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$TaCl_5$-Silicagel and $TaCl_5$ as new Lewis acid systems for selective tetrahydropyranylation of alcohols and thioacetalisation, trimerisation and aldolisation of aldehydes.

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Abstract: $TaCl_5$ adsorbed on silicagel has been utilized for the first time as Lewis acid catalyst for protection of aldehydes and alcohols as thiocetals and THP ethers respectively. Similarly $TaCl_5$ has been exploited as an useful Lewis acid for chemoselective trimerisation and/or aldolisation of aldehydes. © 1997 Elsevier Science Ltd.

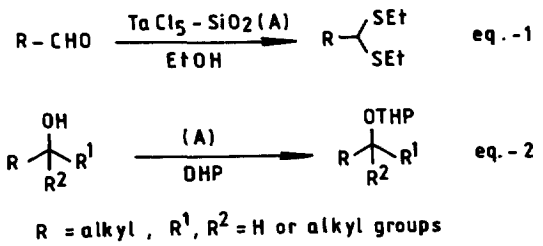
INTRODUCTION

Group VB elements especially low valent tantalum and niobium halides ($TaCl_3$ and $NbCl_3$) have recently come into prominance due to their ability to form complexes with acetylenes and inturn enable to add on to electrophilic sites viz., carbonyl compounds[1], isocyanates[2] and hydrazones.[3] Surprisingly, however, these two elements in higher oxidation state ($TaCl_5$ and $NbCl_5$) have not been utilized for any purposeful transformation. The only report pertaining to utility of $TaCl_5$ as Lewis acid catalyst in Diels Alder reaction is an exception.[4] It is well documented that, Lewis acids are very useful catalysts in tetrahydropyranylation of alcohols and thioacetalisation of aldehydes and extensive studies have been done on this.[5] Similarly the cyclotrimerisations and aldolisations of aldehydes is an inherent phenomenon in presence of Lewis acid.[6] The 1,3,5-trioxanes formed out of cyclotrimerisation are specially useful in colour photography,[7] burning regulators in fumigants for potato sprouting inhibition and separation of closely boiling aldehyde and ketone mixtures.[8] Interestingly the conjugated aldehydes formed out of self aldolisation mediated by Lewis acids are useful in Diels-Alder reaction and are also good Michael acceptors.[9]

RESULTS AND DISCUSSION

Rapid thioacetalisation of aldehydes and tetrahydropyranylation of alcohols using $TaCl_5$-SiO_2.

The recent trends in utilizing solid supported reagents for functional group transformations[10] which offer many advantages has prompted us to explore the possibility of utilizing the hitherto not reported $TaCl_5$-silicagel as an excellent Lewis acid catalyst. The results pertaining to rapid and very high yielding thioacetalisation of aldehydes (equation 1) and tetrahydropyranylation of alcohols (equation 2) are tabulated (table 1). It is very interesting to note that, $TaCl_5$ when adsorbed on silicagel acted as a more efficient catalyst even at low concentrations and required less reaction times when compared to use of $TaCl_5$ alone.



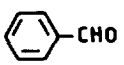
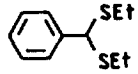
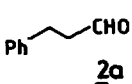
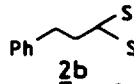
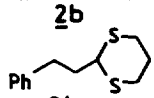
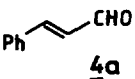
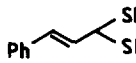
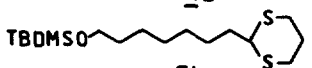
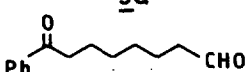
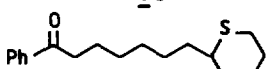
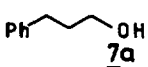
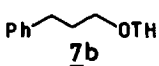
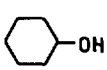
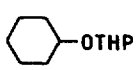
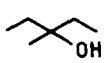
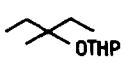
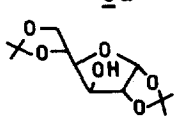
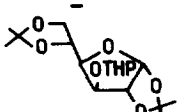
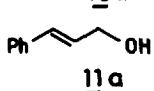
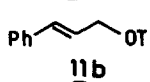
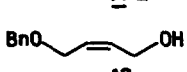
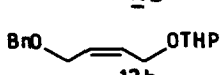
When a range of aldehydes (table 1, entries 1-6) were exposed to ethanethiol or propanedithiol as represented, in dry CH_2Cl_2 containing 10mol% $TaCl_5$-SiO_2, a rapid and clean thioacetalisation was observed in excellent yields. Conjugated aldehyde (entry 4), 8-O-t-butyldimethylsilyl-1-octanal (entry 5) were thioacetalized without any difficulty. The keto aldehyde substrate (entry 6) underwent protection only at the aldehyde site. The usual problem encountered for protection of aldehydes having α-hydrogen (entries 2,3,5 and 6) was not noticed using the present catalyst system.[11]

