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On the Palladium(II)-Catalyzed Rearrangement of Allyl Imidates

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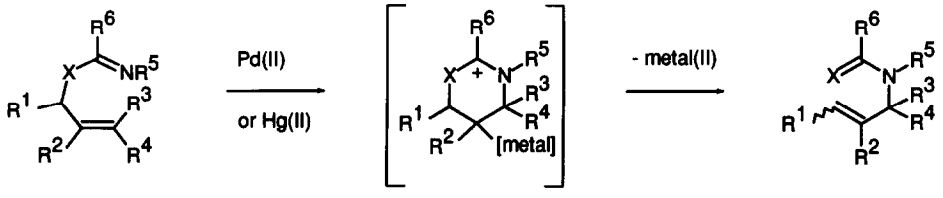
Abstract: *Polyhetero-[3,3]-sigmatropic rearrangements of allyl N-phenylimidates* ***4a-f*** *catalyzed by dichlorobis-(benzonitrile)palladium(II) are shown to afford N-allyl-N-phenylamides in good to excellent yields for substitution patterns that have so far precluded cyclization-induced allyl shifts. Using trichloroacetimidates of secondary allyl alcohols as substrates, the palladium(II)-catalyst effects a completely (E) stereoselective rearrangement at room temperature which proceeds with complete chirality transfer. This reaction has been applied to a synthesis of (R)-N-(trichloroacetyl)norleucinol (**18**) starting from (R)-2,3-O-isopropylideneglyceraldehyde (**17**).*

INTRODUCTION

Metal-catalyzed polyhetero-[3,3]-sigmatropic rearrangements permit the formation of allylic C-heteroatom bonds at significantly lower temperatures than their purely thermal counterparts.[1-3] Among the numerous variants of this reaction type, palladium(II)-[2,4,5] and mercury(II)-promoted[2,3,6] irreversible O→N rearrangements of allyl imidates **1a**, as well as the corresponding palladium(II)-assisted S→N rearrangements of *S*-allyl thioimidates **1b**,[7-9] *S*-allyl iminothiocarbonates **1c**,[1,2] *S*-allyl dithiocarbonimidates **1d**[10] or 3-(allylthio)-1,2,4-triazin-5(2*H*)-ones **1e**[11] offer attractive routes to derivatives **3** of synthetically valuable allyl amines[12] starting from more easily accessible allyl alcohols or halides.



1 **2** **3**

a: X = O, R^6 = H or C; **b**: X = S, R^6 = C; **c**: X = S, R^6 = O; **d**: X = S, R^6 = S; **e**: X = S, R^6 = N

Scheme 1.

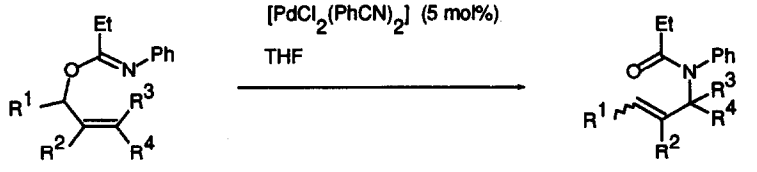
The reports dealing with palladium(II)-promoted O→N or S→N allyl transfers suggest that several major limitations are inherent to these cyclization-induced[13] rearrangements. First, for O→N as well as for S→N shifts, substrates bearing a substituent bigger than hydrogen at the β-position of the allyl moiety ($R^2 \neq H$) were found to be either unreactive[4,5,7,9,10] or to require a temperature of 100°C for rearrangement.[11] Second, a *cis* vinyl substituent which is present in (Z) configured ($R^3 \neq H$, $R^4 = H$) or in γ,γ-disubstituted allyl moieties

(R^3, $R^4 \neq H$) either led to a low yield for the former substitution pattern[1] or completely suppressed S→N rearrangements for the latter,[1,7,10] while corresponding O→N transfers have not been addressed so far. Third, a thorough study of the O→N shift within an optically active *N*-phenylimidate derived from a secondary allyl alcohol ($R^1 \neq H$) revealed an incomplete (*E*) selectivity of this process.[4]

RESULTS AND DISCUSSION

Allyl N-Phenylimidates

Due to our interest in rearrangement reactions of allyl imidates,[14,15] we subjected allyl *N*-phenylimidates **4a - f**, known to undergo purely thermal rearrangement to γ,δ-unsaturated anilides *via* their ketene *O,N*-acetal isomers,[14] to catalytic amounts of dichlorobis(benzonitrile)palladium(II)[16] in tetrahydrofuran (Table 1).



4 **5**

Scheme 2.

Table 1. Rearrangements of Allyl *N*-Phenylimidates **4** Catalyzed by Dichlorobis(benzonitrile)palladium(II).

4	R^1	R^2	R^3	R^4	Temp. (°C)	Time (h) [a]	**5**	Yield (%) [b]
a	H	H	H	Me	20	16	**a**	79
b	H	H	H	*n*-Pr	20	18	**b**	69
c	H	H	*n*-Pr	H	20	21	**b**	74
d	H	H	Me	Me	20	19	**d**	90
e	H	Me	H	Me	20	39	**e**	75
f	Me	H	H	H	67	16	**f** [c]	68

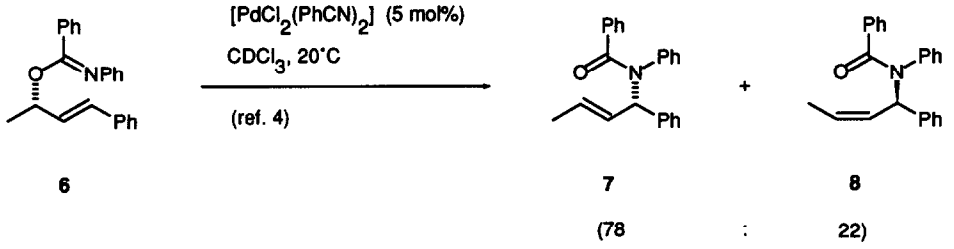
[a] Capillary GC showed complete conversion of **4** after the time listed. [b] Yield of pure product after flash chromatography. [c] (*E*) : (*Z*) = 80 : 20 by capillary GC, no conversion of **4f** after 28 h at 20°C.

