Communications to the Editor

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1-ACYL-3-SUBSTITUTED IMIDAZOLIUM SALTS AS HIGHLY REACTIVE ACYLATING AGENTS

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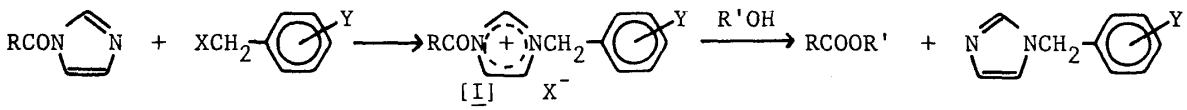
1-Acylimidazoles could be highly activated for acylation by the quarternizing with benzyl halides. 1-Acyl-3-benzylimidazolium halides [I] were powerful acylating agents. Alcohols, phenols, and amines were converted to the corresponding esters and amides in excellent yields under mild conditions.

KEYWORDS——— 1-acyl-3-substituted imidazolium salts; acylating agents; 1-acylimidazoles; 1-acetyl-3-benzylimidazolium bromide; 1-benzoyl-3-benzylimidazolium bromide

1-Acylimidazoles are known as acylating agents of alcohols or amines. However, the acylation is usually slow at room temperature, so the acylation of alcohols and amines is carried out at elevated temperatures or in the presence of a strong base such as sodium alkoxide or sodium amide.[1] T. Katsuki et al. reported that when 1-acylimidazoles were treated with N-bromosuccinimide in the presence of alcohols, rapid esterification took place at room temperature under neutral conditions.[2]

On the other hand, we found that the reaction of 1-acylimidazoles with halides gave the corresponding quarternary salts [I] in high yields and the acyl moieties of the salts [I] were easily transferred to alcohols to give the corresponding esters and 1-substituted imidazoles in excellent yields.[3]

We report here that the 1-acyl-3-benzylimidazolium halides [I] are powerful acylating agents and alcohols, phenols, and amines are converted to the corresponding esters and amides in excellent yields under mild conditions. These halides [I] are easily prepared from 1-acylimidazoles and benzylhalides.[4]

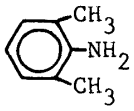
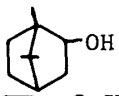
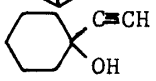
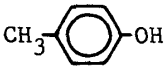
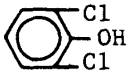


[I]

R: CH_3, Ph, X: halogen
Y: H, Me, OMe, Cl, etc.

[I] a R: CH_3, X: Br, Y: H
b R: Ph, X: Cl, Y: H
c R: Ph, X: Br, Y: H

Table Acylation of Amines or Alcohols with 1-Acyl-3-benzylimidazolium Salts [I]

Entry	Amine or Alcohol	Acylating Agent	Solvent	Conditions Temp. [°C]	Time [h]	Yield[a) [%]
1a	$Ph\text{-}CH_2CH_2NH_2$	Acetyl-Im[c)]	$CHCl_3$	r.t.	0.5	95[b)]
1b		Ia	$CHCl_3$	r.t.	0.5	95[b)]
2a	$(n\text{-}C_5H_{11})_2NH$	Acetyl-Im[c)]	$CHCl_3$	r.t.	0.5	5
2b		Ia	$CHCl_3$	r.t.	0.5	94
3		Ia	$CHCl_3$	r.t.	0.5	93[b)]
4	$Ph\text{-}CH_2NHCH_3$	Ia	$CHCl_3$	r.t.	0.5	91
5		Ia	$CHCl_3$	r.t.	0.5	80[b)]
6a	$Ph\text{-}CH_2OH$	Ia	$CHCl_3$	r.t.	1	97
6b		Ib	$CHCl_3$	reflux	3	84
6c		Ic	$CHCl_3$	r.t.	0.5	96
7a	$Ph\text{-}CH_2CH_2OH$	Acetyl-Im[c)]	$CHCl_3$	r.t.	1	12
7b		Ia	$CHCl_3$	r.t.	1	94[b)]
7c		Ia	CH_2Cl_2	r.t.	1	37
7d		Ia	CH_3CN	r.t.	1	21
7e		Ia	THF	r.t.	1	<5
7f		Ia	CCl_4	r.t.	1	<5
7g		Ia	hexane	r.t.	1	<5
7h		Ib	$CHCl_3$	reflux	3	81
8	$Ph\text{-}CH{=}CHCH_2OH$	Ia	$CHCl_3$	r.t.	1	96
9a	$(CH_3)_2CHCH_2CH(CH_3)OH$	Ia	$CHCl_3$	r.t.	3	80
9b		Ib	$CHCl_3$	reflux	5	75
10		Ia	$CHCl_3$	reflux	3	88
11		Ia	$CHCl_3$	reflux	5	76
12		Ia	$CHCl_3$	r.t.	0.3	99
13		Ia	$CHCl_3$	r.t.	0.5	94
14	$Ph\text{-}SH$	Ia	$CHCl_3$	r.t.	0.5	99
15		Ia	$CHCl_3$	r.t.	1	94[b)]

a) The yields were calculated from NMR spectra.
b) Isolated yield.
c) Im: 1-imidazolyl.

