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# A highly efficient synthesis of (Z) γ-iodo allylic alcohols

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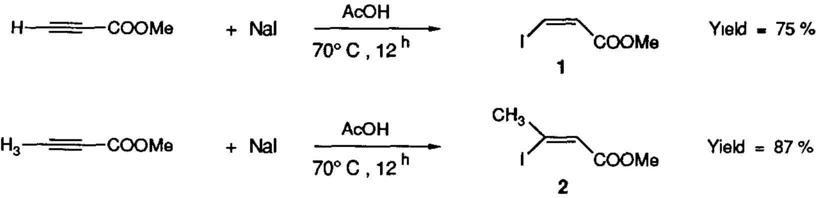
*Key Words β-Halopropenoate, (Z) γ-iodo allylic alcohols, (Z) γ-iodo acrolein equivalent.*

***Abstract:*** *The reaction of (Z) Methyl-β- iodo propenoate with diisobutylaluminium hydride and subsequent reaction with a Grignard reagent allows the synthesis of (Z) γ-iodo allylic alcohols in a very easy way*

The preparation of γ-iodo secondary allylic alcohols of Z configuration has been a challenge in recent years specially in connection with the synthesis of metabolites of arachidonic acid arising either through the cyclooxygenase pathways (prostaglandin PG)[1] or through the lipoxygenase way[2]. The Z iodovinyl alcohols **4** can be prepared from the iodo acetylenic carbinols by reaction with diimide[3], by the Denmark modification[4] of the Corey reductive iodination[5] of ethynyl carbinols, or from the reaction of diisobutylaluminium hydride with propargylic ethers followed by iodonolysis[6] (the hydroxyl group blocked as the ter-butyl ether, leads to a net trans addition of the aluminium hydride to the triple bond, and the easy and mild cleavage of the terbutyl ether into the corresponding acetates has been reported[7]), and finally by synthesis of epoxysilanes and vinylsilanes which are useful precursors of vinyl halides[8].

In this letter, we report a very easy preparation of the title compounds from (Z) Methyl-β-iodo propenoates, which have proved to be versatile and valuable intermediates in organic synthesis due to further elaboration of the three functionnal groups : the halogen atom, the carbon-carbon double bond and the ester group[9]. Among the different ways to obtain 3-halopropenoates[10], Lu et al have found that propiolates or propiolic acid could be hydrohalogenated highly stereoselectively by reaction with lithium halides in acetic acid[11].

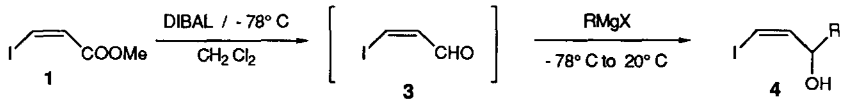
In a similar way, we have found that methyl propiolate and substituted propiolates can be hydroiodinated regio and stereospecifically, in high yield, by reaction with the less expensive sodium iodide in acetic acid as shown in Scheme 1 :



**Scheme 1**

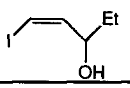
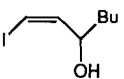
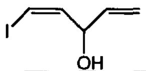
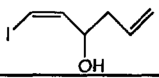
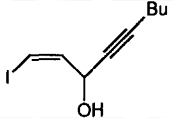
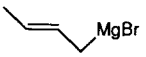
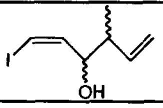
The assignment of the stereochemistry of **1** was based on the coupling constant between the two vicinal vinyl protons (J = 8,6 Hz) in 400 MHz $^1$H NMR spectroscopy, and **2** is similar to the compound obtained by Lu[11].In these cases, we did not detect any E isomers.

By reaction of compound **1** with diisobutylaluminium hydride at low temperature and subsequent reaction with a Grignard reagent, we can obtain very easily the (Z) γ-iodo allylic alcohols, according to Scheme 2 :



**Scheme 2**

**Table** : Reaction of compound **1** with DIBAL and Grignard reagents

| Entry | Grignard reagent | Product(a) | Yield(b) |
|---|---|---|---|
| 1 | EtMgBr |  | 88% |
| 2 | BuMgBr |  | 79% |
| 3 |  |  | 80%(c) |
| 4 |  |  | 72% |
| 5 | nBu—≡—MgBr |  | 81% |
| 6 |  |  | 78%(d) |

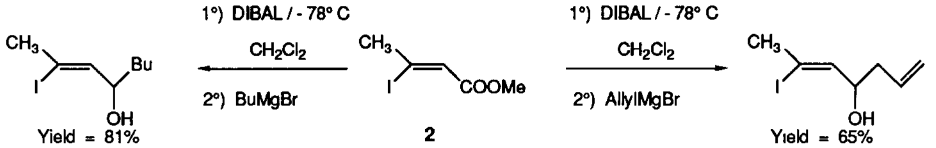
(a) The isolated pure products (except entry 3) gave satisfactory $^1$H and $^{13}$C NMR data. In all these cases, only the Z isomer is obtained

(b) Yield of isolated products by chromatography on silica gel

(c) Compound unstable on silica gel, yield determined from the $^1$H NMR spectrum of the crude product.

(d) Two diastereoisomers are obtained in a 2/1 ratio.

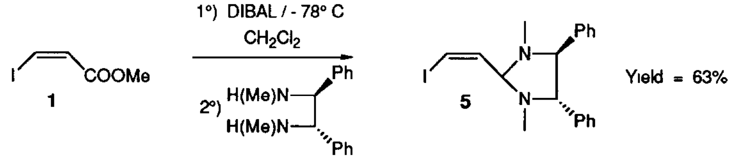
The same procedure can be used for the substituted γ-iodo allylic alcohols as shown in Scheme 3.



