Tetrahedron Letters,Vol.25,No.36,pp 4007-4010,1984 0040-4039/84 $3.00 + .00
Printed in Great Britain

A CONVENIENT SYNTHESIS OF ALLENES BY THE REACTION OF PROPARGYL ALCOHOLS WITH GRIGNARD REAGENTS USING 1-CHLORO-2-METHYL-N,N-TETRAMETHYLENEPROPENYLAMINE

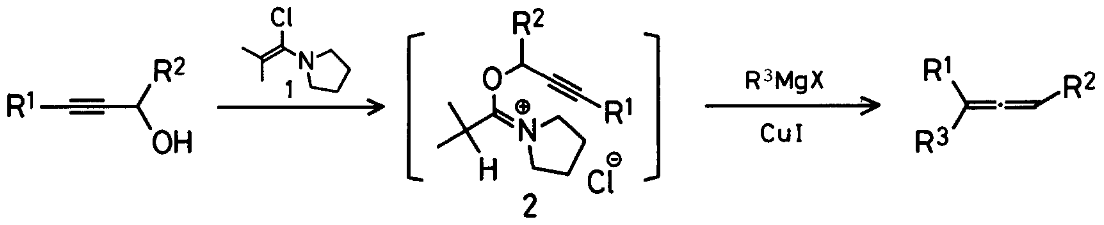
Tamotsu Fujisawa,* Sachio Iida, and Toshio Sato
Chemistry Department of Resources, Mie University, Tsu, Mie 514, Japan

Summary: *1-Chloro-2-methyl-N,N-tetramethylenepropenylamine was found to be an efficient condensation reagent for the regioselective coupling reaction of propargyl alcohols with Grignard reagents to give allenes in good yields with high chemo- and enantioselectivities. The utility of the reaction was demonstrated in the stereocontrolled synthesis of methyl (E)-2,4,5-tetradecatrienoate, the pheromone of the male dried bean beetle.*

Although allenes have been characterized for long time as a distinct class of organic compounds, they have received only limited attention. Recently, an interest in allenic chemistry has been noted from the reactivity and synthetic aspects.[1] Allene synthesis from propargyl alcohols with organometallics has been generally completed by two-step procedure *via* the corresponding ether,[2] acetate,[3] tosylate,[4] halide,[5] sulfinate,[6] carbamate,[7] and so on. Although the direct coupling of free propargyl alcohols with organometallics such as Grignard reagent using 2-fluoropyridinium salt[8] or with alkyllithium using *N*,*N*-methylphenylaminotributylphosphonium iodide[9] have been reported, these methods require excess amount of the organometallics. Recently 1-chloro-2-methyl-*N*,*N*-tetramethylenepropenylamine (1) has been found to be an effective condensation reagent in the equimolar reaction of allyl alcohols with Grignard reagents to give olefins.[10] In the present Communication, we wish to describe a useful method for the transformation of free propargyl alcohols into allenes by the reaction of slightly excess Grignard reagents using α-chloroenamine 1 in the presence of hexamethylphosphoric triamide (HMPA) and copper(I) iodide.

α-Chloroenamine 1, prepared easily from *N*,*N*-tetramethyleneisobutanamide, oxalyl chloride and triethylamine,[11] was subjected to the reaction with 4-heptyn-3-ol in THF-CH_2Cl_2 at 0 °C for 5 h. Then a solution of β-phenethylmagnesium bromide was added into the reaction mixture at -30 °C for 30 min to give the desired S_N2' product, 1-phenyl-3-ethyl-3,4-heptadiene, in 64% yield without any formation of S_N2 product, acetylenic compound. Addition of HMPA (1 ml) or copper(I) iodide (10 mol%) increased the yield of the desired allene to 91% or 93%, respectively. Addition of both HMPA and copper(I) iodide gave the desired allene in a 98% yield. Thus, HMPA and copper(I) iodide were found to be effective additives in this method.

The results of the reaction of various kinds of propargyl alcohols with the Grignard reagents using α-chloroenamine 1 was summarized in Table. Primary, secondary and tertiary alkyl Grignard reagents gave the allenes in



high yields (entries 1,3,5,6,7,8,10,11, and 12). The use of two equivalents of vinyl Grignard reagent increased the yield of the corresponding allene (entry 9). Phenyl and allyl Grignard reagents gave the corresponding allenes in good yields (entries 2,4, and 13). Even the reaction of 2-octyn-1-ol, propargyl alcohol having a long chain group such as pentyl group, with isopropenyl Grignard reagent gave the corresponding triene (entry 14), which is known as a precursor of dihydrojasmone.[12]

The high reactivity of the propargyloxyiminium salt 2, formed initially by the reaction of propargyl alcohols with α-chloroenamine 1, toward Grignard

Table. Yields of Allenes by the Reaction of Various Propargyl Alcohols with Grignard Reagents Using 1-Chloro-2-methyl-*N*,*N*-tetramethylene-propenylamine[a]