All substrates **4** rearranged solely by O→N allyl shift to give propanamides **5a - f** in good to excellent yields. (*E*) and (*Z*) configured allyl moieties reacted equally well (**5b** from **4b** and **4c**) and a bond from nitrogen to a tertiary carbon was easily set up (**4d**).

Most remarkably, even when a σ-bond from a tertiary carbon to palladium had to be formed (see intermediate **2** for **4e**), this sterically demanding reaction still took place at room temperature. Since a longer reaction time was needed for complete conversion of **4e** compared to **4a - d**, this result is still consistent with a cyclization-induced rearrangement involving the intermediacy of cation **2**[4,13] and suggests that stabilization of a partial positive charge at the terminal carbon of the former allyl fragment in **2** by an electron donor group (R^4 = Me) can compensate for an unfavorable steric situation.

Whereas these transformations proceeded readily at room temperature and demonstrate a broader scope for palladium(II)-catalyzed polyhetero-[3,3]-sigmatropic rearrangements than has hitherto been recognized, reflux in tetrahydrofuran was required for the reaction of terminally unsubstituted derivative **4f** and

propanamide **5f** was obtained as 80 : 20 mixture of (*E*) and (*Z*) isomers, supporting the inability of allyl *N*-phenylimidates bearing an electron-donating group R[6] to undergo highly (*E*) selective palladium(II)-mediated O→N rearrangements (cf. Scheme 3).[4] Configurational assignment of the geometrical isomers **5f** rests on the ^{13}C NMR spectrum where a high field shift for the resonances of the allylic carbons in the minor component is seen.[17]



6 **7** (78 : 22) **8**

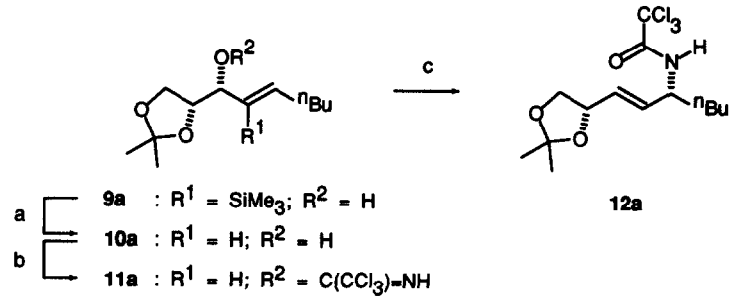
Scheme 3.

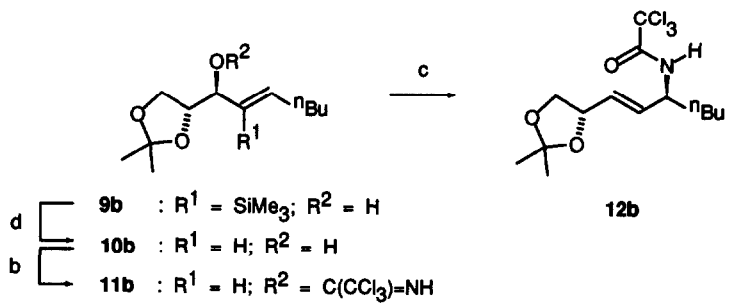
Allyl Trichloroacetimidates

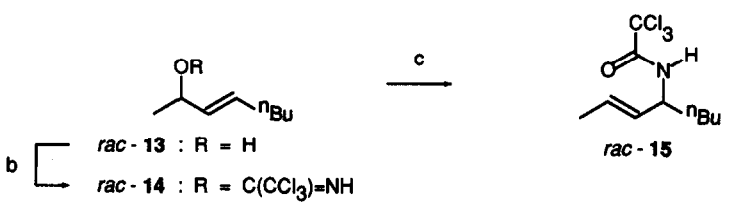
The thermal [3,3]-sigmatropic rearrangement of allyl trichloroacetimidates to allylically transposed *N*-(trichloroacetyl)amines[3,6] is a well known key step for the preparation of primary allyl amines.[18] For trichloroacetimidates of secondary allyl alcohols this rearrangement leads to (*E*) configured products exclusively and is accompanied by a complete chirality transfer in case of optically active substrates.[19] However, owing to the usually long reaction times at high temperatures (110 - 140°C) an elimination of trichloroacetamide can strongly compete.[3,6,19,20] Though the use of analogous trifluoroacetimidates has been shown to suppress diene formation, this alternative still requires a reaction time of 20 h at 140°C.[20] Rearrangement of allyl trichloroacetimidates at room temperature can be achieved by mercury(II)-catalysis (10 - 40 mol%), but under these conditions only derivatives of primary allyl alcohols provide good yields of rearranged amides.[6] Whereas palladium(II)-catalyzed (1 - 10 mol%) rearrangements of allyl *N*-phenylimidates have found some attention[4,5] (*vide supra*), the corresponding reaction of allyl trichloroacetimidates bearing a hydrogen atom on nitrogen has only been mentioned for a derivative of a single primary allyl alcohol.[2]

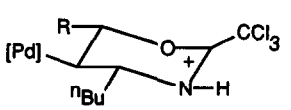
We subjected trichloroacetimidates **11** derived from secondary allyl alcohols to catalytic quantities of dichlorobis(benzonitrile)palladium(II) in tetrahydrofuran and were glad to find that a fast and efficient rearrangement takes place at room temperature to yield only (*E*) configured *N*-allyl-*N*-(trichloroacetyl)amines **12** with complete transfer of chirality (Scheme 4).

