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An Improved and Convenient Procedure for the Synthesis of 1-Substituted Imidazoles

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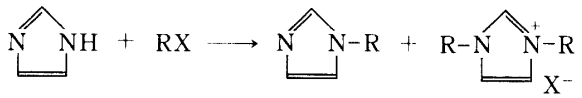
1-Protected imidazoles, such as 1-acetyl- and 1-benzoylimidazoles, react with various halides, such as benzyl, allyl, α-keto, and alkyl halides, to give 1-protected-3-substituted imidazolium salts in high yields. The resultant imidazolium salts are easily deprotected by treatment with water or alcohols to give the corresponding 1-substituted imidazoles in excellent yields. In this reaction the yields of 1-substituted imidazoles vary with the kinds of halides used and/or with the protecting groups, and the yields increase in the following order: benzyl halides≥allyl halides∼α-keto halides>alkyl halides, and acetyl≥benzoyl>ethoxycarbonyl>diethoxymethyl>trimethylsilyl>tosyl.

Keywords——1-substituted imidazole; 1-protected imidazole; 1-acetylimidazole; 1-benzoylimidazole; 1-ethoxycarbonylimidazole; 1-protected-3-substituted imidazolium salt; imidazole

1-Substituted imidazole derivatives (**1**) have been prepared by means of the following reactions: (a) the reaction of imidazole with halides,[1-7] (b) the reaction of imidazole with trialkyl phosphates,[8] (c) the thermal decarboxylation of *N*-alkoxycarbonyl imidazoles,[9] and (d) the reaction of imidazole with alcohols in the presence of an acid catalyst.[10] Among them, method (a) is most commonly used, because the halides can be easily prepared and the reaction conditions are mild compared with those required for other methods. However, the reaction of imidazole with halides does not proceed satisfactorily due to the formation of by-products, that is, 1,3-disubstituted imidazolium salts (**2**), and the purification of 1-substituted imidazoles is troublesome, especially in large-scale preparations, so that the yields of 1-substituted imidazoles are low (Chart 1). Further, this method gives poor results with highly reactive halides, since the formation of the undesirable imidazolium salts (**2**) tends to increase considerably.



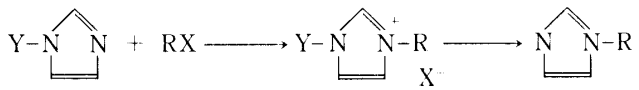
1 **2**

Chart 1

This side reaction can be reduced to some extent (a) by using excess imidazole[1,2,10] and (b) by the addition of a strong base or by using alkali metal salts of imidazole.[1,2,10]

The regioselective *N*-alkylation of 4- or 5-substituted imidazoles *via* the regioselective *N*-acylation, quaternization, and deacylation process is known.[11,12] However, no procedure has yet been reported for the effective synthesis of 1-substituted imidazoles (monosubstituted imidazoles) in excellent yields.

We report here an improved and convenient procedure for the synthesis of 1-substituted imidazoles (**1**) by using 1-protected imidazoles, such as 1-acetyl (**3a**), 1-benzoyl (**3b**), and 1-ethoxycarbonylimidazole (**3c**), in place of imidazole (Chart 2).



3a : Y=CH_3CO **4** **1**
3b : Y=PhCO
3c : Y=EtOCO

Chart 2

Results and Discussion

The properties required for the protecting groups of imidazole are (a) not to reduce the reactivity of imidazole, (b) to be stable in the reaction with halides, and (c) to be easily removed when the reaction is completed. From these viewpoints, we examined various 1-protected imidazoles, such as 1-acetylimidazole (**3a**),[13,14] 1-benzoylimidazoles (**3b**),[14,15] 1-ethoxycarbonylimidazole (**3c**),[9,14] 1-diethoxymethylimidazole,[16] 1-trimethylsilylimidazole,[15] and 1-tosylimidazole.[17] These protected imidazoles, which are easily prepared, were treated with an equimolar amount of halides in acetonitrile. Highly reactive halides, such as benzyl bromides, allyl bromides, and α-bromoketones, reacted easily at room temperature to produce the corresponding 1-protected-3-substituted imidazolium salts (**4**). In the case of inactive halides, addition of an equimolar amount of sodium iodide was necessary and the reactions were carried out under heating. Some of the 1-protected-3-substituted imidazolium salts (**4**) precipitated from the reaction mixture, and these compounds could be separated and purified. However, these salts can be used without purification when they are obtained in high yields. The deprotection of 1-protected-3-substituted imidazolium salts (**4**) can be easily achieved with water or alcohols in the presence of base, and the 1-substituted imidazoles (**1**) are obtained in high yields.

