Effects of Hexamethylphosphoric Triamide (Hempa) upon Allylic Grignard Reagents: Synthesis of Long Chain Alkenol Acetates

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ABSTRACT

E or Z allylic Grignard reagents reacted with allylic halides in tetrahydrofuran-Hempa to give products in which the double bond from the organometallic fragment was predominantly Z. Protonation of the allylic Grignard reagents gave an increased proportion of Δ2-alkene and a higher ratio of Z:E isomers when Hempa was added.

INTRODUCTION

We recently reported our studies on sex pheromones of the adult pink bollworm, *Pectinophora gossypiella*, and the identification of the pheromone as the acetates of (Z,Z)- and (Z,E)-7,11-hexadecadien-1-ol [4] (1). The initial report of these materials was given by Hummel, et al. (2). As part of the structure confirmation, we synthesized these materials and their isomers by coupling the allylic Grignard reagent derived from 1-chloro-2-heptene [1] with Z and E allylic halides [2a] and [2b]. Since allylic Grignard reagents normally react with alkyl halides to give mixtures of Z and E olefins, as well as the product of internal coupling of the Grignard fragment (3), we expected to obtain isomeric pairs of dienes in nearly equal proportions; for example, from [1] and [2a], a mixture of the (Z,Z)- and (Z,E)-7,11-acetates [4] would be expected after acetolysis of the tetrahydropyranyl (THP) group (Scheme I). When Hempa was employed in the solvent mixture, the product of primary coupling was almost exclusively Z,Z-[4]. This article reports these results and the effect of Hempa on the composition of the reaction products.

$CH_3(CH_2)_3CH{=}CHCH_2MgCl + ClCH_2CH{=}CH(CH_2)_6OTHP \rightarrow$

[1] [2]

a, Z
b, E

$CH_3(CH_2)_3CH{=}CH(CH_2)_2CH{=}CH(CH_2)_6OTHP \rightarrow$

[3]

$CH_3(CH_2)_3CH{=}CH(CH_2)_2CH{=}CH(CH_2)_6OAc$

[4]

Scheme I

EXPERIMENTAL PROCEDURES

Materials

Allylic halides were obtained by treating appropriate lithium acetylides with paraformaldehyde (4) to produce propargyl alcohols. Reduction of these with lithium aluminum hydride gave E-allylic alcohols that were then converted to chlorides by tosylation of the alkoxides in the presence of lithium chloride (5). Hydrogenation of the propargyl alcohols in pentane with Lindlar catalyst gave the predominantly Z-allylic alcohols, which similarly were converted to chlorides. Elemental analyses were correct for the bis-α-naphthylurethans of the diols corresponding to [2a] (n_D^{25}, 1.4716) and [2b] (n_D^{25}, 1.4704). In analogous fashion, we synthesized and characterized (E)-1-chloro-2-undecene (boiling point [bp] 108-110 C/1.0 mm; n_D^{25} 1.4515; IR 975 cm^{-1}; NMR [CCl_4], 3.58 ppm, d, allylic CH_2Cl). Magnesium turnings, purchased from Fisher Scientific Co., Fairlawn, N.J., were used directly; tetrahydrofuran (THF) and Hempa were dried and stored over type 4A molecular sieves. The preparations of the isomers of [4] are described in a previous publication (1).

Preparation and Reaction of Allylic Grignard Reagents

Magnesium (60 mmol) was placed in a dry vessel under nitrogen, and reaction was initiated by briefly warming it with a few drops of ethylene bromide, a crystal of iodine, and THF (2 ml). More THF (23 ml) then was added, and, after the mixture had been cooled to 0-5 C, one equivalent of the allylic halide [1] (Z or E) was added over a 2 hr period. The resulting mixture was stirred at 0-5 C for 1 hr longer and then decanted into an addition funnel from which it was subsequently added dropwise to a stirred solution of the appropriate allylic halide [2a] or [2b] (5 mmol)

TABLE I

Analyses of Diene Mixtures[a] Resulting from Reaction of [1] with [2a] or [2b] in Presence of Several Concentrations of Hempa

Reactant	Percent, Hempa	Z:E of Δ11
2a	18	∿96:4[b]
2b	0	43:57
2b	18	94:6
2b	38	92:8

[a] Analyses were performed on a 1500 x 0.05 cm silicone polymer EGGS-X SCOT column at 170 C after a preliminary purification by preparative gas liquid chromatography by using a 910 x 0.6 cm 5% SE-30 silicone oil column at 200 C to remove the products of secondary coupling. These products were not investigated, but they constituted 85-90% of the product in tetrahydrofuran (THF) and 45-50% in 18% Hempa-THF.

