dd, J = 7.5, 5.5 Hz), 5.30 (1H, dd, J = 17, 1 Hz), 5.32 (1H, dd, J = 11, 1 Hz), 5.39 (1H, m), 5.82 (1H, dd, J = 17, 11 Hz), 9.21 (1H, br s). ^{13}C NMR (67.9 MHz, $CDCl_3$) δ 22.7, 26.3, 26.6, 30.1, 35.9, 44.5, 60.0, 76.4, 93.9, 110.0, 116.0, 119.0, 130.8, 133.7, 160.4. Anal. Calcd for $C_{16}H_{23}O_3NCl_3$: C, 50.08; H, 6.04; N, 3.65. Found C, 50.25; H, 5.97; N, 3.59.

Overman Rearrangement of 4 *in the absence of* K_2CO_3. Allylic alcohol **4** (32 mg, 0.086 mmol) was dissolved in dry CH_2Cl_2 (0.8 mL), and the solution was cooled to 0 °C. To this solution were successively added DBU (15 μL, 0.10 mmol) and CCl_3CN (13 μL, 0.13 mmol). The mixture was stirred at 0 °C for 30 min. The reaction was quenched with sat. NH_4Cl solution. The mixture was extracted with CH_2Cl_2 (×2). Combined organic layer was dried over anhydrous Na_2SO_4 and evaporated under reduced pressure. The crude product was dissolved in xylene (3 mL). The mixture was heated at reflux temperature for 15 h. After cooling to rt, the mixture was evaporated in vacuo. The residue was purified by silica gel TLC (ether/hexane = 1:3) to give the trichloroacetamide **6** (16 mg, 37%) and aromatized product **7** (6 mg, 32%).

Overman Rearrangement of 4 *in the presence of* K_2CO_3. To a solution of allylic alcohol **4** (76 mg, 0.21 mmol) in dry CH_2Cl_2 (5 mL) cooled at 0 °C were added DBU (49 μL, 0.32 mmol) and CCl_3CN (39 μL, 0.39 mmol) successively. The mixture was stirred at 0 °C for 45 min. The reaction mixture was diluted with CH_2Cl_2 and washed with sat. NH_4Cl solution (×2), dried over anhydrous Na_2SO_4, and evaporated under reduced pressure to give crude imidate. The crude imidate was dissolved in xylene (10 mL), and powdered K_2CO_3 (20 mg) was added. The mixture was heated at a reflux temperature for 36 h. After cooling to rt, the mixture was filtered through a pad of Super-Cel and washed with toluene. The combined filtrate was evaporated in vacuo. The residue was purified by column chromatography (silica 15 g, ether/hexane = 1:10 → 1:5) to give the trichloroacetamide **6** (65 mg, 62%) and unreacted imidate **4** (11 mg, 10%).

Trichloroacetimidate of 4: ^{1}H NMR (300 MHz, $CDCl_3$) δ 0.11 (3H, s), 0.13 (3H, s), 0.95 (9H, s), 1.29 (3H, s), 1.37 (3H, s), 1.66 (3H, br s), 1.72 (1H, br d, J = 18 Hz), 2.34 (1H, br d, J = 18 Hz), 3.08 (1H, m), 3.62 (1H, dd, J = 8, 6 Hz), 4.05 (1H, dd, J = 8, 6 Hz), 4.14 (1H, dt, J = 9, 6 Hz), 4.82−4.99 (3H, m), 5.36 (1H, br s), 5.95 (1H, td, J = 7, 2 Hz), 8.25 (1H, br s).

