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Selective and Efficient Alcoholyses of Allylic, Secondary- and Tertiary Benzylic Alcohols in the Presence of Iron (III)

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Abstract: An efficient and selective method for the conversion of allylic, secondary- and tertiary benzylic alcohols into their corresponding ethers in the presence of iron(III) as $FeCl_3$ and $Fe(ClO_4)_3$ under solvolytic condition is described. The results obtained from an optically active allylic alcohol show that a carbonium ion is formed during the course of the reaction.

INTRODUCTION

The common method for the conversion of alcohols to ethers consists of the reaction of metal salts of alcohols with different alkylating agents[1-5]. Condensation of alcohols or their salts with aldehydes[6,7], olefins[8], alkyloxides[9], dialkyl phosphites[10] and alcohols[11,12] are also reported. However synthesis of bulky ethers is not possible by most of the reported methods. Furthermore some of these methods suffer from highly acidic or basic conditions or high cost of the reagent.

Ferric perchlorate is a versatile reagent in organic synthesis[14-18]. It is a hygroscopic compound which is easily prepared by the reaction of ferric hydroxide and perchloric acid and can be stored for a long time in a desiccator. We have already reported the use of anhydrous ferric chloride as an efficient and economic catalyst for the alcoholysis of epoxides[13]. In this paper the ability of iron(III) as $FeCl_3$ and $Fe(ClO_4)_3$ as mild reagents for C-O bond cleavage in allylic, secondary- and tertiary benzylic alcohols in the presence of 1°,2° and 3° alcohols is investigated.

RESULTS AND DISCUSSION

Different kinds of allylic, secondary- and tertiary benzylic alcohols were subjected to solvolytic etherification in methanol, n-propanol, i-propanol and t-butanol in the presence of a catalytic amount of Fe(III) (Scheme, Table 1). Comparison of the results show that in similar cases $Fe(ClO_4)_3$ is more reactive

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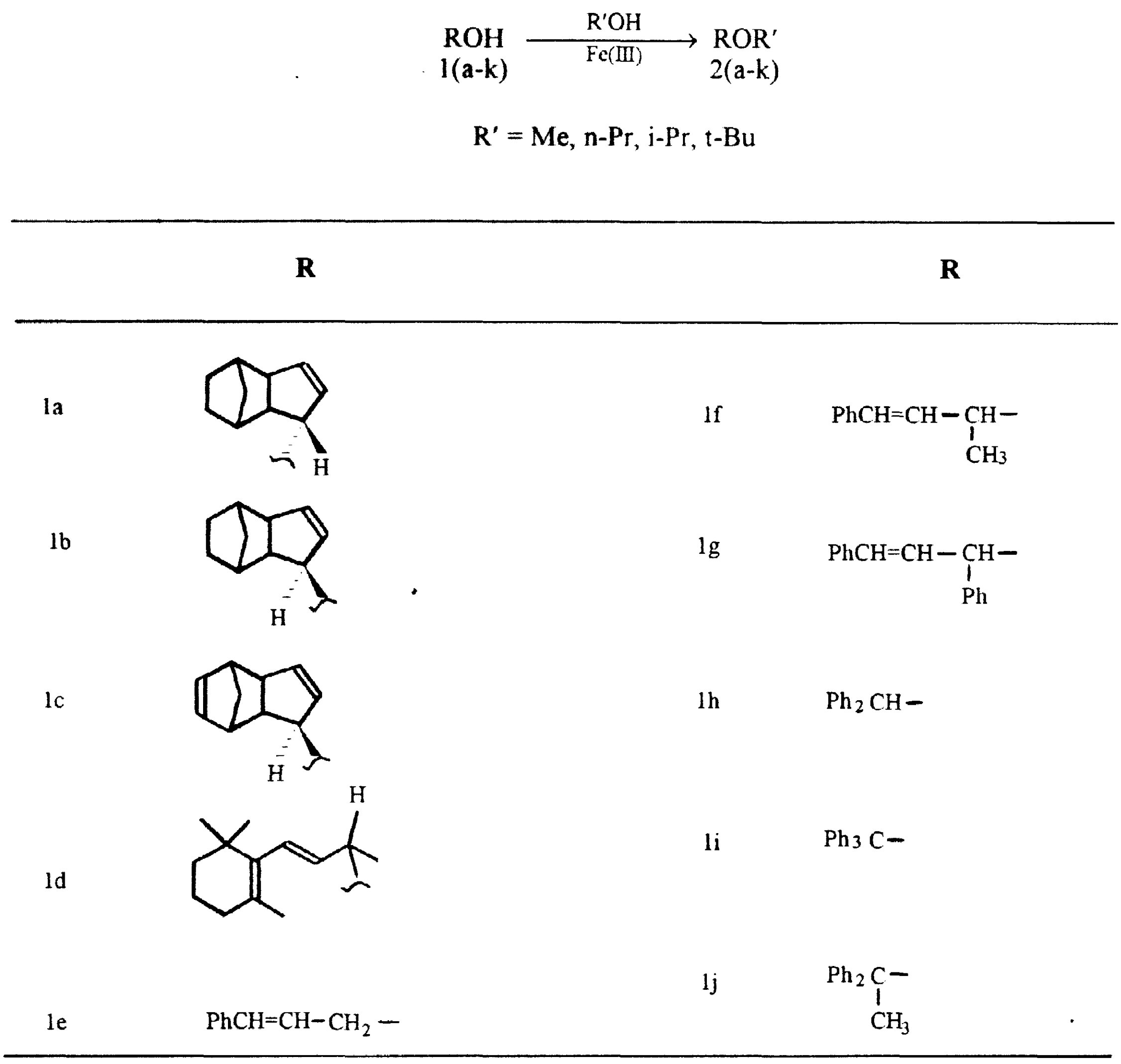