Starting from allyl alcohols **9a**[21] and **9b**,[22] which are both accessible with high stereoselectivity from (*R*)-2,3-*O*-isopropylideneglyceraldehyde (**17**)[23] and 1-trimethylsilyl-1-hexyne by a one pot procedure, substrates **11** were prepared by oxygen assisted desilylation[24] and subsequent addition of **10** to trichloroacetonitrile.[3,6] In the presence of the palladium(II)-catalyst both diastereoisomers **11a** and **11b** reacted within a short time at room temperature to give a single product (**12a** resp. **12b**)[25] in high yield. The purely thermal rearrangement of **11a** also led to **12a** (61%) exclusively, however, reflux in toluene for 8 h was required for complete conversion of **11a**. The stereochemical result of the palladium(II)-catalyzed reactions of **11a** and **11b** was surprising since the reported rearrangement of optically active allyl *N*-phenylimidate **6** under similar conditions yielded a mixture of (*E*) and (*Z*) alkenes **7** and **8** with opposite absolute configurations at the sp^3 center in a ratio of 78 : 22 (Scheme 3).[4] In order to investigate if the bulky dioxolane substituent in **11** is responsible for the complete (*E*) selectivity observed here, allyl trichloroacetimidate *rac*-**14** derived from *rac*-**13**[26] was exposed to the palladium(II)-catalyst. Again, only (*E*) configured product *rac*-**15**[25] could be detected, showing that palladium(II)-promoted cyclization-induced rearrangements of allyl trichloroacetimidates proceed solely *via* cationic intermediate **16**[4,27] with equatorial disposition of substituent R for R = methyl already.









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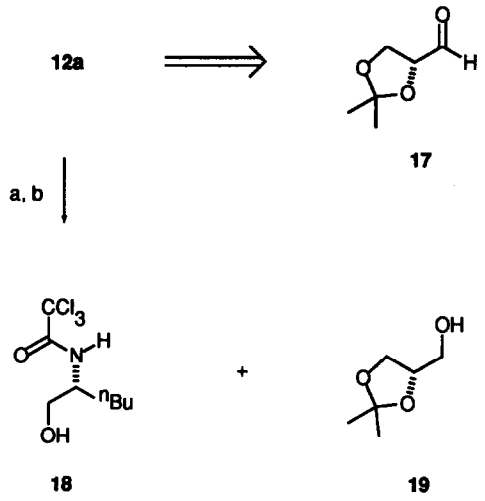
Scheme 4. Synthesis and Palladium(II)-Catalyzed Rearrangement of Allyl Trichloroacetimidates. a) KH, THF, 3 h 20°C, then K_2CO_3, MeOH, H_2O, 1 h 35°C, 92%; b) NaH, ether, 15 min 20°C, then Cl_3C-CN, 15 min -5°C, 79% **11a**, 53% **11b** (from **9b**), 74% *rac*-**14**; c) 4 - 5 mol% $[PdCl_2(PhCN)_2]$, THF, 1.5 - 3 h 20°C, 85% **12a**, 84% **12b**, 62% *rac*-**15**; d) KH, HMPA, 1 h 20°C, then K_2CO_3, H_2O, 1 h 35°C.

The highly diastereoselective palladium(II)-catalyzed rearrangement **11** → **12** allows for a simple synthesis of enantiomerically pure *N*-protected β-amino alcohols from (*R*)-2,3-*O*-isopropylideneglyceraldehyde (**17**) as a chiral template[28] under mild conditions (Scheme 5).



Scheme 5. Synthesis of *N*-Protected β-Amino Alcohol **18**. a) O_3, MeOH, CH_2Cl_2, -78°C, then Me_2S, -78 - 20°C; b) $NaBH_4$, MeOH, 0 - 20°C, 68% **18** and 42% **19** (from **12a**).

Ozonolysis of the C,C double bond in **12a** followed by reductive work up using dimethyl sulfide led to an *N*-protected α-amino aldehyde[31] and regenerated **17**. In order to facilitate reisolation of the chiral template in a storable form, the two aldehydes were reduced with sodium borohydride to yield (*R*)-*N*-(trichloroacetyl)norleucinol (**18**)[32] and (*S*)-2,3-*O*-isopropylideneglycerine (**19**).[33]

Extensions of this concept to other chirality transfer processes are currently under investigation.

EXPERIMENTAL

General remarks. All reactions were run under argon using flame-dried glassware. THF and ether were freshly distilled from benzophenone ketyl. Dichlorobis(benzonitrile)palladium(II) was purchased from Janssen Chimica. Flash chromatography was performed on Merck silica gel 60 (40 - 63 μm). Capillary GC analyses were performed with a Shimadzu GC-14APFsc, a Shimadzu C-R6A integrator, a Rescom OV 225 CB column, 25 m length, 0.25 mm i. d., 0.25 μm film, and a Rescom SE-54 CB column, 25 m length, 0.25 mm i. d., 0.25 μm film. HPLC separations were performed with a Waters Delta Prep 3000, a Waters 404 differential refractometer, a Waters 740 data module, and a Waters Porasil 125 Å (15 - 20 μm) column, 30 cm length, 5 cm i. d.. Optical rotations were measured with a Perkin-Elmer 241 polarimeter. IR spectra ($CHCl_3$) were recorded with a Shimadzu IR-408. ^1H NMR spectra (300 MHz, $CDCl_3$) and ^{13}C NMR spectra (75.47 MHz, $CDCl_3$) were obtained with a Bruker WM 300. ^{13}C multiplicities were determined using INEPT or DEPT pulse sequences. Mass spectra were recorded with a Varian MAT CH-7A and a data system Finnigan MAT 200 (GC / MS) or else with a Varian MAT CH-7 and a data system Varian SS 200. Microanalyses were performed by Mikroanalytisches Laboratorium M. Beller, Göttingen.

