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Esterification of Alcohols with 1-Acylimidazole Assisted by *N*-Bromosuccinimide

Tsutomu KATSUKI

Department of Chemistry, Faculty of Science, Kyushu University, Higashi-ku, Fukuoka 812

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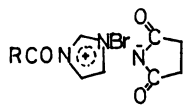
Synopsis. Treatment of 1-acylimidazoles with alcohols in the presence of *N*-bromosuccinimide led to the rapid formation of the corresponding esters. The carboxylic acids with less than two hydrogen atoms at their α-positions generally gave good results. Even such a hindered ester as *t*-butyl pivalate could be prepared by this procedure.

The reaction between alcohols and 1-acylimidazoles[1] is known as one of the elegant esterification methods[2] under mild conditions. Though the above reaction is usually slow at room temperature, the esters of primary and secondary alcohols can be prepared by conducting the reaction at elevated temperatures.[3] For the preparation of hindered esters, however, the method is ineffective and the use of a strong base catalyst, such as sodium alkoxide or sodium amide, is indispensable.[4] *t*-Butyl pivalate, for example, has been prepared by the latter procedure in a 64% yield.[4] The author has found that when 1-acylimidazoles were treated with *N*-bromosuccinimide[5] in the presence of alcohols, rapid esterification took place at room temperature under neutral conditions. In most cases, the reaction terminated within sixty minutes. Hindered esters, such as *t*-butyl pivalate (**2**) and *t*-butyl 2,3,6-trimethylbenzoate (**3**) could be obtained in 48 and 65% yields, respectively, by refluxing the corresponding reactants in methylene chloride for twelve hours.



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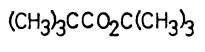

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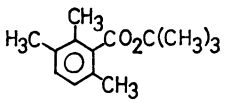

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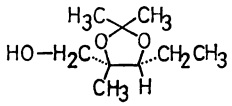

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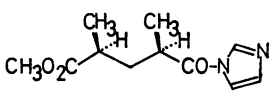

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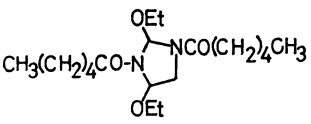

(6)

The esterification is considered to proceed *via* the intermediate represented by **1**. This method could be applied to the acylation of the acid-labile alcohol, 2,3-isopropyridenedioxy-2-methylpentanol (**4**).[6] The imidazolide (**5**) of methyl hydrogen meso-2,4-dimethylglutarate was converted into the corresponding *t*-butyl ester in a 70% yield without any detectable epimerization.

A limitation of the method is that the yield in the esterification of carboxylic acids having two or three hydrogen atoms on the α-carbon atoms, is fairly variable depending on the alcohols used. 1-Hexanoylimidazole was, for example, converted into its ethyl ester in only a 17% yield, and 80% of the product was an unexpected compound for which the tentative formula (**6**) has been given on the basis of spectral data. *s*-Butyl hexanoate was, however, obtained in a 80% yield.

A summary of the yields is given in Table 1 below.

Table 1. Per cent yields of esters

1-Acylimidazole	Alcohol	Solvent	Yield[a]
Pivaloyl	Ethanol	CH_2Cl_2	84
Pivaloyl	2-Methyl-2-propanol	CH_2Cl_2	48[b]
Pivaloyl	Cyclohexanol	THF	95[c]
Pivaloyl	(**4**)	THF	90
2-Methylpentanoyl	Ethanol	CH_2Cl_2	85
2-Methylpentanoyl	Cyclohexanol	CH_2Cl_2	81
2-Methylpentanoyl	2-Methyl-2-propanol	CH_2Cl_2	95
2,3,6-Trimethylbenzoyl	2-Methyl-2-propanol	CH_2Cl_2	65[b]
2,3,6-Trimethylbenzoyl	Benzyl alcohol	CH_2Cl_2	70[d]
Benzoyl	Ethanol	THF	80
Hexanoyl	Ethanol	CH_2Cl_2	17
Hexanoyl	2-Butanol	CH_2Cl_2	80
Hexanoyl	Benzyl alcohol	CH_2Cl_2	80[d]
Hexanoyl	2-Methyl-2-propanol	CH_2Cl_2	57
Acetyl	Cyclohexanol	THF	20

a) All yields are based on 1-acylimidazoles. b) These reactions were run under reflux for 12 h. c) The yield was determined by GLC. d) The yields were calculated from NMR spectra.

The analytical and NMR data of new compounds prepared in this study are given in Table 2.

Experimental

General. All the reactions were carried out in a nitrogen atmosphere. The quality of the reagents employed has a very marked effect upon the yield. Imidazole was purified by sublimation. *N*-Bromosuccinimide was recrystallized from water and dried at 25 °C under reduced pressure (5 mmHg). The alcohols employed were all absolute.