Reaction of 1-Acetylimidazole (3a) with Halides (Table I)

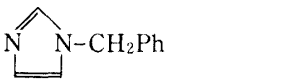
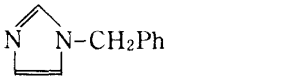
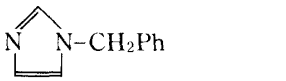
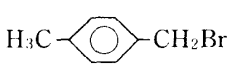
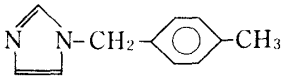
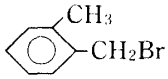
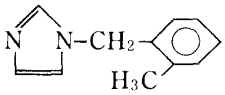
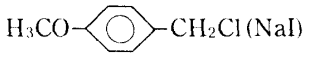
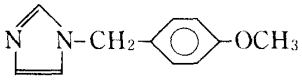
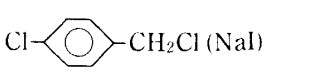
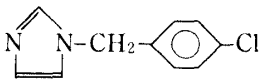
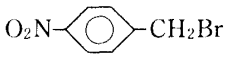
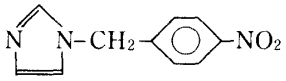
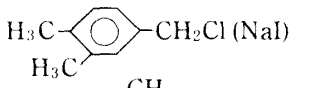
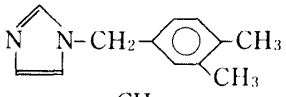
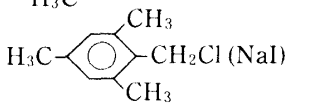
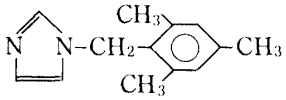
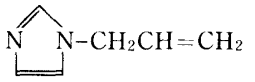
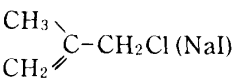
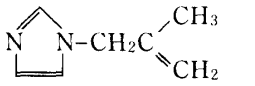
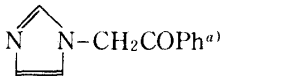
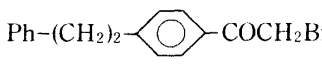
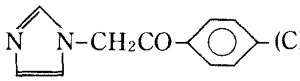
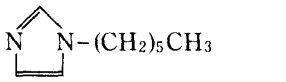
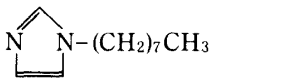
The reaction of 1-acetylimidazole (**3a**) with benzyl bromides gave 1-benzylimidazoles in excellent yields (entries 1, 2, 5, 6, 9). In the case of less reactive benzyl chloride, the addition of an equimolar amount of sodium iodide was effective (entries 3, 4). No substituent effect was observed in the reaction of benzyl halides with a methyl, methoxy, chloro, or nitro group on the benzene ring (entries 5—11). 1-Substituted imidazoles possessing hypolipidemic activity[3] were also prepared in good yields (entries 5, 7). The reaction with allyl or α-keto halides gave 1-substituted imidazoles in yields similar to those of benzyl halides (entries 12—14). 1-Substituted imidazoles possessing anticonvulsant activity[5] were also prepared in good yields (entry 15) after sodium borohydride reduction. In the reaction with alkyl halides, the addition of sodium iodide and prolonged heating above 80°C were necessary because of the low reactivity of alkyl halides (entries 16—20).

Reaction of 1-Benzoylimidazoles (3b) with Halides (Table II)

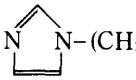
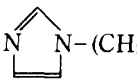
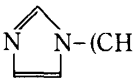
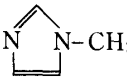
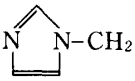
The reaction of 1-benzoylimidazole (**3b**) with benzyl halides also gave the corresponding 1-substituted imidazoles in excellent yields, and no substituent effect was observed (entries 22—25). The reaction with alkyl halides was carried out under prolonged heating, but the yields were below 70% (entry 26). 1-Benzoylimidazole shows reactivities similar to those of 1-acetylimidazole, and gave the corresponding 1-substituted imidazoles in similar yields.

