This article was downloaded by: [University of California Santa Cruz] On: 16 October 2014, At: 13:14 Publisher: Taylor & Francis Informa Ltd Registered in England and Wales Registered Number: 1072954 Registered office: Mortimer House, 37-41 Mortimer Street, London W1T 3JH, UK



Synthetic Communications: An International Journal for Rapid Communication of Synthetic Organic Chemistry

Publication details, including instructions for authors and subscription information: <u>http://www.tandfonline.com/loi/lsyc20</u>

Nitrogen Ligand Complexes of Metal Chlorides as Effective Catalysts for the Highly Regioand Chemoselective Silylation of Hydroxyl Groups with Hexamethyldisilazane (HMDS) at Room Temperature

H. Firouzabadi^a, A. R. Sardarian^a, Z. Khayat^a, B. Karimi^a & S. Tangestaninejad^a ^a Chemistry Department, Shiraz University, Shiraz, 71454, Iran Published online: 22 Aug 2006.

To cite this article: H. Firouzabadi , A. R. Sardarian , Z. Khayat , B. Karimi & S. Tangestaninejad (1997) Nitrogen Ligand Complexes of Metal Chlorides as Effective Catalysts for the Highly Regio- and Chemoselective Silylation of Hydroxyl Groups with Hexamethyldisilazane (HMDS) at Room Temperature, Synthetic Communications: An International Journal for Rapid Communication of Synthetic Organic Chemistry, 27:15, 2709-2719, DOI: <u>10.1080/00397919708004140</u>

To link to this article: <u>http://dx.doi.org/10.1080/00397919708004140</u>

Taylor & Francis makes every effort to ensure the accuracy of all the information (the "Content") contained in the publications on our platform. However, Taylor & Francis, our agents, and our licensors make no representations or warranties whatsoever as to the accuracy, completeness, or suitability for any purpose of the Content. Any opinions and views expressed in this publication are the opinions and views of the authors, and are not the views of or endorsed by Taylor & Francis. The accuracy of the Content should not be relied upon and should be independently verified with primary sources of information. Taylor and Francis shall not be liable for any losses, actions, claims, proceedings, demands, costs, expenses, damages, and other liabilities whatsoever or howsoever caused arising directly or indirectly in connection with, in relation to or arising out of the use of the Content.

This article may be used for research, teaching, and private study purposes. Any substantial or systematic reproduction, redistribution, reselling, loan, sub-licensing, systematic supply, or distribution in any form to anyone is expressly forbidden. Terms & Conditions of access and use can be found at <u>http://www.tandfonline.com/page/terms-and-conditions</u>

NITROGEN LIGAND COMPLEXES OF METAL CHLORIDES AS EFFECTIVE CATALYSTS FOR THE HIGHLY REGIO- AND CHEMOSELECTIVE SILYLATION OF HYDROXYL GROUPS WITH HEXAMETHYLDISILAZANE (HMDS) AT ROOM TEMPERATURE

H.Firouzabadi*, A.R. Sardarian, Z. Khayat, B.Karimi, S. Tangestaninejad

Chemistry Department, Shiraz University, Shiraz 71454, Iran

Abstract: $Zn(bipy)_3Cl_2$, $Fe(bipy)Cl_3$, and Fe(tpp)Cl are effective catalysts for silylation of hydroxy groups with HMDS at room temperature in dry CH₃CN. High selectivity is observed between primary and secondary hydroxy functional groups. This method absolutely discriminates other functional groups containing labile hydrogen atoms.

The importance of the hydroxyl group functionality in organic chemistry is reflected by the continuous appearance of methods for developing complex structures based on the chemical interconversion of this functional group in the literature. A limiting factor in some cases in the presence of more than one oxygen function of comparable reactivity in the molecule to be transformed. This difficulty is circumvented by the use of protective group, a practice which in theory allows free manipulation of the desired functionality. However, it is only in a few cases, this practice reaches an acceptable practical level, mostly due to the difficulties involved in selectivity of protecting and of regenerating specific hydroxyl groups.

^{*} Corresponding author

Since the introduction of silyl ethers for the protection of hydroxy groups, the use of organosilicon compounds as protective groups in organic synthesis has undergone an explosivdevelopment. It is fair to say that, to date, in any synthesis of reasonable complexity, the use of one kind or another of organosilicon reagent is unavoidable¹.

