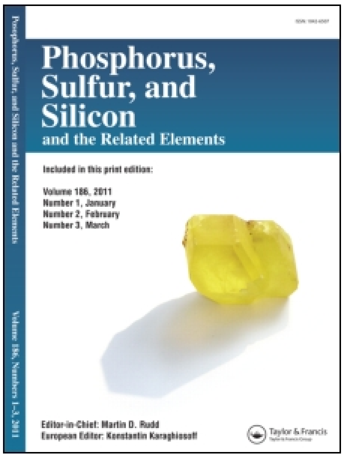

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ALANINE/CHLOROCHROMIC ACID/SILICA GEL: AN EFFICIENT AND SELECTIVE REAGENT FOR THE OXIDATION OF ORGANIC FUNCTIONAL GROUPS

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ALANINE/CHLOROCHROMIC ACID/SILICA GEL: AN EFFICIENT AND SELECTIVE REAGENT FOR THE OXIDATION OF ORGANIC FUNCTIONAL GROUPS

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Alanine/chlorochromic acid/silica gel is a new and selective reagent for the efficient oxidation of sulfides, thiols, oximes, and alcohols. Oxidation of sulfides is solvent dependent. In chloroform at room temperature sulfoxides are formed as the major products, while in carbon tetrachloride or under solvent-free conditions solfones are produced in good-to-excellent yields.

Keywords: Alcohols; chlorochromic acid; oxidation; oximes; sulfides; thiols

Chlorochromic acid and its salts (chlorochromates) are valuable oxidizing agents in organic synthesis.[1] Since the introduction of pyridinium chlorochromate as a reagent for the oxidation of alcohols,[2] many other new derivatives were prepared and applied for the oxidation of organic functional groups.[3–10]

In continuation of our interest in the preparation and application of chlorochromates in the oxidation of organic compounds,[11–16] we wish to introduce a new oxidizing system including alanine, chlorochromic acid, and silica gel(AlCC–SiO_2).

At first, our main intention was to prepare a chiral oxidant for asymmetric oxidation of sulfides to sulfoxides. But attempted preparation of alaninium chlorochromate as a stable compound failed. However,

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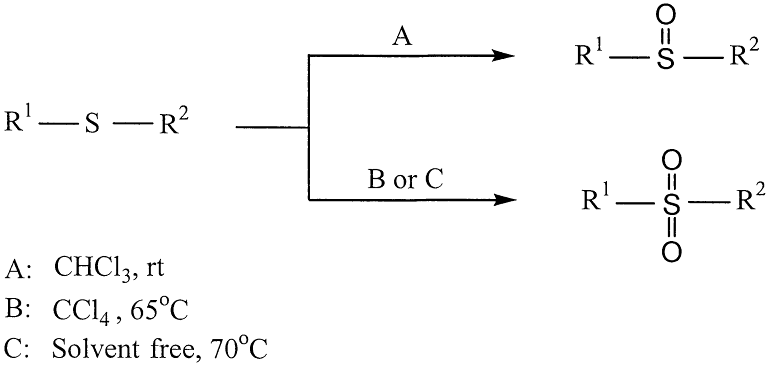
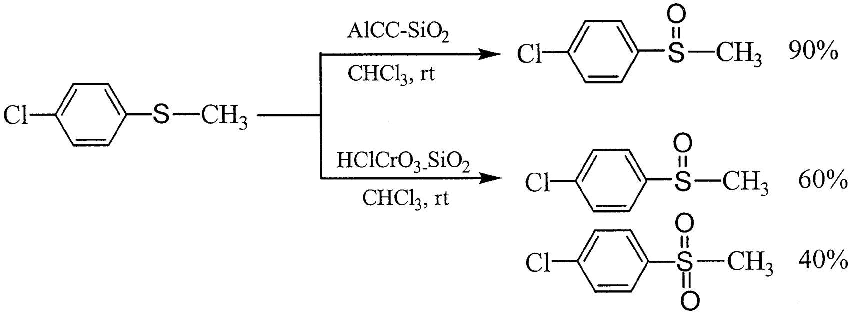
we found that the addition of silica gel to the mixture of alanine and chlorochromic acid gave an orange solid reagent that can be stored and used for several months without any loss of activity. Although we were unsuccessful in the asymmetric oxidation of sulfides to chiral sulfoxides by this reagent, we found many other advantges for the selective oxidation of sulfides, thiols, oximes, and alcohols.