[b] (Z,E)- and (E,Z)-7,11 isomers were indistinguishable by gas liquid chromatography and calculations were made assuming ∿4% 7-E in [2a]. This amount of E is expected from hydrogenation of acetylenes.

TABLE II

Analyses of Protonated Mixtures from Allylic Grignard Reagent[a] with Different Concentrations of Hempa

Percent, Hempa	Z:E	Δ1:Δ2[b]
0	39:61[c]	---
0	47:53	55:45
8	60:40	47:53
18	67:33	37:63
33	73:26	36:64
41	77:23	31:69
50	79:21	18:82

[a] Analyses were performed on the column described in Table I at 90 C. Reagent is 2-undecen-1-yl magnesium chloride.

[b] This ratio is quite sensitive to other variables not identified, and only the trend is meaningful.

[c] Reference (7): 2-penten-1-yl magnesium halide.

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[1] ARS, USDA.

in THF containing the proportions of Hempa listed in Table I. Preparation of the Grignard reagent of (E)-1-chloro-2-undecene was carried out in essentially the same way. Carboxylation of the product was accomplished by decanting onto crushed dry ice and appropriate workup. The resulting acid was esterified with 1-methyl-3-p-tolyltriazene by the usual procedure (6).

RESULTS AND DISCUSSION

The most rigorous investigation of the nature of allylic Grignard reagents (7) revealed them to be rapidly equilibrating Z-E mixtures with some evidence that magnesium is bonded directly to the primary carbon atom. In that study, the Z-E ratios were determined by NMR spectroscopy directly with the equilibrated allylic Grignard isomers and indirectly by protonation of the mixture and determination of the resulting $\Delta 2$-alkenes. Our choice of Hempa as a cosolvent for the alkylation of our allylic Grignards was predicated upon the likelihood that its presence would suppress secondary coupling on the allylic halide and preserve the geometry of the 7-double bond (5).

Regardless of the geometry of [1], the 11-double bond was >90% Z when the solvent mixture for the condensation contained $\sim$18% Hempa. Some results are given in Table I. It has been reported that Hempa can dramatically alter the course of reaction of Grignard reagents with ketones (9); this was explained in terms of Hempa's strong coordinative power. By coordinating with magnesium, the Hempa relieved the allylic anion from its bond to the solvated metal, which enhanced the proportion of Z in the anion equilibrium.

We also prepared the Grignard reagent of (E)-1-chloro-2-undecene in THF and, after adding Hempa to aliquots of this solution, quenched them with 1% hydrochloric acid (HCl). The ratio of (Z)- to (E)-2-undecene we obtained in THF alone was similar to that reported by Grutzner from 2-penten-2-yl magnesium halide (7). (Table II). A gradual increase in the Z:E ratio was noted with increasing Hempa content. We also observed that the proportion of 1-decene decreased, a reasonable consequence if the primary carbon of the anion becomes less encumbered. The effect of Hempa upon the equilibrium as determined by protonation was less pronounced than on the apparent relative reactivities of the Z and E anions with allylic halides.

A final observation was that carboxylation occurred exclusively at the secondary site in 18% Hempa-THF; the same reactivity as has been noted in the usual solvent systems (3). Clearly, however, profound changes occur both in the nature and reactivity of allylic Grignard reagents in solvents of strong basicity. It appears that conditions may be found to produce nearly pure Z olefins with easily prepared allylic halides of mixed geometry. Hopefully, these data will provoke a more thorough mechanistic study.

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