Many reagents, such as; trimethylchlorosilane (TMCS) in presence of basic catalysts^{2,3}or lithium sulfide⁴; hexamethyldisilazane (HMDS)⁵, and hexamethyldisiloxane (HMDSO)⁶ in acidic media⁷; allyl silanes ^{8,9}, etc. ^{10,11}, have been developed for the introduction of trimethylsilyl group to the molecules.

One of the most practical silylating agents is hexamethyldisilazane (HMDS) which has been used for our studies druring this investigation. HMDS is a cheap and commercially available reagent. Its handling does not need special precaution and the work up of the reaction mixture is not time consuming. The main drawback of this reagent is its poor silylating power ⁷, which needs forceful conditions in many instances and long reaction times. In the literature, several procedures have been reported to catalyze silylations with HMDS. This reagent has been used for silylation of various alcohols in the presence of trimethylchlorosilane ¹², sulfonic acids ⁷, amines, and trimethylsilylated amides such as saccharin ¹³. Although the procedures mentioned above provide an improvement, in many cases, reaction times of several hours are still necessary.

We have reported that hexamethyldisilazane (HMDS) protects various types of hydroxy groups in the presence of a catalytic amount of anhydrous ZnCl₂ in dry CH₃CN under reflux conditions with high yields.¹⁴ The reactions are completed within a few minutes with absolute chemoselectivity. ZnCl₂ is a very hygroscopic compound therefore, its handling is difficult and puts restriction on its uses in the reactions. Now, we report that 2,2'-bipyridyl complexes of ZnCl₂, FeCl₃, and Fe(tpp)Cl are effective catalysts (0.02-0.06 mol) for selective silylation of hydroxy groups with HMDS at room temperature in dry CH_3CN . These catalysts are as effective as $ZnCl_2$ are not hygroscopic their handling is easy, and they catalyze the reactions at room temperature.

Primary alcohols are silvlated almost immediately with excellent yields . Secondary hydroxy groups undergo silvlation easily with higher molar ratios of HMDS. The representative results and their reaction conditions by Fe(tpp)Cl catalysis are tabulated (Table 1). The other two catalysts; $Fe(bipy)Cl_3$ and $Zn(bipy)_3Cl_2$ show more or less the same activity as Fe(tpp)Cl. The effects of the catalysts in competitive silvlation reactions of various types of alcohols are also presented (Table 2). By the presented method, primary hydroxy groups are silvlated versus secondary hydroxy groups with high selectivity (Scheme I and Table 2).



Silylation of diarylcarbinols is difficult and does not proceed so easily with HMDS. In a recent report⁷, triflic acid has been used to catalyze this reaction at 80°C. Dismutation of some diarylcarbinols has been observed with this catalyst. In the same report, it has been mentioned that chlorotrimethylsilane (TMSCI) catalyzes the reaction safely and produces the corresponding silyl ethers with high yields⁷.

| Atoms by HMDS in Dry CH3CN at Room Temperature in | |
|---|----------------------------|
| 1. Silylation of Compounds with Labile Hydrogen | the Presence of Fe(tpp)Cl. |
| Table | |

| | | | Molar ratio | | |
|----------|--|---|------------------------|-----------------------|----------|
| No. | Substrate | Product Reactar | nvHMDS / Fe(tpp)Cl | Reaction Time(min) | Yield(%) |
| - | Ph-CH ₂ -OH | PhCH ₂ OTMS | 1/0.7 / 0.06 | ۳, | 100 |
| 7 | PhCH:CHCH ₂ OH | PhCH:CHCH2OTMS | 1/0.7 / 0.06 | е т Г | 93 |
| Э | CH ₃ (CH ₂) ₆ CH ₂ OH | CH ₃ (CH ₂) ₆ CH ₂ OTMS | 1/0.7 / 0.06 | C | 91 |
| 4 | CH ₃ (CH ₂),CH(OH)CH ₃ | CH ₃ (CH ₂) ₅ CH(OTMS)CH ₃ | 1/0.7 / 0.06 | 90 | 45 |
| S | CH ₃ (CH ₂),CH(OH)CH ₃ | CH ₃ (CH ₂) ₅ CH(OTMS)CH ₃ | 1/1.2 / 0.06 | 20 | 80 |
| 9 | CH ₃ (CH ₂),CH(OH)CH ₃ | CH ₃ (CH ₂) ₅ CH(OTMS)CH ₃ | 1/1.7 / 0.06 | 5 | 94 |
| ٢ | 4-MeC ₆ H ₄ CH(OH)Et | 4-MeC ₆ H ₄ CH(OTMS)Et | 1/1.6 / 0.06 | 10 | 95 |
| × | $4-CIC_6H_4NH_2$ | 4-CIC ₆ H ₄ NHTMS | 1/0.8 / 0.06 | 06 | 0 |
| 6 | C ₆ H ₅ SH | C ₆ H ₅ STMS | 1/0.8 / 0.06 | 06 | 0 |
| 10. | Рьсн(он)Рь | PhCH(OTMS)Ph | 1/0.7/0.06 | Ś | 90¢ |
| 10 | Tmmediate reactions occurr | | | | |
| ي ب و | This reaction was also cata | lvzed by ZnCL at reflux condition (9 | 8%) and hy FeCl. at no | om temneratur | e (97%) |
| 5 | 11100 1000 11 11 10 MIC VANA | titere uj zaroj al retran vonuraci (| | mmindum mo | シジャンシ |

