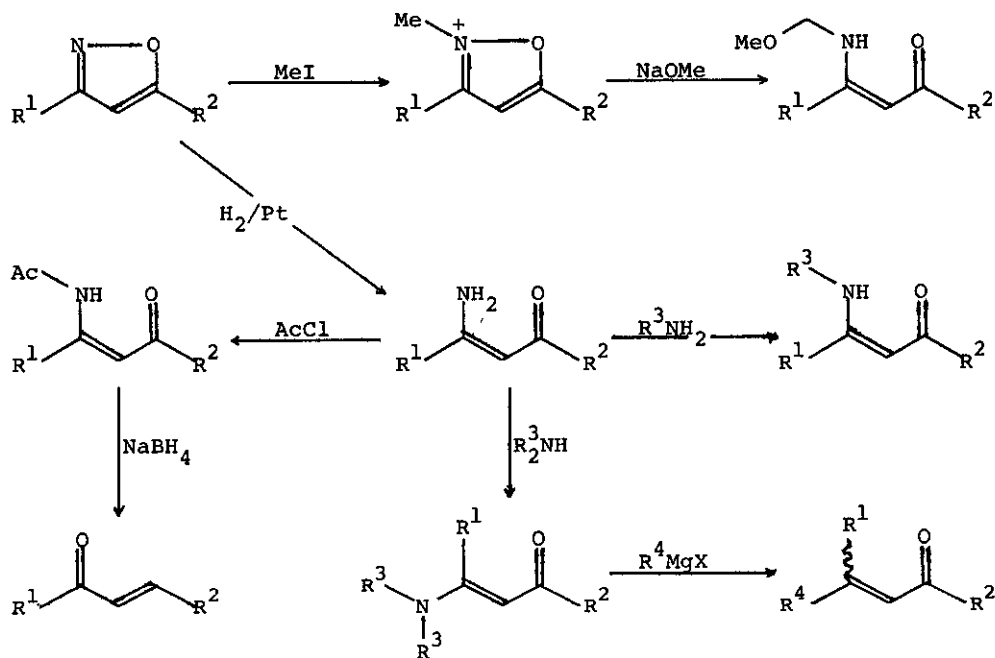


THE PREPARATION OF α,β -UNSATURATED KETONES BY THE GRIGNARD REACTION WITH β -(N-ALKYL-N-ACYLAMINO)ENONES

Choji Kashima* and Yasuhiro Yamamoto
Department of Chemistry, University of Tsukuba,
Sakura-mura, Niihari-gun, Ibaraki 305, Japan

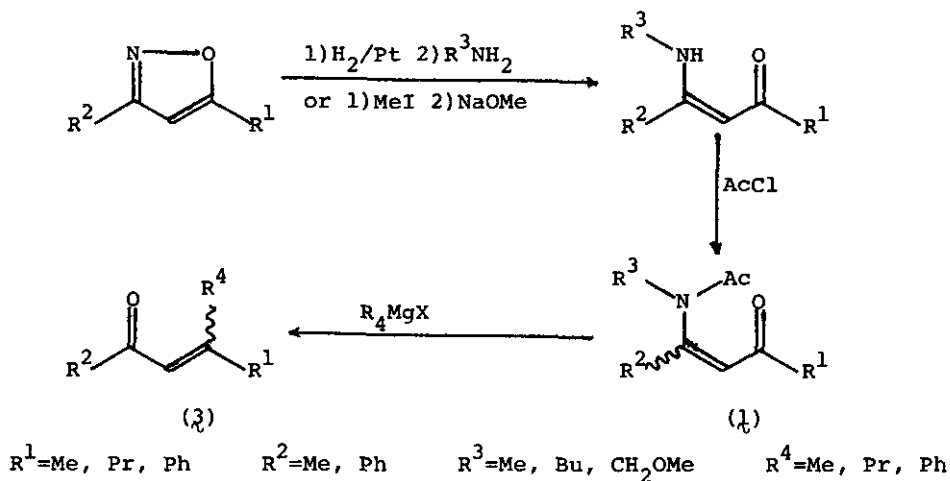
Abstract—The Grignard reaction of β -(N-alkyl-N-acylamino)enones afforded regioselectively α,β -unsaturated β -(N-alkyl-N-acylamino)-alcohols, which were converted into α,β -unsaturated ketones by hydrolysis accompanying dehydration. The resulting α,β -unsaturated ketones were regioisomeric with α,β -unsaturated ketones derived from β -(N,N-dialkylamino)enones by the Grignard reaction.