(1*S*,2*S*,1′*S*)-Trichloro-*N*-[1-vinyl-4-methyl-6-(3′,3′-dimethyl-2′,4′-dioxolanyl)-2-(*tert*-butyldimethylsiloxy)cyclohex-3-enyl]acetamide (6): mp 130−132 °C. $[\alpha]^{27}_D$ +133.7 (*c* 0.40, $CHCl_3$). IR (KBr) 3327, 2930, 1727, 1533, 1256 cm^{-1}. ^{1}H NMR (300 MHz, $CDCl_3$) δ 0.05 (6H, s), 0.85 (9H, s), 1.39 (3H, s), 1.41 (3H, s), 1.51−1.62 (1H, m), 1.69 (3H, s), 1.75 (1H, dd, J = 18.5, 6 Hz), 2.48 (1H, ddd, J = 11.5, 9.5, 6 Hz), 3.68 (1H, m), 4.01−4.11 (2H, m), 4.87 (1H, d, J = 6 Hz), 5.33 (1H, dd, J = 11, 1 Hz), 5.38 (1H, dd, J = 17.5, 1 Hz), 5.56 (1H, dd, J = 6, 1 Hz), 5.68 (1H, dd, J = 17.5, 11 Hz), 8.87 (1H, br s). ^{13}C NMR (100 MHz, $CDCl_3$) δ −4.5, −3.7, 18.1, 22.7, 25.9, 26.3, 26.5, 30.6, 38.6, 64.4, 66.2, 68.7, 75.6, 94.0, 109.9, 116.0, 117.5, 123.1, 132.4, 133.8, 135.4, 159.3. HRMS (FAB) for $C_{22}H_{37}O_4NCl_3Si$ (M + H), 512.1557, found 512.1540. Anal. Calcd for $C_{22}H_{38}O_4NCl_3Si$: C, 51.51; H, 7.07; N, 2.73. Found: C, 51.47; H, 7.07; N, 2.62.

(*S*)-5-(2′-Vinyl-5′-methylphenyl)-2,2-dimethyl-1,3-dioxolane (7): ^{1}H NMR (300 MHz, $CDCl_3$) δ 1.50 (3H, s), 1.57 (3H, s), 2.36 (3H, s), 3.60 (1H, t, J = 8.5 Hz), 4.33 (1H, dd, J = 8.5, 6.5 Hz,), 5.28 (1H, dd, J = 11, 1.5 Hz), 5.35 (1H, dd, J = 8.5, 6.5 Hz), 5.58 (1H, dd, J = 17.5, 1.5 Hz), 6.88 (1H, dd, J = 17.5, 11 Hz), 7.08 (1H, br d, J = 7.5 Hz), 7.34−7.38 (2H, m). MS (FAB) *m*/*z* 219 (M + H).

Typical Experimental Procedure (entries 1−11 in Table 1). Preparation of trichloroacetimidate: Allylic alcohol **13** (152 mg, 1.00 mmol) was dissolved in dry CH_2Cl_2 (5 mL), and the solution was cooled to 0 °C. To this solution were successively added DBU (0.22 mL, 1.50 mmol) and CCl_3CN (0.18 mL, 1.80 mmol). After stirring at 0 °C for 30 min, the reaction was quenched with sat. NH_4Cl solution. The mixture was extracted with CH_2Cl_2 (×2). The combined organic layer was washed with sat. NH_4Cl solution (×2), passed through a column packed with anhydrous Na_2SO_4 and a thin layer of silica gel, and evaporated under reduced pressure to give crude imidate. (a) *Overman rearrangement in the absence of K_2CO_3:* The crude imidate was dissolved in xylene (20 mL). The mixture was heated at reflux temperature overnight. After cooling to rt, the mixture was evaporated in vacuo. The residue was purified by column chromatography (silica 30 g, ether/hexane = 1:40) to give trichloroacetamide **14** (212 mg, 72%). (b) *Overman rearrangement in the presence of K_2CO_3:* To a solution of the crude imidate in xylene (20 mL) was added powdered anhydrous K_2CO_3 (40 mg). The mixture was heated at reflux temperature overnight with vigorous stirring. After cooling to rt, the mixture was filtered through a pad of Super-Cel, and the precipitate was washed with toluene. The combined filtrate was evaporated in vacuo. The residue was purified as described above to give **14** (282 mg, 95%).