To examine the effects of substituents on the benzene ring of the benzoyl group, the reaction of 1-benzoylimidazole carrying a methyl, methoxy, chloro, or nitro group with benzyl bromide was carried out. The reactions of benzyl bromide with 1-(4-methylbenzoyl)-, 1-(4-methoxybenzoyl)-, 1-(4-chlorobenzoyl)-, and 1-(4-nitrobenzoyl)imidazole gave 1-benzylimidazole in quantitative, quantitative, 72, and 34% yields, respectively (entries 27—30). These observations suggest that the reactivities of the nitrogen atom (3 position) of 1-benzoylimi-

TABLE I. Synthesis of 1-Substituted Imidazoles using 1-Acetylimidazole

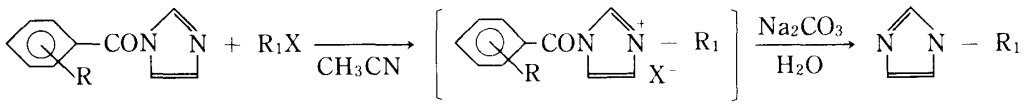
Entry	RX	Reaction Temp. (℃)	Time (h)	Product		Yield (%)
1	$PhCH_2Br$	r. t	15		(1a)	99
2		60	3			92
3	$PhCH_2Cl$	80	4		(1a)	44
4	$PhCH_2Cl$(NaI)	60	3		(1a)	90
5		60	2.5		(1c)	97
6		r. t.	o. n.		(1d)	95
7		60	2		(1e)	Quant.
8		60	3		(1f)	91
9		60	3		(1g)	90
10		70	1.5		(1h)	93
11		r. t.	20		(1i)	95
12	$CH_2=CHCH_2Br$	60	3		(1j)	82
13		60	4		(1k)	89
14	$PhCOCH_2Br$	r. t.	o. n.	 [a]	(1l)	91
15		r. t.	o. n.	 [b]	(1m)	76
16	$CH_3(CH_2)_5Br$ (NaI)	80	5		(1b)	80
17	$CH_3(CH_2)_7Br$ (NaI)	80	6		(1n)	77

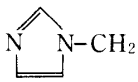
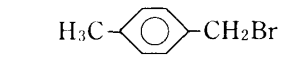
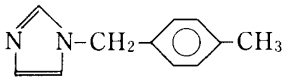
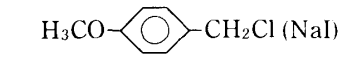
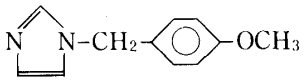
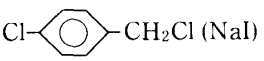
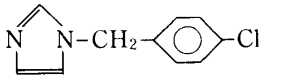
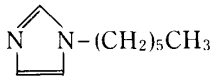
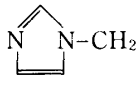
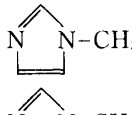
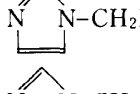
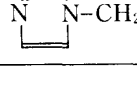
(continued)

Entry	RX	Reaction Temp. (℃)	Time (h)	Product		Yield (%)
18	Br $(CH_2)_3CN$ (NaI)	80	6		**(1o)**	74
19	Br $(CH_2)_3COOEt$ (NaI)	80	5		**(1p)**	80
20	Br $(CH_2)_2Ph$ (NaI)	100	6		**(1q)**	64
21	$BrCH_2COOEt$ (NaI)	60	3		**(1r)**	30
					**(1s)**	55

r. t. = room temperature. o. n. = overnight.
a) Treated with $NaHCO_3/H_2O$.
b) Treated with $NaOH/CH_3OH$ and purified by column chromatography.
c) The ester (**1r**) was easily hydrolyzed to give the acid (**1s**).

TABLE II. Synthesis of 1-Substituted Imidazoles using 1-Benzoylimidazoles



Entry	R	R_1X	Reaction Temp. (°C)	Time (h)	Product		Yield (%)
22	H	$PhCH_2Br$	r. t.	o. n.		**(1a)**	97
23	H		r. t.	o. n.		**(1c)**	97
24	H		r. t.	o. n.		**(1e)**	92
25	H		r. t.	o. n.		**(1f)**	86
26	H	$CH_3(CH_2)_5Br$ (NaI)	80	5		**(1b)**	64
27	4-CH_3O	$PhCH_2Br$	r. t.	o. n.		**(1a)**	Quant.
28	4-CH_3	$PhCH_2Br$	r. t.	o. n.		**(1a)**	Quant.
29	4-Cl	$PhCH_2Br$	r. t.	o. n.		**(1a)**	72
30	4-NO_2	$PhCH_2Br$	r. t.	o. n.		**(1a)**	34

r. t. = room temperature. o. n. = overnight.