Recently we have succeeded in the preparation of isoxazoles having the different substituent groups on C-3 and C-5 position.¹ Isoxazole ring is easily cleaved into β -aminoenones by hydrogenation of isoxazoles² or the reaction of corresponding 2-methylisoxazolium salts with sodium methoxide.³ For the sake of the extension of the synthetic utilities of isoxazoles, we have investigated the chemical properties of β -aminoenones. By the treatment with acyl chloride at low temperature, acylation of β -aminoenones is possible to control at nitrogen atom.⁴ Further, the reactivity⁵ and regioselectivity⁶ of N-substituted β -aminoenones with various nucleophiles are dependent on the properties of N-substituent groups. The β -aminoenones having the electron-donating group on nitrogen react with nucleophiles at β -carbon, while β -aminoenones having the electron-withdrawing group react at carbonyl carbon. Although N-unsubstituted or N-monosubstituted β -aminoenones do not react with Grignard reagents, β -(N,N-dialkylamino)enones regioselectively afford the α,β -unsaturated ketones by the reaction with Grignard reagents at β -position.⁷ Therefore, the Grignard reaction of β -(N-alkyl-N-acylamino)enones, which had the electron-deficient nitrogen on β -position, was carried out.



As a typical example, 3-(N-butylacetamido)-1-phenyl-2-buten-1-one ($1a$) was treated with methylmagnesium iodide. From the ir (3400, 2950, 1620 and 1400 cm^{-1}) and the nmr spectra [$\delta = 0.9$ (t, 3H), 1.2-1.7 (m, 6H), 1.65 (s, 6H), 1.90 (s, 3H), 5.75 (s, 1H) and 7.1-7.5 ppm (m, 5H)], the product was found to be 4-(N-butylacetamido)-2-phenyl-3-penten-2-ol ($2a$) which was hydrolyzed without isolation by hydrochloric acid to give 4-phenyl-3-penten-2-one ($3a$) in 50 % yield based on $1a$. This α,β -unsaturated ketone $3a$ was regioisomeric with 3-methyl-1-phenyl-2-buten-1-one ($4a$), which was obtained by the reaction of 3-(N,N-dimethylamino)-1-phenyl-2-buten-1-one with methylmagnesium iodide. Similarly, some β -(N-alkyl-N-acylamino)enones were treated with Grignard reagents to afford α,β -unsaturated ketones listed in Table.

From these results, the Grignard reagents seemed to attack on carbonyl carbon of β -(N-alkyl-N-acylamino)enones to afford α,β -unsaturated ketones, while the Grignard reagents attacked on β -carbon of β -(N,N-dialkylamino)enones. Thus isoxazoles having a various substituent group on C-3 and C-5 carbons are concluded to be useful precursor for the preparation of α,β -unsaturated ketones via β -aminoenones.



Table

	Starting Material			Reactant (R ⁴ MgX)	Product	Yield* (%)
	R ¹	R ²	R ³			
1a	Ph	Me	Bu	MeMgI	4-Phenyl-3-penten-2-one	50
1b	Ph	Me	Me	MeMgI	4-Phenyl-3-penten-2-one	44
1c	Ph	Me	Me	PhMgBr	4,4-Diphenyl-3-buten-2-one	71
1d	Me	Me	Me	MeMgI	4-Methyl-3-penten-2-one	83
1e	Me	Me	Me	PhMgBr	4-Phenyl-3-penten-2-one	80
1f	Me	Me	Me	PrMgBr	4-Methyl-3-hepten-2-one	86
1g	Pr	Me	Me	MeMgI	4-Methyl-3-hepten-2-one	46
1h	Me	Ph	Me	MeMgI	3-Methyl-1-phenyl-2-buten-1-one	43
1i	Me	Ph	Me	PhMgBr	1,3-Diphenyl-2-buten-1-one	54
1j	Me	Me	MeOCH ₂	MeMgI	4-Methyl-3-penten-2-one	92
1k	Pr	Me	MeOCH ₂	MeMgI	4-Methyl-3-hepten-2-one	40

* Yields of products were based on β-(N-alkyl-N-acylamino)enones (1).

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