Chem. Pharm. Bull. **40**(10) 2834—2835 (1992) Vol. 40, No. 10

Allylation of Aldehydes with Allyl Bromides and Zinc Induced by Pyridinium Perchlorates

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Received March 16, 1992

The effects of inorganic and organic salts on the allylation of benzaldehyde with unactivated zinc powder and allyl bromide in acetonitrile were examined at room temperature. Although Li$^+$, Na$^+$, Mg^{2+}, and R$_4$N$^+$ perchlorates exerted negligible effects on the allylation, various pyridinium perchlorates except the 2,6-lutidinium salt promoted the formation of the corresponding homoallylic alcohol from benzaldehyde. In the presence of pyridinium perchlorate, the allylation of aliphatic and aromatic aldehydes with allyl bromide and zinc smoothly proceeded to give the corresponding products in good yields. Hydroxy-, methoxy-, and halogen-substituted aromatic aldehydes were tolerated under the reaction conditions employed. In the case of cinnamyl aldehyde, only 1,2-addition was observed.

Keywords metallic zinc; pyridinium salt; allylation; aldehyde; allyl bromide; homoallylic alcohol

To understand electrode reactions, electroorganic chemists must take the nature of the supporting electrolyte into account when its constituent ions have weak solvation capability and interact strongly with the electrode surface. That is, in electroorganic chemistry it has been appreciated that the identity of a supporting electrolyte, which is responsible for the structure of the so-called electric double layer built up at an electrode surface, can have great influence on the kinetics of charge transfer and of coupled chemical reactions as well as on the stereochemical outcome, because electrode reactions are supposed to take place only in close proximity to the electrode surface, namely, in the double layer.$^{1)}$

The same phenomenon is observed when a metal is in contact with a solution containing an electrolyte, although the effect is less marked than in electrode reactions. However, the effect of a salt on chemical reactions initiated by heterogeneous electron transfer from zero-valent metals has never been studied in detail. In order to examine how electrolytes will work in such a reaction, we investigated the electrolyte effect on the allylation of aldehydes by unactivated zinc powder and allyl bromide in CH_3CN (Chart 1), and found that pyridinium perchlorate among various salts examined is the electrolyte of choice for the allylation.

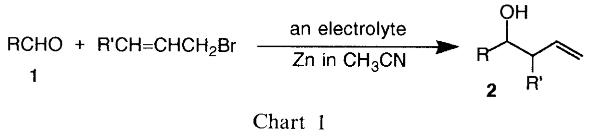

Chart 1

Results and Discussion

Barbier-type reaction of benzaldehyde (**1a**; R = Ph) with allyl bromide and zinc powder in the absence or presence of a salt was investigated first. The results are summarized in Table I.

The formation of the corresponding homoallylic alcohol (**2a**; R = Ph, R′ = H) was aided by the presence of Li$^+$, Na$^+$, Mg^{2+}, or R$_4$N$^+$ perchlorate as compared with that in the absence of a salt, but the yields were not satisfactory (runs 1—6). In contrast, the use of pyridinium (Py$^+$) perchlorate provided **2a** in an excellent yield (run 7). A few examples of similar phenomena have recently appeared in the literature: Py$^+$ tosylate was used to induce allylation of α-phenylpropionaldehyde$^{2)}$ and α-keto amides$^{3)}$ by zinc powder and allyl bromide in H_2O–tetrahydrofuran (THF). But pyridinium salt-induced allylation of aldehydes has not yet been well established. So the effects of counter anions of the pyridinium salts and substitutions on the pyridinium ring upon the allylation were further investigated. With regard to the counter anion, perchlorate was found to be the best anion for the allylation (runs 7—10). On the other hand, substituted pyridinium perchlorates except for the 2,6-lutidinium salt were also shown to be available for this transformation (runs 11—16). Thus, Py$^+$ and γ-picolinium (Pic$^+$) perchlorates seem to be the electrolytes of choice.

Allylation induced by Py$^+$ and γ-Pic$^+$ perchlorates was

TABLE I. The Effect of Electrolytes on the Allylation of Benzaldehyde (**1a**) by Zinc Powder and Allyl Bromide in $CH_3CN^{a)}$