dazoles are enhanced by the presence of an electron-donating group on the benzoyl group, and the 1-benzoyl-3-benzylimidazolium salts (or 1-benzylimidazole) are obtained in high yields. On the other hand, substitution with an electron-withdrawing group decreases the reactivities of the nitrogen atom (3 position) of 1-benzoylimidazoles, so that the yields of 1-benzoyl-3-benzylimidazolium salts (or 1-benzylimidazole) are decreased.

Reaction of 1-Ethoxycarbonylimidazole (3c) and Other 1-Protected Imidazoles with Halides (Table III)

The reaction of 1-ethoxycarbonylimidazole (**3c**) with benzyl halides gave the corresponding 1-substituted imidazoles in 67—77% yields (entries 31—34). The yields of 1-substituted imidazoles were lower than in the cases of the corresponding 1-acetylimidazole or 1-benzoylimidazoles. In the reaction of 1-ethoxycarbonylimidazole with alkyl halides at 100°C, 1,3-dialkylimidazolium salts were obtained (entry 36). Further, the reaction of 1-ethoxycarbonylimidazole (**3c**) with benzyl bromide under heating gave only 1,3-dibenzylimidazolium bromide (87% yield based on benzyl bromide), and not 1-benzylimidazole (entry 35).

TABLE III. Synthesis of 1-Substituted Imidazoles using 1-Ethoxycarbonylimidazole and Other 1-Protected Imidazoles

Entry	Y-N N	RX	Reaction Temp. (°C)	Time (h)	Product (Yield)
31	EtOC(=O)-N N	$PhCH_2Br$	r. t.	o. n.	$PhCH_2$-N N (72 %) **(1a)**
32		H_3CO-C$_6$H$_4$-CH_2Cl (NaI)	r. t.	o. n.	N N-CH_2-C$_6$H$_4$-OCH_3 (77 %) **(1e)**
33		H_3C-C$_6$H$_4$-CH_2Br	r. t.	o. n.	N N-CH_2-C$_6$H$_4$-CH_3 (67 %) **(1c)**
34		O_2N-C$_6$H$_4$-CH_2Br	r. t.	o. n.	N N-CH_2-C$_6$H$_4$-NO_2 (67 %) **(1g)**
35		$PhCH_2Br$	60	4	$PhCH_2$-N$^+$ N-CH_2Ph[a] Br^- (87 % based on bromide)
36		$CH_3(CH_2)_3Br$	100	6	$CH_3(CH_2)_3$-N$^+$ N-$(CH_2)_3CH_3$[a] Br^-
37	$(EtO)_2CHN$ N	$PhCH_2Br$	r. t.	o. n.	$PhCH_2$-N N (66 %) **(1a)**
38		$CH_3(CH_2)_5Br$ (NaI)	80	6	$CH_3(CH_2)_5$-N$^+$ N-$(CH_2)_5CH_3$[a] I^-
39	Me_3Si-N N	$PhCH_2Br$	r. t.	o. n.	$PhCH_2$-N N (54 %) **(1a)** $PhCH_2$-N$^+$ N-CH_2Ph[a] Br^-
40		$CH_3(CH_2)_5Br$	r. t.	o. n.	$CH_3(CH_2)_5$-N$^+$ N-$(CH_2)_5CH_3$[a] Br^-
41	Tosyl-N N	CH_3-C$_6$H$_4$-CH_2Br	80	7	

r. t. room temperature. o. n. overnight
a) IR and NMR spectra were consistent with these structures.

