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Reactions of coordinated geminal dichromium reagents with aldehydes: stereoselective formation of (*Z*)-2-chloroalk-2-en-1-ols†‡

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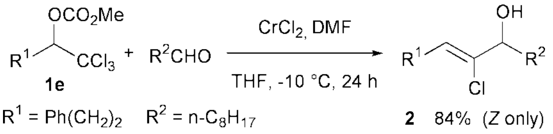
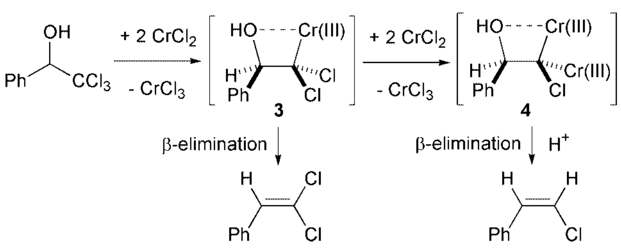
Treatment of a carbonate ester of 2,2,2-trichloroethanol derivative with $CrCl_2$–DMF in THF gives a β-carbonate-coordinated geminal dichromium species, which adds to an aldehyde and eliminates an acyloxychromium group to afford a (*Z*)-2-chloroalk-2-en-1-ol stereoselectively.

Intramolecular coordination of a hetero atom to a metal center often fixes the molecular conformation,[1] and thus carbon–carbon bond formation proceeds in a stereoselective manner. We disclose here that the effect is observed in geminal dichromium species, and that a stereoselective coupling between a geminal trichloroalkane having an adjacent acyloxy group and an aldehyde leading to a (*Z*)-2-chloroalk-2-en-1-ol proceeds with chromium(II) chloride. Chromium(II) reduces geminal dihaloalkanes, such as 1,1-diiodoalkanes,[2a] iodoform,[2b] $Me_3SiCHBr_2$,[2c] and $Bu_3SnCHBr_2$,[2d] to give geminal dichromium species, which add to aldehydes to afford Wittig-type olefins with high *E*-selectivity. However, such Wittig-type olefinations do not proceed in the trichloroalkane **1e**, and a new double bond is formed between the carbons bearing halogen and the acyloxy group [eqn. (1)].



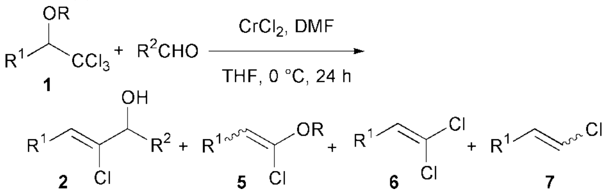
(1)

In 1986, Steckhan reported the reduction of 1-phenyl-2,2,2-trichloroethanol with $CrCl_2$ in aqueous DMF to obtain (*Z*)-2-chlorostyrene in 44% yield, along with 2,2-dichlorostyrene in 10% yield.[3] Although the yield of 2-chlorostyrene was moderate, the observed *Z*-selectivity was quite high. The stereoselectivity was explained by 1) fixation of the conformation by intramolecular coordination of the β-hydroxy group to chromium(III) of the monochromium species **3**, and 2) selective reduction of a chlorine atom at the less hindered side leading to geminal dichromium species **4** (Scheme 1). Because the reduction was performed in the presence of proton sources, *i.e.*, aqueous conditions and the hydroxy group of the starting trichloride, the procedure could not be applied for carbon–carbon formation. Thus, we first examined the effects of solvents using a hydroxy-protected 2,2,2-trichloroethanol **1a** [Table 1, R^1 = $Ph(CH_2)_2$, R = Ac].