Trichloroacetimidate of 10: ^{1}H NMR (300 MHz, $CDCl_3$) δ 1.78 (3H, br d, J = 7 Hz), 4.81 (2H, d, J = 6.5 Hz), 5.68−5.85 (2H, m), 6.09 (1H, ddq, J = 15, 10, 1.5 Hz), 6.35 (1H, dd, J = 15.5, 10.5 Hz), 8.29 (1H, br).

Trichloro-*N*-[(4*E*)-1,4-hexadiene-3-yl]acetamide (11): IR (KBr) 3322, 1697, 1511 cm^{-1}. ^{1}H NMR (300 MHz, $CDCl_3$) δ 1.75(3H, br d, J = 6.5 Hz), 4.94 (1H, m), 5.24 (1H, dt, J = 10.5, 1 Hz), 5.26 (1H, dt, J = 17.5, 1 Hz), 5.48 (1H, ddq, J = 15.5, 6, 1.5 Hz), 5.76 (1H, dqd, J = 15.5, 7, 1.5 Hz), 5.86 (1H, ddd, J = 17.5, 10.5, 5.5 Hz), 6.62 (1H, br). ^{13}C NMR (75 MHz, $CDCl_3$) δ 17.8, 54.8, 92.9, 116.6, 127.9, 129.6, 135.8, 161.1. EI-MS *m*/*z* 241 (M^+), 206 (M-Cl). FAB-MS (positive) *m*/*z* 242 (M + H). HR-MS (FAB) for $C_8H_{11}ONCl_3$ (M + H), calcd 241.9906, found 241.9912.

Trichloroacetimidate of 13: ^{1}H NMR (300 MHz, $CDCl_3$) δ 0.86 (3H, s), 1.22 (1H, d, J = 9 Hz, 1.29 (3H, s), 2.08−2.16 (1H, m), 2.22 (1H, td, J = 6, 15 Hz), 2.28−2.35 (2H, m), 2.42 (1H, dt, J = 6, 6 Hz), 4.67 (2H, m), 5.67 (1H, m), 8.25 (1H, br).

(1*R*,3*S*,5*R*)-Trichloro-*N*-(6,6-dimethyl-2-methylenebicyclo[3.1.1]heptan-3-yl)acetamide (14): mp 61.5−63 °C. $[\alpha]^{27}_D$ +37.3 (*c* 0.89, $CHCl_3$). IR (KBr) 3430, 3336, 2936, 1706, 1508 cm^{-1}. ^{1}H NMR (300 MHz, $CDCl_3$) δ 0.78 (3H, s), 1.17 (1H, d, J = 11 Hz), 1.29 (3H, s), 1.80 (1H, ddd, J = 15.5, 4, 2.5 Hz), 2.07 (1H, m), 2.48−2.62 (3H, m), 4.68 (1H, br t, J = 8 Hz), 4.93 (1H, br s), 5.05 (1H, t, J = 1 Hz), 6.71 (1H, br). ^{13}C NMR (75 MHz, $CDCl_3$) δ 22.0, 25.7, 29.7, 33.7, 39.9, 40.3, 46.8, 51.1, 92.7, 112.9, 152.0, 161.0. FAB-MS (positive) *m*/*z* 296 (M + H). Anal. Calcd for $C_{12}H_{16}ONCl_3$: C, 48.59; H, 5.44; N, 4.72. Found C, 48.56; H, 5.42; N, 4.65.

Trichloroacetimidate of 15: ^{1}H NMR (300 MHz, $CDCl_3$) δ 0.06 (6H, s), 0.89 (9H, s), 3.70 (1H, ddd, J = 8, 5.5, 2 Hz), 3.79 (1H, dd, J = 11.5, 5.5 Hz), 3.89 (1H, dd, J = 11.5, 2 Hz), 4.23−4.26 (2H, m), 5.42 (1H, br d, J = 8 Hz), 5.90−6.01 (2H, m), 8.39 (1H, br).

