Preparation of β-(1-Imidazolyl)-enones

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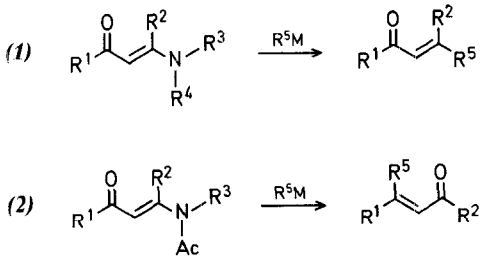
It is known that β-aminoenones exhibit the properties characteristic of enamines, ketones, enones, and amines[1]; furthermore, they also behave as vinylogs of amides. *N*-Substituted β-aminoenones with an electron-withdrawing function at nitrogen react with nucleophiles at the carbonyl carbon atom[2] (Scheme **A**, Reaction *2*), whereas those with an electron-donating function at nitrogen react at the β-carbon atom[3] (Scheme **A**, Reaction *1*).



Scheme **A**

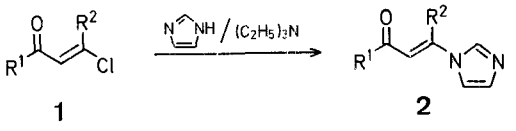
Table. β-(1-Imidazolyl)-enones **2** prepared

Product No.	R^1	R^2	Yield [%]	(*E*)-isomer [%]
2a	*i*-C_3H_7	H	67	100
2b	4-H_3C—C_6H_4	H	57	100
2c	H_3C	H_3C	53	100
2d	C_6H_5	H_3C	70	100
2e	4-H_3C—C_6H_4	H_3C	85	100
2f	—CH_2—$C(CH_3)_2$—CH_2—		35	100
2g	H_3C	C_6H_5	79	66
2h	*i*-C_3H_7	C_6H_5	94	75
2i	C_6H_5	C_6H_5	54	—[c]
2j	C_6H_5	4-H_3C—C_6H_4	63	60
2k	*n*-C_3H_7	H_3C	39	100

[a] The microanalyses were in satisfactory agreement with the calculated values (C ±0.19, H ±0.13, N ±0.24).
[b] $\Delta\delta_{CH}$.
[c] Not determinable.

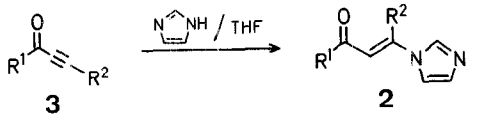
N-Acylated imidazoles have been extensively used as acylating agents because of the good leaving group properties of the imidazole moiety[4]. β-(1-Imidazolyl)-enones should behave similarly to *N*-acylated imidazoles as well as their vinylogs and can be classified as β-aminoenones with a strong electron-withdrawing group on nitrogen. In spite of these interesting properties, there have been only few reports on the synthesis of 4-(1-imidazolyl)-3-buten-2-ones[5]. β-Substituted β-(1-imidazolyl)-enones, such as 4-(1-imidazolyl)-penten-2-one, were previously unknown.

We now report on the synthesis of β-(1-imidazolyl)-enones **2**. These compounds were not formed by reaction of imidazole with β-diketones, their enol ethers, enol thioethers, or β-aminoenones under the usual conditions[1]. Thus, we turned to the reaction of imidazole with β-chloroenones **1**, prepared from the β-diketone and carbon tetrachloride/triphenylphosphine[6], (Scheme **B**). The preparation of **1** is, however, limited: regioselective preparations of 4-chloro-4-phenyl-3-buten-2-one and 2-chloro-2-hepten-4-one were difficult.