This remarkably efficient Lewis acidity of $TaCl_5$-silicagel has also been demonstrated in tetrahydropyranylation of a variety of alcohols which include 1° alcohol (entry 7), 2° alcohol (entry 8), 3° alcohol (entry 9), an acid labile sugar substrate (entry 10), cinnamyl alcohol (entry 11) and benzyloxy substrate (entry 12). In all the cases studied, the reaction was completed within 4-10 minutes yielding 72-98% of the isolated products.

Trimerisation and aldolisation of aldehydes using $TaCl_5$:

While working on the establishment of $TaCl_5$ as a mild Lewis acid for tetrahydropyranylation and thioacetalisation of alcohols and aldehydes respectively (vide supra), we have noticed that selective trimerisation and/or aldolisation (equation 3) could be achieved with $TaCl_5$ by varying the solvent. The results are presented in Table 2.

Table 1 Thioacetalisation and tetrahydropyranylation

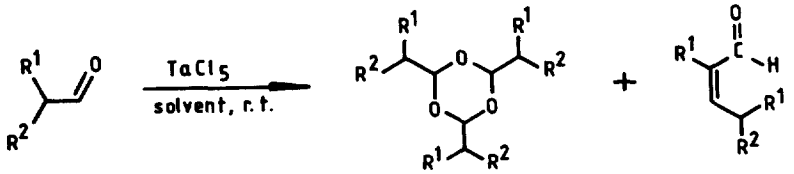
Entry	Substrate	Reaction condition	Product (Time)	Yield (%)
1	 1a	A	 (2 min) 1b	98 (60)
2	 2a	A	 (5min) 2b	92 (55)
3	〃	B	 (4min) 3b	93 (58)
4	 4a	A	 (5min) 4b	96
5	 5a	B	 (8min) 5b	89
6	 6a	A	 (5min) 6b	91
7	 7a	C	 (4min) 7b	98 (56)
8	 8a	C	 (5min) 8b	94
9	 9a	C	 (10min) 9b	76
10	 10a	C	 (10 min) 10b	71
11	 11a	C	 (5min) 11b	88
12	 12a	C	 (6 min) 12b	86

A. $TaCl_5$ -silicagel, Ethanethiol, CH_2Cl_2.

B. $TaCl_5$-silicagel, Propanedithiol, CH_2Cl_2.

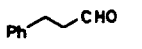
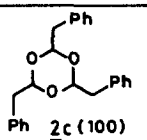
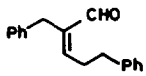
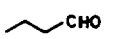
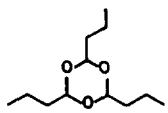
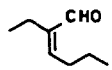
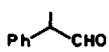
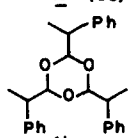
C. $TaCl_5$-silicagel, Di hydropyran, CH_2Cl_2.

Yields in parentheses represent to isolated yield of the product when 20 mole % $TaCl_5$ alone was used.



eq. 3

Table 2: Trimerisation and/or aldolisation

Entry	Aldehyde	Solvent	Reaction time (h)	Trimer (%)	(%) Aldol product	Overall yield (%)
1	 **2a**	Neat	2	 **2c** (100)	 **2d** (0)	82
2	**2a**	Ether	4	**2c** (50)	**2d** (50)	76
3	**2a**	CH_2Cl_2	4	**2c** (20)	**2d** (80)	72
4	**2a**	DME	4	**2c** (15)	**2d** (85)	80
5	 **13a**	Neat	2	 **13c** (100)	 **13d** (0)	81
6	**13a**	Ether	4	**13c** (40)	**13d** (60)	69
7	**13a**	CH_2Cl_2	5	**13c** (50)	**13d** (50)	75
8	**13a**	DME	6	**13c** (50)	**13d** (50)	70
9	 **14a**	Neat	2	 **14c** (100)	–	86

In a typical experiment when 3-phenyl propanaldehyde **2a** and $TaCl_5$ (25 mole%) were stirred together in absense of solvent, the 1,3,5-cyclotrimer **2c** was formed exclusively. However when CH_2Cl_2 or DME or dry ether were used as solvent, self aldolisation was competetive and **2c** was formed in varying ratios (see table 2). This selelctive trimerisation and/or aldolisation has been achieved on few other commercial aldehydes which include butyraldehyde **13a** and 2-phenyl propanaldehyde **14a**. However benzaldehyde and anisaldehyde resisted the reaction conditions and were recovered intact.

