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A convenient synthesis of (*Z*)-1-chloro-1-alkenes and (*Z*)-1-chloro-2-alkoxy-1-alkenes

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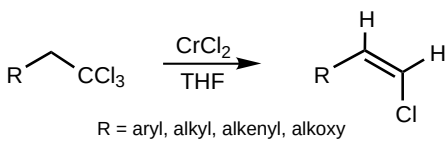
Abstract—Mild, room temperature $CrCl_2$ reduction of 1,1,1-trichloroalkanes stereoselectively generates (*Z*)-1-chloro-2-substituted-1-alkenes in excellent yields.

(*Z*)-1-Chloro-1-alkenes are useful synthetic intermediates[1] as well as structural components in some medicinally significant pharmaceuticals[2] and natural products.[3] They are most often prepared by Wittig and related olefinations,[4] selective hydrogenation,[5] hydroboration/protonolysis[6] of 1-chloro-1-alkynes, transition metal-catalyzed additions,[7] or E_2-eliminations.[8] However, extant methodology is sometimes unreliable, inefficient, and/or generates mixtures of geometric isomers. These limitations are particularly relevant for conjugated systems and for (*Z*)-1-chloro-2-alkoxy-1-alkenes (α-chloroenol ethers), whose sensitivity to a wide variety of reagents and acids makes their preparation quite challenging.[9] In continuation of our investigations[10] of organochromium methodology, we report herein a broadly applicable and convenient preparation of (*Z*)-1-chloro-1-alkenes and (*Z*)-1-chloro-2-alkoxy-1-alkenes via $CrCl_2$ reduction of 1,1,1-trichloroalkanes in THF at ambient temperature (Eq. (1)).[11]



(1)

R = aryl, alkyl, alkenyl, alkoxy

The results from subjecting a panel of substituted 1,1,1-trichloroalkanes[12] to $CrCl_2$ reduction are summarized in Table 1 and illustrate the generality of the method. As determined by ^1H NMR analysis, stereochemically pure (*Z*)-α-chlorostyrene (**2**) was smoothly generated from (2,2,2-trichloroethyl)benzene (**1**) in excellent yield (entry 1). Likewise, furan **3**[13] and thiophene **5** gave good yields of the corresponding heterocyclic (*Z*)-olefins **4** and **6**, respectively. Notably, reduction of unactivated trichloride **7** to **8** (entry 4) and its homoallylic homolog **9** to *E*,*Z*-diene **10** (entry 5) proceeded with complete stereochemical integrity. The compatibility of the general procedure with a variety of common functionality was demonstrated by the conversion of aryl bromide **11**, acetonide **13**, and bis-acetate **15** to **12** (entry 6), **14** (entry 7), and **16** (entry 8), respectively. Access to α-chloroenol ethers was achieved with outstanding results. Benzyl ether **17**, phenacyl **19**, α,β-unsaturated ester **21**, and allylic ether **23** provided the (*Z*)-1-chloro-2-alkoxy-1-alkenes **18** (entry 9), **20** (entry 10), **22** (entry 11), and **24** (entry 12) without incident.

Recent mechanistic studies[14] provide important insights into the remarkable stereospecificity observed above. The 1,1,1-trichloroalkanes are initially transformed by $CrCl_2$ to a labile 1-chloro-1,1-dichromium carbenoid **25** (Scheme 1). Formally, the oxidative addition of Cr(II) into a C–Cl bond involves two consecutive single-electron transfers,[15] thus accounting for the four equivalents of $CrCl_2$ needed for the generation of **25** (see General procedure). As a consequence of the high steric presentation by the *gem*-chromiums, **25** adopts a conformation that minimizes the interaction between the R group and the two chromiums. From this eclipsed conformation, *syn*-β-elimination of chromium hydride gives rise to (*E*)-chromium vinylidene carbenoid **26** exclusively and whence to (*Z*)-1-chloro-1-alkene upon quenching.

Keywords: alkenyl halides; carbenoids; chromium; enol ethers.

