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Montmorillonite K 10 (Clay) Catalyzed Hydrolysis of Aryl-substituted α,β-Difluoroallyl Alcohols Leading to (Z)-α-Fluoro-β-aryl-substituted Acrylaldehydes

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Abstract

Aryl-substituted α,β-difluoroallyl alcohols **1** were readily hydrolyzed in the presence of a catalytic amount of montmorillonite K 10 (clay) in hexane at reflux temperature for 1 h to give the corresponding (*Z*)-α-fluoro-β-aryl-substituted acrylaldehydes **2** in good yields.

Keywords: Fluorine and compounds, Clays and earths, Supported reagents/reaction, Enals, Hydrolysis, Stereoselection

Introduction

Considerable attention has been focused on the development of effective organic syntheses using a number of solid catalysts, which have marked advantages such as ease of handling, non-corrosiveness, low cost, and regeneration and modification of the catalytic activity. Notably, clays (montmorillonite) are one of the most versatile catalysts, and are being employed in various types of organic reactions [1-21]. However, widely applicable synthetic methods involving stereoselectivity are still limited [22-25]. On the other hand, fluorinated compounds are widely used in the field of materials and medicinal chemistry because of their unique properties. Among them, stereo-defined α-fluoroacrylaldehydes are some of the most important and useful intermediates for the preparation of fluorine-containing bioactive compounds, such as dipeptide isosteres [26,27], insect sex pheromones [28], inhibitors [29,30], and agonists [31]. In the future, therefore, more clean and environmental routes will be required, although some reports on the synthesis of

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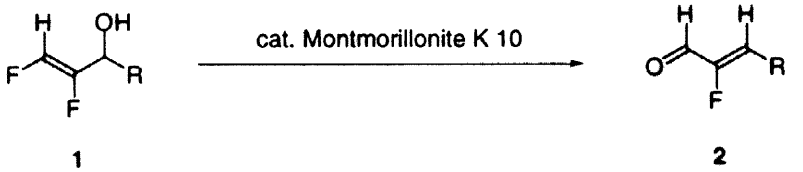
α-fluoroacrylaldehydes have so far appeared [32-39]. In this paper, we present in full detail, the montmorillonite K 10 catalyzed hydrolysis of aryl-substituted α,β-difluoroallyl alcohols, which is utilized recycling, waste-minimium, and non-hazardous systems, leading to (Z)-α-fluoro-β-aryl-substituted acrylaldehydes (Scheme 1) [40].



1 2

Scheme 1 Hydrolysis of **1** in the presence of montmorillonite K 10

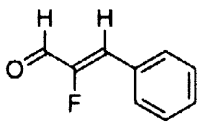
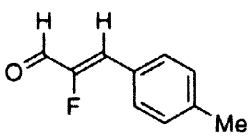
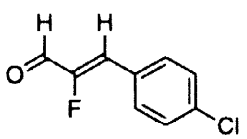
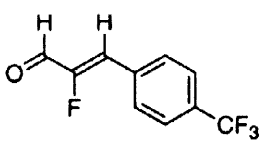
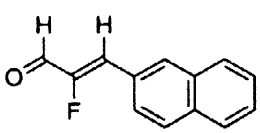
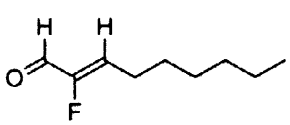
Results and Discussion

α,β-Difluoroallyl alcohols **1** were prepared according to our previously reported procedure [40]. Treatment of alcohol **1a** with a catalytic amount of montmorillonite K 10 (M K 10) at room temperature for 1 h gave the corresponding α-fluoroacrylaldehydes **2a** in only 6% yield, the alcohol **1a** being unchanged in 67% yield (Table 1, Entry 1). When the reaction was carried out at reflux temperature, **1a** was completely consumed to give the aldehyde **2a** as the only (Z)-isomer in the 78% yield (Entry 2). Benzene was equally employable as a solvent (Entry 4). However, the use of acetonitrile (MeCN) or tetrahydrofuran (THF) decreased the yield of **2a**, together with the recovery of the starting alcohol **1a** (5-36%), probably due to the Lewis basicity of the solvents [41] (Entries 6 and 8). A small amount of water (0.1 ml) did not effect on the yields in hexane or benzene (Entries 2 and 5), on the other hand, the reaction in MeCN or THF resulted in a significant yield reduction of **2a** (Entries 7 and 9). These results suggest not only that an excess amount of water will deactivate the catalytic activity of M K 10 [5], but that the water in M K 10 will also be sufficient for the hydrolysis of the alcohol **1a**. It is noteworthy that the reaction in the presence of triethylamine hardly proceeded resulting in the quantitative recovery of the starting alcohol **1a** (Entry 12). Presumably triethylamine poisons the Brønsted acid sites of M K 10 [5]. The recovered M K 10 catalyst was still effective in the reaction (Entries 10 and 11).