Oxidation of sulfides by AlCC–SiO_2 was solvent dependent. As shown in Scheme 1, oxidation in chloroform at room temperature resulted in the formation of sulfoxides as the sole products, while in carbon tetrachloride at 65°C sulfones were produced in high yields. The results are summarized in the Table I.



SCHEME 1

Different types of sulfides were subjected to oxidation under both conditions, and the corresponding products were isolated satisfactorily (Table I, entries 1–8). In the case of dibutyl sulfide the corresponding sulfone was produced in CCl_4 in 95% yield, but in chloroform the



SCHEME 2

TABLE I Oxidation of Sulfides by AlCC–SiO_2 under Different Conditions

			$CHCl_3$, rt[a]			CCl_4, 65°C[b]			Solvent-free, 70°C[b]		
Entry	R^1	R^2	Time (h)	Oxid./sub. (mole ratio)	Yield (%)	Time (h)	Oxid./sub. (mole ratio)	Yield (%)	Time (h)	Oxid./sub. (mole ratio)	Yield (%)
1	Ph	$PhCH_2$	10	3.5	75	5	3	92	5	3	90
2	4-MeC_6H_4	$PhCH_2$	3.5	3.5	90	4.5	3	94	4	3	92
3	4-ClC_6H_4	$PhCH_2$	8	3.5	70	5.5	3	95	5	3	92
4	Ph	Me	2	3	92	4	3	90	6	3	90
5	4-Cl C_6H_4	Me	2.5	3	93	6.5	3	87	7.5	3	90
6	Ph	Allyl	8	4	85	7.5	3.5	80	7.5	3.5	85
7	4-MeC_6H_4	*n*-Bu	4	3.5	90	6	3	85	7	3	83
8	*n*-Bu	*n*-Bu	5	3.5	65	4.5	3	97	5	3	95

[a] Sulfoxides were produced as the final products.
[b] Sulfones were produced as the final products.

sulfoxide was contaminated with a few percent of the sulfone (Table I, entry 8).

We also studied the same reaction in the absence of solvent and observed that under solvent-free conditions sulfones were formed as the only product. The results are shown in the last column of Table I.

In order to show the role of the amino acid in the selectivity of these reactions, we conducted the oxidation of 4-chlorophenyl methyl sulfide in the absence of the amino acid and observed that the selectivity decreased significantly, and a mixture of the corresponding sulfoxide and sulfone was produced.

AlCC–SiO_2 is also the reagent of choice for the oxidative coupling of thiols to disulfides (Scheme 3 and Table II).

$$R^3\text{—SH} \xrightarrow[\text{CH}_2\text{Cl}_2\text{, rt}]{\text{AlCC-SiO}_2} R^3\text{S—SR}^3$$

SCHEME 3

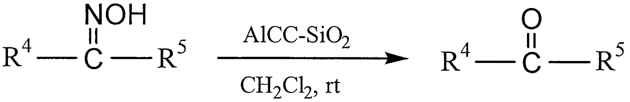
The reactions were performed at room temperature in dichlromethane. Aromatic and benzylic thiols were coupled in the presence of one molar equivalent of the oxidant (Table II, entries 1–4), while in the case of aliphatic thiols the reactions were completed with two molar equivalents of the reagent (Table II, entries 5–8). The primary alcohol group in 2-mercaptoethanol remained intact in the course of the reaction (Table II, entry 8). Overoxidation of the produced disulfides was not observed in any case.

Oximes are a class of important organic compounds both for characterization and purification of aldehydes and ketones.[17] An alternative pathway to aldehydes and ketones is the synthesis of oximes from

TABLE II Oxidation of Thiols by AlCC–SiO_2 in Dichloromethane at Room Temperature

Entry	R^3	Time (h)	Oxid./sub. (mole ratio)	Yield (%)
1	Ph	3	1:1	90
2	4-MeC_6H_4	1	1:1	90
3	4-ClC_6H_4	3.5	1:1	92
4	$PhCH_2$	9	1:1	90
5	Cyclohexyl	7	2:1	85
6	*n*-Bu	5	2:1	70
7	*n*-Octyl	10	2:1	80
8	$HOCH_2CH_2$	11	2:1	50

noncarbonyl substrates followed by a deoximation step.[18] Therefore, we studied the ability of AlCC–SiO$_2$ for the conversion of aldoximes and ketoximes into the carbonyl compounds (Scheme 4).



$$R^4-\overset{NOH}{\overset{\|}{C}}-R^5 \xrightarrow[CH_2Cl_2,\ rt]{AlCC\text{-}SiO_2} R^4-\overset{O}{\overset{\|}{C}}-R^5$$