1 **2**

Scheme **B**



3 **2**

Scheme **C**

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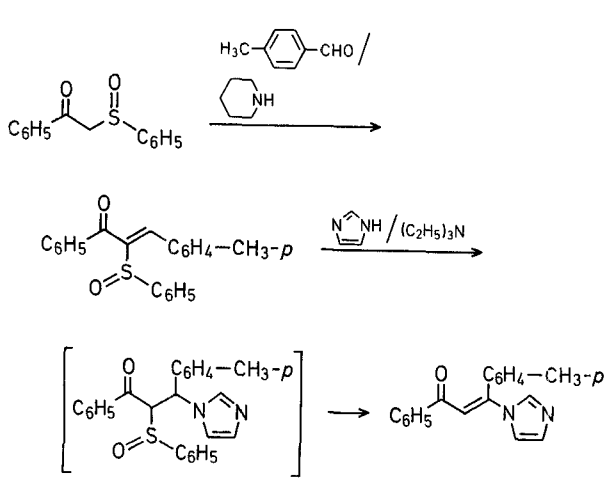
Method	m.p. [°C]	Molecular formula[a]	I.R. (KBr) $\nu_{C=O}$, $\nu_{C=C}$ [cm^{-1}]	^{1}H-N.M.R. ($CDCl_3$) δ [ppm]			
				R^1	R^2	—CH=	Imidazole
A	74.5–75.5°	$C_9H_{12}N_2O$ (164.2)	1615, 1685	1.17, 2.82	7.95	6.44	7.20, 7.35, 7.90
A	151–152°	$C_{13}H_{12}N_2O$ (212.2)	1600, 1610, 1670	2.44, 7.33, 7.94	8.08	7.27	7.20, 7.39, 7.90
A	80–81°	$C_8H_{10}N_2O$ (150.2)	1600, 1670	2.32	2.69	6.43 (4.26)[b]	7.18, 7.39, 7.90
A	64–64.5°	$C_{13}H_{12}N_2O$ (212.2)	1600, 1660	7.4–8.1	2.74	7.10	7.23, 7.4–8.1
A	115–116°	$C_{14}H_{14}N_2O$ (226.3)	1610, 1660	2.42, 7.30, 7.88	2.72	7.06 (4.31)[b]	7.23, 7.37, 7.99
A	87.5–88.5°	$C_{11}H_{14}N_2O$ (190.2)	1620, 1655	(1.19, 2.37, 2.75)		6.20 (4.81)[b]	7.23, 7.34, 7.97
B	81–82°	$C_{13}H_{12}N_2O$ (212.2)	(*E*): 1600, 1675 (*Z*): 1610, 1660	1.97 2.03	7.0–7.7 7.0–7.7	6.43 (4.78)[b] 6.51	7.0–7.7 7.0–7.7
B	80–81°	$C_{15}H_{16}N_2O$ (240.3)	1605, 1616, 1680	1.09, 2.4–2.9	7.1–7.7	6.50	7.1–7.7
B	93.5–94.5°	$C_{18}H_{14}N_2O$ (274.3)	1615, 1655	(7.0–8.0)			
C	142–143°	$C_{19}H_{16}N_2O$ (288.3)	1600, 1660	7.0–8.2	2.37, 7.0–8.2	(7.0–8.2)	
B	43.5–44.5°	$C_{10}H_{14}N_2O$ (178.2)	1605, 1680	0.99, 1.3–1.9, 2.55	2.66	6.44	7.13, 7.34, 7.97

We have also reacted imidazole with the conjugated ynones **3**, prepared by acylation of acetylenes[7] or by oxidation of ynols[8], (Scheme **C**).

The β-(1-imidazolyl)-enones could also be prepared, although in lower yields with longer reaction times, by condensation of the phenylsulfinylmethyl ketone with an aldehyde, Michael addition of imidazole, and thermal elimination of sulfenic acid (Scheme **D**).



Scheme **D**

β-(1-Imidazolyl)-enones 2; Typical Procedures:

Method A: from β-chloroenones **1**; A mixture of the β-chloroenone **1** (0.05 mol), imidazole (4.1 g, 0.06 mol), triethylamine (25.3 g, 0.25 mol), and a catalytic amount of potassium hydrogen carbonate (100 mg) is stirred for 10 h at room temperature in benzene (30 ml). The mixture is then extracted with dichloromethane (3 × 20 ml). The organic layer is washed with water (3 × 100 ml) and dried with anhydrous magnesium sulfate. After removal of the solvent, the residue is chromatographed on a column of silica gel, eluting with chloroform/acetone/ethanol (100:10:2). The product is recrystallized from hexane/benzene.

The structures of compounds **2** were determined by microanalysis, ^{1}H-N.M.R. spectral data ($CDCl_3$), and I.R. spectral data (KBr disk). Determination of the configuration of compounds **2** was carried out by ^{1}H-N.M.R. spectroscopy using the shift reagent $Eu(fod)_3$. Physical properties and spectral data of **2** are listed in the Table.

Method B: from conjugated ynones **3**: The ynone **3** (0.05 mol) and imidazole (4.1 g, 0.06 mol) are heated under reflux in tetrahydrofuran (30 ml) for 10 h. The reaction mixture is worked up as described in Method A. Compounds **2g–j** are prepared as a mixture of (*E*)- and (*Z*)-isomers which could not be separated by chromatography or fractional recrystallization.

Method C: from phenylsulfinylmethyl ketones: A mixture of phenylsulfinylmethyl phenyl ketone (1.22 g, 5 mmol), 4-methylbenzaldehyde (0.6 g, 5 mmol), and catalytic amount of piperidine (100 mg) in benzene (75 ml) is heated under reflux for 5 h. The resulting residue is then treated with imidazole (0.68 g, 10 mmol), triethylamine (0.51 g, 5 mmol) in tetrahydrofuran (25 ml) and heated under reflux for 68 h. The product is purified by the procedure described above.

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