(*Z*)-3-heptenyl mesylate, 105281-66-1; (±)-2-carbomethoxycyclopentanone, 53229-93-9; (±)-2-(3(*E*)-hepten-1-yl)-2-carbomethoxycyclopentanone, 105281-67-2; (±)-2-(3(*Z*)-hepten-1-yl)-2-carbomethoxycyclopentanone, 105281-68-3; 3-heptynol, 14916-79-1.

Supplementary Material Available: Experimental procedures for compounds **1** and **3**–**9** (5 pages). Ordering information is given on any current masthead page.

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Reaction of (α-Thioalkyl)chromium Compounds Prepared by Chromium(II) Reduction of α-Halo Sulfides

Summary: Reduction of α-chloroalkyl phenyl (or methyl) sulfides with chromium(II) chloride in THF proceeds smoothly in the presence of LiI. The resulting (α-thioalkyl)chromium reagents add to aldehydes in a chemo- and stereoselective manner.

Sir: Because of the versatility of sulfur, carbanions stabilized by adjacent sulfur are widely employed in organic synthesis.[1] The preparation of α-thio carbanions, compared to their sulfinyl[2] or sulfonyl counterparts,[3] requires very strong base combinations such as BuLi–DABCO,[4a] BuLi–TMEDA,[4b] or *t*-BuLi–HMPA.[4c,5] We report here that α-phenyl (or -methyl) thio carbanions are produced smoothly by chromium(II) reduction[6,7] of the corresponding α-halo sulfides (Scheme I).[8] The resulting (α-thioalkyl)chromium reagents add to aldehydes in a chemo- and stereoselective manner which could not be achieved by employing the former strong-base combinations.

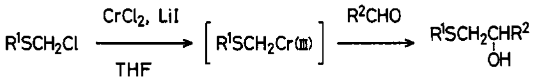
A typical procedure is as follows. To a stirring suspension of commercial CrCl$_2$[9] (0.49 g, 4.0 mmol) in THF (6 mL) at 25 °C under an argon atmosphere was added successively a solution of benzaldehyde (0.11 g, 1.0 mmol) in THF (2 mL), chloromethyl methyl sulfide (0.17 mL, 2.0 mmol), and a THF solution of LiI (1.0 M, 2.0 mL, 2.0 mmol). The resulting mixture was stirred at 40 °C for 5 h and then poured into water (25 mL). The mixture was extracted with ether (3 × 15 mL), and the combined extracts were dried (Na$_2$SO$_4$) and concentrated. Purification by silica gel column (5:1 hexane–ethyl acetate) gave 2-(methylthio)-1-phenyl-1-ethanol (**1**) in 88% (0.15 g) yield.[10,11] The yield of **1** without LiI was 16% even at 60 °C for 6 h. Lithium iodide is added to generate in situ iodomethyl methyl sulfide[12] which is reduced smoothly with CrCl$_2$.

Table I. Reaction of α-Halo Sulfides with Aldehydes Using CrCl$_2$[a]

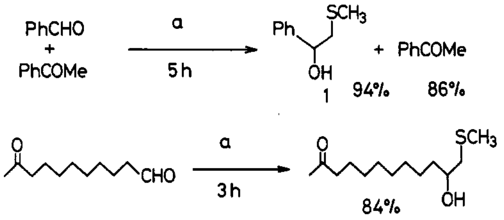
run	α-halo sulfide, R^1	aldehyde, R^2	temp, °C	time, h	yeild,[b] %
1	Me	Ph	40	5	88
2		Oct	40	9	72
3		PrCH=CH	40	13	64
4	Ph	Ph	60	10	63[c]
5		Oct	40	10	48[d]

[a] The aldehyde (1.0 mmol) was treated with α-halo sulfide (2.0 mmol), LiI (2.0 mmol), and CrCl$_2$ (4.0 mmol) in THF. [b] Isolated yields. [c] Reaction was conducted without LiI. [d] Four mmoles of α-halo sulfide, 4.0 mmol of LiI, and 8.0 mmol of CrCl$_2$ were employed per mol of the aldehyde.