Scheme 1

Table 1 Reactions of 2,2,2-trichloroalkanol derivatives and nonanal with chromium(II)[a]



		Yield (%)[b]				Recov. (%)	
Run	R	**2**	**5**	**6**	**7**	Aldehyde	**1**
1	Ac (**a**)	62	29	< 5	< 5	15	7
2		30[c]	2	35	16	33	0
3		27[d]	52	0	0	56	32
4	COPh (**b**)	61	23	7	2	15	13
5	$CO(C_5H_4N)$ (**c**)[e]	< 5	0	89	0	94	0
6	Ms (**d**)	0	0	96	0	91	0
7	CO_2Me (**e**)	77	8	19	6	8	13
8	Me_3Si (**f**)	60	0	< 5	< 5	< 5	44

[a] R^1 = $Ph(CH_2)_2$, R^2 = n-C_8H_{17}; Reaction was conducted on a 1.0 mmol scale. Two mmol of trichloride **1**, 8 mmol of $CrCl_2$, 8 mmol of DMF were used per mmole of nonanal. [b] Isolated yields. [c] The reaction was conducted in DMF solvent. [d] The reaction was conducted without addition of DMF. [e] $CO(C_5H_4N)$ = pyridine-2-carbonyl.

Treatment of **1a** in the presence of nonanal with $CrCl_2$ in DMF at 0 °C for 24 h gave the desired coupling product **2** in 30% yield along with **6** and **7** in 35% and 16% yields, respectively (Table 1 run 2).[4] A *Z*-isomer was obtained exclusively as expected.[5] Although the yield could not be improved in THF solvent (run 3), pre-treatment of 1 equiv. of $CrCl_2$ with DMF before addition of the trichloride **1a** and nonanal accelerated the reaction, and the yield was improved to 62% (run 1).[2a] Benzoate **1b** gave almost the same yield with **2**. However, reactions with the pyridine-2-carbonyloxy compound **1c** and mesylate **1d** produced the 1,1-dichloroalkene **6** as a main product, and most of the aldehyde was recovered. Among the protecting groups examined, a carbonate gave the best result (run 7).

There are three possible reaction pathways which have different timings of the elimination steps of acyloxychromium (Scheme 2). In Path A, acyloxychromium is smoothly eliminated when one of the chlorine atoms is reduced, and 1,1-dichloroalkene **10** is produced as an intermediate. Then, the chlorine atom at the less hindered *trans* position of **10** is selectively reduced to give **11**, which adds to an aldehyde. In Path B, acyloxychromium is eliminated after the second reduction to the geminal dichromium species **9**.[2,6] The elimination gives the alkenylchromium **11** directly, and addition to an aldehyde proceeds. The third Path C also includes the acyloxy-coordinated geminal dichromium species **9**, and addition to an aldehyde at a non-coordinated chromium of **9** occurs before elimination of acyloxychromium.

The hydroxy-protecting groups with oxygen act as leaving groups in the reaction sequence.[7] Trichlorides **1c** and **1d**, which

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† Electronic supplementary information (ESI) available: experimental procedure. See http://www.rsc.org/suppdata/cc/b1/b102387j/
‡ Dedicated to Professor Jean F. Normant on the occasion of his 65th birthday.

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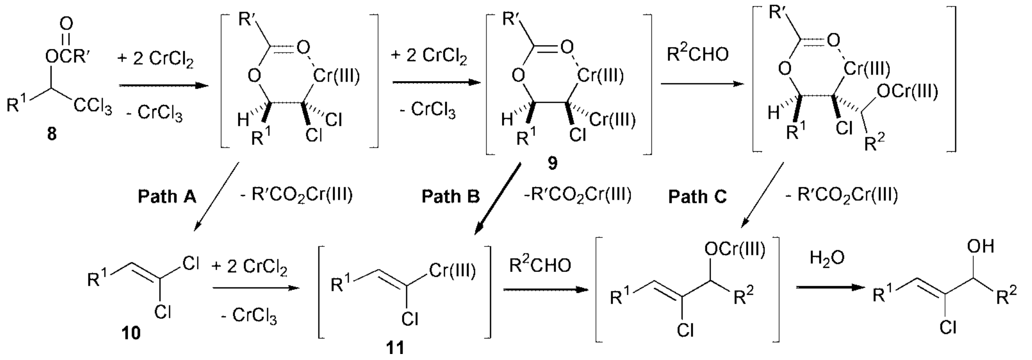
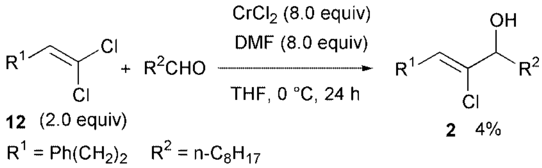