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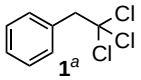
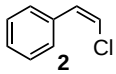
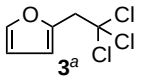
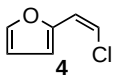
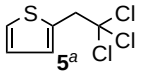
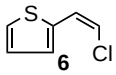
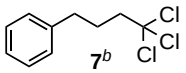
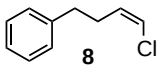
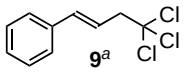
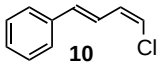
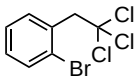
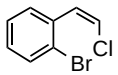
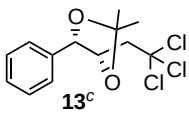
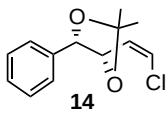
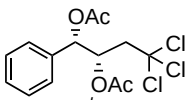
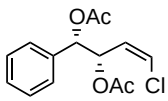
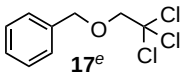
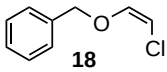
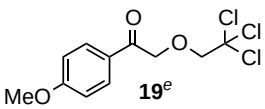
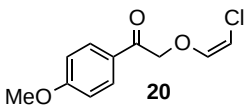
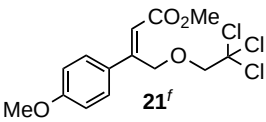
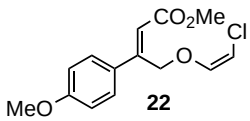
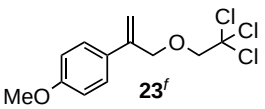
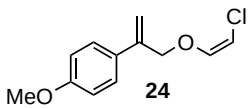
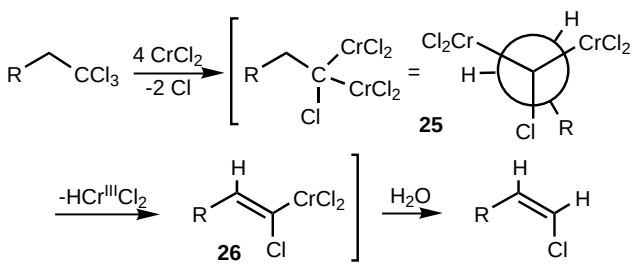
Table 1. Synthesis of (*Z*)-1-chloro-1-alkenes and (*Z*)-1-chloro-2-alkoxy-1-alkenes

Entry	Reactant	Product	Yield (%)
1	 **1**[a]	 **2**	93
2	 **3**[a]	 **4**	91
3	 **5**[a]	 **6**	89
4	 **7**[b]	 **8**	98
5	 **9**[a]	 **10**	95
6	 **11**[a]	 **12**	83
7	 **13**[c]	 **14**	97
8	 **15**[d]	 **16**	93
9	 **17**[e]	 **18**	92
10	 **19**[e]	 **20**	95
11	 **21**[f]	 **22**	92
12	 **23**[f]	 **24**	97

[a]Ref. 12a. [b]Ref.12b. [c]Ref. 12c. [d]Ref. 12d. [e]Ref. 12e. [f]Ref. 12f.

General procedure: 1,1,1-Trichloroalkane (0.4 mmol) in THF (2 mL) was added to a stirring, rt suspension of anhydrous $CrCl_2$[16] (1.6 mmol, 4 equiv.) in THF (8 mL) under argon. After 10–12 h, the reddish reaction mixture was quenched with water and extracted with ether (3×8 mL). The combined ethereal extracts were evaporated in vacuo and the residue was purified by SiO_2 chromatography to give stereochemically pure (>98% by ^1H NMR) (*Z*)-1-chloro-1-alkene in the indicated yields (Table 1).



Scheme 1.