Scheme

than $FeCl_3$ which is consistent with previous reports[19]. Although ferric perchlorate promoted the etherification of secondary benzylic alcohols the same reaction did not proceed in the presence of ferric chloride (Table 1, entries 17-19). Under the same condition etherification of primary benzylic alcohols were not achieved.

In cases where the elimination reaction competed with substitution, the yield of the desired ethers were increased by performing the reactions at lower temperatures (Table 1, entries 23,24).

The formation of oxidation side products was not observed in the cases reported in Table 1. But attempted alcoholyses of 1-phenyl ethanol in the presence of ferric perchlorate ended up with the formation of acetophenone as the sole product. Apparently, oxidation becomes important when C-O bond cleavage is suppressed.

Table 1. Solvolytic Etherification of Allylic, Secondary- and Tertiary Benzylic Alcohols in the Presence of Fe(III) Under Reflux Condition.

Entry	R	$FeCl_3$			$Fe(ClO_4)_3$			R′	Product
		Molar / ratio	Time / (min)	Yield (%)	Molar / ratio	Time / (min)	Yield (%)		
1	1a	0.2	120	75	0.05	5	87	Me	2b
2	1b	0.2	45	83	0.05	5	90	Me	2b
3	1c	0.2	90	90	0.05	5	86	n-Pr	2c
4	1c	0.2	90	75	0.05	5	89	i-Pr	2c
5	1c	0.2	120	60	0.05	10	91	t-Bu	2c
6	1d	0.2	30	87	0.05	60	85	Me	2d
7	1d	0.2	25	95	0.05	5	87	n-Pr	2d
8	1d	0.2	30	83	0.05	10	93	i-Pr	2d
9	1e	0.4	360	85	0.05	5	97	n-Pr	2e
10	1e	0.4	480	78	0.05	30	98	i-Pr	2e
11	1f	0.2	90	87	0.05	20	97	Me	2f
12	1f	0.2	60	90	0.05	10	90	n-Pr	2f
13	1f	0.2	60	78	0.05	10	84	i-Pr	2f
14	1f	0.2	120	62	0.05	65	78	t-Bu	2f
15	1g	0.2	75	85	0.02	5	94	Me	2g
16	1g	0.2	100	70	0.02	5	97	t-Bu	2g
17	1h	no reaction			0.1	50	94	Me	2h
18	1h	no reaction			0.1	75	85	n-Pr	2h
19	1h	no reaction			0.2	105	97	i-Pr	2h
20	1i	0.2	120	45	0.05	5	90	Me	2i
21	1i	0.2	150	90	0.05	5	96	n-Pr	2i
22	1i	no reaction			0.05	40	-	i-Pr	-[I]
23	1j	0.2	120	87	0.05	60	93[II]	Me	2j
24	1j	0.2	120	20[II,III]	0.05	50	25[II,IV]	n-Pr	2j