Scheme 2 Possible reaction pathways for the coupling reaction.

have good leaving groups, afforded **6** as a major product, and only a small amount of the 1,1-dichloroalkene **6** was produced when the adduct **2** was obtained in high yield. In addition, treatment of a mixture of 1,1-dichloroalkene **12** and nonanal with CrCl$_2$–DMF in THF at 0 °C for 24 h produced the adduct **2** in only 4% yield, and most of **12** (75%) was recovered unchanged [eqn. (2)].[8] These results suggest that this addition reaction does not proceed through the 1,1-dichloroalkene **10** (Path A) but through the geminal dichromium species **9**.

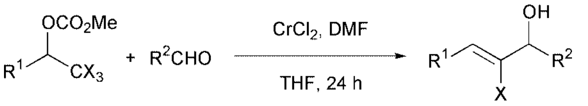


(2)

During the reactions of **1a**, **1b** and **1e** with nonanal, the Wittig-type olefination[2a] leading to 1-phenyl-4-chlorotridec-4-en-3-ol derivatives was not observed. This suggests that the coupling reaction does not proceed *via* Path C either, leaving Path B as the only possible reaction pathway.

The results of the coupling reactions between carbonates of 2,2,2-trichloroethanols and aldehydes are shown in Table 2.[9]

Table 2 (*Z*)-Selective coupling of 2,2,2-trihaloalkyl carbonates and aldehydes with chromium(II)[a]



Run	R^1	R^2	X	Temp/°C	Yield (%)[b]
1	Ph(CH$_2$)$_2$	n-C$_8$H$_{17}$	Cl	−10	84
2				0	77
3				25	52[c]
4			Br	−10	X = Br 16[d] X = Cl 31[d]
5		c-C$_6$H$_{11}$	Cl	−10	69
6		Ph	Cl	−10	71
7		(*E*)-PrCH=CH	Cl	−10	46
8	c-C$_6$H$_{11}$	n-C$_8$H$_{17}$	Cl	−10	68
9	Ph	n-C$_8$H$_{17}$	Cl	−10	63

[a] Reaction was conducted on a 1.0 mmol scale. Two mmol of trihalides, 8 mmol of CrCl$_2$, and 8 mmol of DMF were used per mmole of an aldehyde. [b] Isolated yields. Isomer ratios were determined by isolation, GLPC, and/or NMR. [c] 0.8 mmol of CrCl$_2$, 9 mmol of manganese, and 9 mmol of Me$_3$SiCl were employed per mmole of nonanal. [d] *Z*-Isomers were obtained exclusively.

2-Chloroalk-2-en-1-ols having a *Z*-configuration were produced selectively in all cases. To reduce the amount of chromium salt used in the reaction, we attempted a catalytic reaction using manganese as a reductant of chromium(III).[10] The reaction proceeded at 25 °C, however, the yield decreased to 52% (run 3). When 2,2,2-tribromoethanol derivative was used as the trihalide, the corresponding bromo and chloro compounds were obtained (run 4).[2b,11,12]

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1 (*a*) For geminal dimetallic species, see: I. Marek and J. F. Normant, *Chem., Rev.*, 1996, **96**, 3241; J. F. K. Müler, *Eur. J. Inorg. Chem.*, 2000, 789; (*b*) J. M. Concellón, P. L. Bernad and J. A. Pérez-Andrés, *Angew. Chem., Int. Ed.*, 1999, **38**, 2384; (*c*) R. W. Hoffmann, M. Bewersdorf, K. Ditrich, M. Krüger and R. Stürmer, *Angew. Chem., Int. Ed. Engl.*, 1988, **27**, 1176.

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9 Reactions using the corresponding benzoates gave about 5–10% less yields of the same products.

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12 For the synthesis of (*Z*)-alkenyl bromides, see: B. M. Trost and A. B. Pinkerton, *Angew. Chem., Int. Ed.*, 2000, **39**, 360.