Scheme I



Scheme II



(a) CH$_3$SCH$_2$Cl, CrCl$_2$, LiI, THF, 40°C

The addition of the [(methylthio)methyl]chromium (or [(phenylthio)methyl]chromium) reagent to several aldehydes is summarized in Table I. In the reaction of an α,β-unsaturated aldehyde, the 1,2-addition product was produced exclusively (run 3).[6]

Treatment of a mixture of benzaldehyde and acetophenone at −78 °C with [(methylthio)methyl]lithium, prepared by using the BuLi–TMEDA system, gave a mixture of **1** and 1-(methylthio)-2-phenyl-2-propanol (**2**) in a 7:5 ratio, in our hands. In contrast, the chromium reagent reported here reacts with an aldehyde selectively (Scheme II).[6]

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(7) Other reducing agents have been examined in the reaction between chloromethyl methyl sulfide and benzaldehyde. Among them, zinc has also proved to promote the reaction (23% yield of **1**). Little or no adduct was obtained with the following reducing agents: VCl$_3$–LiAlH$_4$, Mn, MnCl$_2$–LiAlH$_4$, Sn, SnCl$_2$, SmI$_2$, and Bi.

(8) α-Halo sulfides were prepared by chlorination of the corresponding sulfides with *N*-chlorosuccinimide in CCl$_4$ and were used after filtration and removal of the solvent in vacuo. Tuleen, D. L.; Stephens, T. B. *Chem. Ind. (London)* **1966**, 1555.

(9) Anhydrous CrCl$_2$ (90% assay) was purchased from Aldrich Chemical Co.

(10) During the reaction, benzyl alcohol and 1,2-diphenyl-1,2-ethanediol were not observed (<1%).

(11) Treatment of a mixture of benzaldehyde and CrCl$_2$ with (or without) LiI in THF at 40 °C for 5 h resulted in recovery of benzaldehyde (93% or 94%) along with 1,2-diphenyl-1,2-ethanediol (<5%). Benzyl alcohol was not detected. These observations suggest to eliminate another possibility for the reaction path that the carbonyl moiety is attacked first by Cr(II) to yield Cr(III)–O–CRH–Cr(III) and this anion attacks the (phenyl- or (methylthio)methyl iodide. See, Castro, C. E.; Kray, W. C., Jr. *J. Am. Chem. Soc.* **1966**, *88*, 4447. Davis, D. D.; Bigelow, W. B. Ibid. **1970**, *92*, 5127.

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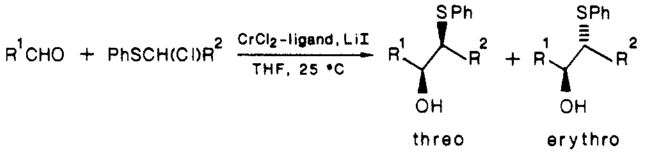
Table II. Diastereoselective Addition of α-Halo Sulfides to Aldehydes Using $CrCl_2$[a]



run	R^1	R^2	ligand	time, h	yield,[b] %	threo/erythro	aldol adduct[c]	recov R^1CHO
1	Ph	Me		16	58	80/20		17
2			TMEDA	6	96	88/12		0
3		Pr	TMEDA[d]	6	95	86/14		0
4		*i*-Pr	TMEDA[d]	25	46	80/20		25
5	Oct	Me		17	17	86/14	11	0
6			TMEDA	1.5	25	90/10	19	0
7			HMPA[e]	20	33	97/3	23	5
8			Ph_3P[f]	20	23	84/16	10	24
9			DIPHOS	20	56	90/10	<3	24
10			DIPHOS[g]	19	53	>98/<2	<3	32
11		Pr	DIPHOS[g]	40	8	>98/<2	<5	71
12	$\overline{(CH_2)_5CH}$	Me	DIPHOS	18	11	90/10	<5	50
13			TMEDA[d]	18	65	81/19	<5	13