Acknowledgements

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12. (a) Prepared (86–96% yield) from commercial bromide (1 mmol), $CHCl_3$ (2 mmol), and NaH (2 mmol) in DMF (15 mL) at 0°C for 6 h. See, Rachid Baati, Ph.D. Thesis, Université Louis Pasteur de Strasbourg, 2000; (b) from **9** (95%) via $Pd/C/H_2$ in EtOH; (c) from **9** via α-AD-mix (CH_2Cl_2, 4°C; 89%), then $Me_2C(OMe)_2$/PTSA (CH_2Cl_2, 23°C; 95%); (d) from **9** via α-AD-mix (CH_2Cl_2, 4°C; 89%), then Ac_2O/py (CH_2Cl_2, 23°C; 92%); (e) according to Morimoto, T.; Sekiya, M. *Synthesis* **1981**, 308–310 using trichloroethanol and benzyl bromide (85%) or 2-bromo-4′-methoxybenzophenone (82%); (f) from **19** via olefination with Ph_3PCHCO_2Me (C_6H_6, 100°C; 85%) or Ph_3PCH_3Br (BuLi, −78°C to rt, THF; 80%).
13. Spectral data for **3**: ^1H NMR ($CDCl_3$, 300 MHz) δ 4.01 (s, 2H), 6.39–6.42 (m, 1H), 6.45–6.48 (m, 1H), 7.43–7.46 (m, 1H); ^{13}C NMR ($CDCl_3$, 75 MHz) δ 53.21, 97.35, 110.90, 111.37, 143.13, 147.87. **9**: ^1H NMR ($CDCl_3$, 300 MHz) δ 4.22 (s, 2H), 7.40–7.60 (m, 2H), 7.80–7.86 (m, 2H); ^{13}C NMR ($CDCl_3$, 75 MHz) δ 57.97, 98.71, 16.98, 127.37, 130.20, 133.24, 133.65. **10**: ^1H NMR ($CDCl_3$, 300 MHz) δ 6.41 (d, 1H, $J=6.0$ Hz), 6.86 (d, 1H, $J=6.0$ Hz), 7.14–7.22 (m, 1H), 7.30–7.36 (m, 1H), 7.56–7.66 (m, 1H), 7.83 (d, 1H, $J=5.7$ Hz); ^{13}C NMR ($CDCl_3$, 75 MHz) δ 120.09, 124.17, 127.16, 129.14, 129.71, 130.91, 132.87, 134.12. **12**: ^1H NMR ($CDCl_3$, 300 MHz) δ 2.50–2.60 (m, 2H), 2.73 (t, 2H, $J=7.2$ Hz), 5.77 (dd, 1H, $J=7.2$, 14.1 Hz), 6.04 (d, 1H, $J=6.9$ Hz), 7.20–7.38 (m, 5H); ^{13}C NMR ($CDCl_3$, 75 MHz) δ 28.87, 34.66, 117.37, 118.85, 126.26, 128.63, 130.95, 141.45. **15**: ^1H NMR ($CDCl_3$, 300 MHz) δ 2.02 (s, 3H), 2.12 (s, 3H), 2.89 (dd, 1H, $J=1.80$, 15.30 Hz), 2.99 (dd, 1H, $J=7.5$, 15.3 Hz), 5.78–5.90 (m, 2H), 7.30–7.42 (m, 5H); ^{13}C NMR ($CDCl_3$, 75 MHz) δ 21.09, 21.12, 54.71, 71.03, 75.74, 96.66, 127.44, 128.90, 129.18, 135.66, 169.46, 169.74. **16**: ^1H NMR ($CDCl_3$, 300 MHz) δ 2.03 (s, 3H), 2.10 (s, 3H), 5.60–5.70 (m, 1H), 5.94 (d, 1H, $J=9.0$ Hz), 6.06–6.17 (m, 2H), 7.20–7.40 (m, 5H). **19**: ^1H NMR ($CDCl_3$, 300 MHz) δ 3.88 (s, 3H), 4.30 (s, 2H), 5.08 (s, 2H), 6.96 (d, 2H, $J=9.0$ Mz), 7.92 (d, 2H, $J=9.0$ Hz). **20**: ^1H NMR ($CDCl_3$, 300 MHz) δ 3.88 (s, 3H), 5.08 (s, 2H), 5.24 (d, 1H, $J=4.2$ Hz), 6.38 (d, 1H, $J=4.2$ Hz), 6.96 (d, 2H, $J=9.0$ Mz), 7.92 (d, 2H, $J=9.0$ Hz).
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16. Alternatively, $CrCl_2$ can be prepared from less expensive $CrCl_3$ via reduction with In powder (THF, 65°C, 10 h).