Run	Electrolyte		Yield of **2a**	Run	Electrolyte		Yield of **2a**
	Cation$^{b)}$	Anion	(%)$^{c)}$		Cation$^{b)}$	Anion$^{d)}$	(%)$^{c)}$
1	None		4	9	Py$^+$	TS$^-$	74
2	Li$^+$	ClO_4^-	23	10	Py$^+$	CAS$^-$	64
3	Na$^+$	ClO_4^-	21	11	β-Pic$^+$	ClO_4^-	90
4	Mg^{2+}	ClO_4^-	10	12	γ-Pic$^+$	ClO_4^-	98
5	Et$_4$N$^+$	ClO_4^-	7	13	2,6-Lut$^+$	ClO_4^-	9
6	Bu$_4$N$^+$	ClO_4^-	26	14	3,5-Lut$^+$	ClO_4^-	92
7	Py$^+$	ClO_4^-	95	15	2-EtO$_2$C–Py$^+$	ClO_4^-	70
8	Py$^+$	BF_4^-	39	16	Q$^+$	ClO_4^-	89

a) A mixture of **1a** (3 mmol), allyl bromide, zinc powder, and an electrolyte (3.6 mmol each) in CH_3CN (20 ml) was stirred at room temperature for 20 h. *b*) Py$^+$, Pic$^+$, Lut$^+$, and Q$^+$ stand for pyridinium, picolinium, lutidinium, and quinolinium ions, respectively. *c*) Determined by GLC. *d*) TS$^-$ and CAS$^-$ denote *p*-toluenesulfonate and (*S*)-(+)-camphor-10-sulfonate anions, respectively.

TABLE II. Allylation of Aldehydes in CH_3CN Induced by Zinc–Pyridinium Perchlorates$^{a)}$

	R	R′	Yield of **2** (%)$^{b)}$			R	R′	Yield of **2** (%)$^{b)}$	
			By Py$^+$	By γ-Pic$^+$				By Py$^+$	By γ-Pic$^+$
a	Ph	H	81	86	**g**	*p*-Cl-Ph	H	85	37
b	CH$_3$(CH$_2$)$_8$	H	85	73	**h**	Ph	CH$_3$	86	85
c	PhCH$_2$CH$_2$	H	76	78				(1.9 : 1)$^{c)}$	(1.8 : 1)$^{c)}$
d	PhCH=CH	H	77	81	**i**	PhCH(CH$_3$)	H	77	83
e	*o*-HO–Ph	H	75	43				(2.8 : 1)$^{d)}$	(2.9 : 1)$^{d)}$
f	*p*-CH$_3$O–Ph	H	65	76	**a**	Ph$^{e)}$	H	38	41

a) General procedure, see Experimental. *b*) Isolated yield. *c*) The number in parentheses shows the ratio of *erythro*/*threo* in the formation of **2h** determined by ^{1}H-NMR (ref. 11). *d*) The number in parentheses shows the ratio of Cram/anti-Cram selectivity in the formation of **2i** determined by ^{1}H-NMR (ref. 8*b*). *e*) Dimethyl acetal was used instead of the aldehyde.

Table III. The Effect of Additives on the Allylation of Benzaldehyde (**1a**) with Allyl Bromide and Zinc Powder in CH_3CN[a)]

Run	Additive	Yield of **2a** (%)[b)]
1	Pyridine and camphorsulfonic acid[c)]	64
2	Camphorsulfonic acid[c)]	34
3	Bu_3N and camphorsulfonic acid[c)]	6
4	*N*-Methyl pyridinium perchlorate	50

a) A mixture of **1a** (3 mmol), allyl bromide, zinc powder, and an additive (3.6 mmol each) in CH_3CN (20 ml) was stirred at room temperature for 20 h. *b)* Determined by GLC. *c)* (*S*)-(+)-Camphor-10-sulfonic acid was used.

applied to various aldehydes. As is apparent from Table II, the present method using Py^+ perchlorate is general, and a variety of aromatic and aliphatic aldehydes are converted to homoallylic alcohols **2** in good yields. Furthermore, the presence of a free hydroxy group does not affect the reaction course. In the case of cinnamyl aldehyde, only 1,2-addition was observed, as in the allylation of α,β-unsaturated carbonyl compounds by other methods using zinc powder.[4)]

It is noteworthy that the present method has high chemoselectivity. Thus, benzaldehyde could be converted to **2a** in as high as 83% yield in the presence of acetophenone, while the homoallylic alcohol ($Ph-CCH_3(OH)-CH_2-CH=CH_2$) was not detected at all.

In order to understand how pyridinium salts favor the allylation, several sets of experiments were carried out (Table III). In the presence of pyridine and (*S*)-(+)-camphor-10-sulfonic acid,[5)] **2a** was obtained in the same yield as in the presence of Py^+ (*S*)-(+)-camphor-10-sulfonate prepared in advance (run 1; *cf.* run 10, Table I). (*S*)-(+)-Camphor-10-sulfonic acid itself is expected to activate the zinc surface and induce the allylation, based on the fact that an acid is known to catalyze zero valent metal induced allylation.[6)] Indeed, this was the case (run 2). But the yield was considerably lower than that in the presence of pyridine. The addition of tributylamine and the acid to the reaction mixture gave a poor result (run 3). It is of great interest that *N*-methylpyridinium perchlorate, which does not work as an acid, could induce the allylation (run 4) though less effectively than Py^+ perchlorate. These results suggest that both a pyridinium ring and an acidic proton in the salts can facilitate the electron transfer from metallic zinc so as to spur the allylation.

