3040 © 1994 The Chemical Society of Japan *Bull. Chem. Soc. Jpn.*, **67**, 3040—3043(1994) [Vol. 67, No. 11

The Ene and the Diels–Alder Reactions of CF_3CHO with Dienes Using ZnX_2 (X: Cl, OTf)

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(Received April 14, 1994)

The reaction of CF_3CHO with dienes using ZnX_2 (X: Cl, OTf) in organic solvents (CH_2Cl_2 or CH_3NO_2) gave fairly good results in depressing unfavorable reactions and affording the preferential formation of the ene reaction products, 1-trifluoromethyl-3-buten-1-ols, together with the Diels–Alder reaction products. Particularly, $Zn(OTf)_2$, which is insoluble in CH_2Cl_2, had some predominance for the formation of ene-type products in preference to $ZnCl_2$, and could be recycled without any deterioration in its catalytic activity.

Trifluoroacetaldehyde is a useful building block for the preparation of organic compounds having a trifluoromethyl group.[1] The ene reaction of trifluoroacetaldehyde with alkenes promoted by $AlCl_3$ has been extensively studied by Kumadaki[1f,1g,1h] to produce the corresponding 1-trifluoromethyl-3-buten-1-ols. However, it is anticipated that the reaction of trifluoroacetaldehyde with dienes would afford Diels–Alder reaction products in very low yield together with the ene reaction products. The reaction of trichloroacetaldehyde and isoprene using $AlCl_3$ was reported to afford the corresponding Diels–Alder reaction products as major products, and the ene reaction products as minor ones with a considerable amount of unfavorable complicated byproducts.[2] Our own investigation in this area has focused on the reaction of trifluoroacetaldehyde with conjugated dienes, which are very sensitive to the acid, and undergo such unfavorable reactions as polymerization. Conjugated dienes **2a**—**2d** were used as substrates to examine the influence of the position of methyl groups and the conformation of dienes in ene and Diels–Alder reactions.

Although $ZnCl_2$ and $Zn(OTf)_2$ are very weak Lewis acids,[3,4] they are hardly employed as carbon–carbon bond-formation catalysts. However, we have recently reported that $ZnCl_2$ can be successfully employed in the Friedel–Crafts benzylation of benzenes as a useful catalyst in the presence of polar solvents.[5] We now wish to report that ZnX_2 (X: Cl, OTf) is a useful catalyst for the reaction of conjugated dienes (**2**) with trifluoroacetaldehyde (**1**), providing ene products (**3**) and Diels–Alder products (**4**) with a depression of unfavorable side reaction (see Scheme 1).

Experimental

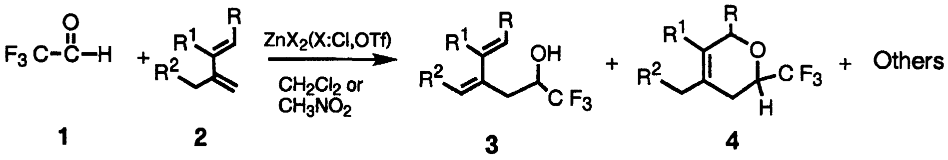
A typical procedure for the reaction of **2a** with **1** is as follows. A dry solvent (8 ml), **2a** (2 ml, 20 mmol) and a catalyst (1 mmol) were cooled to −78 °C in a 50 ml glass flask with a two-way cock, and **1** (1 ml, 10 mmol) was distilled into the reactor through a calibrated trap. The reactor was sealed and stirred for 5 h at either 25 or 50 °C. After the resulting solution was treated in the usual manner, the products were isolated by column chromatography on silica gel with dichloromethane used as an eluent. All pure products were fully characterized by IR, NMR, and MS. The ^{1}H NMR (90 MHz), ^{19}F NMR (86 MHz), and ^{13}C NMR (26 MHz) spectra were measured with a Hitachi R-1900 high-resolution NMR spectrometer. ^{1}H NMR (400 MHz) spectra were measured with a JEOL JNM-Ex 400 and HR-MS spectra were obtained with a JEOL JMS Dx-303 at the Center for the Instrumental Analysis, Hokkaido University. GC/MS was analyzed using a Hewlett–Packard 5890/5970 gas chromatography/mass spectrometer. Analytical GC was performed using an internal standard on a Shimadzu GC-14A gas chromatograph with a 25 m OV-1 capillary column. Infrared spectra were taken on a Hitachi 260-30 Infrared Spectrometer. UV-vis spectra were obtained with a Union Giken MCPD-350 spectro multi-channel detector for a liquid chromatography.

