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## REGIOSELECTIVE ALKYLATION OF ALLYLIC GRIGNARD REAGENTS . A NEW SYNTHESIS OF GERANIOL.

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The allylic Grignard reagents<sup>1,2</sup> provide a useful method of introducing a double bond into a molecule. However, the synthetic utility is often impeded by the formation of both isomers when an unsymetrical substrate is utilized.

We wish to report the copper catalyzed alkylation<sup>3</sup> of such species and the selective coupling reaction in the  $\alpha$  or  $\gamma$  position.



When allyImagnesium bromide (1.3 equiv.) was treated with octyl iodide (1 equiv.) and copper iodide (0.13 equiv.) in ether at 0° for 1.5 hr, pure 1-undecene<sup>4</sup> was obtained in 80% yield<sup>5</sup>. Without copper iodide, the reaction was very slow (22% of 1-undecene, 66% of unreacted iodide after 28hr at 0°).

The crotyl Grignard reagent<sup>1</sup>, prepared from 1-bromo-2-butene<sup>6</sup>, treated with copper iodide<sup>7</sup> and heptyl iodide (1 hr at -20° in tetrahydro-furan) gave  $(85\%)^5$  a mixture (50: 50) of (E) and (Z) 2-undecene<sup>4</sup>. Less than 5% of 3-methyl-1-decene <u>4</u>b was formed.

3-methyl-2-butenylmagnesium chloride  $\underline{2}d$  is a very useful reagent for the introduction of the isoprene unit. This reagent, when treated with copper iodide and alkyl electrophiles undergoes alkylation in high yield exclusively in the  $\alpha$  position. Thus, reaction of this organometallic (2 equiv.) with copper iodide (0.2 equiv.) and heptyl iodide<sup>8</sup>, bromide, or tosylate<sup>9</sup> (1 equiv.) in tetrahydrofuran at 0° for 2 hr gave 2-methyl-2-undecene<sup>4</sup> 3d (80-90%)<sup>5</sup> as a sole product.

However, without copper iodide, in ether at 0°, alkyl tosylates<sup>10</sup> react selectively with the allylic Grignard reagents in the  $\gamma$  position to furnish high yields of substituted olefins as the major products : <u>2</u>b gave (1.25 hr, 0°, 85%) <u>4</u>b<sup>11</sup>, (4% of <u>3</u>b and <u>3</u>c were also detected ); <u>2</u>d<sup>12</sup> gave (94%) a mixture (14 : 86) of <u>3</u>d and <u>4</u>d<sup>11</sup>.



The regioselective alkylation of the "prenyl" Grignard reagent\_2d has been utilized in a new synthesis of geraniol<sup>13</sup> : (E) 4-chloro-3-methyl -2-buten-1-ol  $5^{14,15}$  (l equiv.), was added at -50° to a mixture of reagent 2d (2.5 equiv.) and copper iodide (0.25 equiv.) in tetrahydrofuran, then allowed to warm to room temperature in 4 hr, and provided 60% of pure geraniol 6 after distillation.

We are continuing our investigations on the extension and applications of the cross coupling method reported here.

## NOTES AND REFERENCES

- (1) R.A. Benkeser, Synthesis, 347 (1971)
- (2) G. Courtois and L. Miginiac, J. Organometal. Chem., 69, 1 (1974)
- (3) Without copper salts, the alkylation of allylic Grignard reagents has been reported, by reactive halides : G. Stork, P.A. Grieco and M. Gregson, <u>Tetrahedron Letters</u>, 1393 (1969); A.F. Thomas and W. Pawlak <u>Helv. Chim. Acta</u>, <u>54</u>, 1822 (1971), and by an alkyl bromide (65 hr in refluxing ether) : R.L. Letsinger and J.G. Traynham, <u>J. Amer. Chem. Soc.</u>, <u>72</u>, 849 (1950)
- (4) These compounds are identical to samples prepared by known procedures,
   G. Linstrumelle, <u>Tetrahedron Letters</u>, 3809 (1974); J. Millon, R. Lorne and G. Linstrumelle, <u>Synthesis</u>, 434 (1975); F. Derguini-Boumechal and
   G. Linstrumelle, <u>Tetrahedron Letters</u>, 3225 (1976)
- (5) All yields are based upon distilled products.
- (6) Containing 13% of 3-bromo-1-butene. There is no need to remove this impurity since both of these bromo isomers produce the same Grignard reagent<sup>1,2</sup>
- (7) Without copper iodide, 4 hr from -40° to room temperature, a mixture
  ( 10:10:80) of 3b, 3c, 4c was obtained in 83% yield.
- (8) Without copper iodide, at 0° for 3 hr, a mixture (70:30) of <u>4</u>d and 3d was obtained in 88% yield.
- (9) In this case, some 3-3-dimethyl -1-decene (2%) could also be detected.
- (10) The influence of the leaving group on sodium and lithium mesomeric carbanion alkylations has been reported : W.S. Murphy, R. Boyce and E.A. O'Riordan, <u>Tetrahedron Letters</u>, 4157 (1971); W. Oppolzer and R.L. Snowden, Tetrahedron Letters, 4187 (1976)
- (11) All new compounds were identified by satisfactory analytical and spectral data.
- (12) In tetrahydrofuran, this reaction was very slow : 60% of a mixture (8:92) of 3d and 4d and 40% of unreacted tosylate after 28 hr at 0°.
- (13) An attempted synthesis of geraniol with a similar procedure, without copper salts, failed : H. Kwart and R.K. Miller, <u>J. Amer Chem. Soc.</u>, <u>76</u>, 5403 (1954)

- (14) Prepared by hydrolysis of (E) -4-chloro-3-methyl-2-buten-1-ol acetate, W. Oroshnik and R.A. Mallory, <u>J. Amer. Chem. Soc</u>.,
  <u>72</u>, 4608 (1950); A. Allais, D. Bertin and G. Nominé, <u>Bull. Soc.Chim. Fr.</u>, 209 (1955)
- (15) The reaction of (E) -4-bromo-3-methyl-2-buten-1-ol with 5 molar equivalents of lithium di-n-butyl-copper in ether has been reported: J.H. Babler and W.J. Buttner, <u>Tetrahedron Letters</u>, 239 (1976). We have found that (E) -4-chloro-3-methyl-2-buten-1-ol <u>5</u>, (1 equiv.) with butylmagnesium bromide (2.4 equiv.) and copper iodide (0.24 equiv.), 1.5 hr from -50° to room temperature, in tetrahydrofuran, gave 65% of (E) -3-methyl-2-octen-1-ol.