(3*R*,6*S*)-6-[(*tert*-butyldimethylsiloxy)methyl]-3-trichloroacetamido-3,6-2*H*-pyran (16): mp 70−71.5 °C. $[\alpha]^{27}_D$ −138 (*c* 1.10, $CHCl_3$). IR (KBr) 3266, 2929, 2858, 1686, 1541 cm^{-1}. ^{1}H NMR (300 MHz, $CDCl_3$) δ 0.06 (6H, s), 0.89 (9H, s), 3.60 (1H, dd, J = 11.5, 4.5 Hz), 3.64 (1H, dd, J = 10.5, 5.5 Hz), 3.74 (1H, dd, J = 10.5, 6 Hz), 4.14 (1H, dd, J = 11.5, 4 Hz), 4.20 (1H, m), 4.42 (1H, m), 5.93 (1H, ddd, J = 10, 4, 2 Hz), 6.03 (1H, ddd, J = 10, 2, 1 Hz), 6.76 (1H, br d, J = 8 Hz). ^{13}C NMR (75 MHz, $CDCl_3$) δ −5.5, −5.4, 18.3, 25.8, 44.7, 64.2, 65.2, 74.1, 92.4, 124.7, 131.9, 161.7. Anal. Calcd for $C_{14}H_{24}O_4NSiCl_3$: C, 43.25; H, 6.22; N, 3.60. Found: C, 43.33; H, 6.33; N, 3.53.

Trichloroacetimidate of 17: ^{1}H NMR (300 MHz, $CDCl_3$) δ 0.06 (6H, s), 0.89 (9H, s), 1.26 (3H, t, J = 7.5 Hz), 3.57 (1H, dq, J = 10, 7.5 Hz), 3.80 (1H, dd, J = 12, 6 Hz), 3.87 (1H, dd, J = 12, 2.5 Hz), 3.91 (1H, dq, J = 10, 7.5 Hz), 4.12 (1H, m), 5.07 (1H, m), 5.41 (1H, ddt, J = 9.5, 1.5, 1.5 Hz), 5.87 (1H, ddd, J = 10, 3, 2 Hz), 6.07 (1H, br d, J = 10 Hz), 8.40 (1H, br s).

Ethyl 6-*O*-(*tert*-butyldimethylsilyl)-2-trichloroacetamido-2,3,4-trideoxy-α-D-*erythro*-hex-3-enopyranoside (18): $[\alpha]^{27}_D$ −41.7 (*c* 1.10, $CHCl_3$). IR (KBr) 3423, 3345, 2930, 1720, 1506 cm^{-1}. ^{1}H NMR (300 MHz, $CDCl_3$) δ 0.08 (6H, s), 0.90 (9H, s), 1.25 (3H, t, J = 7.5 Hz), 3.62 (1H, dq, J = 10.5, 7.5, Hz), 3.63 (1H, dd, J = 11, 6 Hz), 3.74 (1H, dd, J = 11, 6 Hz), 3.88 (1H, dq, J = 10.5, 7.5 Hz), 4.18 (1H, m), 4.66 (1H, m), 5.03 (1H, d, J = 5 Hz), 5.63 (1H, br d, J = 11 Hz), 5.96 (1H, dt, J = 11, 2.5 Hz), 7.07 (1H, br d, J = 9 Hz). ^{13}C NMR (75 MHz, $CDCl_3$) δ −5.4, 15.0, 18.2, 25.8, 47.2, 64.1, 65.2, 68.8, 92.5, 94.7, 123.0, 129.3, 161.7. FAB-MS (positive) *m*/*z* 432 (M + H), 386 (M-OEt). HR-MS (FAB) for $C_{16}H_{29}O_4NSiCl_3$ (M + H), calcd 432.0931, found 432.0928.

