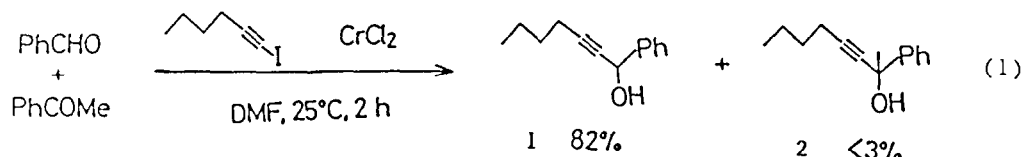


ALDEHYDE-SELECTIVE ADDITION OF ALKYNYLCHROMIUM COMPOUNDS  
PREPARED BY REDUCTION OF ALKYNYL HALIDES WITH CHROMIUM(II) REAGENT

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Abstract: Alkynyl halides are reduced by chromium(II) chloride in DMF to give unisolable alkynylchromium compounds which add selectively to an aldehyde moiety without affecting the coexisting ketone group of the substrate.

Nucleophilic addition of an alkynylmetal compound to a carbonyl group has been widely employed in carbon-chain extension reactions.<sup>2</sup> Unfortunately, alkynyllithium and -magnesium compounds add to both aldehyde and ketone groups indiscriminately. Thus, treatment of a mixture of benzaldehyde (1.0 mmol) and acetophenone (1.0 mmol) in THF with hexynyllithium (1.0 mmol) at 0°C for 30 min gave 53% of 1 and 45% of 2. In the reaction between hexynylmagnesium bromide (1.0 mmol) and a mixture of benzaldehyde (1.0 mmol) and acetophenone (1.0 mmol) in THF at 0°C for 15 min, the yields of 1 and 2 were 52% and 42% respectively. In this letter we report a chemoselective addition of alkynylchromium compounds to aldehydes and its application.



To a suspension of commercial  $\text{CrCl}_2$ <sup>3</sup> (0.25 g, 2.0 mmol) in dimethylformamide (DMF, 5 mL) at 25°C was added a mixture of benzaldehyde (0.11 g, 1.0 mmol), acetophenone (0.12 g, 1.0 mmol), and 1-iodo-1-hexyne<sup>4</sup> (0.21 g, 1.0 mmol) in DMF (3 mL) over a period of 10 min under stirring. After 2 h at 25°C, the mixture was poured into water (20 mL) and extracted with ether (3x15 mL). The organic extracts were washed with water, dried

Table 1. Reactions between alkynyl halides and aldehydes by means of chromium(II) reagent<sup>a</sup>

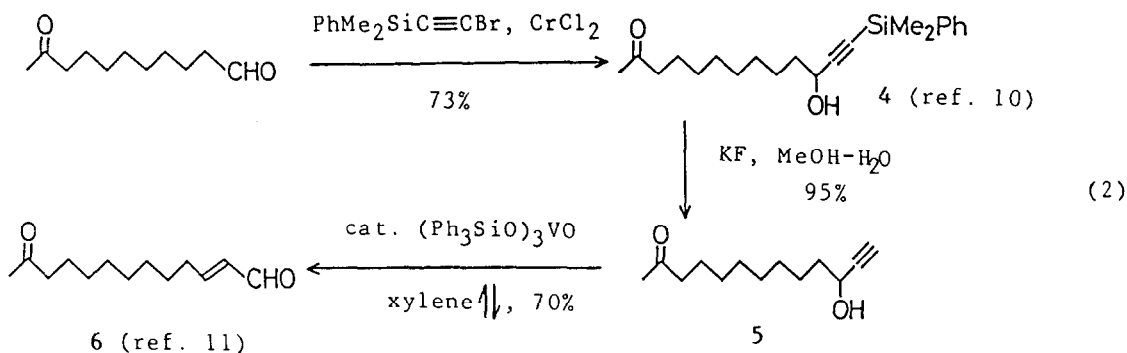
| Runs | Alkynyl Halides                               | Aldehydes<br>RCHO                   | Time<br>(h) | Products | Yield (%) <sup>b</sup> |                 |
|------|---|-------------------------------------|-------------|----------|------------------------|-----------------|
|      |   |                                     |             |          | Method A <sup>c</sup>  | B <sup>d</sup>  |
| 1    | BuC≡Cl  | PhCHO                               | 2           |          | 82                     | 74              |
| 2    |   | C <sub>8</sub> H <sub>17</sub> CHO  | 1           |          | 72                     | 65              |
| 3    |   | CH <sub>3</sub> CH=CHCHO            | 0.5         |          | 62 <sup>e</sup>        | 87 <sup>e</sup> |
| 4    |   | (PhCOMe)                            | 19          |          | < 5 <sup>f</sup>       |                 |
| 5    |   |                                     | 6           |          | 76                     |                 |
| 6    |   |                                     | 1           |          | 78 <sup>g</sup>        |                 |
| 7    | PhC≡Cl  | PhCHO                               | 0.5         |          | 83                     | 89              |
| 8    |   | C <sub>8</sub> H <sub>17</sub> CHO  | 0.5         |          | 71                     | 70              |
| 9    |   | CH <sub>3</sub> CH=CHCHO            | 0.5         |          | 87 <sup>e</sup>        | 73 <sup>e</sup> |
| 10   | PhMe <sub>2</sub> SiC≡CBr <sup>h</sup><br>(3) | PhCHO                               | 3           |          | 79 <sup>i</sup>        |                 |
| 11   |   | C <sub>11</sub> H <sub>23</sub> CHO | 4           |          | 68 <sup>i</sup>        |                 |