N-Allyl-N-phenylpropanamides **5** *- general procedure*. A solution of the allyl *N*-phenylimidate **4**[14] (1 mmol) in dry THF (4 ml) is added to a solution of dichlorobis(benzonitrile)palladium(II) (19 mg, 0.05 mmol) in dry THF (1 ml). The resulting mixture is stirred at room temperature (**4a - e**) or at reflux (**4f**) for the time listed in Table 1. The solvent is removed *in vacuo* and the crude product is purified by flash chromatography using ethyl acetate / petroleum ether 1 : 4 (**5a, 5e, 5f**) or ethyl acetate / petroleum ether 1 : 6 (**5b, 5d**) as eluent to give **5** as an oil (for yields see Table 1).

***N*-Phenyl-*N*-propionyl-2-amino-3-butene (5a)**: IR 1630, 1595 cm^{-1}; ^1H NMR δ 1.03 (t, 3 H, J = 7.5), 1.14 (d, 3 H, J = 6.9), 1.96 (m, 2 H), 5.07 (d, 1 H, J = 10.5), 5.10 (d, 1 H, J = 17.3), 5.45 (m, 1 H), 5.81 (ddd, 1 H, J = 6.1, J = 10.5, J = 17.3), 7.0 - 7.5 (m, 5 H_{arom}); ^{13}C NMR δ 9.52 (q), 17.45 (q), 28.36 (t), 51.91 (d), 115.79 (t), 128.07 (d), 129.03 (d), 130.22 (d), 138.60 (d), 139.10 (s), 173.23 (s); MS (GC / MS) *m/e* 203 (M^+, 26), 132 (100). Anal. Calcd for $C_{13}H_{17}NO$: C, 76.80; H, 8.43. Found: C, 76.65; H, 8.59.

***N*-Phenyl-*N*-propionyl-3-amino-1-hexene (5b)**: IR 1635, 1590 cm^{-1}; ^1H NMR δ 0.92 (t, 3 H, J = 7.1), 1.03 (t, 3 H, J = 7.4), 1.2 - 1.6 (m, 4 H), 1.96 (q, 2 H, J = 7.4), 5.08 - 5.24 (m, 3 H), 5.61 (ddd, 1 H, J = 8.0, J = 10.2, J = 17.5), 7.0 - 7.5 (m, 5 H_{arom}); ^{13}C NMR δ 9.65 (q), 13.87 (q), 19.60 (t), 28.31 (t), 34.31 (t), 57.80 (d), 117.55 (t), 128.14 (d), 129.13 (d), 130.13 (d), 137.25 (d), 139.52 (s), 173.66 (s); MS *m/e* 231 (M^+, 2), 132 (100). Anal. Calcd for $C_{15}H_{21}NO$: C, 77.89; H, 9.15. Found: C, 78.01; H, 9.31.

***N*-Phenyl-*N*-propionyl-2-amino-2-methyl-3-butene (5d)**: IR 1635, 1590 cm^{-1}; ^1H NMR δ 0.95 (t, 3 H, J = 7.4), 1.34 (s, 6 H), 1.85 (q, 2 H, J = 7.4), 5.00 (d, 1 H, J = 10.7), 5.07 (d, 1 H, J = 17.5), 6.26 (dd, 1 H, J = 10.7, J = 17.5), 7.1 - 7.4 (m, 5 H_{arom}); ^{13}C NMR δ 9.30 (q), 27.54 (q), 30.14 (t), 60.46 (s), 110.25 (t), 127.97 (d), 129.03 (d), 130.23 (d), 141.69 (s), 145.54 (d), 173.56 (s); MS *m/e* 217 (M^+, 11), 93 (100). Anal. Calcd for $C_{14}H_{19}NO$: C, 77.38; H, 8.81. Found: C, 77.28; H, 8.82.

***N*-Phenyl-*N*-propionyl-2-amino-3-methyl-3-butene (5e)**: IR 1640, 1600 cm^{-1}; ^1H NMR δ 1.03 (t, 3 H, J = 7.4), 1.11 (d, 3 H, J = 7.0), 1.83 (s, 3 H), 1.90 - 2.07 (m, 2 H), 4.60 (s, 1 H), 4.85 (s, 1 H), 5.50 (q, 1 H, J = 7.0), 7.0 - 7.4 (m, 5 H_{arom}); ^{13}C NMR δ 9.73 (q), 16.58 (q), 21.50 (q), 28.45 (t), 52.97 (d), 112.92 (t), 127.96 (d), 128.82 (d), 129.90 (d), 138.81 (s), 144.81 (s), 173.68 (s); MS (GC / MS) *m/e* 217 (M^+, 73), 57 (100). Anal. Calcd for $C_{14}H_{19}NO$: C, 77.38; H, 8.81. Found: C, 77.53; H, 8.81.