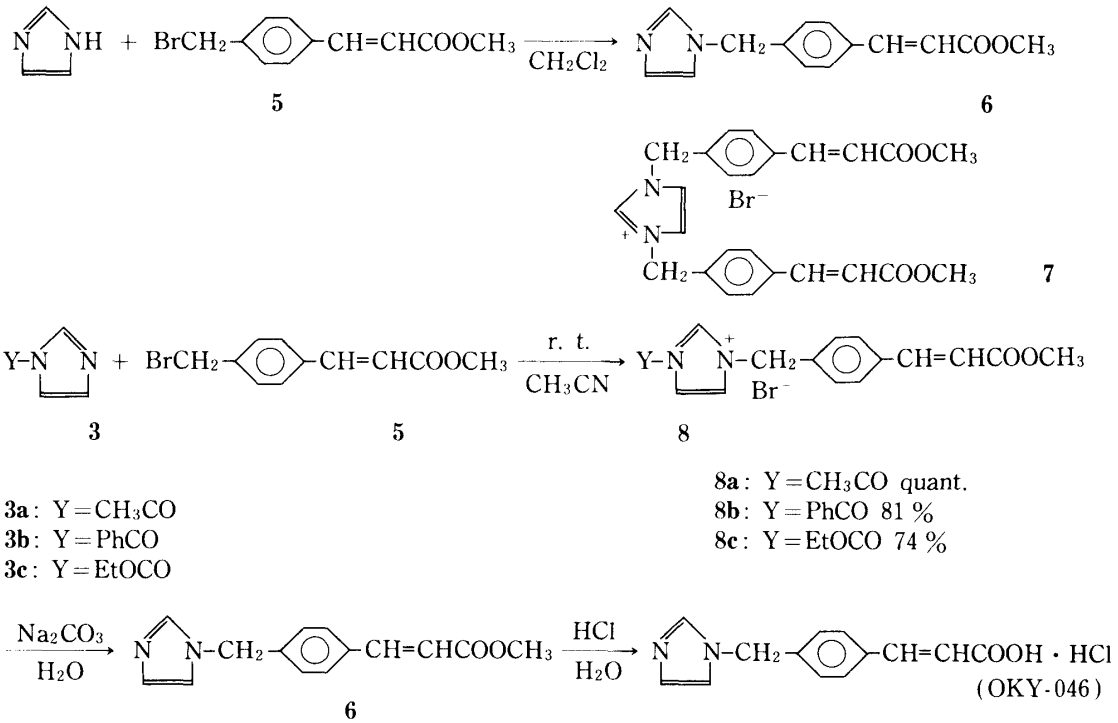
These results suggest that the quaternary salts of 1-ethoxycarbonylimidazole are thermally unstable and the protecting groups are cleaved during the reaction at elevated temperature; further, *N*-alkylation proceeds to form the 1,3-disubstituted imidazolium salts. Similarly, the formation of 1,3-disubstituted imidazolium salts was observed in the cases of 1-diethoxymethylimidazole and 1-trimethylsilylimidazole (entries 38, 40). This probably results from cleavage of the protecting groups of the quaternary salts during the reaction. The reaction of 1-tosylimidazole with 4-methylbenzyl bromide gives an inseparable mixture (entry 41).

From these data, it appears that acetyl and benzoyl groups are effective protecting groups, but ethoxycarbonyl, diethoxymethyl and trimethylsilyl groups are unstable in the reaction with halides, and the tosyl group greatly reduces the reactivity of imidazole; the latter protecting groups are therefore unsuitable. The yields of 1-substituted imidazoles (**1**) in relation to the protecting groups increase in the following order: acetyl≥benzoyl>ethoxycarbonyl>diethoxymethyl>trimethylsilyl>tosyl.

This method is especially useful in reactions with highly reactive halides which produce large amounts of by-product (**2**) in the usual methods.

Synthesis of a Biologically Active 1-Substituted Imidazole (OKY-046)

(*E*)-4-(1-Imidazolylmethyl)cinnamic acid hydrochloride (OKY-046) is a highly selective inhibitor of thromboxane synthetase.[18] The maximum yield of OKY-046 methyl ester (**6**) obtained by the usual methods (*e.g.*, the reaction of methyl 4-bromomethylcinnamate (**5**) with excess imidazole) is 40—50%.



3a: Y=CH_3CO
3b: Y=PhCO
3c: Y=EtOCO

8a: Y=CH_3CO quant.
8b: Y=PhCO 81%
8c: Y=EtOCO 74%

Chart 3

On the other hand, the reaction of 1-protected imidazoles (**3a**, **b**, and **c**) with methyl 4-bromomethylcinnamate (**5**) in acetonitrile at room temperature give the imidazolium salts (**8**) in quantitative, 81%, and 74% yields, respectively. The imidazolium salt **8a** was easily deprotected with water in the presence of sodium carbonate to give OKY-046 methyl ester (**6**) in 96% yield. The ester was hydrolyzed with hydrochloric acid to give OKY-046 in excellent yield.

