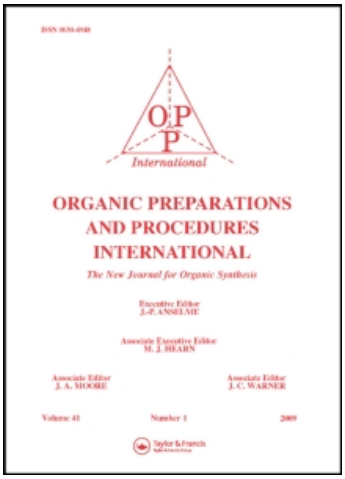


Organic Preparations and Procedures International
Publication details, including instructions for authors and subscription information:
http://www.informaworld.com/smpp/title~content=t902189982

FERRIC CHLORIDE-CATALYZED REDUCTIVE HALOGENATION OF CARBONYL COMPOUNDS TO BROMIDES AND IODIDES

Zhifang Li[a]; Chunqi Sheng[a]; Chengjun Yang[a]; Huayu Qiu[a]
[a] Key Laboratory of Organosilicon Chemistry and Material Technology of Ministry of Education Hangzhou Normal University, Hangzhou, PR CHINA

To cite this Article Li, Zhifang , Sheng, Chunqi , Yang, Chengjun and Qiu, Huayu(2007) 'FERRIC CHLORIDE-CATALYZED REDUCTIVE HALOGENATION OF CARBONYL COMPOUNDS TO BROMIDES AND IODIDES', Organic Preparations and Procedures International, 39: 6, 608 — 611
To link to this Article: DOI: 10.1080/00304940709458645
URL: http://dx.doi.org/10.1080/00304940709458645

8. R. Zong, D. Wang, R. Hammitt and R. P. Thummel, *J. Org. Chem.*, **71**, 167 (2006).

9. B. E. Halcrow and W. O. Kermack, *J. Chem. Soc.*, 155 (**1946**).

10. C. R. Rice and K. M. Anderson, *Polyhedron*, **19**, 495 (2000).

11. M. R. Johnson, D. Bell and L. Shanaman, *Heterocycles*, **45**, 1059 (1997).

12. Y. Engel, A. Dahan, E. Rozenshine-Kemelmakher and M. Gozin, *J. Org. Chem.*, **72**, 2318 (2007).

13. J. Lewis and T. D. O'Donoghue, *J. Chem. Soc. Dalton Trans.*, 736 (**1980**).

****

FERRIC CHLORIDE-CATALYZED REDUCTIVE HALOGENATION OF CARBONYL COMPOUNDS TO BROMIDES AND IODIDES

Submitted by (06/15/07)

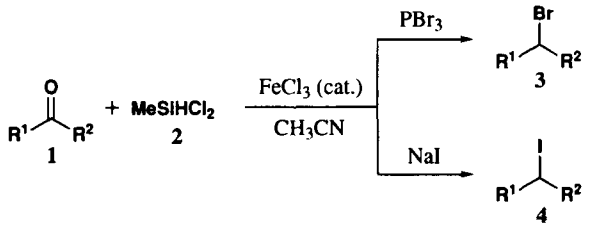
Zhifang Li, Chunqi Sheng, Chengjun Yang and Huayu Qiu*

Key Laboratory of Organosilicon Chemistry and Material Technology of Ministry of Education
Hangzhou Normal University, Hangzhou, 310012, P. R. CHINA
e-mail: huayuqiu@hotmail.com

The direct replacement of the hydroxy group by halogen is a well-known method for the synthesis of aralkyl halides.[1] Other methods such as bromodecarboxylation of carboxylates of Ag (I), Hg (II), Pb (IV) and Tl (I) with bromine[2] or, less frequently, the photocatalyzed side-chain halogenation of alkylarenes have also been reported.[3] Iodoalkanes are usually obtained by halogen exchange from an alkyl chloride or bromide.[4] However, the direct conversion of carbonyl compounds into organic halides has remained largely unexplored. Corre and co-workers[5] described the reductive bromination of aromatic carbonyl compounds using trimethylamine-borane complex (TMAB) and bromine, however, with a strong electron-withdrawing substituent on the benzene ring, the amount of bromination was low. The direct synthesis of benzyl halides from aromatic aldehydes using alkylboron dibromides[6] or a combination of chlorotrimethylsilane (TMSCl), 1,1,3,3-tetramethyldisiloxane (TMDS) and either LiBr or NaI[7] has been reported, but these methods failed with ketones. In our studies for the direct conversion of carbonyl compounds into the halides, it was found that $FeCl_3$ is a versatile catalyst for the synthesis of organic chlorides.[8] Herein we report the $FeCl_3$ catalyzed one-flask conversion of

carbonyl compounds (**1**) into the corresponding bromides and iodides in the presence of dichloromethylsilane.