***N*-Phenyl-*N*-propionyl-1-amino-2-butene (5f)**: IR 1630, 1590 cm^{-1}; ^1H NMR δ 1.05 (t, 3 H, J = 7.4), 1.46 for (*Z*)-**5f** and 1.64 for (*E*)-**5f** (d, 3 H, J = 6.6 for (*Z*)-**5f** and J = 4.2 for (*E*)-**5f**), 2.07 (q, 2 H, J = 7.4), 4.22 for (*E*)-**5f** and 4.36 for (*Z*)-**5f** (d, 2 H, J = 5.0 for (*E*)-**5f** and J = 6.7 for (*Z*)-**5f**), 5.4 - 5.7 (m, 2 H), 7.1 - 7.5 (m, 5 H_{arom}); ^{13}C NMR δ 9.48 (q), 12.46 (q, (*Z*)-**5f**), 17.51 (q, (*E*)-**5f**), 27.57 (t, (*Z*)-**5f**), 27.65 (t, (*E*)-**5f**), 45.53 (t, (*Z*)-**5f**), 51.30 (t, (*E*)-**5f**), 125.12 (d), 125.82 (d), 127.57 (d), 128.24 (d), 129.04 (d), 129.31 (d), 129.37 (d), 142.50 (s, (*Z*)-**5f**), 142.55 (s, (*E*)-**5f**), 173.26 (s); MS (GC / MS) *m/e* (*E*)-**5f**: 203 (M^+, 48), 93 (100), (*Z*)-**5f**: 203 (M^+, 41), 93 (100). Anal. Calcd for $C_{13}H_{17}NO$: C, 76.80; H, 8.43. Found: C, 76.88; H, 8.47.

Preparation of vinylsilanes **9** *from (R)-2,3-O-isopropylideneglyceraldehyde (17)*. **9a** was prepared *via* addition of a vinylcopper species to **17**.[21] In our hands, this method led to **9a** : **9b** = 88 : 12 according to capillary GC (66% yield). **9b** was prepared *via* addition of a vinyl cuprate to **17**.[22] Here, we obtained **9a** : **9b** = 4 : 96 according to capillary GC (50% yield). Purification of **9a** and **9b** by preparative HPLC using petroleum ether / ethyl acetate / triethylamine 85 : 14 : 1 afforded the pure isomers as colorless oils.

(*Z*)-(1*S*,4'*R*)-1-(2,2-Dimethyl-1,3-dioxolane-4-yl)-2-trimethylsilyl-hept-2-en-1-ol (9a): $[\alpha]_D^{20}$ = -4.7 (*c* = 10, $CHCl_3$); IR (film) 3480, 840 cm^{-1}; ^1H NMR δ 0.16 (s, 9 H), 0.87 (t, 3 H, *J* = 7.1), 1.27 - 1.31 (m, 4 H), 1.35 (s, 3 H), 1.40 (s, 3 H), 2.12 (dt, 2 H, J_t = 7.1, J_d = 7.4), 2.31 (d, 1 H, *J* = 3.0), 3.56 (dd, 1 H, *J* = 6.5, *J* = 8.5), 3.85 (dd, 1 H, *J* = 6.3, *J* = 8.5), 3.98 (dd, 1 H, *J* = 3.0, *J* = 7.9), 4.11 (m, 1 H), 6.20 (dt, 1 H, J_d = 0.7, J_t = 7.4); ^{13}C NMR δ 1.04 (q), 14.00 (q), 22.42 (t), 25.60 (q), 26.94 (q), 31.61 (t), 31.64 (t), 66.36 (t), 78.99 (d), 80.01 (d), 109.80 (s), 138.21 (s), 147.49 (d); MS (GC / MS) *m/e* 271 (M^+ - CH_3, 0.7), 101 (100). Anal. Calcd for $C_{15}H_{30}O_3Si$: C, 62.89; H, 10.56. Found: C, 62.70; H 10.60.

(*Z*)-(1*R*,4'*R*)-1-(2,2-Dimethyl-1,3-dioxolane-4-yl)-2-trimethylsilyl-hept-2-en-1-ol (9b): $[\alpha]_D^{20}$ = +23.1 (*c* = 1.06, $CHCl_3$), $[\alpha]_{365}^{20}$ = +54.3 (*c* = 1.06, $CHCl_3$); IR (film) 3450, 830 cm^{-1}; ^1H NMR δ 0.15 (s, 9 H), 0.88 (t, 3 H, *J* = 7.1), 1.22 - 1.39 (m, 4 H), 1.35 (s, 3 H), 1.42 (s, 3 H), 2.10 - 2.17 (m, 3 H), 3.74 (dd, 1 H, *J* = 6.7, *J* = 8.3), 3.86 (m, 1 H), 4.10 (m , 1 H), 4.47 (m, 1 H), 6.43 (dt, 1 H, J_d = 1.6, J_t = 7.6); ^{13}C NMR δ 0.24 (q), 13.92 (q), 22.33 (t), 25.19 (q), 26.35 (q), 31.58 (t), 31.86 (t), 63.85 (t), 71.81 (d), 77.89 (d), 109.22 (s), 136.12 (s), 143.27 (d); MS (GC / MS) *m/e* 271 (M^+ - CH_3, 2), 101 (100). Anal. Calcd for $C_{15}H_{30}O_3Si$: C, 62.89; H, 10.56. Found: C, 63.09; H 10.55.