For 3a: ^{1}H NMR (90 MHz, $CDCl_3$) $\delta=2.48$ (d, $J=9.5$ Hz, 1H), 2.26—2.86 (m, 2H), 3.90—4.4 (m, 1H), 5.21 (m, 4H), 6.42 (m, 1H); ^{13}C NMR (26 MHz, $CDCl_3$) $\delta=32.51$ (q, $J=2.4$ Hz), 68.79 (q, $J=36.45$ Hz), 114.45, 119.76, 125.02 (q, $J=322.66$ Hz), 137.71, 140.28; ^{19}F NMR (86 MHz, $CDCl_3$) ($CFCl_3$ as an internal standard) $\delta=-80.34$ (d, $J=6.7$ Hz); MS m/z 166 (M^+). HRMS Calcd for $C_7H_6OF_3$: M, 166.0606. Found: m/z 166.0585.

For 4a: ^{1}H NMR (400 MHz, $CDCl_3$) $\delta=1.76$ (s, 3H), 1.98 (d, $J=16.9$ Hz, 1H), 2.32 (dd, $J=16.9$, 11.0 Hz, 2H), 3.93 (m, 1H), 4.26 (AB system, $2J=15.6$ Hz, 2H), 5.46 (s, 1H); ^{13}C NMR (26 MHz, $CDCl_3$) $\delta=22.37$, 28.10, 65.91, 71.77 (q, $J=36.45$ Hz), 119.27, 124.33 (q, $J=319.49$ Hz), 129.60; ^{19}F NMR (86 MHz, $CDCl_3$) ($CFCl_3$ as an internal standard) $\delta=-79.63$ (d, $J=6.4$ Hz); MS m/z 166 (M^+). HRMS Calcd for $C_7H_9OF_3$: M, 166.0606. Found: m/z 166.0599.

For 3b: ^{1}H NMR (90 MHz, $CDCl_3$) $\delta=1.79$ (d, $J=6.2$ Hz, 3H), 2.16—2.84 (m, 3H), 3.96—4.23 (m, 1H), 5.06 (d, $J=5.9$ Hz, 2H), 5.53—5.91 (m, 1H), 6.13 (d, $J=16.2$ Hz, 1H); ^{19}F NMR (86 MHz, $CDCl_3$) ($CFCl_3$ as an internal standard) $\delta=-80.32$ (d, $J=6.6$ Hz); MS m/z 180 (M^+). HRMS Calcd for $C_8H_{11}OF_3$: M, 180.0762. Found: m/z 180.0748.

For 4b: ^{1}H NMR (90 MHz, $CDCl_3$) $\delta=1.25$ (d, $J=6.6$ Hz, 3H), 1.73 (s, 3H), 1.90—2.53 (m, 2H), 3.85—4.08 (m, 1H), 4.23—4.30 (m, 1H), 5.29—5.38 (m, 1H); ^{19}F NMR (86 MHz, $CDCl_3$) ($CFCl_3$ as an internal standard) $\delta=-78.95$ (d, $J=6.9$ Hz), −79.71 (d, $J=6.4$ Hz); MS m/z 180 (M^+). HRMS Calcd for $C_8H_{11}OF_3$: M, 180.0762. Found: m/z 180.0777.



2, 3, 4	R	R^1	R^2
a	H	H	H
b	Me	H	H
c	H	Me	H
d	H	-$(CH_2)_3$-	

Scheme 1.

For 3c: ^{1}H NMR (90 MHz, $CDCl_3$) $\delta=1.94$ (s, 3H), 2.09—2.98 (m, 3H), 4.00—4.20 (m, 1H), 5.07 (s, 2H), 5.16 (s, 1H), 5.30 (s, 1H); ^{19}F NMR (86 MHz, $CDCl_3$) ($CFCl_3$ as an internal standard) $\delta=-80.32$ (d, $J=7.0$ Hz); MS m/z 180 (M^+). HRMS Calcd for $C_8H_{11}OF_3$: M, 180.0762. Found: m/z 180.0745.

For 4c: ^{1}H NMR (90 MHz, $CDCl_3$) $\delta=1.56$ (s, 3H), 1.69 (s, 3H), 1.83—2.49 (m, 2H), 3.78—3.99 (m, 1H), 4.08 (s, 2H); ^{19}F NMR (86 MHz, $CDCl_3$) ($CFCl_3$ as an internal standard) $\delta=-79.53$ (d, $J=6.5$ Hz); MS m/z 180 (M^+). HRMS Calcd for $C_8H_{11}OF_3$: M, 180.0762. Found: m/z 180.0761.