CONCLUSION

In conclusion, $TaCl_5$-SiO_2 system has been utilised for the first time as a new and fairly efficient catalyst for thioacetalisation and tetrahydropyranylation even at low concentrations. Similarly $TaCl_5$ was demonstrated as a useful reagent for selective trimerisation and/or aldolisation of aldehyde which is dependent on the nature and presence or absence of solvent. The further usefulness in other Lewis acid mediated reactions viz., Prins and Ritter reactions is currently being investigated.

EXPERIMENTAL SECTION

IR spectra were recorded on Perkin-Elmer infrared 683 spectrophotometer with NaCl optics. ^1H NMR spectra were recorded on varian Gemini - 200 MHz. The samples were made in $CDCl_3$ using tetramethyl silane as the internal standard and are given in the δ scale. Mass measurements were carried out on CEC-21-110B double focussing mass spectrometer operating at 70 eV and are given in mass units (m/z). TLC was performed on 0.25 mm E. Merck precoated silica plates (60F-254). All the products were purified by column chromatography on silica gel (100-200 mesh). Dihydropyran, ethanethiol and 1,3-propane dithiol were purchased from Aldrich and used directly. All reagents including $TaCl_5$ and substrates 1a, 2a, 4a, 7a, 8a, 10a, 11a, 13a and 14a were obtained from Aldrich Chemical Company and were used as such without any further purification.

Preparation of $TaCl_5$-silica gel:

The tantalum (V) chloride - silica gel was prepared by mechanically shaking chromatography grade silica gel (10g, 100-200 mesh, dried overnight at 100°C) and tantalum (V) chloride (3g) for 20 h.

General Procedure for thioacetalisation of aldehydes:

To a mixture of anhydrous CH_2Cl_2 (10 ml), benzaldehyde **1a** (0.53g, 5 mmol) and ethanethiol (0.75 ml, 10 mmol) at room temperature under N_2 was added 10 mole percent of $TaCl_5$-SiO_2 (180 mg wt which is equivalent to 42 mg of $TaCl_5$ and 138 mg of SiO_2) and stirred for 2 min. To the reaction mixture was added $NaHCO_3$ (60 mg) and stirred for further 5 min followed by filtration through a small pad of silica gel, evaporation of volatiles produced benzaldehyde diethylthioacetal **1b**[12] (1.03g, 98%) as a colorless liquid. bp 115°-121°/5mm (lit[12] 125-130°/5mm); ^1H NMR: δ 7.30 (m, 5H), 4.89 (s, 1H), 2.50 (q, 4H, J = 8Hz), 1.20 (t, 6H, J = 8 Hz); MS : m/z 212 (M^+).

3-Phenyl-propan-1-al-diethylthioacetal (2b): Yield : 1.11g, 92%; ^1H NMR ($CDCl_3$): δ 7.15-7.35 (m, 5H), 3.7 (t, 1H, J = 4.4 Hz), 2.85 (t, 2H, J = 6.6 Hz), 2.55-2.75 (m, 4H), 2.1 (q, 2H, J = 6 Hz), 1.30 (t,

6H, J = 6 Hz) ; MS: m/z 240 (M^+); HRMS Calcd. for $C_{13}H_{20}S_2$: 240.4210 ; Found : 240.4221.

3-Phenyl-propan-1-al-1,3-propanedithioacetal (3b): 3b was prepared from **2a** (5 mmol) following an identical procedure by suing 1,3-propanedithiol (5 mmol) instead of ethanethiol. Yield : 1.04 g, 93% ; ^1H NMR ($CDCl_3$): δ 7.15-7.35 (m, 5H), 3.95 (t, 1H, J = 7.7 Hz), 2.80 (t, 2H, J = 8 Hz), 2.75-2.95 (m, 4H), 2.0-2.15 (m, 2H), 1.25-1.4 (m, 2H) ; HRMS : Calcd. for $C_{12}H_{16}S_2$: 224.3784, Found 224.3791.