*Oxygen assisted desilylation[24] of **9** to allyl alcohols **10**.*

(*E*)-(1*R*,4'*R*)-1-(2,2-Dimethyl-1,3-dioxolane-4-yl)-hept-2-en-1-ol (10a): A solution of the allyl alcohol **9a** (1.90 g, 6.63 mmol) in dry THF (20 ml) is added to a suspension of KH (53 mg, 1.32 mmol) in dry THF (25 ml) under argon. The solution is stirred at room temperature for 3 h and then treated with K_2CO_3 (5 g) in water (10 ml) and methanol (30 ml) at 35°C for 1 h. The aqueous phase is separated and extracted with ether (4 x 10 ml). The combined organic phases are dried over $MgSO_4$ and concentration *in vacuo* yields **10a** (1.313 g, 92%) as an oil: $[\alpha]_D^{20}$ = +1.2 (*c* = 1, $CHCl_3$), $[\alpha]_{365}^{20}$ = +5.6 (*c* = 1, $CHCl_3$); IR (film) 3450, 960 cm^{-1}; ^1H NMR δ 0.87 (t, 3 H, *J* = 7.1), 1.28 - 1.33 (m, 4 H), 1.35 (s, 3 H), 1.43 (s, 3 H), 2.02 (m, 2 H), 2.14 (s, 1 H), 3.67 - 3.72 (m, 1 H), 3.92 - 4.02 (m, 3 H), 5.36 (dd, 1 H, *J* = 6.9, *J* = 15.5), 5.77 (dt, 1 H, J_t = 6.8, J_d = 15.3); ^{13}C NMR δ 13.78 (q), 22.07 (t), 25.27 (q), 26.73 (q), 31.00 (t), 31.91 (t), 65.91 (t), 74.38 (d), 78.99 (d), 109.75 (s), 127.58 (d), 135.41 (d); MS (GC / MS) *m/e* 199 (M^+ - CH_3, 3), 101 (100). Anal. Calcd for $C_{12}H_{22}O_3$: C, 66.94; H, 10.77. Found: C, 66.90; H 10.82.

(*E*)-(1*S*,4'*R*)-1-(2,2-Dimethyl-1,3-dioxolane-4-yl)-hept-2-en-1-ol (10b): **10b** is prepared from **9b** using the same procedure as for **10a** with the exception that the solvent THF is replaced by HMPA in the first step and methanol is omitted in the second step. The crude product is purified by bulb to bulb distillation and used directly for preparation of **11b**. An analytical sample of **10b** was characterized as follows: IR (film) 3450, 980 cm^{-1}; ^1H NMR δ 0.87 (t, 3 H, *J* = 7.1), 1.25 - 1.33 (m, 4 H), 1.34 (s, 3 H), 1.42 (s, 3 H), 2.03 (m, 2 H), 2.11 (d, 1 H, *J* = 2.5), 3.90 (dd, 1 H, *J* = 5.1, *J* = 8.2), 3.96 (dd, 1 H, *J* = 6.5, *J* = 8.2), 4.10 (m, 1 H), 4.25 (m, 1 H), 5.39 (ddt, 1 H, J_t = 1.4, J_d = 6.4, J_d = 15.5), 5.78 (ddt, 1 H, J_d = 1.2, J_t = 6.8, J_d = 15.5); ^{13}C NMR δ 13.74 (q), 22.02 (t), 25.09 (q), 26.32 (q), 31.05 (t), 31.89 (t), 64.93 (t), 71.63 (d), 78.47 (d), 109.11 (s), 127.56 (d), 133.70 (d); MS (GC / MS) *m/e* 199 (M^+ - CH_3, 6), 101 (100); MS (GC / MS; high resolution) Calcd for $C_{11}H_{19}O_3$ (M^+ - CH_3): 199.1334. Found: 199.1336.

*Allyl 2,2,2-Trichloroacetimidates **11a**, **11b**, and rac-**14** - general procedure.*[6] A solution of the allyl alcohol **10a**, **10b**, or *rac*-**13**[26] in dry ether is added to a suspension of hexane washed NaH in dry ether under argon. After 15 min the solution is cooled to -5°C and a solution of trichloroacetonitrile in dry ether is added. The solution is stirred for additional 15 min, the solvent is removed *in vacuo* and the residue is treated with pentane containing 0.3% methanol. The suspension is filtered and the precipitate is washed with pentane. After concentration by evaporation and flash chromatography using petroleum ether / ethyl acetate / triethylamine 96 : 3 : 1 compounds **11a**, **11b**, and *rac*-**14** were obtained as colorless oils.

***O*-[(*E*)-(1*R*,4'*R*)-1-(2,2-Dimethyl-1,3-dioxolane-4-yl)-hept-2-en-1-yl] 2,2,2-trichloroacetimidate (11a)**: 70 mg (2.34 mmol) NaH (80%) in ether (6 ml), 1.00 g (4.67 mmol) **10a** in ether (6 ml), 720 mg (5.00 mmol) trichloroacetonitrile in ether (5 ml), 20 ml pentane / methanol (99.7 : 0.3). Yield: 1.325 g (79%) **11a**: $[\alpha]_D^{20}$ = -14.6 (*c* = 1, $CHCl_3$), $[\alpha]_{365}^{20}$ = -61.3 (*c* = 1, $CHCl_3$); IR (film) 3330, 1660 cm^{-1}; ^1H NMR δ 0.84 (t, 3 H, *J* = 7.1), 1.20 - 1.32 (m, 4 H), 1.32 (s, 3 H), 1.40 (s, 3 H), 2.04 (m, 2 H), 3.82 (dd, 1 H, *J* = 6.0, *J* = 8.5), 3.98 (dd, 1 H, *J* = 6.5, *J* = 8.5), 4.29 (m, 1 H), 5.39 (m, 1 H), 5.46 (ddt, 1 H, J_t = 1.4, J_d = 7.4, J_d = 14.8), 5.89 (dt, 1 H, J_t = 6.8, J_d = 14.7), 8.31 (s, 1 H); ^{13}C NMR δ 13.72 (q), 21.94 (t), 25.38 (q), 26.28 (q), 30.79 (t), 31.89 (t), 65.38 (t), 76.34 (d), 78.97 (d), 91.55 (s), 109.79 (s), 122.76 (d), 137.55 (d), 161.51 (s); MS *m/e* 359 / 357 (M^+, 1 / 2), 43 (100). Anal. Calcd for $C_{14}H_{22}Cl_3NO_3$: C, 46.88; H, 6.18. Found: C, 47.06; H 6.36.