FIROUZABADI ET AL.

 $Zn(bipy)_3 Cl_2$ was not effective as catalyst.

| | Fe(bipy)Cl, Zn(bipy) ₃ Cl, | and Fe(tpp)Cl * as Catalysts. | | | | |
|--------------|---|---|---|---------------------|----------------|--|
| [山本 | ltry Curbotrato | Decidinat | Cotolicot | Molar Ratio | | |
| - | 10. 3 0050 atC | riouuci | Catalyst | Alc./Alc./HMDS/Cat. | Vo CUITVEISIUI | |
| - | CH ₃ (CH ₂) ₆ CH ₂ OH | CH ₃ (CH ₂) ₆ CH ₂ OTMS | Eothian) CI | 0 0/L 0/ 1/ 1 | 70 | |
| | CH ₃ (CH ₂) ₅ CH(OH)CH ₃ | CH ₃ (CH ₂) ₅ CH(OTMS)CH ₃ | re(upy) CI3. | CO.0/1.0/1 /1 | 10 | |
| c | CH ₃ (CH ₃) ₆ CH ₂ OH | CH ₃ (CH ₃) ₆ CH ₂ OTMS | | | 80 | |
| 4 | CH ₃ (CH ₂) ₅ CH(OH)CH ₃ | CH ₃ (CH ₂),CH(OTMS)CH ₃ | Z ii(0ipy) ₃ U ₂ | CU.U/C/.U/1/1 | 11 | |
| , , | CH ₃ (CH ₂) ₆ CH ₂ OH | CH ₃ (CH ₂) ₆ CH ₂ OTMS | | | 62 | |
| n | CH ₃ (CH ₂) ₅ CH(OH)CH ₃ | CH ₃ (CH ₂) ₅ CH(OTMS)CH ₅ | re(upp)ci | 0/.U/I.UI | × | |
| - | PhCH ₂ OH | PhCH ₂ OSiMe ₃ | Eothian) CI | 111/0 6/0 03 | 65 | |
| 1 | CH ₃ (CH ₂) ₅ CH(OH)CH ₃ | CH ₃ (CH ₂),CH(OTMS)CH ₃ | re(upp) c13. | CO.0/0.0/1/1 | 8 | |
| ų | PhCH ₂ OH | PhCH ₂ OSiMe ₃ | | | 82 | |
| r | CH ₃ (CH ₂) ₅ CH(OH)CH ₃ | CH ₃ (CH ₂),CH(OTMS)CH ₃ | 212512 | CU.UII.UIII | 10 | |

Competitive Silylation Reactions with HMDS in Dry CH₃CN at Room Temperature, in the Presence of Table 2. 2713

(continued)

Table 2. Continued.