a) A mixture of an alkynyl halide (4.0 mmol) and an aldehyde (2.0 mmol) in DMF was treated with the chromium(II) reagent (8.0 mmol) at 25°C. b) Isolated yields. c) Anhydrous CrCl<sub>2</sub> was employed as Cr(II) reagent. d) Chromium(II) reagent was prepared from CrCl<sub>3</sub> and LiAlH<sub>4</sub> in THF (ref. 5). e) With crotonaldehyde 1,2-addition products were produced exclusively. f) Acetophenone was recovered unchanged in 87% yield. g) THF was used as a solvent. h) See ref. 7. i) An aldehyde was treated with 4.0 equiv. of the alkynylchromium reagent.

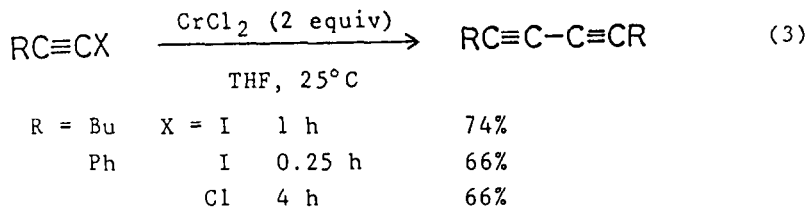
and concentrated. Purification by silica gel column chromatography (hexane-ethyl acetate, 10:1) gave 0.15 g (82%) of 1-phenyl-2-heptyn-1-ol (1) and 0.11 g (92%) of the unreacted acetophenone. The chromium(II) reagent prepared from CrCl<sub>3</sub> and LiAlH<sub>4</sub> was also effective for the reaction.<sup>5</sup>

Table 1 summarizes the results. Alkynylchromium compounds add to crotonaldehyde to give exclusively 1,2-addition product similarly to allylic-<sup>5</sup> and alkenylchromium compounds<sup>6</sup> (runs 3 and 9). Addition of hexynylchromium to an aldehyde moiety proceeded smoothly, while ketone and cyano groups in the same molecule remained unchanged (runs 5 and 6). Bromoacetylene was rather unreactive than iodoacetylene, thus the reaction with  $\text{PhMe}_2\text{SiC}\equiv\text{CBr}$  (3) was conducted at  $40^\circ\text{C}$  in DMF (runs 10 and 11).

The reaction sequence of Eq. 2 completes a two-carbon homologation of an aldehyde without affecting the coexisting ketone group of the substrate. Selective addition of the chromium dimethylphenylsilylacetylide to the aldehyde followed by desilylation with potassium fluoride afforded a propargylic alcohol 5 in 70% yield. The alcohol 5 was converted to an  $\alpha,\beta$ -unsaturated aldehyde 6 by vanadium-catalyzed isomerization.<sup>9</sup>



Reduction of 1-halo-1-alkyne in the absence of an aldehyde with chromium(II) chloride in THF resulted in reductive dimerization<sup>12,13,14</sup> (Eq. 3).