Cinnamaldehyde diethylthiocetal (4b)[11] : Yield : 1.14 g, 96% ; ^1H NMR ($CDCl_3$) : δ 7.3 (m, 5H), 6.4 (d, 1H, J = 15.5 Hz), 6.0 (dd, 1H, J = 6.5, 15.5 Hz), 4.4 (d, 1H, J = 6.5 Hz), 2.4-2.6 (m, 4H), 1.1-1.3 (m, 6H) ; MS: m/z 238 (M^+); HRMS Calcd for $C_{13}H_{18}S_2$: 238.4052 ; Found : 238.4061.

8-O-tert-butyldimethylsilyl octan-1-al-1,3-propanedithioacetal (5b): Yield: 1.56 g, 89%; ^1H NMR ($CDCl_3$) : δ 4.00 (t, 1H, J = 6 Hz), 3.60 (t, 2H, J = 6 Hz), 2.75-2.90 (m, 4H), 1.80-2.00 (m, 2H), 1.2-1.6 (m, 12H), 0.91 (s, 9H), 0.25 (s, 6H); MS : m/z 348 (M^+); HRMS Calcd for $C_{17}H_{36}OS_2Si$: 348-6763 ; Found : 348-6771.

8-Oxo-8-phenyl-octan-1-al-1,3-propane dithioacetal (6b) : Yield : 1.41 g, 91%; ^1H NMR ($CDCl_3$) : δ 7.95 (d, 2H, J = 6 Hz), 7.40-7.60 (m, 3H), 4.00 (t, 1H, J = 5 Hz), 2.95 (t, 2H, J = 5 Hz), 2.75-2.90 (m, 4H), 2.2-2.4 (m, 2H), 1.3-1.6 (m, 8H) ; IR ($CHCl_3$) : ν 1700 cm^{-1} ; MS: m/z 308 (M^+); Analysis calcd for $C_{17}H_{24}OS_2$: C, 66.29; H, 7.85; Found: C, 66.31, H, 7.89.

General procedure for tetrahydropyranylation of alcohols:

To a stirred mixture of 3-phenylpropan-1-ol **7a** (0.68 g, 5 mmol), DHP (0.63 ml, 7 mmol) in CH_2Cl_2 (12 ml) at room temperature was added 10 mol percent of $TaCl_5$ silica gel (180 mg wt) and stirred for 4 min. The usual workup (vide supra) furnished the desired tetrahydropyranyl ether **7b**[13] as colorless liquid (1.07 g), in 98% yield. ^1H NMR : δ 7.2-7.3 (m, 5H), 4.55 (br s, 1H) 3.8 (m, 2H), 3.7-3.9 (m, 2H), 2.7 (t, 2H, J = 5 Hz), 1.85 (m, 2H), 1.45-1.8 (m, 6H) ; MS: m/z 220 (M^+).

O-Tetrahydropyranyl cyclohexanol (8b)[14]**:** Yield: 0.86 g, 94%, b.p 79-80°/2 torr ^1H NMR ($CDCl_3$) : δ 4.65 (br s, 1H), 3.80-3.95 (m, 1H), 3.40-3.60 (m, 2H), 1.1-1.9 (m, 16H); MS: m/z 184 (M^+); HRMS Calcd. for $C_{11}H_{20}O_2$: 184.2670; Found: 184.2674.

3-O-Tetrahydropyranyl-3-methyl pentane (9b)[15]**:** Yield : 0.7 g, 76% ; ^1H NMR ($CDCl_3$) : δ 4.85 (dist. t, 1H), 3.8-4.1 (m, 1H) 3.5-3.7 (m, 1H), 1.3-2.0 (m, 10H), 1.2 (s, 3H), 0.8-1.0 (m, 6H); MS: m/z 186 (M^+).

1,2:5,6-Di-O-isopropylidene-3-O-tetrahydropyranyl glucofuranoside (10b)[16]: Yield: 1.22 g, 71%; ^1H NMR ($CDCl_3$): δ 5.85 (d, 1H, J = 4 Hz), 4.7-4.85 (m, 1H), 4.3-4.5 (m, 2H), 3.8-4.2 (m, 4H), 3.4-3.6 (m, 2H), 1.0-1.95 (m, 18H); MS: m/z 344 (M^+); HRMS calcd. for $C_{17}H_{28}O_7$: 344.4040; Found: 344.4042.