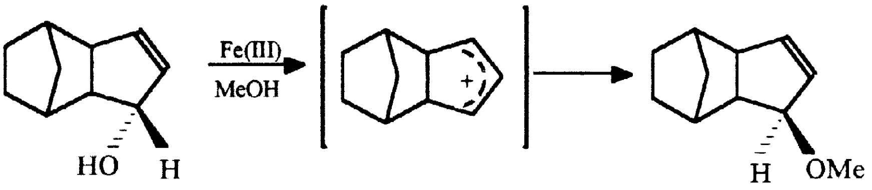
I- Unidentified product.

II- The reaction was performed at 50 °C.

III- Plus 67% elimination product.

IV- Plus 60% elimination product.

Formation of exo-3-methoxy-endo-tricyclo[5,2,1,0^{2,6}]dec-4-ene (**2b**,R′=Me) from both endo-endo-tricyclo[5,2,1,0,^{2,6}]dec-4-ene-3-ol (**1a**) and exo-endo-tricyclo[5,2,1,0^{2,6}]dec-4-ene-3-ol (**1b**) could be strong evidence for the formation of a carbonium ion as an intermediate. There remains a possibility that exo-ether **2b**(R′=Me) has been formed from endo-alcohol **1a** by a S_N2 mechanism. This doubt was overcome by studying the reaction of optically active **1a** in methanol and in the presence of catalytic amount of Fe(III). It was observed that corresponding optically inactive exo-ether **2b**(R'=Me) was formed. This result clearly showed the intermediacy of a carbocation with a plane of symmetry which reacted with nucleophile to form a racemic modification.



$[\alpha]_D^{25}$ = +50° ($CHCl_3$)

exo -racemic dl pair

In Table 2 we have compared our results with some of those which have already reported[11, 12]. In all cases the reactions which were promoted by $Fe(ClO_4)_3$ took place faster and smaller molar equivalents of the reagent was consumed, although in some cases our yields are lower.

Table 2. Comparison of the Results Obtained from Etherification of Alcohols by $Fe(ClO_4)_3$, with CAN[I] and DDQ[II] Under Reflux Condition.

Entry	R	R'	$Fe(ClO_4)_3$			CAN[11]			DDQ[12]		
			Molar ratio	Time (min)	Yield (%)	Molar ratio	Time (min)	Yield (%)	Molar ratio	Time (min)	Yield (%)
1	1b	Me	0.05	5	90	-	-	-	0.2	15	92
2	1c	n-Pr	0.05	5	86	-	-	-	0. 2	120	94
3	1c	i-Pr	0.05	5	89	0.2	30	97	-	-	-
4	1c	t-Bu	0.05	10	91	0.2	15	95	-	-	-
5	1f	n-Pr	0.05	10	90	0.2	60	97	-	-	-
6	1f	i-Pr	0.05	10	84	0.2	60	96	-	-	-
7	1i	Me	0.05	5	90	0.2	15	98	0.2	45	92
8	1i	n-Pr	0.05	5	96	-	-	-	0.2	60	97

I- Ceric ammonium nitrate.