Entry	R^1	R^2	R^3	Time(h)[b]	Yield(%)[c]
1	H	H	$PhCH_2CH_2$	0.25	96
2	H	H	Ph	0.25	74
3	H	CH_3CH_2	$PhCH_2CH_2$	6	79
4	H	CH_3CH_2	Ph	6	78
5	CH_3	CH_3CH_2	$PhCH_2CH_2$	0.25	84
6	CH_3CH_2	CH_3CH_2	$PhCH_2CH_2$	5	98
7	CH_3	Ph	$PhCH_2CH_2$	6	85
8	CH_3	Ph		6	78
9	CH_3	Ph	$CH_2{=}CH$	6	41 (61)[d]
10	Ph	CH_3CH_2	$PhCH_2CH_2$	3	90
11	Ph	CH_3CH_2		3	91
12	Ph	CH_3CH_2	t-C_4H_9	3	81
13	Ph	CH_3CH_2	$CH_2{=}CHCH_2$	3	87
14	n-C_5H_{11}	H	$CH_2{=}CMe$	6	58[d]
15	H	(R)-(+)-n-C_4H_9	n-C_4H_9	6	65

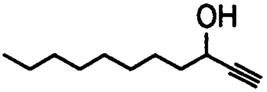
[a] All reactions were performed on 1 mmol scale with the same procedure as described in the text. [b] Reaction time of propargyl alcohols with 1-chloro-2-methyl-*N*,*N*-tetramethylene-propenylamine. [c] The products were identified by NMR and IR spectra. [d] Two equivalents of RMgBr were used.

reagents makes possible the chemoselective coupling of propargyl alcohols and Grignard reagents in the co-existence of ketone, ester, nitrile, or halide. When a 1:1 mixture of 4-heptyn-3-ol and propiophenone was treated with β-phenethylmagnesium bromide using 1-chloro-2-methyl-*N*,*N*-tetramethylenepropenylamine (1), the desired allene was obtained in 94% yield and propiophenone was recovered in 98% yield. The similar reactions in co-existence of ethyl laurate, benzonitrile or octyl bromide instead of the ketone gave the allenes in 93 ∿ 96% yields with recovery of them in over 92% yields.

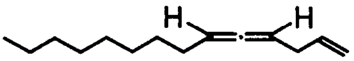
Further, the stereochemistry of the γ-alkylation of optically active propargyl alcohol was examined, since the S_N2' reaction has been interested from standpoints of both mechanism and utility for organic synthesis. Definitive investigations of the stereochemistry, however, are limited to a few cases.[13] The reaction of (*R*)-(+)-1-heptyn-3-ol ($[\alpha]_D^{23}$ +26.32° (c 0.874, Et_2O), 98%ee)[14] with butyl Grignard reagent gave selectively (*S*)-(+)-5,6-undecadiene ($[\alpha]_D^{23}$ +17.27° (c 0.85, CCl_4))[15] in 65% yield (entry 15). This result clearly shows that the transformation of alcohol to allene proceeds predominantly *via* syn type of S_N2' reaction.

To demonstrate the utility of the enantioselective method, a stereocontrolled synthesis of both enantiomers of optically active methyl 4,5-tetradecadienoate (6), a precursor of methyl (*E*)-2,4,5-tetradecatrienoate (7), the sex pheromone of the male dried bean beetle *Acauthoscelides obtectus* (Say),[16] was carried out using the present method as a key step. The reaction of both enantiomers of 1-undecyn-3-ol ((*S*)-(−)-(3), $[\alpha]_D^{23}$ −15.3°, and (*R*)-(+)-(3), $[\alpha]_D^{23}$ +15.9° (Et_2O), 99%ee)[16g] with allyl Grignard reagent using α-chloroenamine (1) gave 1,4,5-tetradecatrienes ((*R*)-(−)-(4), $[\alpha]_D^{23}$ −45.47°, and (*S*)-(+)-(4), $[\alpha]_D^{23}$ +49.69° ($CHCl_3$)) in 84 and 85% yields. Hydroboration of trienes 4 with 9-BBN in THF at room temperature gave 4,5-tetradecadiene-1-ols ((*R*)-(−)-(5), $[\alpha]_D^{23}$ −60.74°, and (*S*)-(+)-(5), $[\alpha]_D^{23}$ +66.1° (Et_2O)) in 85 and 90% yields. By the oxidation of the alcohols 5 with PCC (CH_2Cl_2, rt, 5 h), the corresponding aldehydes were obtained in 85 and 87% yields, which were then converted to methyl 4,5-tetradecadienoates ((*R*)-(−)-(6), $[\alpha]_D^{23}$ −54.2°, 86%ee, and (*S*)-(+)-(6), $[\alpha]_D^{23}$ +58.2° (*n*-hexane), 92%ee)[16g] in 69 and 67% yields (Ag_2O and CH_2N_2). Synthesis of methyl (*E*)-2,4,5-tetradecatrienoate (7) from methyl-4,5-tetradecadienoate (6) was already reported.[16g]

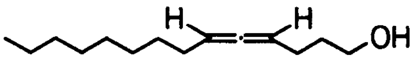
A typical procedure is described for the preparation of 1-phenyl-3-ethyl-