1-O-Tetrahydropyranyl-3-phenyl-2-E-propen-1-ol (11b)[17]: Yield: 0.96 g, 88%; b.p 125-130°/ 1 torr; ^1H NMR ($CDCl_3$): δ 7.30 (m, 5H), 6.48-6.62 (d, 1H, J = 18.1 Hz), 6.20-6.39 (dt, 1H), 4.95 (dt, 1H), 4.03-4.22 (m, 2H), 3.79-3.98 (m, 1H), 3.45-3.62 (m, 1H), 1.50-2.00 (m, 6H) ; MS: m/z 218 (M^+).

4-Benzyloxy-1-O-tetrahydropyranyl-2-Z-buten-1-ol (12b): Yield: 1.12 g, 86%; ^1H NMR ($CDCl_3$): δ 7.2-7.5 (m, 5H), 5.7-5.9 (m, 2H), 5.0 (br s, 1H), 4.52 (s, 2H) 4.0-4.35 (m, 2H), 3.8-4.0 (m, 2H), 3.41-3.6 (m, 2H), 1.5-2.0 (m, 6H); MS: m/z 262 (M^+); HRMS Calcd for $C_{16}H_{22}O_3$: 262.3480 ; Found : 262.3487.

Typical experimental procedure for trimerisation of aldehydes:

To $TaCl_5$ (175 mg, 1 mmol) under nitrogen atmosphere was added 3-phenyl propanaldehyde **2a** (0.67 g, 5 mmol) and stirred for 2h. Reaction mixture was diluted with 25 ml of ether, washed with saturated sodium bicarbonate solution (10 ml), water (10 ml), and brine (10 ml). Evaporation of volatiles furnished the desired 2,4,6-tri (2'-phenyl ethyl)-1,3,5-trioxane **2c**[18] (0.55 g, 82%) as a colorless syrup. ^1H NMR ($CDCl_3$): δ 7.10-7.41 (m, 15H), 4.80 (t, 3H, J = 4 Hz), 2.75 (t, 6H, J = 6 Hz), 1.90-2.110 (m, 6H); IR (neat) : 2900, 2750, 1150, 3050, 1600 cm^{-1}. MS: m/z 402 (M^+).

2,4,6, Tri-n-propyl-1,3,5-trioxane (13c)[19]: Yield (0.25 g, 81%), ^1H NMR ($CDCl_3$) : δ 4.85 (t, 3H), 1.15-1.70 (m, 12H), 0.91 (dist. t, 9H); IR (neat) : 2950, 2750, 1150 cm^{-1}. MS : m/z 236 (M^+).

2,4,6 Tri-(1'-phenyl ethyl)-1,3,5-trioxane (14c): Yield (0.57 g, 86%), ^1H NMR ($CDCl_3$) : δ 7.1-7.4 (m, 15H), 4.80 (m, 3H), 3.05 (m, 3H), 1.25-1.50 (three sets of doublets, 9H J = 6.3 Hz): IR (neat) : 2950, 2750, 1150, 3050, 1600 cm^{-1}. MS: m/z 402 (M^+).

Typical experimental procedure for aldolisation and trimerisation:

To $TaCl_5$ (175 mg, 1mmol) in argon atmosphere anhydrous ether or DME or CH_2Cl_2 (5 ml, see table) was added phenyl propanaldehyde **2a** (340 mg, 5 mmol) and stirred for 4h. Reaction mixture was diluted with water (10 ml) and extracted with ether (3x15 ml). Organic layer was evaporated under reduced pressure, to produce mixture of trimer (**2c**) and aldol product of (**2d**) in varying ratios (see table 2). ^1H NMR ($CDCl_3$) of **2d** : δ 9.40 (s, 1H), 6.90-7.32 (m, 10H), 6.55 (t, 1H, J = 5.2 Hz), 3.52 (s, 2H), 2.62-2.75 (m, 4H); IR (neat): 2950, 3100, 2750, 1710, 1600 cm^{-1}. MS: m/z 250 (M^+).

2-Ethyl-2-hexen-1al (13d) : With the above general procedure butyraldehyde **13a** produced mixture of trimer **13c** and aldol product of **13d** in varying ratios (see table 2). ^{1}H NMR ($CDCl_3$) of **13d**: δ 9.26 (s, 1H), 6.31 (t, 1H, J = 6 Hz), 2.10-2.35 m, 4H), 1.15-1.30 (m, 2H), 0.95 (t, 6H, J = 7.6 Hz); IR (neat) : 2950, 3100, 1600, 2750, 1710 cm^{-1}. MS: m/z 127 (M^+).

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