

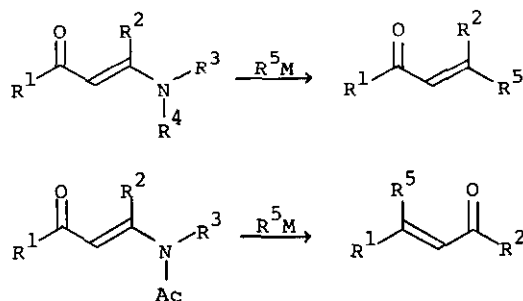
A Convenient Synthesis of β -(1-Imidazolyl)enones from α,β -Dibromoketones

C. Kashima*, M. Shimizu, and T. Tajima

Department of Chemistry, University of Tsukuba,
Sakura-mura, Niihari-gun, Ibaraki 305, Japan

As the convenient preparative method of β -(substituted)-phenyl- β -(1-imidazolyl)enones, we succeeded in the preparation of β -aryl- β -(1-imidazolyl)enones from α,β -dibromo- β -arylketones with imidazole in the presence of triethylamine.

Previously we reported¹⁾ that β -aminoenones had the properties of enamines, ketones, and amines. Moreover, β -aminoenones behave as the vinylogues of amides. N-Substituted- β -aminoenones, having the electron-withdrawing group on the nitrogen atom, react with nucleophiles on the carbonyl carbon²⁾. On the contrary, N-substituted- β -aminoenones having the electron-donating group on nitrogen, react with nucleophiles on the β -carbon³⁾ (Scheme 1). In a meanwhile, N-acylated imidazoles have extensively been investigated as the acylating agent, because



Scheme 1

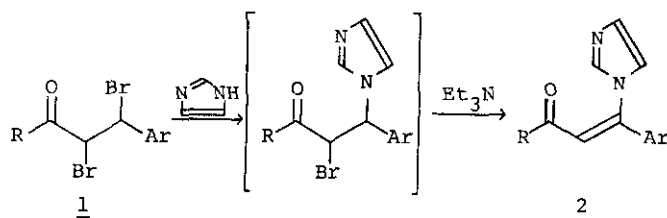
imidazolyl group behaves as a strong electron-withdrawing group and a good leaving group⁴⁾.

β -(1-Imidazolyl)enones are expected to be one of the β -aminoenones having the strong electron-withdrawing group on β -carbon. Further β -(1-imidazolyl)enones will show the properties of N-acylated imidazoles as their vinylogues. Though β -(1-imidazolyl)enones are of interest in these points of view, few papers

concerning the synthesis of 1-(imidazol-1-yl)-1-buten-3-one have been reported⁵⁾. Further, imidazole derivatives manifested the biological activity⁶⁾. Recently, we reported the preparations of β -substituted- β -(1-imidazolyl)enones from conjugated ynones and imidazole. However, the resulting β -(1-imidazolyl)enones were the mixture of E- and Z-forms⁷⁾. Further the preparations of conjugated ynones as the starting material were subject to some limitations; for example, the preparations of β -(substituted)phenyl-ynones, such as β -(p-tolyl)ynone, were quite difficult. In this paper we will show new synthetic method of β -aryl- β -(1-imidazolyl)enones from α,β -dibromo- β -arylketones with imidazole.

α,β -Dibromoketones were prepared from enones with bromine in dichloromethane under cooling in an ice-ethanol mixture. A solution of 5 mmol of α,β -dibromoketone, 7 mmol of imidazole, and 25 mmol of triethylamine in 20 ml of benzene were refluxed for 12h. The mixture was extracted with dichloromethane and the organic layer was washed with water. After removal of the solvent, the residue was distilled under reduced pressure or chromatographed on silica gel. In this procedure, β -(1-imidazolyl)enones were easily prepared in good yield.

It is well-known that α -bromo-enones are easily prepared from α,β -dibromoketones by the treatment with the weak base such as sodium acetate⁸⁾. Therefore we examined the reaction of α -bromo-enone with imidazole in the presence of triethylamine for the determination of the reaction mechanism. A mixture of



	R	Ar
a	Me	Ph
b	Me	p-Tol
c	Ph	Ph
d	Ph	p-Tol
e	p-Tol	p-Tol
f	MeO	Ph

Scheme 2

α -bromoenones, imidazole, and triethylamine was refluxed in benzene for 12 h. However, α -bromoenones was recovered. From this fact, the reaction mechanism was speculated as follows. Initial step was a replacement of β -bromine atom with imidazole. Then, an elimination of hydrogen bromide was accelerated by the activation of β -proton according to the strong electron-withdrawing effect of imidazolyl group (Scheme 2). Thus, in the case of using erythro α,β -dibromo-ketones, β -(1-imidazolyl)enones were prepared only Z-form under kinetic control.

In the reaction of α,β -dibromoketone with imidazole, β -(imidazolyl)enones having various substituent groups were able to prepare in good yield. β -(1-imidazolyl)- α,β -unsaturated acid esters, the preparation of which had never reported in the literature, were also prepared from α,β -dibromoesters in good yield.

Spectral Data of β -(1-imidazolyl)enones

	$^1\text{H-Nmr} (\delta, \text{CDCl}_3)$			=CH	$\text{Ir (cm}^{-1}\text{)}$ (CHCl_3)	Yield (%)
	R	Ar	Imidazole			
2a	1.97		7.0 - 7.7	6.43	1600, 1675	70
2b	2.02	2.40, 7.23	7.00, 7.32, 7.65	6.43	1605, 1660	74
2c			7.0 - 8.0		1615, 1665	48
2d			6.9 - 8.1		1605, 1685	67
2e		2.38, 2.41, 6.9 - 7.9			1610, 1655	63
2f	3.68		6.9 - 7.7		1635, 1720	53

References

1. T. Nishio, C. Kashima, Y. Omote, J. Synthetic Org. Chem. Jpn., **34**, 526 (1976).
2. C. Kashima, Y. Omote, Y. Tsuda, J. Org. Chem., **40**, 526 (1975).
3. C. Kashima, Y. Yamamoto, Bull. Chem. Soc. Jpn., **52**, 1735 (1979).
4. H. A. Staab, Angew. Chem., **74**, 407 (1962).
5. S. Hoffmann, Z. Chem., **7**, 12 (1967); *ibid.*, **8**, 381 (1968).
6. P. B. Sologood, Jpn. Kokai Tokkyo Koho, 79-145665;
G. Jaeger, U. Kraz, K. H. Buechel, *ibid.*, 80-59169.
7. C. Kashima, T. Tajima, Synthesis, in press.
8. N. H. Cromwell, D. J. Cram, C. E. Harris, "Org. Synth." Coll. Vol. III, Wiley, New York, 1955, p 125.

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