For 5c: ^{1}H NMR (90 MHz, $CDCl_3$) $\delta=1.76$ (s, 3H), 1.92—2.57 (m, 5H), 3.83—4.10 (m, 2H), 4.19 (s, 2H); ^{19}F NMR (86 MHz, $CDCl_3$) ($CFCl_3$ as an internal standard) $\delta=-79.65$ (d, $J=6.6$ Hz), -79.69 (d, $J=6.8$ Hz), -80.77 (d, $J=6.8$ Hz), -80.93 (d, $J=6.8$ Hz); MS m/z 278 (M^+). HRMS Calcd for $C_8H_{11}OF_3$: M, 278.0742. Found: m/z 278.0745.

For 3d: ^{1}H NMR (90 MHz, $CDCl_3$) $\delta=1.63$—1.88 (m, 2H), 2.16—2.91 (m, 5H), 3.60—3.79 (m, 2H), 3.83—4.19 (m, 1H), 4.86 (d, $J=4.6$ Hz, 2H), 5.86 (t, $J=3.6$ Hz, 1H); ^{19}F NMR (86 MHz, $CDCl_3$) ($CFCl_3$ as an internal standard) $\delta=-80.32$ (d, $J=7.0$ Hz); MS m/z 206 (M^+). HRMS Calcd for $C_8H_{11}OF_3$: M, 206.0918. Found: m/z 206.0900.

For 4d: ^{1}H NMR (90 MHz, $CDCl_3$) $\delta=1.48$—2.26 (m, 10H), 3.80—4.00 (m, 1H), 4.07 (s, 2H); ^{19}F NMR (86 MHz, $CDCl_3$) ($CFCl_3$ as an internal standard) $\delta=-79.67$ (d, $J=6.3$ Hz); MS m/z 206 (M^+). HRMS Calcd for $C_8H_{11}OF_3$: M, 206.0918. Found: m/z 206.0926.

For 5d: ^{1}H NMR (90 MHz, $CDCl_3$) $\delta=1.80$—2.72 (m, 10H), 3.84—4.06 (m, 2H), 5.85 (s, 2H); ^{19}F NMR (86 MHz, $CDCl_3$) ($CFCl_3$ as an internal standard) $\delta=-80.37$ (d, $J=6.7$ Hz), -80.35 (d, $J=7.0$ Hz); UV-vis λ_{max} 259 nm; MS m/z 304 (M^+). HRMS Calcd for $C_8H_{11}OF_3$: M, 304.0898. Found: m/z 304.0903.

Results and Discussion

Representative results are shown in Table 1. The reactivity of conjugated dienes was greatly affected by their structures and the Lewis acids employed. The reaction of isoprene (**2a**) with trifluoroacetaldehyde (**1**) using $AlCl_3$ in CH_2Cl_2 gave both the Diels–Alder adduct (**4a**) and an ene product (**3a**), but in very poor yields (Entry 5). In this case, because of the high acidity of the catalyst, a further reaction of the formed ene product (**3a**) with **1** or **2a** and the self-polymerization of **1** and **2a** significantly took place, affording unfavorable complicated products. Even under conditions using a smaller amount of catalyst, the yields of **3a** and **4b** were not remarkably improved (Entry 6). On the contrary, by employing ZnX_2 (X: Cl, OTf) having a relatively lower acidity,[4] such unfavorable reactions were greatly depressed to give **3a** together with **4a** in good to excellent yields by using CH_2Cl_2 or CH_3NO_2 as solvent (Entries 1—4). The ratio of **3a** and **4a** formed in the reaction of **1** and **2** was also affected by the catalyst used, and a more predominant formation of **3a** was observed in the case of $Zn(OTf)_2$ (Entries 1 and 2).

The reactions of **2c** and **2d** with **1** gave good results, affording the corresponding products, **3c** and **4c**, and **3d** and **4d**, respectively, by using $ZnCl_2$ or $Zn(OTf)_2$ (Entries 10—12, 14, and 15). In the reactions of **2c** and **2d**, the formation of **4c** and **4d** was always predominantly observed, particularly in the case of using $ZnCl_2$ (Entries 10, 11, and 14). Interestingly, however, by using $Zn(OTf)_2$, the ene product **3d** was formed even during the reaction of **2d**, which has an advantageous structure to allow the Diels–Alder reaction (Entry 14).