| ļ | | | | | |
|---|---|---|-------------------------|--------------|----|
| 9 | PhCH:CHCH ₂ OH | PhCH:CHCH2OTMS | Fe(bipy)Cl ₃ | 1/1/0.7/0.04 | 80 |
| | CH ₃ (CH ₂) ₅ CH(OH)CH ₃ | CH ₃ (CH ₂),CH(OTMS)CH ₃ | 5 • • | | × |
| ۲ | PhCH:CHCH ₂ OH | PhCH:CHCH2OTMS | 7n(hinu) (J | 11110 7/0 03 | 86 |
| - | CH ₃ (CH ₂) ₅ CH(OH)CH ₃ | CH ₃ (CH ₂) ₅ CH(OTMS)CH ₃ | 211(U1P7)3~12 | 60.01.01 H | 6 |
| c | PhCHOH | PhCH ₂ OSiMe ₃ | Esthian | | 80 |
| ø | 4-MeC ₆ H ₄ CH(OH)CH ₂ CH ₃ | 4-MeC ₆ H ₄ CH(OTMS)CH ₂ CH | re(uipy)~13 I3 | CO.071.01111 | 10 |
| c | PhCH ₂ OH | PhCH ₂ OSiMe ₃ | Tr(hini) | 11110 710 03 | 74 |
| ע | 4-MeC ₆ H ₄ CH(OH)CH ₂ CH ₃ | 4-MeC ₆ H ₄ CH(OTMS)CH ₂ CH | | 60.01.011 | 5 |
| 1 | PhCH:CHCH ₂ OH | PhCH:CHCH2OTMS | Ea(hinu)Ol | 20 0/2 0/1/1 | 64 |
| 1 | CH ₃ (CH ₂), CH ₂ OH | CH ₃ (CH ₂) ₆ CH ₂ OTMS | | CO:011011 | 46 |

FIROUZABADI ET AL.

| PhCH:CHCH ₂ OH | PhCH:CHCH20TMS | | | 60 |
|--|--|---------------------------------------|--------------|--------------|
| 11 | | Zn(bipy) ₃ Cl ₂ | 1/1/0.7/0.03 | |
| CH ₃ (CH ₂) ₆ CH ₂ OH | CH ₃ (CH ₂) ₆ CH ₂ OTMS | | | 4 |
| PhCH ₂ OH 12 | PhCH ₃ OSiMe ₃ | Fe(bipy) Cl ₃ . | 1/1/0.7/0.03 | 58 |
| PACH:CHCH ₂ OH | PhCH:CHCH ₂ O1MS | | | 4/ |
| PhCH ₂ OH | PhCH ₂ OSiMe ₃ | Zn/hinu) | 111/0 7/0 03 | 54 |
| ^{L1} PhCH:CHCH ₂ OH | PhCH:CHCH20TMS | zu(utpy)3~12 | CO-04-0414 | 31 |
| PhCH ₂ OH | PhCH ₂ OSiMe ₃ | | | 38 |
| L4 CH ₃ (CH ₂) ₆ CH ₂ OH | CH ₃ (CH ₂) ₆ CH ₂ OTMS | re(uipy) Ui3. | c0.0/1.0/1/I | 41 |
| PhCH ₂ OH | PhCH ₂ OSiMe ₃ | Zn(hinu) (J | 1/1/0 7/0 03 | 39 |
| CH ₃ (CH ₂) ₆ CH ₂ OH | CH ₃ (CH ₂) ₆ CH ₂ OTMS | | 1110.01 | 42 |
| a. Iron (III) tetraphenylporphirin | Chloride. | | | |

HEXAMETHYLDISILAZINE

2715

We have found that Fe(tpp)Cl and $Fe(bipy)Cl_3$ are excellent catalysts for the high yield silvlation of diphenylcarbinol with HMDS at room temperature in dry CH₃CN (Scheme II).

| PhCH Ph | OH + HMDS | $\frac{\text{Cat./CH}_3\text{CN}}{\text{RT}}$ | PhCHOTMS Ph |
|-----------------|-------------------------|---|---------------------|
| Cat: | Fe(bipy)Cl ₃ | | 91% |
| | Fe(tpp)Cl | | 90% |

Scheme II

Conclusion

In this study, we have developed methods for absolute silylation of hydroxy groups in the presence of other functional groups with replaceable hydrogen atoms. In addition, by this method discrimination between primary and secondary hydroxy groups is also observed. Diphenylcarbinol which is resistant towards silylation with HMDS could be silylated very easily and with excellent yields in the presence of Fe(tpp)Cl and Fe(bipy)Cl at room temperature. The reaction condition is aprotic and the catalysts are not hygroscopic. Reactions are usually fast and proceed at room temperature in excellent yields. Discrimination among various types of primary alcohols has not been observed by the present method.