[a] The aldehyde (1.0 mmol) was treated with α-halo sulfide (2.0 mmol), LiI (2.0 mmol), and $CrCl_2$ (4.0 mmol)–TMEDA (4.0 mmol) (ref 17) in THF. [b] Isolated yields. [c] α,β-Unsaturated aldehyde was produced by self-condensation of the reactant aldehyde; for instance, $C_7H_{15}C(CHO){=}CHC_8H_{17}$ in the case of nonanal. [d] An aldehyde (1.0 mmol) was treated at 25 °C with the reagent prepared from an α-halo sulfide (4.0 mmol), LiI (4.0 mmol), $CrCl_2$ (8.0 mmol), and TMEDA (8.0 mmol) in THF. [e] $CrCl_2$ was suspended in THF–HMPA (5:1, v/v). [f] Two moles of Ph_3P were employed per mole of $CrCl_2$. [g] The reagent was prepared from α-halo sulfide (2.0 mmol), LiI (2.0 mmol), $CrCl_2$ (6.0 mmol), and DIPHOS (6.0 mmol).

Phenylthio-stabilized ethyllithium, derived from phenyl ethyl sulfide and *t*-BuLi–HMPA, reacts with benzaldehyde to provide a 1:1 mixture of *threo*-2-(phenylthio)-1-phenyl-1-propanol (**3**) and *erythro*-**4**.[5] In contrast, the [1-(phenylthio)ethyl]chromium reagent adds to benzaldehyde to give a mixture of **3** and **4** in an 80:20 ratio, though the yield is about 60% (run 1). Pretreatment of $CrCl_2$ with TMEDA has proved to accelerate the reaction rate and improve both the yield and the diastereoselectivity (run 2).[13] In the case of nonanal, addition of TMEDA, HMPA, or Ph_3P to $CrCl_2$ did not give satisfactory results because of the formation of aldol dimer **5** (runs 6–8). A most effective ligand for the reaction of nonanal has been found to be 1,2-bis(diphenylphosphino)ethane (DIPHOS). Thus, reaction of 1-chloroethyl phenyl sulfide and nonanal by means of $CrCl_2$–DIPHOS (1:1 molar ratio) proceeded in 53% yield to give the threo adduct almost exclusively, along with unchanged nonanal (32%) (run 10).

The threo/erythro product ratios for α-phenylthiochromium reagents[14] are summarized in Table II. The stereochemistry of the β-hydroxy sulfides[15] was confirmed by transformation of the adducts to the corresponding epoxides with $Me_3O^+BF_4^-$ and aqueous sodium hydroxide.[16]

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(13) The reduction potential of the Cr(II)–Cr(III) couple in aqueous media is reported to be enhanced significantly by complex formation with ethylenediamine. Kochi, J. K.; Singleton, D. M. *J. Org. Chem.* **1968**, *33*, 1027.

(14) Butylchromium reagent prepared by chromium(II)-reduction of 1-iodobutane in DMF reacted at 25 °C for 24 h with benzaldehyde to give 1-phenyl-1-pentanol in 11% yield. The presence of a phenylthio group at the α-position has a significant effect upon the rate of reduction of a halide and/or reactivity of an alkylchromium species.

(15) Stereoselective formation of threo and erythro β-methylthio or -phenylthio alcohols was achieved by reduction of α-methylthio or -phenylthio ketones with L-Selectride (Aldrich) or $Zn(BH_4)_2$. Shimagaki, M.; Maeda, T.; Matsuzaki, Y.; Hori, I.; Nakata, T.; Oishi, T. *Tetrahedron Lett.* **1984**, *25*, 4775.

(16) (a) Townsend, J. M.; Sharpless, K. B. *Tetrahedron Lett.* 1972, 3313. (b) Shanklin, J. R.; Johnson, C. R.; Ollinger, J.; Coates, R. M. *J. Am. Chem. Soc.* **1973**, *95*, 3429. The cis and trans epoxides were assigned by the coupling constant of the epoxide protons (trans 2.2–2.3 Hz; cis 4.1–4.4 Hz). See also ref 15.

(17) To a stirred suspension of $CrCl_2$ (4.0 mmol) in THF (6 mL) at 25 °C under an argon atmosphere was added TMEDA (4.0 mmol). The resulting light blue suspension was stirred at 25 °C for 1 h, before addition of an aldehyde, an α-halo sulfide, and LiI.