Typical Experimental Procedure (entries 12−15 in Table 1). To a solution of **19** (112 mg, 1.00 mmol) in dry CH_2Cl_2 (5 mL) was added DBU (0.22 mL, 1.50 mmol) and cooled to −20 °C. To this solution was added CCl_3CN (0.18 mL, 1.8 mmol) dropwise. After stirring at −20 °C for 1 h, the reaction mixture was quenched with cold saturated aq. NH_4Cl solution. The combined organic layer was washed with saturated NH_4Cl solution (×2), passed through a column packed with anhydrous Na_2SO_4 and a thin layer of anhydrous K_2CO_3,[27] and evaporated under reduced pressure to give crude trichloroacetimidate which was used for the following reaction without any purifications: ^{1}H NMR (300 MHz, $CDCl_3$) δ 1.60−2.10 (6H, m), 1.74 (3H, s), 5.38 (1H, m), 5.62 (1H, m), 8.22 (1H, br). The crude imidate was dissolved in toluene (10 mL), and powdered anhydrous K_2CO_3 (20 mg) was added. The mixture was heated at reflux temperature for 13 h with vigorous stirring. After cooling to rt, the mixture was filtered through a pad of Super-Cel, and the precipitate was washed with toluene. The combined filtrate was evaporated in vacuo. The residue was purified by column chromatography (silica 15 g, only hexane → ether/hexane = 1:20) to give **20** (205 mg, 80%).

Trichloro-*N*-(1-methyl-2-cyclohexen-1-yl)acetamide (20): mp 50−51 °C. IR (KBr) 3426, 3348, 2934, 1717, 1499 cm^{-1}. ^{1}H NMR (300 MHz, $CDCl_3$) δ 1.52 (3H, s), 1.58−1.73 (3H, m), 1.90−2.16 (2H, m), 2.24−2.35 (1H, m), 5.75 (1H, br d, J = 10 Hz), 5.89 (1H, dt, J = 10, 3.5 Hz), 6.49 (1H, br). ^{13}C NMR (75 MHz, $CDCl_3$) δ 18.9, 24.8, 25.9, 33.4, 53.9, 93.3, 130.7, 131.0, 160.3. Anal. Calcd for $C_9H_{12}ONCl_3$: C, 42.13; H, 4.71; N, 5.46. Found: C, 42.12; H, 4.83; N, 5.42.

Trichloroacetimidate of 21: ^{1}H NMR (300 MHz, $CDCl_3$) δ 0.98 (3H, s), 1.04 (3H, s), 1.60 (1H, dd, J = 13, 7 Hz), 1.73 (3H,

(27) Silica gel should not be used for removal of polymeric products due to acid lability of the imidate.

s), 1.74 (1H, br d, J = 18 Hz), 1.86 (1H, dd, J = 13, 6 Hz), 1.91 (1H, br d, J = 18 Hz), 5.46 (1H, m), 5.57 (1H, m), 8.22 (1H, br s).

Trichloro-*N*-(1,5,5-trimethyl-2-cyclohexen-1-yl)acetamide (22): IR (KBr) 3429, 3349, 2954, 1717, 1506 cm^{-1}. ^1H NMR (300 MHz, $CDCl_3$) δ 0.99 (3H, s), 1.01 (3H, s), 1.48 (1H, d, J = 15 Hz), 1.52 (3H, s), 1.88 (2H, m), 2.21 (1H, br d, J = 15 Hz), 5.78−5.89 (2H, m), 6.54 (1H, br). ^{13}C NMR (75 MHz, $CDCl_3$) δ 27.2, 27.3, 29.1, 31.3, 38.7, 45.7, 54.2, 93.4, 128.8, 129.4, 159.8. EI-MS m/z 268 (M-CH_3), 248 (M-Cl). HR-MS (FAB) for $C_{10}H_{13}ONCl_3$ (M-CH_3), calcd 268.0062, found 268.0060.

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