EXPERIMENTAL

All yields refer to isolated yields unless otherwise indicated.All silylation

products were characterized by comparison of their spectral data and GC chromatograms with authentic samples. Chemicals were either prepared in our laboratories or were purchased from Fluka, Merck, and BDH Chemical Companies. Iron(III) tetraphenylporphyrin chloride (Fe(tpp)Cl) is commercially available. Fe(bipy)Cl₃ and Zn(bipy)₃ Cl₂ were prepared by the addition of ethereal solutions of 1 and 3 molar ratios of 2,2'-bipyridyl to 1 molar equivalent of ethereal solutions of FeCl₃ and ZnCl₂ respectively. The precipitated complexes were dried under reduced pressure and used as catalysts.

Silylation of 1-Octanol in Presence of Fe(tpp)Cl with HMDS. A Typical Procedure.

In a round-bottomed flask (50 ml) equipped with a drying tube and a magnetic stirrer, a solution of 1-octanol (520 mg, 4 mmol) in dry CH_3CN (20 ml) was prepared. Fe(tpp)Cl (169 mg, 0.24 mmol) was then added and the mixture was stirred at room temperature. HMDS (0.6 ml, 2.8 mmol) was added to the mixture over a period of 2-4 min. The progress of the reaction was monitored by GC. After completion of the reaction, the mixture was extracted with hexane (3 x15 ml). The hexane extracts were concentrated on a rotary evaporator, and then filtered through a silica gel pad. The filter cake was washed with CCl_4 (3 x 15 ml). The filtrates were added together and the solvent was evaporated under diminished pressure to give the corresponding silyl ether, yield 735 mg, 91% (100% conversion).

Silylation of Diphenylcarbinol with HMDS in Presence of Fe(tpp)Cl. A Typical Procedure

In a round-bottomed flask (50 ml) equipped with a drying tube and a magnetic stirrer, a solution of diphenylcarbinol (0.74 g, 4 mmol) and HMDS (0.45 gr, 2.8 mmoles) in CH_3CN (20 ml) was prepared. To the resulting solution

Fe(tpp)Cl (0.039 gr, 0.24 mmol) was added in one portion. The resulting mixture was stirred at room temperature for 5 min. Solvent was evaporated under reduced pressure and to the resulting mixture CCl_4 (15 ml) was added and filtered through a silica-gel pad. The filter cake was washed twice with CCl_4 (each 15 ml) and the filtrates were combined together. Evaporation of the solvent afforded pure silylated compound (0.947 g, 92% yield).

Acknowledgment:

We are thankful to Shiraz University Research Council for the partial support of this work.

REFERENCES:

- (1) Lalonde, M.; Chan, T.H. Synthesis, 1985, 817.
- (2) Corey, E.J.; Snider, B.B. J. Am. Chem. Soc. 1972, 94, 2549.
- (3) Haslam, E. Tetrahedron 1980, 36, 2409.
- (4) Olah, C.A.; Gupta, B.G.B.; Narang, S.C.; Molhotra, R. J. Org. Chem..
 1979, 44, 4272.
- (5) Goldschmidt A.G., German Patent 2758884; *Chem. Abst.* 1979, *90*, 65300.
- (6) Pinnick, H.W.; Bal, B.S.; Lajis, N. H. Tetrahedron Lett. 1978, 4261.
- (7) Gautret, P.; Ep-Ghammarti,S.; Legrand, A. Synth. Commun. 1996, 26, 707.
- (8) Morita, T.; Okamoto, Y.; Sakurai, H. Tetrahedron Lett. 1980, 21, 835.
- (9) Olah, G.A.; Husain, A.; Gupta, B.G.; Salem, G.F.; Narang, S.C. J. Org. Chem. 1981, 46, 5212.

HEXAMETHYLDISILAZINE

- (10) Evans, D.A.; Hoffman, J. M.; Truesdale, L.K.J. J. Am. Chem. Soc.
 1973, 95, 5822.
- (11) Lipshutz, B.H.; Burgess-Henry, J.; Roth, G.P. Tetrahedron Lett. 1993, 34, 995.
- (12) Langer, S.H.; Connell, S.; Wender, I. J. Org. Chem. 1958, 23, 50.
- (13) Bruynes, C.A.; Jurriens, T.K. J. Org. Chem. 1982, 47, 3966 and references cited therein.
- (14) Firouzabadi, H.; Karimi, B. Synth. Commun. 1993, 23, 1633.

(Received in the UK 24 January 1997)