Tetrahedron Letters,Vol.30,No.46,pp 6409-6412,1989
Printed in Great Britain

0040-4039/89 $3.00 + .00
Pergamon Press plc

NICKEL-CATALYZED REGIOSELECTIVE ALLYLATION OF ALLYLIC ALCOHOLS

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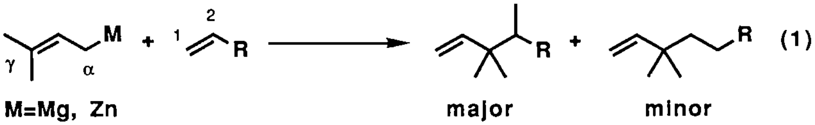
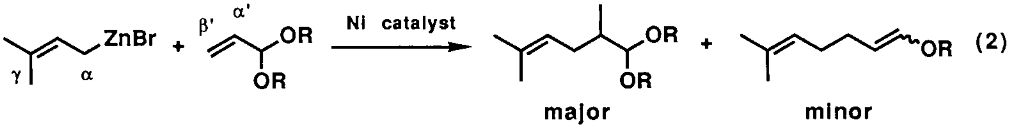
Abstract: Regioselective allylmetallation of allylic alcohol has been accomplished by treatment with allylzinc in the presence of a nickel catalyst. Benzylic protective group of allyl alcohol facilitates the allylmetallation.

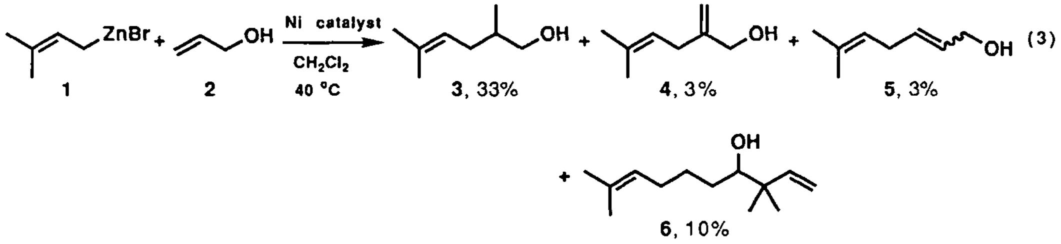
During the past two decades many investigations in the field of allylmetallation of alkenes using allylic Grignard reagents or zinc reagents have been reported.[1] For example, unsymmetrical allylic metal compounds added to 1-alkene are known to give the product (γ--C-2) in eq. 1.[1a] We have recently shown that an α,β-unsaturated acetal undergoes rapid metallation upon treatment with allylzinc in the presence of nickel catalyst.[2] Thus, the allylic zinc reagent regiospecifically reacted at the α carbon and attacked at the α' carbon of the acetal selectively, eq. 2. Here, we wish to report further studies of this new process on allylic alcohols and their derivatives.

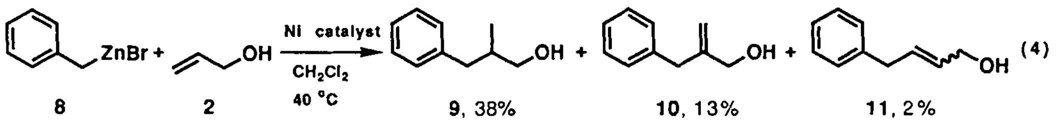




Treatment of 1 equiv of allyl alcohol (**2**) with a solution of 3-methyl-2-butenylzinc bromide (**1**) (4 eq) in CH_2Cl_2 under the influence of catalytic $NiBr_2(PBu_3)_2$ (10 mol%) at 40 °C for 35 min gave a mixture of the C-2 adduct **3** and **4** and C-3 adduct **5**[3] and **6**[4] in low combined yield, eq. 3.[5] Thus, allyl alcohol was found to be less reactive towards allylic metal reagent than α,β-unsaturated acetal, probably due to its higher basicity.

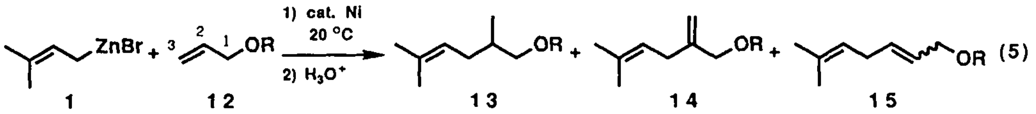
Benzylzinc reagent gave similar results: The reaction of benzylzinc bromide (**8**) with allyl alcohol (**2**) furnished the benzylated products **9**, **10**, and **11**, eq. 4.