Tetrahydrofuran or dichloromethane was used as the solvent. But dichloromethane was preferable because tetrahydrofuran polymerized slowly under the reaction conditions.

Procedure. All the esters were prepared by almost the same procedure as exemplified by that of *t*-butyl 2-methyl-

Table 2. Analytical and NMR data of new compounds

Compound	Characteristic chemical shifts (δ) and analysis[a)]
1-(2-Methylpentanoyl)imidazole[b)]	0.93(m, 3H), 1.35(d, 3H), 3.13(m, 1H), 7.00(double-d, 1H), 7.12(double-d, 1H), 8.22(broad-s, 1H). Found: C, 64.77; H, 8.40. Calcd: C, 65.03; H, 8.49.
1-(2,3,6-Trimethylbenzoyl)imidazole[b)]	2.11(s, 3H), 2.17(s, 3H), 2.28(s, 3H), 6.95—8.00(m, 5H). Found: C, 72.51; H, 6.63. Calcd: C, 72.87; H, 6.59.
Benzyl 2,3,6-trimethylbenzoate	2.14(s, 3H), 2.20(s, 6H), 4.33(s, 2H), 6.97(qualtet, 2H), 7.30—7.46(m, 5H). Found: C, 79.85; H, 7.04. Calcd: C, 80.28; H, 7.13.
t-Butyl 2,3,6-trimethylbenzoate (**3**)	1.61(s, 9H), 2.23(s, 6H), 2.30(s, 3H), 6.98(qualtet, 2H). Found: C, 76.45; H, 9.28. Calcd: C, 76.32; H, 9.15.
Cyclohexyl 2-methylpentanoate	0.90(m, 3H), 1.11(d, 3H), 2.43(m, 1H), 4.75(m, 1H). Found: C, 72.33; H, 11.22. Calcd: C, 72.68; H, 11.18.
2,3-Isopropyridenedioxy-2-methylpentyl pivalate	1.05(m, 3H), 1.20(s, 9H), 1.30(s, 3H), 1.38(s, 3H), 1.41(s, 3H), 3.70(t, 1H), 3.93(s, 2H). Found: C, 64.01; H, 10.11. Calcd: C, 65.08; H, 10.14.

a) The C and H analyses were carried out on the samples which were obtained by the simple distillation of the reaction products by applying the micro pot-style molecular distillation apparatus at the appropriate bath temperature. b) The 1-acylimidazoles were prepared from the corresponding acyl chlorides and imidazole following the usual procedure.

pentanoate. The esters thus obtained were spectroscopically identified.

t-Butyl 2-Methylpentanoate (**7**): 1-(2-Methylpentanoyl)-imidazole prepared from 2-methylpentanoyl chloride (592 mg) and imidazole (610 mg) was dissolved in dichloromethane (25 ml). To this solution were added 2-methyl-2-propanol (422 mg) and then *N*-bromosuccinimide (814 mg) at one time at room temperature. After 1 h, the mixture was analyzed by GLC. GLC analysis indicated the formation of **7** in a 95% yield. The resulting mixture was distributed between water (20 ml) and pentane (100 ml). The organic layer was separated, washed successively with a saturated aqueous solution of citric acid, water, and a saturated aqueous solution of sodium hydrogencarbonate, dried over anhydrous sodium sulfate, and concentrated to a colorless oil (95%). The ester thus obtained was identified with an authentic sample by NMR spectroscopy.

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2) The reagents employed are, for example, dimethylaminopyridine [G. Hofle and W. Steglich, *Synthesis*, **1972**, 620], triphenylphosphine–dipyridyldisulfide [T. Mukaiyama, R. Matsueda, and M. Suzuki, *Tetrahedron Lett.*, **1970**, 1901 and E. J. Corey and K. C. Nicolaou, *J. Am. Chem. Soc.*, **96**, 5614 (1974)], tosyl chloride–triethylamine [J. H. Brewster and C. J. Ciotti Jr, *J. Am. Chem. Soc.*, **77**, 6214 (1655)], and trifluoroacetylimidazole [H. A. Staab and G. Walther, *Chem. Ber.*, **95**, 2070 (1962) and H. D. Law, *J. Chem. Soc.*, **1965**, 3897].

3) H. A. Staab, *Angew. Chem.* **71**, 194 (1959).

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5) *N*-Chlorosuccinimide was also used but it was less effective than *N*-bromosuccinimide.

6) J. Inanaga, A. Takeda, N. Okukado, and M. Yamaguchi, *Mem. Fac. Sci., Kyushu Univ., C*, **9**, 293 (1975).