Allyl alcohols **1b-e** carrying other aromatic substituents, such as *p*-tolyl, *p*-chlorophenyl, *p*-(trifluoromethyl)phenyl and 2-naphthyl groups, participated well in the reaction producing the corresponding (Z)-α-fluoro-β-aryl-substituted acrylaldehyde **2** in good yields (Entries 13-16). Unfortunately, the hydrolysis of **1f** bearing the *n*-hexyl group did not occur. The starting alcohol **1f** was recovered under the usual conditions (Entry 17), or even if the reaction time was prolonged (3 h) (Entry 18) and the Sn^{2+} ion-exchanged montmorillonite was employed (Entry 19).

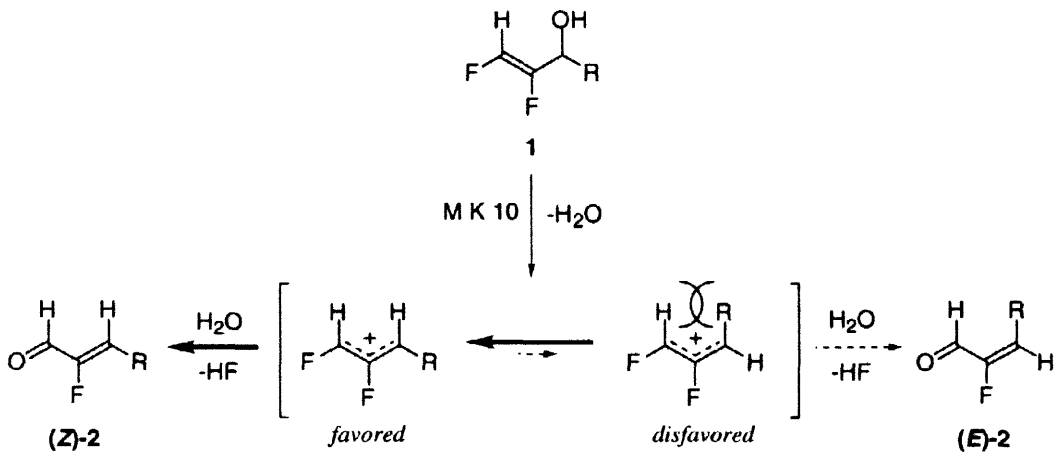
It should be noted that only one geometrical isomer was produced under the various conditions. At present, although it is unclear whether or not the restricted environment of the M K 10 interlayer influences the (Z)-stereoselectivity, the reaction probably proceeds through the allyl cation species, whose relative stability plays a significant role in the

Table 1. Montmorillonite K 10 Catalyzed Hydrolysis of **1**[a]

Entry	Solvent	Temp.	Product		Yield[b]/% of **2**	(*Z*/*E*)[c] of **2**
1[d]	Hexane	r.t.		**2a**	6 (67)	(>99/<1)
2[d]	Hexane	reflux		**2a**	78	(>99/<1)
3	Hexane	reflux		**2a**	78	(>99/<1)
4	Benzene	reflux		**2a**	72	(>99/<1)
5[d]	Benzene	reflux		**2a**	69	(>99/<1)
6	MeCN	reflux		**2a**	57 (5)	(>99/<1)
7[d]	MeCN	reflux		**2a**	44 (38)	(>99/<1)
8	THF	reflux		**2a**	34 (36)	(>99/<1)
9[d]	THF	reflux		**2a**	3 (76)	(>99/<1)
10[e]	Hexane	reflux		**2a**	69	(>99/<1)
11[f]	Hexane	reflux		**2a**	56	(>99/<1)
12[g]	Hexane	reflux		**2a**	0 (71)	–
13	Hexane	reflux		**2b**	71	(>99/<1)
14	Hexane	reflux		**2c**	68	(>99/<1)
15	Hexane	reflux		**2d**	61	(>99/<1)
16	Hexane	reflux		**2e**	64	(>99/<1)
17	Hexane	reflux			0 (75)	–
18[h]	Hexane	reflux		**2f**	0 (74)	–
19[i]	Hexane	reflux			0 (73)	–

[a] Unless otherwise noted, all the reaction was carried out with alcohol **1** (2 mmol) and M K10 (0.4 g) in a solvent (6 ml) for 1 h. [b] Isolated yields of analytically pure products. Values in parentheses stand for the recovery of **1**. [c] Determined by ^{19}F NMR of the crude products prior to isolation. [d] H_2O (0.1 ml) was added. [e] The 2nd use of M K10. [f] The 3rd use of M K10. [g] Et_3N (0.1 ml) was added. [h] The reaction was carried out for 3 h. [i] Sn-montmorillonite (0.4 g) was employed.

stereoselective formation of the (*Z*)-isomer (Scheme 2) [42].