Scheme 3

As described in the Table and Scheme 3, this simple methodology is the only one which allows the synthesis of (Z) γ-iodo allylic alcohols *substituted*, or *not*, in γ position in a very easy and straightforward way

Independently, we have trapped the intermediate aldehyde **3** with a diamine (DMPEDA)[12] to prepare the imidazolidine **5** (scheme 4) which is a protected form of Z β-iodo acrolein with a $C_2$ axis of symmetry



Scheme 4

In conclusion, we have shown that Methyl propiolate can be used for the rapid construction of γ-iodo allylic alcohols with a perfect stereoselectivity by hydroiodination followed by a one-pot treatment with diisobutylaluminium hydride and a Grignard reagent.

## References.

1. (a) Roberts, S.M. ; Scheinmann, F., "New synthetic routes to prostaglandins and thromboxanes", Academic Press", N.Y., 1982.
   (b) Noyori, R. ; Suzuki, M., *Angew. Chem , Int. Ed. Engl.*, **1984**, *23*, 847
2. (a) Green, R.H. ; Lambeth, P., *Tetrahedron* **1983**, *39*, 1687.
   (b) Rokach, J. ; Adams, J., *J Acc. Chem. Res.*, **1985**, *18*, 87.
   (c) Kobayashi, Y. ; Shimazaki, J. , Taguchi, H. ; Sato, F., *J. Org. Chem.*, **1990**, *55*, 5324.
   (d) Kobayashi, Y. ; Otamato, S. ; Shimazaki, T. ; Ochiai, Y. ; Sato, F., *Tetrahedron Lett.*, **1987**, *28*, 3959.
   (e) Kobayashi,Y.; Shimazaki, T ; Sato, F.,*Tetrahedron Lett*, **1987**, *28*, 5849
3. Kluge, A.F. ; Untch, K.G. ; Fried, J.H., *J Am. Chem Soc* , **1972**, *94*, 9256
4. Denmark, S.E. ; Jones, T.K., *J. Org. Chem.*, **1982**, *47*, 4595

5. Corey, E.J. ; Katzenellenbogen, J.A. ; Posner, G.H., *J. Am. Chem. Soc.*, **1967**, *89*, 4245

6. (a) Bernady, K.F. ; Floyd, M.B. ; Poletto, J.F. ; Weiss, M.J., *J. Org. Chem.*, **1979**, *44*, 1438.
   (b) Alexakis, A. ; Duffault, J.M., *Tetrahedron Lett.*, **1988**, *29*, 6243

7. Alexakis, A. ; Gardette, M. ; Colin, S., *Tetrahedron Lett.*, **1988**, *29*, 2951

8. (a) Colvin, E.W., "Silicon in Organic Synthesis", Butterworths London, **1981**.
   (b) Okamoto, S. ; Shimazaki, T. ; Kobayashi, Y. ; Sato, F., *Tetrahedron Lett*, **1987**, *28*, 2033

9. (a) Smith, A.B. ; Kilenyl, S., *Tetrahedron Lett.*, **1985**, *26*, 4419.
   (b) Terao, Y. ; Imai, N. ; Achiwa, K. ; Sekiya, M., *Chem. Pharm. Bull*, **1982**, *30*, 3167.
   (c) Chalchat, J.C. ; Garry, R.P. ; Lacroix, B. ; Michet, A. ; Vessiere, R., *C.R. Seances Acad. Sci. Ser. 2*, **1983**, *296*, 253.
   (d) Miyaura, N. ; Sasaki, N. ; Itoh, M. ; Suzuki, A., *Tetrahedron Lett.*, **1977**, 3369.
   (e) Oppolzer, W. ; Robbiani, C. ; *Helv. chim. Acta.*, **1980**, *63*, 2010

10. (a) Kuitz, A.N. ; Billups, W.E. ; Greenlee, R.B. ; Hamil, H.F. ; Pace, W.T., *J. Org Chem.*, **1965**, *30*, 3141.
    (b) Bowden, K., *Can. J Chem.*, **1966**, *44*, 661.
    (c) Wingfort Corp. Brit., **1944**, 564, 261, *Chem Abstr.*, **1946**, *40*, 37688.
    (d) Takagi, K. ; Hayama, N. ; Inokawa, S., *Chem. Lett.*, **1978**, 1435.
    (e) Maclness, L. ; Schorstein, D.E. ; Suckling, C.J. ; Wngglesworth, R., *J Chem. Soc. Perkin Trans.1*, **1981**, 1103.
    (f) Biougne, J. ; Thenon, F., *C.R. Acad Sci , Ser. C*, **1971**, *272*, 858.
    (g) Winterfeldt, E., *Angew. Chem Int. Ed. Engl.*, **1967**, *6*, 423.
    (h) Jung, M. E ; Hagenah, J. A ; Mei, Z. L., *Tetrahedron Lett.*, **1983**, *24*, 3973

11. (a) Ma, S. ; Lu, X., *J. Chem. Soc., Chem. Commun*, **1990**, 1643.
    (b) Ma, S. ; Lu, X., *Tetrahedron Lett*, **1990**, *31*, 7653

12. (a) Mangeney, P. ; Grojean, F. ; Alexakis, A. ; Normant, J.F., *Tetrahedron Lett.*, **1988**, *29*, 2675.
    (b) Gosmini, R. ; Mangeney, P. ; Alexakis, A. ; Commerçon, M. ; Normant, J.F., *Synlett*, **1991**, *2*, 111 and references cited therein.

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