***O*-[(*E*)-(1*S*,4'*R*)-1-(2,2-Dimethyl-1,3-dioxolane-4-yl)-hept-2-en-1-yl] 2,2,2-trichloroacetimidate (11b)**: 52 mg (1.75 mmol) NaH (80%) in ether (5 ml), crude **10b** from 1.00 g **9b** (3.49 mmol) in ether (5 ml), 580 mg (4.02 mmol) trichloroacetonitrile in ether (4 ml), 15 ml pentane / methanol (99.7 : 0.3). Yield: 660 mg (53% from **9b**) **11b**: $[\alpha]_D^{20}$ = +21.6 (*c* = 1.05, $CHCl_3$), $[\alpha]_{365}^{20}$ = +81.1 (*c* = 1.05, $CHCl_3$); IR (film) 3340, 1660 cm^{-1}; ^1H NMR δ 0.86 (t, 3 H, *J* = 7.1), 1.26 - 1.37 (m, 4 H), 1.35 (s, 3 H), 1.41 (s, 3 H), 2.05 (m, 2 H), 3.91 (dd, 1 H, *J* = 6.2, *J* = 8.4), 4.06 (dd, 1 H, *J* = 6.4, *J* = 8.4), 4.25 (m, 1 H), 5.41 (m, 1 H), 5.46 (ddt, 1 H, J_t = 1.4, J_d = 6.8, J_d = 14.8), 5.87 (dt, 1 H, J_t = 6.7, J_d = 14.7), 8.34 (s, 1 H); ^{13}C NMR δ 13.84 (q), 22.05 (t), 25.42 (q), 26.52 (q), 30.93 (t), 32.02 (t), 65.98 (t), 76.59 (d), 78.43 (d), 91.59 (s), 109.85 (s), 123.41 (d), 136.82 (d), 161.51 (s); MS *m/e* 359 / 357 (M^+, 4 / 4), 101 (100). Anal. Calcd for $C_{14}H_{22}Cl_3NO_3$: C, 46.88; H, 6.18. Found: C, 46.96; H 6.09.

***O*-[(*E*)-Oct-3-en-2-yl] 2,2,2-trichloroacetimidate (*rac*-14)**: 60 mg (2.00 mmol) NaH (80%) in ether (10 ml), 641 mg (5.00 mmol) *rac*-**13** in ether (10 ml), 870 mg (6.00 mmol) trichloroacetonitrile in ether (8 ml), 20 ml pentane / methanol (99.7 : 0.3). Yield: 1.016 g (74%) *rac*-**14**: IR (film) 3360, 1660 cm^{-1}; ^1H NMR δ 0.89 (t, 3 H, *J* = 7.0), 1.25 - 1.46 (m, 4 H), 1.42 (d, 3 H, *J* = 6.2), 2.01 - 2.08 (m, 2 H), 5.45 (m, 1 H), 5.55 (ddt, 1 H, J_t = 1.4, J_d = 6.6, J_d = 15.0), 5.79 (dt, 1 H, J_t = 6.7, J_d = 15.0), 8.25 (s, 1 H); ^{13}C NMR δ 13.83 (q), 19.79 (q), 22.07 (t), 31.05 (t), 31.81 (t), 76.07 (d), 91.99 (s), 128.57 (d), 133.75 (d), 161.83 (s). Anal. Calcd for $C_{10}H_{16}Cl_3NO$: C, 44.06; H, 5.92. Found: C, 44.10; H 6.03.

*N-Allyl-2,2,2-trichloroacetamides **12a**, **12b**, and rac-15 - general procedure.* A solution of dichlorobis(benzonitrile)palladium(II) in dry THF is added to a solution of allyl 2,2,2-trichloroacetimidate **11a**, **11b**, or *rac*-**14** in dry THF and the solution is stirred for 1.5 - 3 h at room temperature. The reaction is complete when the color turnes from yellow to orange. The solvent is removed *in vacuo* and the crude product is purified by flash chromatography using petroleum ether / ethyl acetate / triethylamine 93 : 6 : 1 yielding **12a**, **12b**, or *rac*-**15** as colorless oils which slowly solidify upon cooling.

***N*-[(*E*)-(3*R*,4'*S*)-1-(2,2-Dimethyl-1,3-dioxolane-4-yl)-hept-1-en-3-yl]-2,2,2-trichloroacetamide (12a)**: 100 mg (0.28 mmol) **11a** in THF (2.5 ml), 4.4 mg (0.011 mmol) $[PdCl_2(PhCN)_2]$ in THF (0.2 ml). Yield: 85 mg (85%) **12a**: $[\alpha]_D^{20}$ = +36.3 (*c* = 1.03, $CHCl_3$), $[\alpha]_{365}^{20}$ = +140.3 (*c* = 1.03, $CHCl_3$); IR (film) 1700, 1520 cm^{-1}; ^1H NMR δ 0.88 (t, 3 H, *J* = 6.9), 1.26 - 1.37 (m, 4 H), 1.37 (s, 3 H), 1.40 (s, 3 H), 1.56 - 1.67 (m, 2 H), 3.56 (m , 1 H), 4.08 (dd, 1 H, *J* = 6.2, *J* = 8.2), 4.40 (m, 1 H), 4.50 (m, 1 H), 5.61 (ddd, 1 H, *J* = 1.2, *J* = 7.1, *J* = 15.5), 5.77 (dd, 1 H, *J* = 5.0, *J* = 15.5), 6.50 (d, 1 H, *J* = 7.9); ^{13}C NMR δ 13.79 (q), 22.19 (t), 25.73 (q), 26.53 (q), 27.66 (t), 34.20 (t), 52.34 (d), 69.30 (t), 76.17 (d), 92.67 (s), 109.40 (s), 129.02 (d), 132.46 (d), 161.07 (s); MS (GC / MS) *m/e* 346 / 344 / 342 (M^+ - CH_3, 3 / 10 / 12), 72 (100). Anal. Calcd for $C_{14}H_{22}Cl_3NO_3$: C, 46.88; H, 6.18. Found: C, 46.73; H 6.40.

