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SELECTIVE GRIGNARD-TYPE CARBONYL ADDITION OF ALKENYL HALIDES MEDIATED BY CHROMIUM(II) CHLORIDE

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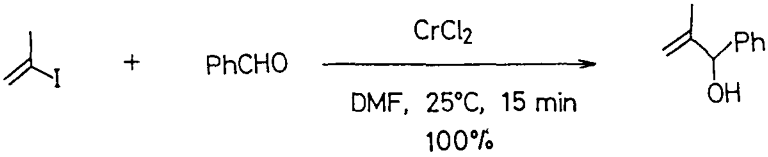
Abstract: Alkenyl (or aryl) iodide (or bromide) is readily reduced with $CrCl_2$ in N,N-dimethylformamide at 25°C to give the corresponding organochromium species which adds selectively to an aldehyde moiety without affecting the coexisting ketone or cyano group of the substrate.

The reaction of alkenylmetal reagents such as alkenyllithium,[1] -magnesium,[2] or -copper[3] with carbonyl compounds is a useful process for the synthesis of allylic alcohols. We report here that alkenylchromium compounds are readily derived from alkenyl halides and anhydrous chromium(II) chloride[4] in N,N-dimethylformamide (DMF) and that the organometals add selectively to aldehydes to produce allylic alcohols.



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The simple operation of the procedure is illustrated for the synthesis of 2-methyl-1-phenyl-2-propen-1-ol (1). To a stirred suspension of chromium(II) chloride (0.98 g, 8.0 mmol) in DMF (8 ml) was added at 25°C a solution of 2-iodopropene (0.67 g, 4.0 mmol) and benzaldehyde (0.21 g, 2.0 mmol) in DMF (6 ml) over a period of 10 min under an argon atmosphere. After being stirred at 25°C for 15 min, the mixture was quenched by addition of water (20 ml) and extracted with ether. The extracts were dried over anhydrous magnesium sulfate and concentrated. Purification of the crude product by short column chromatography (hexane-ethyl acetate, 5 : 1) gave 1 quantitatively (0.30 g). The chromium reagent prepared from $CrCl_3$-$LiAlH_4$[5] was less effective for this reaction (8% of 1). DMF solvent was essential for this reaction; tetrahydrofuran turned out futile.

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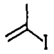
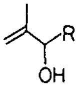
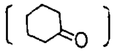
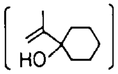
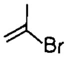
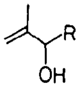
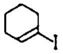
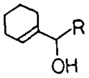
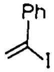
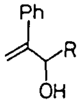
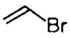
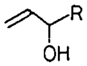
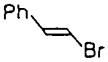
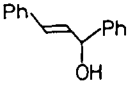
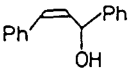
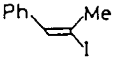
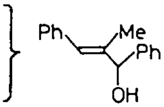
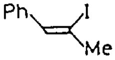
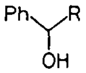
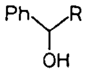
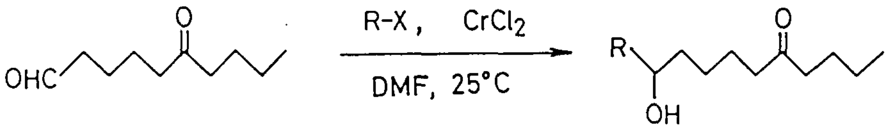
Table 1. Reaction of Alkenyl Halides with Aldehydes Using $CrCl_2$[a]