On the other hand, a remarkable distinction of catalytic activities between $ZnCl_2$ and $Zn(OTf)_2$ was observed during the reaction of 2-methyl-1,3-pentadiene (**2b**) (Entries 7 and 8). The acidity of $ZnCl_2$ seemed to be too strong for the selective formation of **3b** and **4b**, and only a 7.1% yield of **4b** was obtained along with a considerable formation of undesirable products (Entry 8). $Zn(OTf)_2$, however, gave fairly good results in depressing unfavorable reactions and affording a preferential formation of the ene product **3b** together with the Diels–Alder product **4b** as a minor side reaction (Entry 7).

In the reaction of **2a**—**c**, the methyl group at the 2-position was responsible for the formation of **3a**—**c**. Because of **2c** having a symmetric structure, the methyl group at the 2- or 3-position took part in the production of **3c**, which further reacted with **1** to produce **5c**. In the case of **2d** having a cisoid conformation, a Diels–Alder product **4d** was obtained as a major product, and ene products **3d** and **5d** as minor ones.

$Zn(OTf)_2$ is insoluble in CH_2Cl_2 and is readily isolated from the reaction mixture by conventional filtra-

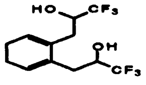
Table 1. Reaction of Trifluoroacetaldehyde **1** and Dienes **2** Using Various Lewis Acids[a)]

Entry	Diene	Catalyst[b)]		Temp	Products yield/%[c)]			Total yield[d)]
		mmol		°C	**3**	**4**	Others	%
1	**2a**	A	(1)	25	54.4	14.5	—[e)]	68.9
2		A	(1)	50	68.9	19.4	—[e)]	88.3
3		B	(1)	25	41.8	30.3	—[e)]	72.1
4		B	(1)	50	55.0	41.0	—[e)]	96.0
5		C	(1)	25	0.3	8.1	—[e)]	8.1
6		C	(0.1)	25	11.9	6.7	—[e)]	18.6
7	**2b**	A	(1)	25	33.9	19.0	—[e)]	52.9
8		B	(1)	25	0	7.1	—[e)]	7.1
9		B	(0.1)	25	15.1	19.2	—[e)]	34.3
10		C	(0.1)	25	0	0	—[e)]	0
11	**2c**	A	(1)	25	24.5	30.6	6.1[f)]	61.2
12		A	(1)	50	29.4	30.9	11.5[f)]	71.8
13		B	(1)	50	11.9	51.6	2.6[f)]	66.2
14		C	(0.1)	25	0	11.9	—[e)]	11.9
15	**2d**	A	(1)	25	7.4	47.9	4.3[g)]	59.6
16		B	(1)	25	0	54.1	13.3[g)]	67.3
17		C	(0.1)	25	0	24.4	0.7[g)]	25.1

a) Reaction conditions; **1** (10 mmol), **2** (20 mmol), solvent (8 ml), time (5 h). b) A: $Zn(OTf)_2/CH_2Cl_2$, B: $ZnCl_2/CH_3NO_2$, C: $AlCl_3/CH_2Cl_2$. c) **3**: the ene product, **4**: the Diels–Alder product. The yield was determined by GC analysis, based on **1**. d) Total yield is **3**+**4** in the Entries 1—9 and **3**+**4**+**5** in the Entries 10—16. e) In the reactions of **2a**, **2b**, and **2c** (Entry 1—10 and 14), complicated products were obtained but could not be identified. f)

5c

g)



5d

tion. This recovered $Zn(OTf)_2$ was successfully used repeatedly in a reaction without any deterioration in its catalytic activity, as shown in Table 2. Consequently, $Zn(OTf)_2$ with CH_2Cl_2 is a useful catalyst that has a great advantage in the reaction of trifluoroacetaldehyde with dienes to produce the corresponding ene products together with Diels–Alder products.

The present work was supported by a Grant-in-Aid for Scientific Research No. 04555200 from the Ministry of Education, Science and Culture.

Table 2. Repeated Use of $Zn(OTf)_2$ in the Reaction of Trifluoroacetaldehyde **1** with Isoprene **2a**[a)]

Number of repeated experiment	Products yield/%[b)]		Total yield/%
	3a	**4a**	
0	54.3	14.6	68.9
1	45.1	14.7	59.8
2	48.2	15.6	63.8

a) Reaction conditions; **1** (10 mmol), **2a** (20 mmol), $Zn(OTf)_2$ (1 mmol), CH_2Cl_2 (8 ml), temp (25 °C), time (5 h). b) The yield was determined by GC analysis, based on **1**.

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