TABLE IV. 1-Substituted Imidazoles

Compd. No.	R	Formula[a]	mp (°C)	IR (cm^{-1})	NMR (δ) ($CDCl_3$)
1a	$-CH_2Ph$	$C_{10}H_{10}N_2$	69—70 (benzene-petroleum ether)	1505, 1240, 1075	5.10 (s, 2H, CH_2), 6.90 (m, 1H, imidazole H), 7.02—7.46 (m, 6H), 7.53 (m, 1H, imidazole H)
1b	$-(CH_2)_5CH_3$	$C_9H_{16}N_2$	Oil	2950, 1505, 1230	0.75—2.00 (m, 11H), 3.93 (t, 2H, J=7Hz, CH_2), 6.90 (m, 1H, imidazole H), 7.05 (m, 1H, imidazole H), 7.47 (m, 1H, imidazole H)
1c	$-CH_2$-C$_6$H$_4$-CH_3	$C_{11}H_{12}N_2$	49—50 (benzene-petroleum ether)	1505, 1395, 1240	2.33 (s, 3H, CH_3), 5.05 (s, 2H, CH_2), 6.87 (m, 1H, imidazole H), 6.95—7.25 (m, 5H), 7.50 (m, 1H, imidazole H)
1d	$-CH_2$-C$_6$H$_4$-CH_3	$C_{11}H_{12}N_2$	Oil	1500, 1230, 1080	2.29 (s, 3H, CH_3), 5.10 (s, 2H, CH_2), 6.80—7.35 (m, 6H), 7.50 (m, 1H, imidazole H)
1e	$-CH_2$-C$_6$H$_4$-OCH_3	$C_{11}H_{12}N_2O$	55—58 (benzene-petroleum ether)	1610, 1510, 1250	3.78 (s, 3H, CH_3), 5.04 (s, 2H, CH_2), 6.70—7.45 (m, 6H), 7.55 (m, 1H, imidazole H)
1f	$-CH_2$-C$_6$H$_4$-Cl	$C_{10}H_9ClN_2$	Oil	3120, 1500, 1080	5.05 (s, 2H, CH_2), 6.87 (m, 1H, imidazole H), 6.95—7.43 (m, 5H), 7.50 (m, 1H, imidazole H)
1g	$-CH_2$-C$_6$H$_4$-NO_2	$C_{10}H_9N_3O_2$	48—51 (benzene-petroleum ether)	1600, 1510, 1340	5.30, (s, 2H, CH_2), 6.95 (m, 1H, imidazole H), 7.12 (m, 1H, imidazole H), 7.30 (d, 2H, J=9 Hz, aromatic H), 7.60 (m, 1H, imidazole H), 8.22 (d, 2H, J=9 Hz, aromatic H)
1h	$-CH_2$-C$_6$H$_3$-(CH_3)$_2$	$C_{12}H_{14}N_2$	<30 (benzene-petroleum ether)	1500, 1230, 1075	2.20 (s, 6H, CH_3), 4.98 (s, 2H, CH_2), 6.75—7.30 (m, 5H), 7.50 (m, 1H, imidazole H)
1i	$-CH_2$-C$_6$H$_2$-(CH_3)$_3$	$C_{13}H_{16}N_2$	Oil	2950, 1615, 1500, 1230	2.25—2.35 (m, 9H, CH_3), 5.07 (s, 2H, CH_2), 6.70 (m, 1H, imidazole H), 6.90 (s, 2H, aromatic H), 7.00 (m, 1H, imidazole H), 7.30 (m, 1H, imidazole H)