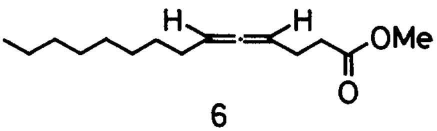
3



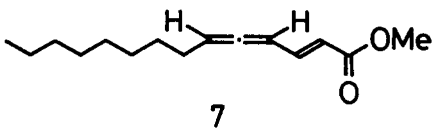
4



5



6



7

3,4-heptadiene: To a solution of 1-chloro-2-methyl-*N*,*N*-tetramethylenepropenylamine (1.3 ml of 0.923M CH_2Cl_2 solution, 1.2 mmol) was added a solution of 4-heptyn-3-ol (1.0 mmol) in THF (3 ml) at 0 °C under an argon atomosphere, and the reaction mixture was stirred for 5 h at the same temperature. Then, hexamethylphosphoric triamide (1 ml), copper(I) iodide (10 mol%) and a solution of β-phenethylmagnesium bromide (1.50 ml of 0.865M THF solution, 1.3 mmol) was subsequently added to the reaction mixture at -30 °C. After stirring for 30 min, the reaction was quenched by the addition of saturated aq. ammonium chloride solution. The organic layer was extracted with ether and dried over $MgSO_4$. After removal of the solvent, the residue was chromatographed on silica-gel TLC (hexane, Rf = 0.85) to give 1-phenyl-3-ethyl-3,4-heptadiene in 98% yield.[17]

It is noted that propargyl alcohols were selectively coupled with the Grignard reagents using 1-chloro-2-methyl-*N*,*N*-tetramethylenepropenylamine to give allenes under mild conditions by simple one-pot procedure.

The present work was partially supported by a Grant-in-Aid for Special Project Research from Ministry of Education, Science and Culture in Japan, and the Asahi Glass Foundation.

References and Notes

1. J. C. Clinet and G. Linstrumelle, *Synthesis*, 1981, 875; J. Meijer, K. Ruitenberg, H. Westmijze, and P. Vermeer, *ibid.*, 1981, 551.
2. L. I. Olason and A. Claesson, *Acta Chem. Scand., Ser. B*, 1979, 679.
3. P. Rona and P. Crabbé, *J. Am. Chem. Soc.*, 91, 3289 (1969).
4. P. Vermeer, J. Meijer, and L. Brandama, *Recl. Trav. Chim. Pays-Bas*, 94, 112 (1975).
5. D. J. Pasto, S.-K. Chou, E. Fritzen, R. H. Shults, A. Waterhouse, and G. F. Hennion, *J. Org. Chem.*, 43, 1389 (1978).
6. H. Kleijn, C. J. Elsevier, H. Westmijze, J. Meijer, and P. Vermeer, *Tetrahedron Lett.*, 1979, 3101.
7. W. H. Pirkle and C. W. Boeder, *J. Org. Chem.*, 43, 1950 (1978).
8. T. Mukaiyama and K. Kawata, *Chem. Lett.*, 1978, 785.
9. Y. Tanigawa and S. Murahashi, *J. Org. Chem.*, 45, 4536 (1980).
10. T. Fujisawa, S. Iida, H. Yukizaki, and T. Sato, *Tetrahedron Lett.*, 24, 5745 (1983).
11. B. Haveaux, A. Dekoker, M. Rens, A. R. Sidani, J. Toye, and L. Ghosez, *Org. Synth.*, 59, 26 (1979).
12. R. Baudouy, F. Delbecq, and J. Gore, *Tetrahedron*, 36, 189 (1980).
13. F. G. Bordwell, P. F. Wiley, and T. G. Mecca, *J. Am. Chem. Soc.*, 97, 132 (1975); G. Stork and A. F. Kreft, III, *ibid.*, 99, 3850 (1977).
14. The optical purity of the acetylenic alcohol obtained by the resolution of the corresponding phthalic half ester with (*R*)-(+)-1-(α-naphthyl)ethylamine was determined by the NMR analysis in the presence of $Eu(hfc)_3$.
15. J. M. Walbrick, J. W. Wilson, Jr., and W. M. Jones, *J. Am. Chem. Soc.*, 90, 2895 (1968), and references cited therein.
16. D. F. Horler, *J. Chem. Soc., (C)*, 1970, 859. Reports for the synthesis are as follows; a) C. Descoins, C. A. Henrick, and J. B. Siddall, *Tetrahedron Lett.*, 1972, 3777. b) R. Bandony and J. Gore, *Synthesis*, 1974, 573. c) D. Michelot and G. Linstrumelle, *ibid.*, 1976, 275. d) P. J. Kocienski, G. Cernigliaro, and G. Feldstein, *J. Org. Chem.*, 42, 353 (1977). e) W. H. Pirkle and C. W. Boeder, *J. Org. Chem.*, 43, 2091 (1978). f) M. Franck Franck-Neumann and F. Brion, *Angew. Chem., Int. Ed. Engl.*, 18, 688 (1979). g) K. Mori, T. Nakada, and T. Ebata, *Tetrahedron*, 37, 1343 (1981).
17. The analysis of the product by GLC showed a single peak of allene without any acetylenic compound formed by S_N2 reaction.

(Received in Japan 21 May 1984)