Scheme 2

Of much significance is that the reaction using M K 10 has marked advantages: (1) the ease of the recovery of the catalyst by filtration; (2) the facile reuse of the catalyst by convenient treatment; and (3) the low cost of commercially available material.

In conclusion, montmorillonite K 10 was an efficient catalyst in the hydrolysis of aryl-substituted α,β-difluoroallyl alcohols **1**, providing exclusively (*Z*)-α-fluoro-β-aryl-substituted acrylaldehydes **2** in good yields. Further studies on the montmorillonite K 10 (clay) catalyzed stereoselective synthesis of fluorinated compounds are now in progress.

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Experimental

Melting points were obtained on a Yanagimoto MP-S2 micro melting point apparatus and are uncorrected. Infrared spectra (IR) were recorded on a Perkin Elmer FT-IR 1640 spectrometer. ^{1}H NMR spectra were measured with a JEOL α-400 (400 MHz) FT-NMR spectrometer in deuteriochloroform ($CDCl_3$) solutions with tetramethylsilane (Me_4Si) as the internal standard. ^{19}F NMR spectra were recorded on a JEOL α-400 (376 MHz) FT-NMR in $CDCl_3$ solutions using trifluoroacetic acid as the external standard. Mass spectra (MS) were taken on a Hitachi-80B spectrometer operating at an ionization potential of 70 eV. Elemental analyses were made on a Yanaco MT-5 CHN corder. The isolation of pure products was carried out by column chromatography using silica gel (Wakogel C-200, 100-200 mesh, Wako Pure Chemical Ind., Ltd.). Montmorillonite K 10 was commercially available from Aldrich Chemical Co. Inc., and dried at 120 °C under vacuum for 3 h prior to use. According to a previous report [43], Sn^{2+}-exchanged

montmorillonite was prepared from Na^+-montmorillonite (Kunipia F), which was obtained from Kinimine Industries Co., Ltd. Tetrahydrofuran (THF) was freshly distilled from sodium benzophenone ketyl. Hexane, benzene and acetonitrile were distilled over calcium hydride under argon. All chemicals were of reagent grade and, if necessary, were purified in the usual manner prior to use.

A typical procedure for the hydrolysis of α,β-difluoroallyl alcohol in the presence of montmorillonite K 10. A mixture of 2,3-difluoro-1-phenyl-2-propen-1-ol (**1a**) (2 mmol, 0.340 g) and montmorillonite K 10 (M K 10, 0.4 g) in hexane (6 mL) was heated at reflux temperature for 1 h. After the resultant mixture had been cooled, the M K 10 was filtered for recovery, and washed with diethyl ether (100 mL). The ethereal mixture was washed with brine (30 mL X 3), dried over anhydrous Na_2SO_4, and concentrated. After the distribution of the isomers was determined by ^{19}F NMR, the residue was subjected to chromatography on a column of silica gel using benzene as the eluent, giving (*Z*)-2-fluoro-3-phenyl-2-propenal (**2a**) (0.234 g, 78%, Table 1, Entry 2).

Compounds **2a** [33, 34, 37, 39], **2b** [33, 39], and **2c** [39] are known.

(Z)-2-Fluoro-3-phenyl-2-propenal (2a) [32, 33, 34, 37, 39]. mp 48.0-48.4 °C (hexane); IR (CCl_4) 1648.5 (C=C), 1699.0 (C=O) cm^{-1}; ^1H NMR ($CDCl_3$) δ 6.62 (d, J = 34.15 Hz, 1H), 7.43-7.49 (m, 3H), 7.69-7.75 (m, 2H), 9.37 (d, J = 16.83 Hz, 1H); ^{13}C NMR ($CDCl_3$) δ 126.89, 129.01, 130.61, 130.78 (d, J = 19.85 Hz), 130.90, 154.76 (d, J = 271.27 Hz), 183.98 (d, J = 24.81 Hz); ^{19}F NMR ($CDCl_3$) δ -50.82 (dd, J = 34.15, 16.83 Hz, 1F); MS *m/z* (rel intensity) 150 (M^+; 100.0), 149 (99.7), 122 (24.5), 121 (19), 101 (23.8), 96 (13.6), 78 (15.4), 75 (11.7); HRMS (EI) Found: *m/z* 150.0482. Calcd for C_9H_7FO: M, 150.0481.