***N*-[(*E*)-(3*S*,4'*S*)-1-(2,2-Dimethyl-1,3-dioxolane-4-yl)-hept-1-en-3-yl]-2,2,2-trichloroacetamide (12b)**: 100 mg (0.28 mmol) **11b** in THF (2.5 ml), 5.5 mg (0.014 mmol) $[PdCl_2(PhCN)_2]$ in THF (0.2 ml). Yield: 84 mg (84%) **12b**: $[\alpha]_D^{20}$ = -5.3 (*c* = 1, $CHCl_3$), $[\alpha]_{365}^{20}$ = -29.0 (*c* = 1, $CHCl_3$); IR (film) 1700, 1515 cm^{-1}; ^1H NMR δ 0.88 (t, 3 H, *J* = 7.0), 1.29 - 1.34 (m, 4 H), 1.37 (s, 3 H), 1.41 (s, 3 H), 1.56 - 1.66 (m, 2 H), 3.58 (m, 1 H), 4.09 (dd, 1 H, *J* = 6.3, *J* = 8.0), 4.40 (m, 1 H), 4.50 (m, 1 H), 5.66 (dd, 1 H, *J* = 5.8, *J* = 15.6), 5.74 (dd, 1 H, *J* = 5.4, *J* = 15.6), 6.48 (d, 1 H, *J* = 8.0); ^{13}C NMR δ 13.85 (q), 22.28 (t), 25.82 (q), 26.60 (q), 27.68 (t), 34.10 (t), 52.66 (d), 69.40 (t), 76.12 (d), 92.75 (s), 109.52 (s), 130.02 (d), 132.00 (d), 161.06 (s); MS (GC / MS) *m/e* 346 / 344 / 342 (M^+ - CH_3, 3 / 7 / 7), 72 (100). Anal. Calcd for $C_{14}H_{22}Cl_3NO_3$: C, 46.88; H, 6.18. Found: C, 46.74; H 6.08.

***N*-[(*E*)-Oct-2-en-4-yl]-2,2,2-trichloroacetamide (*rac*-15)**: 137 mg (0.50 mmol) *rac*-**14** in THF (5 ml), 9.6 mg (0.025 mmol) $[PdCl_2(PhCN)_2]$ in THF (0.5 ml). Yield: 85 mg (62%) *rac*-**15**: IR (film) 1695, 1515 cm^{-1}; ^1H NMR δ 0.90 (t, 3 H, *J* = 6.8), 1.28 - 1.38 (m, 4 H), 1.54 - 1.65 (m, 2 H), 1.71 (d, 3 H, *J* = 6.5), 4.33 (m, 1 H), 5.39 (ddq, 1 H, J_q = 1.6, J_d = 6.5, J_d = 15.3), 5.69 (ddq, 1 H, J_d = 1.2, J_q = 6.5, J_d = 15.3), 6.46 (d, 1 H, *J* = 6.0); ^{13}C NMR δ 13.89 (q), 17.72 (q), 22.33 (t), 27.74 (t), 34.51 (t), 53.32 (d), 94.53 (s), 127.89 (d), 129.62 (d), 160.90 (s); MS (GC / MS) *m/e* 238 / 236 (M^+ - Cl, 17 / 26), 218 / 216 / 214 (31 / 95 / 100). Anal. Calcd for $C_{10}H_{16}Cl_3NO$: C, 44.06; H, 5.92. Found: C, 44.26; H 6.05.

*Ozonolysis of trichloroacetimidate **12a**.*

***(R)*-*N*-(Trichloroacetyl)norleucinol (18)**: A solution of **12a** (150 mg, 0.42 mmol) in methanol (15 ml) and CH_2Cl_2 (30 ml) is ozonized at -78°C until the mixture turns blue. Excess ozone is removed by purging with nitrogen. Dimethyl sulfide (2 ml) is added and the solution is stirred overnight at room temperature. CH_2Cl_2

and dimethyl sulfide are removed by distillation using a Vigreux column and 24 mg $NaBH_4$ (0.63 mmol) are added at 0°C to the remaining solution. The reaction mixture is stirred overnight while the temperature rises up to room temperature. Water (15 ml) is added and the aqueous phase is extracted with CH_2Cl_2 (5 x 20 ml). The combined organic phases are dried over $MgSO_4$ and concentrated under reduced pressure. The remaining oil is purified by flash chromatography with petroleum ether / ethyl acetate 1 : 1 yielding 23.5 mg (42%) **19**[33] and 75 mg (68%) **18**[32]: $[\alpha]_D^{20}$ = +23.7 (*c* = 1, $CHCl_3$), $[\alpha]_{365}^{20}$ = +74.4 (*c* = 1, $CHCl_3$); IR (film) 1695, 1525 cm^{-1}; ^1H NMR δ 0.89 (t, 3 H, *J* = 7.0), 1.31 - 1.36 (m, 4 H), 1.55 - 1.66 (m, 2 H), 1.92 (s, 1 H), 3.70 (dd, 1 H, *J* = 4.3, *J* = 11.0), 3.76 (dd, 1 H, *J* = 3.3, *J* = 11.0), 3.88 - 3.97 (m, 1 H), 6.64 (s, 1 H); ^{13}C NMR δ 13.88 (q), 22.40 (t), 27.96 (t), 30.48 (t), 53.29 (d), 63.82 (t), 92.70 (s), 162.09 (s); MS (GC / MS) *m/e* 234 / 232 / 230 (M^+ - CH_2OH, 31 / 87 / 93), 69 (100). Anal. Calcd for $C_8H_{14}Cl_3NO_2$: C, 36.60; H, 5.37. Found: C, 36.84; H 5.61.

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