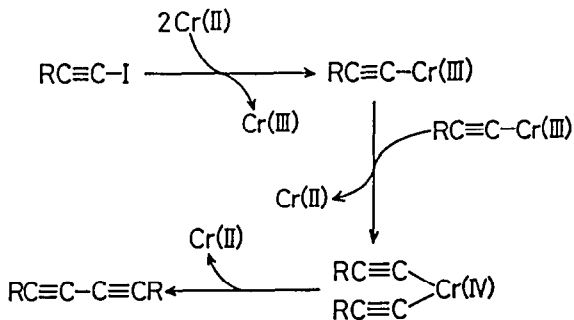


#### References and Notes

- 1) Present address: Okayama University of Science, Ridai-cho, Okayama 700, Japan.
- 2) P. F. Hudrlik and A. M. Hudrlik, "The Chemistry of the Carbon-carbon Triple Bond," part 1, ed by S. Patai, New York, John Wiley and Sons, 1978, p. 256.
- 3) Anhydrous chromium(II) chloride was purchased from Aldrich Chemical Co.

and was used without further purification.

- 4) For review see, S. Y. Delavareme and H. G. Viehe, "Chemistry of Acetylenes," ed by H. G. Viehe, Marcel Dekker, New York, 1969, Chap. 6, pp. 651-750.
- 5) T. Hiyama, Y. Okude, K. Kimura, and H. Nozaki, Bull. Chem. Soc. Jpn., 55, 561 (1982) and references cited therein.
- 6) K. Takai, K. Kimura, T. Kuroda, T. Hiyama, and H. Nozaki, Tetrahedron Lett., 24, 5281 (1983).
- 7) Lithium 2-bromoacetylide<sup>8</sup> generated by treatment of 1,1,2,2-tetrabromoethane with phenyllithium (3 equiv) in ether was trapped in situ by chlorodimethylphenylsilane at 0°C.  $\text{PhMe}_2\text{SiC}\equiv\text{CBr}$ : Bp 70°C (bath temp, 3 Torr); IR (neat): 2960, 2120, 1428, 1250, 1120, 1109, 845, 830  $\text{cm}^{-1}$ ; NMR ( $\text{CCl}_4$ ):  $\delta$ 0.39 (s, 6H), 7.22-7.75 (m, 5H); MS m/z (%): 240 (0.3,  $\text{M}^+$ ), 238 (0.3), 225 (100), 223 (100), 159 (82).
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- 10) Bp 148°C (bath temp, 0.14 Torr); IR (neat): 3410, 2928, 2168, 1713, 1428, 1249, 1115  $\text{cm}^{-1}$ ; NMR ( $\text{CCl}_4$ ):  $\delta$ 0.37 (s, 6H), 1.12-1.84 (m, 15H), 2.00 (s, 3H), 2.29 (t,  $\underline{J}$ =7 Hz, 2H), 4.30 (t,  $\underline{J}$ =5 Hz, 1H), 7.20-7.72 (m, 5H); MS m/z (%): 344 (2,  $\text{M}^+$ ), 329 (60), 267 (58), 145 (58), 137 (100), 135 (60), 75 (50).
- 11) Bp 110°C (bath temp, 0.11 Torr); IR (neat): 2926, 2852, 1713, 1690, 1636, 1359, 1159  $\text{cm}^{-1}$ ; NMR ( $\text{CCl}_4$ ):  $\delta$ 1.10-1.70 (m, 14H), 2.04 (s, 3H), 2.33 (t,  $\underline{J}$ =7 Hz, 2H), 6.03 (dd,  $\underline{J}$ =8,16 Hz, 1H), 6.78 (dt,  $\underline{J}$ =7,16 Hz, 1H), 9.47 (d,  $\underline{J}$ =8 Hz, 1H); MS m/z (%): 211 (7,  $\text{M}^++1$ ), 210 (2,  $\text{M}^+$ ), 153 (34), 134 (48), 98 (100), 58 (75).
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- 13) P. Cadiot and W. Chodkiewicz, ref. 4, Chap. 5, pp. 597-647.
- 14) We are tempted to assume the following mechanism (Scheme 1): (1) An alkynyl iodide was reduced by 2 equiv. of Cr(II) reagent to give an alkynyl-chromium(III) compound. (2) Disproportionation of the Cr(III) compound followed by reductive elimination afforded the homo-coupling product.



Scheme 1

(Received in Japan 8 August 1985)