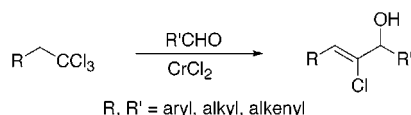


Chromium Vinylidene Carbenoids:  
Stereospecific Synthesis of  
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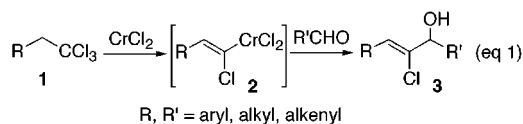
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## ABSTRACT



(Z)-2-Chloroalk-2-en-1-ols are obtained in excellent yields from a wide variety of aldehydes by addition of (*E*)-chromium vinylidene carbenoids, stereospecifically generated from trichloroalkanes using  $\text{CrCl}_2$  in THF at room temperature.

Our laboratories recently described an efficient synthesis of terminal 2-chloropropenyl alcohols via in situ  $\alpha$ -chloro-vinylation of aldehydes using 1,1,1-trichloroethane and  $\text{CrCl}_2$ .<sup>1,2</sup> Subsequent mechanistic investigations identified a chromium vinylidene carbenoid as the penultimate intermediate.<sup>3</sup> Herein, we report that homologous trichloroalkanes **1** are stereoselectively transformed to (*E*)-chromium vinylidenes **2** which efficiently add to aldehydes affording (Z)-2-chloroalk-2-en-1-ols **3** (eq 1).<sup>4</sup> Halogenated alkenols such



as **3** are versatile synthetic intermediates<sup>5</sup> as well as critical structural units in a variety of biologically active natural products of current interest.<sup>6</sup> However, their accessibility is often hampered by multistep routes and/or poor stereo-selectivity.<sup>7</sup>

The results from a panel of representative substrates are summarized in Table 1.<sup>8,9</sup> For simple, unactivated trichlo-

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(4) 2,2,2-Trichloroethanol derivatives also yield (Z)-2-chloroalk-2-en-1-ols accompanied by variable amounts of 1,1-dichloroalkene, (*E*)/(*Z*)-1-chloroalkene, and 1-alkoxy-1-chloroalkene: Takai, K.; Kokumai, R.; Nobunaka, T. *Chem. Commun.* **2001**, 1128–1129.

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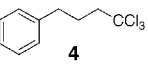

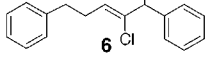
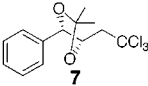

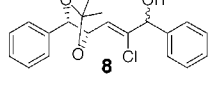
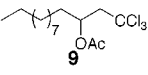

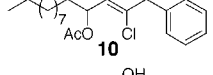
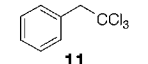

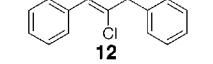
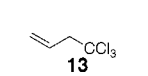

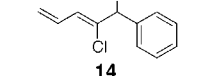
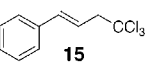

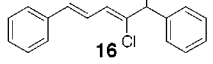
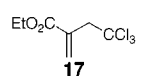

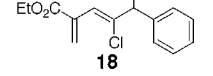

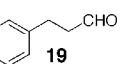
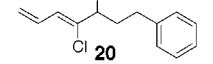

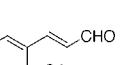
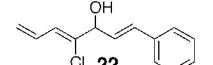

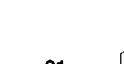
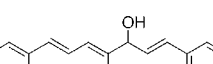


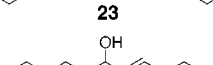
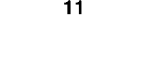

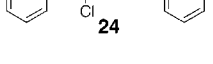
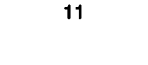
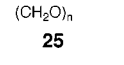
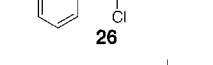
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(8) **General procedure:** 1,1,1-Trichloroalkane (0.4 mmol) and aldehyde (0.4 mmol) in THF (1 mL) were added to a stirring, grayish suspension of anhydrous  $\text{CrCl}_2$  (1.6 mmol) in THF (10 mL) under argon at ambient temperature. After 10–12 h, the resultant reddish reaction mixture was quenched with water and extracted thrice with ether, and the combined ethereal extracts were evaporated in vacuo. Chromatographic purification on  $\text{SiO}_2$  gave the (Z)-chloroalkenol adducts in the indicated yields (Table 1).