(Z)-2-Fluoro-3-(4-methylphenyl)-2-propenal (2b) [32, 33, 39]. mp 45.5-46.3 °C (hexane); IR (CCl_4) 1649.7 (C=C), 1701.5 (C=O) cm^{-1}; ^1H NMR ($CDCl_3$) δ 2.40 (s, 3H), 6.59 (d, J = 34.40 Hz, 1H), 7.26 and 7.62 (AB quartet, J = 8.05 Hz, 4H), 9.37 (d, J = 17.08 Hz, 1H); ^{19}F NMR ($CDCl_3$) δ -51.72 (dd, J = 34.40, 17.07 Hz, 1F); MS *m/z* (rel intensity) 164 (M^+; 54.7), 163 (27.6), 150 (10.3), 149 (100), 135 (21.6), 133 (17.5), 116 (7.4), 115 (24.0), 109 (9.1), 92 (11.7), 91 (6.6); HRMS (EI) Found: *m/z* 164.0638. Calcd for $C_{10}H_9FO$: M, 164.0638.

(Z)-3-(4-Chlorophenyl)-2-fluoro-2-propenal (2c) [32, 39]. mp 67.0-67.9 °C (hexane); IR (CCl_4) 1635.0 (C=C), 1704.9 (C=O) cm^{-1}; ^1H NMR ($CDCl_3$) δ 6.59 (d, J = 33.67 Hz, 1H), 7.43 and 7.65 (AB quartet, J = 8.54 Hz, 4H), 9.37 (d, J = 16.59 Hz, 1H); ^{19}F NMR ($CDCl_3$) δ -50.07 (dd, J = 33.67, 16.59 Hz, 1F); MS *m/z* (rel intensity) 186 (M^++2; 20.4), 184 (M^+; 55.0), 183 (23.4), 149 (100.0), 136 (6.0), 121 (16.8), 113 (6.1), 112 (14.4), 101 (19.2), 99 (6.6), 75 (8.3); HRMS (EI) Found: *m/z* 186.0058. Calcd for $C_9H_6{}^{37}ClFO$: M, 186.0062; Found: *m/z* 184.0101. Calcd for $C_9H_6{}^{35}ClFO$: M, 184.0092.

(Z)-2-Fluoro-3-(4-trifluoromethylphenyl)-2-propenal (2d) [32]. mp 61.8-62.2 °C (hexane); IR (CCl_4) 1649.7 (C=C), 1705.9 (C=O) cm^{-1}; ^1H NMR ($CDCl_3$) δ 6.67 (d, J = 33.42 Hz, 1H), 7.71 and 7.83 (AB quartet, J = 8.30 Hz, 4H), 9.43 (d, J = 16.10 Hz, 1H); ^{19}F NMR ($CDCl_3$) δ -47.71 (dd, J = 33.42, 16.10 Hz, 1F); MS *m/z* (rel intensity) 218 (M^+; 94.1), 217 (38.2), 199 (23.1), 197 (5.4), 190 (21.1), 189 (11.9), 171 (10.4), 170 (11.5), 151 (16.4), 149 (100.0), 146 (19.7), 145 (6.9), 140 (13.3), 121 (17.4), 120 (20.1), 101 (12.0); HRMS (EI) Found: *m/z* 218.0358. Calcd for $C_{10}H_6F_4O$: M, 218.0355. Anal. Calcd for : C, 55.06; H, 2.77. Found: C, 55.02; H, 2.90.

(Z)-2-Fluoro-3-(2-naphthyl)-2-propenal (2e) [32]. mp 83.9-84.5 °C (hexane); IR (CCl_4) 1648.0 (C=C), 1703.0 (C=O) cm^{-1}; ^1H NMR ($CDCl_3$) δ 6.75 (d, J = 34.16 Hz, 1H), 7.50-7.64 (m, 2H), 7.80-7.98 (m, 4H), 8.19 (s, 1H), 9.42 (d, J = 16.84 Hz, 1H); ^{19}F NMR ($CDCl_3$) δ -50.74 (dd, J = 34.16, 16.84 Hz, 1F); MS *m/z* (rel intensity) 200 (M^+; 100.0), 199 (35.9), 172 (55.2), 171 (38.4), 152 (16.6), 151 (12.6), 150 (8.1), 128 (27.4); HRMS (EI) Found: *m/z* 200.0641. Calcd for $C_{10}H_9FO$: M, 200.0638.

Anal. Calcd for : C, 77.99; H, 4.53. Found: C, 78.23; H, 4.69.

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