SCHEME 4

As shown in the Table III, regeneration of benzaldehyde and its derivatives was achieved at room temperature without any overoxidation of the produced aldehydes (Table III, entries 1–5). Aromatic and cyclic ketoximes were also converted to the corresponding ketones in the presence of 1.5 molar equivalents of the oxidant (Table III, entries 6–13). Decanal oxime and 2-heptanonoxime as two model compounds

TABLE III Oxidation of Oximes by AlCC–SiO$_2$ in Dichloromethane at Room Temperature

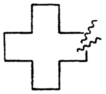
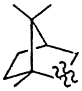
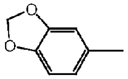
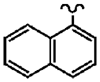
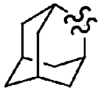
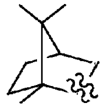
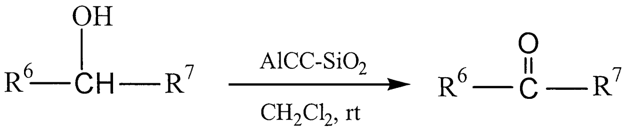
Entry	R^4	R^5	Time (h)	Oxid./sub. (mole ratio)	Yield (%)
1	Ph	H	1	1.5	85
2	4-ClC$_6$H$_4$	H	1.5	1.5	92
3	4-O$_2$NC$_6$H$_4$	H	4	1.5	85
4	2-HOC$_6$H$_4$	H	11	1.5	75
5	2,4-(MeO)$_2$C$_6$H$_3$	H	2	1.5	85
6	Ph	Me	2.	1.5	85
7	4-MeC$_6$H$_4$	Me	1.5	1.5	90
8	4-BrC$_6$H$_4$	Me	2.5	1.5	92
9	Ph	Ph	2	1.5	90
10			4	1.5	92
11			5	1.5	90
12			12	1.5	65
13			9	1.5	90
14	PhCH=CH	H	4	1.5	85
15	*n*-Nonyl	H	9	1.5	85
16	*n*-Pentyl	Me	14	1.5	80

TABLE IV Oxidation of Alcohols by AlCC–SiO_2 in Dichloromethane at Room Temperature

Entry	R^6	R^7	Time (h)	Oxid./sub. (mole ratio)	Yield (%)
1	4-$PhCH_2OC_6H_4$	H	0.5	1.5:1	85
2	4-ClC_6H_4	H	1.5	1.5:1	91
3	2-$O_2NC_6H_4$	H	15	1.5:1	61
4	4-$MeOC_6H_4$	H	1.2	1.5:1	92
5	2-$PhOC_6H_4$	H	15	2:1	80
6		H	2.5	1.5:1	92
7	PhCO	Ph	8	2:1	65
8	Ph	Ph	2	1.5:1	90
9		Me	1.5	1.5:1	91
10			3	2:1	90
11			3.5	2:1	93
12			20	2:1	85
13	*n*-Hexyl	H	4	2:1	80
14	*n*-Pentyl	Me	3.5	2:1	85

of linear aliphatic aldoximes and ketoximes were subjected to oxidation under the same conditions, and the carbonyl compounds were produced in 85 and 80% yields, respectively (Table III, entries 15 and 16).

Selective oxidation of primary and secondary alcohols was also achieved by AlCC–SiO_2 at room temperature (Scheme 5 and Table IV).



$$R^6-\overset{\large OH}{\overset{|}{C}H}-R^7 \xrightarrow[CH_2Cl_2,\ rt]{AlCC\text{-}SiO_2} R^6-\overset{O}{\overset{\|}{C}}-R^7$$

SCHEME 5

Primary benzylic alcohols with electron-releasing and electron- withdrawing substituents were oxidized by using 1.5–2 molar equivalents of the oxidant, and the corresponding carbonyl compounds were obtained in good-to-excellent yields (Table IV, entries 1–6).

Benzhydrol and 1-(1-naphthyl) ethanol, as two model compounds for secondary benzylic alcohols, were also subjected to oxidation satisfactorily (Table IV, entries 8 and 9).

Oxidation of linear and cyclic saturated primary and secondary alcohols was also achieved in the presence of 2 molar equivalents of AlCC–SiO_2 at room temperature (Table IV, entries 10–14).

In conclusion, AlCC–SiO_2 is a very efficient and selective reagent for the oxidation of sulfides, thiols, oximes, and alcohols. The yields are high and the workup procedure is very simple, including filtration followed by evaporation of the solvent.