Regarding the mechanism of the allylation by the present method, two pathways can be envisaged. One of them is nucleophilic attack of an allyl zinc compound on the aldehyde carbon. The other involves coupling of an allylic radical with the carbon–oxygen double bond or with a ketyl radical generated by one electron reduction of the aldehyde. The latter ketyl radical process has been proposed by Luche and Einhorn for their allylation method in THF–aqueous NH_4Cl.[4b)] For the pyridinium salt-induced allylation, it is not likely that the products are formed *via* nucleophilic attack or radical–radical coupling, because the allyl zinc compound is supposed to be protonated by pyridinium salts, being good proton donors, before it would attack the aldehyde carbon, and benzaldehyde was not reduced under these reaction conditions to give the corresponding alcohol and pinacol, which would imply the formation of the ketyl radical. At present, it can be proposed that the initially formed allylic radical somehow executes the addition onto aldehyde carbons, although pyridinium salts are known to be better acceptors for carbon radicals than a carbon–oxygen double bond.[7)]

In summary, the present study indicates that allylation of aldehydes by allyl bromide and zinc powder in CH_3CN can be effectively performed by the use of Py^+ perchlorate, which appears to activate the zinc surface. Further studies to shed light on the exact role of pyridinium perchlorates in the allylation are in progress.

Experimental

Infrared (IR) spectra were taken on a JASCO A-202 spectrometer. ^1H-NMR spectra were obtained at 200 MHz on a Varian VXR-200 spectrometer in $CDCl_3$ with tetramethylsilane (TMS) as an internal standard. Gas liquid chromatography (GLC) was performed on a JEOL JGC-20K gas chromatography with a PEG 20M glass column (2 m × 3 mm). For column chromatography, SiO_2 (Wakogel C-200) was used.

Materials Pyridinium salts except Py^+ tosylate were prepared as described previously.[9)] All other chemicals were of reagent grade, and were used without further purification. CH_3CN was distilled from P_2O_5.

General Procedure for the Runs in Table II Zinc powder (3.6 mmol) was added gradually at room temperature to a stirred solution of an aldehyde (3 mmol), allyl bromide, and Py^+ or γ-Pic^+ perchlorate (3.6 mmol each) in CH_3CN (20 ml). An exothermic reaction was occurred, and after 4 h, the mixture was poured into 10% HCl (80 ml). The whole was extracted with ether (60 ml × 3). The combined organic layer was washed with brine, dried over $MgSO_4$, and evaporated *in vacuo*. The residue was subjected to column chromatography (SiO_2; hexane–ethyl acetate) to afford a pure homoallyl alcohol. The ^1H-NMR and IR spectra of **2a**,[10)] **2d**,[8a)] **2e**,[4b)] **2f**,[8a)] **2h**,[11)] and **2i**[8a)] coincided with those in the literature. All other products are also known compounds and gave satisfactory ^1H-NMR and IR spectra (see below).

1-Tridecen-4-ol (**2b**): A colorless oil. IR (neat) 3380, 1645 cm^{-1}. ^1H-NMR ($CDCl_3$) δ 5.98—5.72 (1H, m), 5.32—5.00 (2H, m), 3.72—3.56 (1H, m), 2.44—2.01 (2H, m), 1.58—1.08 (16H, m), 0.88 (3H, t, $J=6.2$ Hz).

1-Phenyl-5-hexen-3-ol (**2c**): A colorless oil. IR (neat) 3400, 1645 cm^{-1}. ^1H-NMR ($CDCl_3$) δ 7.46—7.17 (5H, m), 5.96—5.71 (1H, m), 5.24—5.08 (2H, m), 3.77—3.60 (1H, m), 2.92—2.61 (2H, m), 2.42—2.14 (2H, m), 1.84—1.73 (2H, m).

1-(4-Chlorophenyl)-3-buten-1-ol (**2g**): A colorless oil. IR (neat) 3400, 1645 cm^{-1}. ^1H-NMR ($CDCl_3$) δ 7.51—7.07 (4H, m), 5.90—5.64 (1H, m), 5.31—5.00 (2H, m), 4.74—4.67 (1H, m), 2.63—2.31 (2H, m).

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