II- 2,3-Dichloro -5,6-dicyanobenzoquinone.

In conclusion, according to the catalytic nature of the reaction, mildness and neutrality of the condition, availability and low cost of the reagent, high yield and ease of work up procedure, the present method could be a useful addition to the available methods in organic synthesis.

EXPERIMENTAL

Products were characterized by comparison of their spectral data and physical properties with those of authentic samples prepared by other methods[11,12,20]. Progress of the reactions were followed by t.l.c. using silica gel polygrams SIL G/UV 254 plates or by g.l.c. using a Shimadzu gas chromatograph GC 14A equipped with flame ionization detector and a glass column packed with DC-200 or SE-30 stationary phases. Infrared spectra were obtained using a Shimadzu 470 spectrophotometer. ^{1}HNMR spectra were run on a Jeol JNM-PMX 60 MHz or a Varian XL-100 spectrometer. Mass spectra were recorded on a Shimadzu GCMS-QP 1000 EX. Optical rotations were measured by a Perkin-Elmer 241 polarimeter. All yields refer to the isolated products.

General Procedure for the Etherification of Alcohols in the Presence of Anhydrous Ferric Chloride.

Anhydrous ferric chloride (0.4-0.8 mmol) was added to a solution of substrate (2 mmol) in an alcoholic solvent (15 mL). The mixture was stirred magnetically under reflux condition for the appropriate time (Table 1). The solvent was evaporated on a rotaryevaporator using a water bath lower than 40 °C. Chromatography on a short silica gel column gave the pure product (45-95%).

Methanolysis of 4-Phenyl-3-Propen-2-ol (2f) as a Typical procedure.

A mixture of 4-phenyl-3-propen-2-ol (0.324 g, 2 mmol), methanol (15 mL) and anhydrous ferric chloride (0.065 g, 0.4 mmol) stirred magnetically under reflux condition. Monitoring by t.l.c. (eluent: n-hexane/ether: 2/1) showed the completion of the reaction after 1.5 hours. The solvent removed in vacuum and the pure product (2f, R'=Me) was isolated by chromatography on a short silica gel column (0.31 g, 87% yield). M^+ (162); ^{1}HNMR ($CDCl_3$), δ (ppm): 7.1 (5H, s), 6.2 (1H, d, J = 16Hz), 5.9 (1H, dd, J = 16, 8Hz) 3.7 (1H, quintet, J = 8 Hz), 3.2 (3H, s), 1.3 (3H, d, J = 6 Hz); n_D^{25}: 1.5488 (Lit[11], 1.5490).

General Procedure for the Conversion of Alcohols to their Corresponding Ethers in the Presence of Ferric Perchlorate.

A solution of the substrate (2 mmol) and the alcoholic solvent (15 mL) was treated with 0.02 to 0.2 molar equivalents of ferric perchlorate (CAUTION: Do not contact metallic equipments with anhydrous ferric perchlorate) and stirred magetically under reflux condition. The progress of reaction was monitored by t.l.c. using n-hexane: ether (5:1) as eluent or by gas chromatography. The mixture was concentrated in vacuum. Chromatography on a short silica gel column gave the desired product(25-98%).

Conversion of Triphenylcarbinol (1i) to its Corresponding Methylether as a Typical Procedure.

In a round-bottomed flask equipped with a condenser and a magnetic stirrer, a solution of triphenylcarbinol (0.52 g, 2 mmol) in methanol (15 mL) was prepared. Ferric perchlorate (0.035 g, 0.1 mmol) was added and the reaction mixture was stirred under reflux condition for 5 minutes. Concentration of the mixture followed by column chromatography gave the desired product (2i, R′ = Me) (0.49 g, 90% yield). M. P. 83-84 °C (Lit[11], 83-84 °C); ^{1}HNMR ($CDCl_3$), δ (ppm): 7.2 (15H, multiplet), 3.0 (3H, s).

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