EXPERIMENTAL

All products are known compounds and were characterized by comparison of their spectral data (^{1}H NMR and IR) and physical properties with those reported in the literature. Carbonyl compounds were characterized by comparasion of the melting point of their 2,4-dinitrophenylhydrazone derivatives with the data reported in the literature. Yields refer to isolated products or are based on the weight of 2,4-dinitrophenylhydrazone derivatives.

Preparation of AlCC–SiO_2

CrO_3 (2.52 g, 25 mmol) was added gradually to 6M HCl (4.8 ml, 29 mmol) with stirring at room temperature. L-(+)-alanine (2.25 g, 25 mmol) was added slowly to the solution over 15 min. While the mixture was stirred vigorously, a mixture of silica gel (13.9 g, silica gel 60, 70–230 mesh; Fluka) in acetone (20 ml) was added within 15 min at room temperature. Acetone was evaporated under reduced pressure. The resulting yellow-orange powder was dried in a vacuum desiccator at ambient temperature.

General Procedure for the Oxidation of Sulfides to Solfoxides in Chloroform

A mixture of sulfide (1 mmol) and the oxidant (3–4 mmol) was prepared in chloroform (8 ml). The mixture was stirred at room temperature for the appropriate period of time (Table I). The completion of the reaction was confirmed by TLC (eluent: ethyl acetate/*n*-hexane, 1/1). Then the mixture was filtered on a sintered glass funnel and the residue was washed thoroughly with chloroform (30 ml). Evaporation of the solvent gave the corresponding sulfoxides, which were recrystallized from ethanol-water (5:1 v/v).

General Procedure for the Oxidation of Sulfides to Sulfones in CCl_4

Sulfide (1 mmol) was dissolved in CCl_4 (10 ml), and the oxidizing agent (3–3.5 mmol) was added in small portions to the solution. The heterogeneous mixture was magnetically stirred at 65°C (reaction times are indicated in Table I). The mixture was then filtered on a sintered glass funnel and the residue was washed thoroughly with chloroform. Evaporation of the solvent gave the coresponding sulfones in 80–90% yields after recrystallization from ethanol.

General Procedure for the Oxidation of Sulfides to Sulfones under Solvent-Free Conditions

The oxidizing agent (3–3.5 mmol) and sulfide (1 mmol) were placed in a mortar and mixed. The mixture was heated in an oven at 70°C for the appropriate period (Table I). Porgress of the reactions was monitored by dissolving a sample in chloroform and using thin layer chromatography on silica gel (eluent: diethyl ether/*n*-hexane, 1/1). Chloroform was added (30 ml) to the resulting solid mixture, and the mixture was then filtered on a sintered glass funnel, and the residue was washed with chloroform (30 ml). Evaporation of the solvent gave the corresponding sulfones in 80–95% yields.

General Procedure for the Oxidation of Thiols by AlCC–SiO_2

The oxidant (1–2 mmol) was added to a solution of thiol (1 mmol) in dichloromethane (7 ml). The mixture was stirred at room temperature for the approprite period (Table II). The completion of the reaction was confirmed by TLC (eluent: MeOH/ HOAc, 5/1). Then the mixture was filtered on a sintered glass funnel, and the residue was washed thoroughly with diethyl ether (30 ml). Finally, evaporation of the solvent gave the corresponding disulfides, which were recrystallized from methanol to afford the pure products.

General Procedure for the Conversion of Oximes into Carbonyl Compounds

A mixture of oxime (1 mmol), AlCC–SiO_2 (1.5 mmol), and dichloromethane (7 ml) was stirred at room temperature for the specified time

(Table III). The reaction was monitored by TLC (eluent: diethyl ether/*n*-hexane, 1/4). After completion of the reaction, the mixture was filtered on a sintered glass funnel and the residue was washed thoroughly with dichloromethane (30 ml). Evaporation of the solvent gave the corresponding carbonyl compounds in 70–95% yields, which were isolated as their 2,4-dinitrophenylhydrazone derivatives.

General Procedure for the Oxidation of Alcohols by AlCC–SiO_2

In a round-bottomed flask, the oxidizing agent (1.5–2 mmol) was added to a solution of alcohol (1 mmol) in dichloromethane (7 ml). The reaction mixture was stirred at room temperature until the alcohol was completely consumed (Table IV). Progress of the reaction was monitored by TLC (eluent: toluene/ethyl acetate, 2/1). The mixture was filtered on a sintered glass funnel, and the residue was washed thoroughly with dichloromethane (30 ml). Evaporation of the solvent gave the corresponding carbonyl compounds in 80–94% yields, which were isolated as their 2,4-dinitrophenylhydrazone derivatives.

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