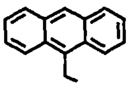


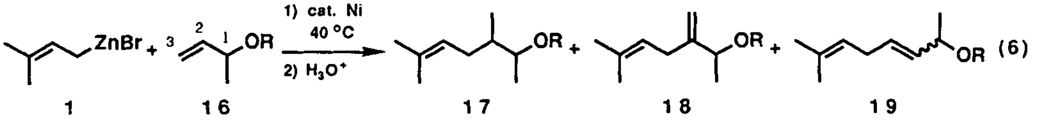


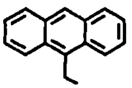
We then turned our attention to the various protective forms of allyl alcohol to facilitate the allylmetallation. Among a variety of protective groups,[6] benzyl allyl ether rapidly reacted with allylic zinc reagent. Some of our examples (eq. 5) show the following features. (1) Unsymmetrical allylic zinc reagent reacted at the primary carbon almost exclusively. (2) Higher C-2/C-3 regioselectivity was achieved by increasing the number of phenyl groups of R. Thus, high regioselectivity of 15/1 was realized in the case of triphenylmethyl allyl ether, while the combined yield of products was lowered, probably due to the steric bulkiness of the protective group. Use of allyl 9-anthrylmethyl ether, in contrast, proved satisfactory in both regioselectivity and chemical yields (C-2/C-3 ratio = 6.9/1, 66% combined yield). Introduction of alkyl substituent at C-1 position of allyl alcohol resulted in higher regioselectivity, eq. 6, and the diastereomeric ratio of C-2 adduct **17** was 4.8:1 in 9-anthrylmethyl ether.[7] Obviously, the intermediate organozinc reagent can be trapped effectively with D_2O to afford the corresponding deuteriated products.

The following procedure for prenylation of allyl 9-anthrylmethyl ether is illustrative. To a solution of 3-methyl-2-butenylzinc bromide (**1**) (3.00 mmol)[2] in CH_2Cl_2 (1.5 mL) was added catalytic $NiBr_2(PBu_3)_2$ (62.9 mg, 0.101 mmol) at 20 °C. After 10 min, allyl 9-anthrylmethyl ether (244.3 mg, 0.984 mmol) was added at 20



R	13	14	15	ratio (C-2/C-3)
Et	14%	0%	12%	1.2/1
$PhCH_2$	48%	0%	18%	2.7/1
Ph_2CH	34%	3%	7%	5.3/1
Ph_3C	26%	4%	2%	15/1
	40%	15%	8%	6.9/1



R	17	18	19	ratio (C-2/C-3)
$PhCH_2$	52%	3%	4%	13.8/1
	60%	11%	5%	14.2/1

°C, and the resulting mixture was stirred at this temperature for 3 h. The mixture was poured into a saturated NH_4Cl aqueous solution and extracted with ether. The combined extracts were dried and concentrated, and the crude product was purified by column chromatography on silica gel (AcOEt/hexane = 15/1) to give a mixture of prenylated ether **13**, **14**, and **15** (240.5 mg, 63% combined yield) as a yellow solid. The product ratio (**13**/**14**/**15**) was determined by 500 MHz ^1H NMR analysis.

Acknowledgement: The present work was partially supported by a Grant-in-Aid for Scientific Research from the Ministry of Education, Science and Culture of Japan.

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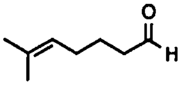
2) A. Yanagisawa, S. Habaue, and H. Yamamoto, *J. Am. Chem. Soc.*, **111**, 366 (1989).
3) *trans*-Allylic alcohol was obtained as major isomer judged by 500MHz ^{1}H NMR analysis.
4) Compound **6** was supposed to be produced by reaction between the remaining 3-methyl-2-butenylzinc bromide (**1**) and aldehyde **7**, another isomer of C-3 adduct.



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5) Alkyllithium or allylic Grignard reagents are known to be readily added to allyl alcohols. The importance of intramolecular coordination was clearly demonstrated. Alkyllithiums: J. K. Crandall and A. C. Clark, *J. Org. Chem.*, **37**, 4236 (1972); J. K. Crandall and A. C. Rojas, *Org. Synth.*, **55**, 1 (1976). Allylic Grignard reagents: H. Felkin and C. Kaeseberg, *Tetrahedron. Lett.*, 4587 (1970); H. G. Richey, Jr. and C. W. Wilkins, Jr., *J. Org. Chem.*, **45**, 5027 (1980).
6) T. W. Greene, "Protective Groups in Organic Synthesis"; John Wiley & Sons, Inc., New York, 1981.
7) The reaction between 1-methyl-2-propen-1-ol (**16**, R=H) and 3-methyl-2-butenylzinc bromide (**1**) in the presence of $NiBr_2(PBu_3)_2$ catalyst at 40 ^{o}C afforded **17** (R=H) in 11% yield accompanied with a trace amount of **18** (R=H) and **19** (R=H).

(Received in Japan 5 August 1989)