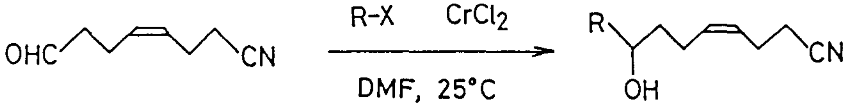
Run	Alkenyl Halide	RCHO	Time (h)	Yield[b] (%)	Product
1		PhCHO	0.25	100	
2		$^nC_8H_{17}CHO$	0.25	100	
3			3	22^c	
4		PhCHO	3	77	
5		$^nC_8H_{17}CHO$	3	62	
6		PhCHO	3	79	
7		$^nC_8H_{17}CHO$	0.5	93	
8		Me_2CHCHO	17	72	
9		PhCHO	5.5	89	
10		$^nC_8H_{17}CHO$	7	83	
11		PhCHO	15	80^d	
12		$^nC_8H_{17}CHO$	1.5	77	
13		PhCHO	1	82^e	
14		PhCHO	1	78^e	
15	 (2)	PhCHO	3	91^f	
16	 (3)	PhCHO	3	90^f	
17	PhI	PhCHO	2	85	
18		$^nC_8H_{17}CHO$	3	83	
19	PhBr	PhCHO	5^g	31	
20		$^nC_8H_{17}CHO$	5^g	13^h	

a) All the reactions were performed in 2.0 mmol scale at 25°C in DMF. Two mol of alkenyl halides and four mol of $CrCl_2$ were employed per mol of aldehydes. b) Isolated yields. c) Reaction mixture was heated at 50°C for 3 h. d) The resulting mixture was acetylated prior to purification by column chromatography. e) Ref. 1b. f) Ref. 9. g) Reaction mixture was heated at 90°C for 5 h. h) An aldolic product, $^nC_8H_{17}CH=C(^nC_7H_{15})CHO$ (19%), was also obtained.

The results shown in Table 1 disclose the wide applicability of the chromium procedure. The salient features of the process follow. (1) Iodoalkenes are more reactive than bromoalkenes (compare runs 1,2 and 4,5). (2) While the reaction of (*E*)- and (*Z*)-2-bromostyrene[1b] and benzaldehyde proceeded stereospecifically[6] (runs 13 and 14), both (*E*)- and (*Z*)-2-iodo-1-phenyl-1-propene[8] reacted with benzaldehyde to give (*E*)-1,3-diphenyl-2-methyl-2-propen-1-ol[9] as the sole product (runs 15 and 16). (3) Chromium(II) chloride is also effective for the addition of halobenzenes to aldehydes (runs 17-20) to afford benzyl alcohols. (4) Ketones are much less reactive (run 3), and therefore a chemoselective addition of isopropenyl-, vinyl-, and phenylchromium to aldehydes was easily achieved.[10]

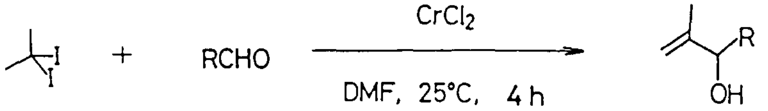


R : $H_2C{=}C(Me)$-	X : I	15 min	94% yield[12]
$H_2C{=}CH$-	Br	3 h	86%
Ph	I	4 h	81%



R : $H_2C{=}C(Me)$-	X : I	15 min	96% yield
$H_2C{=}CH$-	Br	1 h	92%
Ph	I	1.5 h	87%

(5) In place of 2-iodopropene 2,2-diiodopropane can be employed for the preparation of the isopropenyl adduct.



R : Ph	86%
$^{n}C_8H_{17}$	78%

References and Notes

1. (a) G. Cahiez, D. Bernard, and J. F. Normant, *Synthesis*, 1976, 245. (b) H. Neumann and D. Seebach, *Chem. Ber.*, 111, 2785 (1978).
2. (a) D. Seyferth, L. G. Vaughan, and R. Suzuki, *J. Organomet. Chem.*, 1, 437 (1964). (b) E. C. Ashby and J. R. Bowers, Jr., *J. Am. Chem. Soc.*, 103, 2242 (1981).
3. (a) G. M. Whitesides, C. P. Casey, and J. K. Krieger, *J. Am. Chem. Soc.*, 93, 1379 (1971). (b) J. W. Patterson, Jr., and J. H. Fried, *J. Org.*

Chem., 39, 2506 (1974).