<sup>†</sup> University of Texas.<sup>‡</sup> Université Louis Pasteur.<sup>⊥</sup> Services des Molécules Marquées.<sup>§</sup> E-mail: mioskow@aspirine.u-strasbg.fr.(1) Falck, J. R.; Barma, D. K.; Mioskowski, C.; Schlama, T. *Tetrahedron Lett.* **1999**, *40*, 2091–2094.(2) For additional examples of recent  $\text{CrCl}_2$ -based methodology, see: (a) Falck, J. R.; Barma, D. K.; Baati, R.; Mioskowski, C. *Angew. Chem., Int. Ed.* **2001**, *40*, 1281–1283. (b) Baati, R.; Valleix, A.; Mioskowski, C.; Barma, D. K.; Falck, J. R. *Org. Lett.* **2000**, *2*, 485–487.

**Table 1.** Synthesis of (*Z*)-2-Chloroalk-2-en-1-ols

entry	trichloroalkane	aldehyde	adduct	yield (%)
1				91
2				91
3				89
4				82
5				77
6				89
7				48
8				88
9				97
10				79
11				89
12				95
13				89

roalkanes, e.g., **4**, stirring with 4 equiv of commercial  $\text{CrCl}_2$  at room temperature for several hours generated the corre-

(9) Additions to ketones were sluggish, even at 75–80 °C, and gave low yields (10–15%) of the chloroalkenol adducts under the standard reaction conditions.

sponding (*E*)-vinylidene intermediate **2** ( $\text{R} = \text{PhCH}_2\text{CH}_2-$ ) which gave rise to **6** in excellent yield (entry 1) upon addition of benzaldehyde (**5**). None of the (*E*)-isomer could be detected by NMR analysis, indicating >95% stereochemical purity. Alternatively and more conveniently, **6** could be obtained under Barbier-type conditions in the same yield and stereochemical purity by simultaneous addition of both **4** and **5** to a slurry of  $\text{CrCl}_2$  at room temperature. A catalytic system,<sup>10</sup> utilizing Mn powder to recycle chromium(III) to chromium(II), proved disappointing, and only small amounts of the desired adducts could be isolated.

Under the standard stoichiometric conditions, oxygenated trichloroalkanes **7** and **9** behaved analogously with **5** furnishing acetone **8** (entry 2) and acetate **10** (entry 3), respectively, as ~7:3 diastereomeric mixtures based on  $^1\text{H}$  NMR analysis. Conjugated versions of **2**, derived from benzyl **11**, allyl **13**, and cinnamyl **15** trichloromethyls, added smoothly to benzaldehyde providing adducts **12**<sup>7b</sup> (entry 4), **14**<sup>a</sup> (entry 5), and **16** (entry 6), respectively. Notably, even the redox sensitive  $\alpha,\beta$ -unsaturated ester **17** could be induced to add to **5** leading to diene **18**, albeit in modest yield (entry 7).

A wide variety of aldehydes were suitable coupling partners, inter alia, aliphatic **19** (entry 8), cinnamaldehyde **21** (entries 9, 10, and 11), and paraformaldehyde **25** (entry 12) which gave their respective (*Z*)-chloroalkenols **20**, **22**, **23**, **24**, and **26** free of regio- or geometric isomers. Condensation of chiral carboxaldehyde **27** with the chromium vinylidene derived from **11** (entry 13) evolved **28** in good yield as a chromatographically separable ~2:1 mixture of syn/anti-isomers. This level of stereoselection is typical of vinylchromium additions to aldehydes bearing chiral  $\alpha$ -heteroatoms.<sup>11</sup>

In summary, we report a convergent, one-pot method for the creation of (*Z*)-2-chloroalk-2-en-1-ols under mild conditions from readily available trichloroalkanes and aldehydes. Modifications to achieve synthetically useful chiral induction are under active investigation.

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**Supporting Information Available:** Spectral data for all new compounds. This material is available free of charge via the Internet at <http://pubs.asc.org>.

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