The acylation of alcohols and amines was carried out with an equimolar amount of the imidazolium salts [I]. A typical experimental procedure for the acylation of alcohols is as follows (entry 7b): A mixture of 1-acetyl-3-benzylimidazolium bromide [Ia] (2.8 g), phenethyl alcohol (1.22 g), and dry chloroform (5 ml) was stirred at room temperature for 1 hr. The reaction solution was washed with dil. HCl, aq. $NaHCO_3$, and water, dried ($MgSO_4$), and evaporated under reduced pressure. The residual oil was distilled (117-119°C/12 mmHg) to obtain phenethyl acetate (1.54 g, 94%).

The results are summarized in the Table. Primary amines were converted to the corresponding amides in high yields by 1-acetylimidazole (entry 1a), but, secondary amines were acetylated in very low yields (entry 2a). On the other hand, both primary and secondary amines were acetylated in high yields by using 1-acetyl-3-benzylimidazolium bromide [Ia] (entries 1b, 2b-5). Similarly, primary and secondary alcohols were also acetylated by the imidazolium salt [Ia] in high yields at room temperature (entries 6a, 7b, 8 and 9a). Sterically hindered alcohols such as borneol (entry 10) and tertiary alcohol (entry 11) were acetylated under reflux in 88 and 76% yields, respectively. Phenols and thiols were also acetylated at room temperature in excellent yields (entries 12-15). Furthermore, in the solvent effects on the acylation, chloroform was most prefered for the acetylation of phenethyl alcohol with 1-acetyl-3-benzylimidazolium bromide [Ia] among the tested solvents (entries 7b-g).

From these results, we found that the acyl moieties of the 1-acyl-3-substituted imidazolium salts [I] were highly activated to a nucleophilic attack as compared with those of 1-acylimidazoles. This high reactivity of the acyl moiety of the imidazolium salts [I] for acylation seems to be due to the positively charged imidazole ring which reduces the electron density of the carbon atom of the carbonyl group.

Thus, 1-acylimidazoles can be highly activated for acylation of alcohols and amines by quarternizing with benzyl halides.

REFERENCES AND NOTES

1) H.A. Staab and W. Rohr, "Newer Methods of Preparative Organic Chemistry," Vol. V, Academic Press, New York and London, (1968) p. 61.
2) T. Katsuki, Bull. Chem. Soc. Jpn., 49, 2019 (1976).
3) T. Kamijo, R. Yamamoto, H. Harada, and K. Iizuka, to be published.
4) Preparation of 1-acetyl-3-benzylimidazolium bromide [Ia]: To 20 ml of dry acetonitrile were added 5.0 g of 1-acetylimidazole and 7.8 g of benzylbromide, and the mixture was stirred overnight at room temperature. The precipitated crystals were collected by filtration to give 11.8 g (93.3 %) of 1-acetyl-3-benzylimidazolium bromide as colorless crystals: mp 125-127°C; IR (KBr): 1770 (C=O) cm^{-1}; NMR (DMSO-d_6) δ: 1.95(s, 3H, CH_3CO-), 5.56(s, 2H, $PhCH_2$-), 7.50(s, 5H, Ar-H), 7.82(m, 1H), 7.92(m, 1H), 9.48(m, 1H). By the same procedure, 1-benzoyl-3-benzylimidazolium chloride [Ib] and bromide [Ic] were obtained in quantitative yields. [Ib]: colorless hygroscopic crystals; IR (KBr): 1740, 1785 (C=O) cm^{-1}; NMR (DMSO-d_6) δ: 5.35(s, 2H, $PhCH_2$-), 7.3-8.2(m, 12H), 9.10(m, 1H). [Ic]: colorless hygroscopic crystals; IR ($CHCl_3$): 1750, 1790 (C=O) cm^{-1}; NMR (DMSO-d_6) δ: 5.60(s, 2H, $PhCH_2$-), 7.3-8.2(m, 12H), 9.52(m, 1H).

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