4. Anhydrous chromium(II) chloride was purchased from ROC/RIC Corp. (507-519 Main Street, Belleville, NJ 07109, U.S.A.) and was used without further purifications. The colour should be grey. We must keep it in mind that the salt is highly air sensitive and hygroscopic. A greenish grey coloured lot resulted in the complete failure of the reaction.
5. T. Hiyama, Y. Okude, K. Kimura, and H. Nozaki, *Bull. Chem. Soc. Jpn.*, 55, 561 (1982) and references cited therein.
6. Addition of alkenyllithium or -magnesium to carbonyl compounds has been reported to proceed stereospecifically.[1a, b, 2b] The lack of stereospecificity in the present chromium reaction is attributed to the equilibrium[7] between the (*E*)- and (*Z*)-alkenyl radicals produced by one electron reduction of the alkenyl halides.
7. L. A. Singer and N. P. Kong, *J. Am. Chem. Soc.*, 88, 5213 (1966); A. J. Fry and M. Mitnick, *ibid.*, 91, 6207 (1969).
8. Prepared from 1-phenyl-2,2-diiodopropane according to the reported procedure. Configuration of the starting iodoalkenes 2 and 3 was determined by aqueous quenching of the corresponding alkenyllithiums derived from these iodoalkenes and butyllithium in THF. The recorded *cis*- and *trans*-isomers of 2-iodo-1-phenyl-1-propene in the literature (A. Poss and S. Sternhell, *Aust. J. Chem.*, 23, 989 (1970)) are established to be (*Z*)- and (*E*)-ones respectively.
9. (*E*)-1,3-Diphenyl-2-methyl-2-propen-1-ol: Bp 131°C (bath temp, 0.1 Torr); IR (neat): 3370, 1604, 1498, 1454, 1010, 915, 740, 700 cm^{-1}; NMR (CCl$_4$): δ1.64 (s, 3H), 2.18 (s, 1H), 5.07 (s, 1H), 6.61 (s, 1H), 7.00-7.40 (m, 10H); MS *m/e* (%): 224 (M$^+$, 4), 206 (19), 91 (53), 77 (100). E. J. Corey and H. Yamamoto, *J. Am. Chem. Soc.*, 92, 226 (1970). The absence of (*Z*)-isomer was confirmed by GLPC (Silicone SE-30) and NMR analysis. The authentic sample of (*Z*)-isomer was prepared by the addition of butyllithium to a THF solution of (*Z*)-2-iodo-1-phenyl-1-propene and benzaldehyde at -78°C. Bp 139°C (bath temp, 0.1 Torr); NMR (CCl$_4$): δ 1.67 (s, 3H), 1.90 (s, 1H), 5.68 (s, 1H), 6.45 (s, 1H), 7.05-7.40 (m, 10H).
10. Although organotitanium compounds have been used for the selective addition to aldehydes, alkenyltitanium reagents can not be utilized similarly due to the dimerization by oxidative coupling.[11]
11. For reviews, see: M. T. Reetz, *Top. Curr. Chem.*, 106, 1 (1982); B. Weidmann and D. Seebach, *Angew. Chem., Int. Ed. Engl.*, 22, 31 (1983).
12. Bp 103°C (bath temp, 0.6 Torr); IR (neat): 3420, 2945, 2885, 1718, 1655, 1458, 1378, 1050, 995, 895 cm^{-1}; NMR (CCl$_4$): δ0.90 (t, $J = 6$ Hz, 3H), 1.10-1.67 (m, 10H), 1.70 (s, 3H), 2.00 (s, 1H), 2.30 (t, $J = 6$ Hz, 4H), 3.93 (t, $J = 6$ Hz, 1H), 4.70 (s, 1H), 4.83 (s, 1H); MS *m/e* (%): 194 (M$^+$-H$_2$O, 12), 113 (49), 94 (45), 85 (100).

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