1j	$-CH_2CH=CH_2$	$C_6H_8N_2$	Oil	3120, 1640, 1505	4.50—4.65 (m, 2H, CH_2), 5.03—5.40 (m, 2H, $=CH_2$), 5.70—6.20 (m, 1H, CH), 6.90 (m, 1H, imidazole H), 7.05 (m, 1H, imidazole H), 7.46 (m, 1H, imidazole H)
1k	$-CH_2C(CH_3)=CH_2$	$C_7H_{10}N_2$	Oil	3120, 1660, 1500	1.65 (s, 3H, CH_3), 4.42 (s, 2H, CH_2), 4.57 (s, 1H), 4.94 (s, 1H), 6.85 (m, 1H, imidazole H), 7.01 (m, 1H, imidazole H), 7.42 (m, 1H, imidazole H)
1l	$-CH_2COPh \cdot HCl \cdot H_2O$	$C_{11}H_{13}ClN_2O_2$	131—135 (methanol-acetone)	3400, 1690, 1230	[b] 6.15 (s, 2H, CH_2), 7.50—8.20 (m, 7H), 9.17 (m, 1H, imidazole H)
1m	$-CH_2CO$-C$_6$H$_4$-$(CH_2)_2Ph$	$C_{19}H_{18}N_2O$	134—135 (ethyl acetate)	1690, 1600[b], 1220	[b] 2.97 (br, 4H, CH_2CH_2), 5.70 (s, 2H, CH_2), 6.93 (m, 1H, imidazole H), 7.10 (m, 1H, imidazole H), 7.24 (s, 5H), 7.41 (d, 2H, J=8 Hz), 7.59 (m, 1H), 7.95 (d, 2H, J=8 Hz)
1n	$-(CH_2)_7CH_3$	$C_{11}H_{20}N_2$	Oil	2950, 1505, 1230	0.75—2.00 (m, 15H), 3.95 (t, 2H, J=7 Hz, CH_2), 6.90 (m, 1H, imidazole H), 7.06 (m, 1H, imidazole H), 7.49 (m, 1H, imidazole H)
1o	$-(CH_2)_3CN$	$C_7H_9N_3$	Oil	3120, 2950, 2250, 1505	1.90—2.50 (m, 4H), 4.10 (t, 2H, J=6 Hz, CH_2), 6.95 (m, 1H, imidazole H), 7.06 (m, 1H, imidazole H), 7.50 (m, 1H, imidazole H)
1p	$-(CH_2)_3COOEt$	$C_9H_{14}N_2O_2$	Oil	3120, 3000, 1730	1.20 (t, 3H, J=8 Hz, CH_3), 1.90—2.45 (m, 4H), 3.95—4.32 (m, 4H), 6.90 (m, 1H, imidazole H), 7.05 (m, 1H, imidazole H), 7.46 (m, 1H, imidazole H)
1q	$-(CH_2)_2Ph$	$C_{11}H_{12}N_2$	Oil	3100, 1600, 1500	3.02 (t, 2H, J=7 Hz, CH_2), 4.15 (t, 2H, J=7 Hz, CH_2), 6.82 (m, 1H, imidazole H), 6.95—7.45 (m, 7H)
1r	$-CH_2COOEt$	$C_7H_{10}N_2O_2$	Oil	3120, 1750, 1215	1.25 (t, 3H, J=7 Hz, CH_3), 4.25 (q, 2H, J=7 Hz, CH_2), 4.68 (s, 2H, CH_2), 6.93 (m, 1H, imidazole H), 7.07 (m, 1H, imidazole H), 7.50 (m, 1H, imidazole H)
1s	$-CH_2COOH \cdot HCl$	$C_5H_7ClN_2O_2$	193—195 (ethanol)	3150, 2850, 1735	[b] 5.22 (s, 2H, CH_2), 7.70 (m, 1H, imidazole H), 7.80 (m, 1H, imidazole H), 9.22 (m, 1H, imidazole H)

a) All compounds gave C, H, and N analyses within ±0.4% of the theoretical values.
b) DMSO-d_6.

Experimental

The infrared (IR) spectra were obtained with a Hitachi Model 260-10 infrared spectrophotometer. The nuclear magnetic resonance (NMR) spectra were taken with a Hitachi Model R-22 high-resolution nuclear magnetic resonance spectrometer in $CDCl_3$ or $(CD_3)_2SO$ with Me_4Si as an internal standard. The melting points were measured with a Yanagimoto micro melting point apparatus and are uncorrected. Elemental analyses were performed with a Yanaco CHN Corder MT-2.

General Procedure——A 1-protected imidazole (1-acetylimidazole, 1-benzoylimidazoles, 1-ethoxycarbonylimidazole, *etc.*) was allowed to react with an equimolar amount of a halide (and an equimolar amount of sodium iodide in the case of an inactive halide) in dry acetonitrile. The reaction mixture was treated with water and base, and extracted with chloroform. The extract was concentrated and the residue was purified by recrystallization or distillation to give the 1-substituted imidazole.

1-Benzylimidazole (Entry 1)——A mixture of 1-acetylimidazole (5.5 g), benzyl bromide (8.5 g) and dry acetonitrile (8 ml) was stirred at room temperature for 15 h. The reaction mixture was dissolved in water (100 ml), and a small amount of insoluble oil was filtered off. The filtrate was made basic with sodium carbonate, and the liberated oil was extracted with chloroform. The extract was dried ($MgSO_4$) and concentrated under reduced pressure. The residual solid was recrystallized from benzene–petroleum ether to give 1-benzylimidazole (7.8 g, 99%).

By the same procedure, the compounds listed in Tables I—III were prepared.

Methyl 4-(1-Imidazolylmethyl)cinnamate (6)——A mixture of 1-acetylimidazole (1.43 g), methyl 4-bromomethylcinnamate (**5**, 3.33 g), and dry acetonitrile (7.0 ml) was stirred at room temperature for 15 h. The precipitated crystals were collected by filtration, and recrystallized from acetonitrile–ether to give 1-acetyl-3-[4-(2-methoxycarbonylvinyl)benzyl]imidazolium bromide (**8a**, 4.75 g, quantitative): mp 153—154°C. IR (KBr): 1770 (C=O), 1715 (C=O) cm^{-1}; ^1H NMR (DMSO-d_6) δ: 1.90 (s, 3H, CH_3CO), 3.75 (s, 3H, CH_3), 5.50 (s, 2H, CH_2), 6.67 (d, 1H, $J=16$ Hz, olefinic H), 7.36—7.90 (m, 7H), 9.31 (m, 1H, imidazole H). *Anal.* Calcd for $C_{16}H_{17}BrN_2O_3$: C, 52.61; H, 4.69; N, 7.67. Found: C, 52.80; H, 4.60; N, 7.83.

The imidazolium salts (**8b** and **8c**) were also prepared in a similar manner in 81 and 74% yields, respectively.

1-Benzoyl-3-[4-(2-methoxycarbonylvinyl)benzyl]imidazolium Bromide (**8b**): mp 154—156°C. IR (KBr): 1785 (C=O), 1745 (C=O), 1720 (C=O) cm^{-1}; ^1H NMR (DMSO-d_6) δ: 3.72 (s, 3H, CH_3), 5.50 (s, 2H, CH_2), 6.60 (d, 1H, $J=16$ Hz, olefinic H), 7.33—8.07 (m, 12H), 9.36 (m, 1H, imidazole H). *Anal.* Calcd for $C_{21}H_{19}BrN_2O_3$: C, 59.02; H, 4.48; N, 6.56. Found: C, 59.03; H, 4.46; N, 6.55.

1-Ethoxycarbonyl-3-[4-(2-methoxycarbonylvinyl)benzyl]imidazolium Bromide (**8c**): mp 129°C (dec.). IR (KBr): 1785 (C=O), 1715 (C=O) cm^{-1}; ^1H NMR (DMSO-d_6) δ: 1.35 (t, 3H, $J=7$ Hz, CH_3), 3.70 (s, 3H, OCH_3), 4.53 (q, 2H, $J=7$ Hz, CH_2), 5.60 (s, 2H, NCH_2), 7.47—8.00 (m, 5H), 8.10 (m, 1H), 8.25 (m, 1H), 8.65 (d, 1H, $J=16$ Hz, olefinic H), 10.27 (m, 1H, imidazole H). *Anal.* Calcd for $C_{17}H_{19}BrN_2O_4$: C, 51.66; H, 4.85; N, 7.09. Found: C, 51.64; H, 4.93; N, 7.12.

A solution of 1-acetyl-3-[4-(2-methoxycarbonylvinyl)benzyl]imidazolium bromide (**8a**, 3.65 g) in water (30 ml) was made basic with sodium carbonate. The precipitated crystals were collected by filtration, and recrystallized from carbon tetrachloride to give methyl 4-(1-imidazolylmethyl)cinnamate (2.3 g, 96%): mp 116—117°C. IR (KBr): 1705 (C=O) cm^{-1}; ^1H NMR ($CDCl_3$) δ: 3.80 (s, 3H, CH_3), 5.13 (s, 2H, CH_2), 6.40 (d, 1H, $J=16$ Hz, olefinic H), 6.90 (m, 1H, imidazole H), 7.05—7.80 (m, 7H). *Anal.* Calcd for $C_{14}H_{14}N_2O_2$: C, 69.40; H, 5.82; N, 11.56. Found: C, 69.13; H, 5.84; N, 11.35.

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