When a mixture of carbonyl compounds, dichloromethylsilane and PBr_3 or NaI was treated with catalytic amount of $FeCl_3$ in CH_3CN for 4-24 h (*Table*), the corresponding organic bromides (**3**) or iodides (**4**) were obtained in moderate to good yields. Both aromatic carbonyl compounds (aldehydes and ketones) (***1a-1j***) and aliphatic aldehydes (***1k, 1l***) underwent the deoxygenative halogenation catalyzed by the $FeCl_3$. Ester and nitro groups (***1f, 1g, 1h***) were not affected (*Scheme 1*).



a) $R^1 = C_6H_5$, R^2 = H; b) R^1 = 4-ClC_6H_4, R^2 = H; c) R^1 = 2-ClC_6H_4, R^2 = H; d) R^1 = 4-MeC_6H_4, R^2 = H; e) R^1 = 4-$MeOC_6H_4$, R^2 = H; f) R^1 = 4-$MeO_2CC_6H_4$, R^2 = H; g) R^1 = 3-$NO_2C_6H_4$, R^2 = H; h) R^1 = 4-$NO_2C_6H_4$, R^2 = H; i) $R^1 = C_6H_5$, R^2 = Me; j) R^1 = 4-ClC_6H_4, R^2 = Me; k) $R^1 = C_5H_{11}$, R^2 = H; l) $R^1 = C_7H_{15}$, R^2 = H

Scheme 1

Table. FeCl-Catalyzed Deoxygenative Bromination and Iodination of Carbonyl Compounds

	Reductive Bromination[a]				Reductive Iodination[b]			
Entry	Product	Yields[c] (%)	Time (h)	mp. or bp./mm (*lit.*) (°C)	Product	Yields[c] (%)	Time (h)	mp. or bp./mm (*lit.*) (°C)
1	**3a**	97	4	197-199 (198)[7a]	**4a**	94	6	23-24 (25)[7a]
2	**3b**	92	5	48-51 (48-50)[7a]	**4b**	72	23	57-61 (59-61)[7a]
3	**3c**	93	4	107-109/8 (95-98/0.4)[7a]	**4c**	81	17	25-26 (26-27)[10b]
4	**3d**	90	5	103-104/10 (106-109/15)[7b]	**4d**	62	13	44-46 (46)[10a]
5	**3e**	55	4	145-147/30 (145-148/30)[7b]	**4e**	90	16	25-27 (27)[10a]
6	**3f**	82	4	54-55 (53-55)[7b]	**4f**	95	21	76 (76-77)[10c]
7	**3g**	75	6	56-58 (57-58)[7c]	**4g**	95	21	83-85 (82-85)[7b]
8	**3h**	92	6	94-98 (95-98)[7c]	**4h**[d]	90	15	
9	**3i**	87	4	96 (16mm)[7c]	**4i**	71	24	71-82/2 (70-80/2)[10d]
10	**3j**	90	10	57-58 (0.11mm)[7c]	**4j**[d]	82	23	
11	**3k**	42	7	128-130 (130)[9]	**4k**	65	12	170-172 (174)[10c]
12	**3l**	50	7	112-114/27 (83-85/10)[9]	**4l**	66	12	119-120/65 (120-121/65)[10f]

a) All reactions were carried out with carbonyl compounds **1** (10.0 mmol), $FeCl_3$ (0.5 mmol), PBr_3 (11.0 mmol) and dichloromethylsilane (15.0 mmol) in reflux CH_3CN. b) Reaction conditions: carbonyl compounds **1** (10.0 mmol), $FeCl_3$ (0.5 mmol), NaI (15.0 mmol) and dichloromethylsilane (15.0 mmol) in reflux CH_3CN. c) Yields based on **1** used. d) The products exhibited physical and spectral characteristics in accord with literature values.

In summary, we have described the first $FeCl_3$ catalyzed reductive bromination and iodination of carbonyl compounds as a useful method for the synthesis of organic bromides or iodides.

EXPERIMENTAL SECTION

Acetonitrile was distilled from phosphorus pentaoxide immediately prior to use. Infrared spectra were recorded on a Perkin-Elmer 683 spectrometer in KBr with absorption in cm^{-1}. ^1H-NMR spectra were determined on a Bruker AC 400 MHz instrument with CCl_4 used as the solvent. Chemical shifts are expressed in δ downfield from internal standard tetramethylsilane. Mass spectra were recorded on a HP5989B mass spectrometer. Elemental analyses were carried out on an EA 1110 instrument.

General Procedure for the Synthesis of Organic Bromides (3a-3l) and Iodides (4a-4l). Anhydrous $FeCl_3$ (81 mg, 0. 5 mmol) in acetonitrile (50 mL) was added to a three-necked flask with stirring at room temperature. When the color of the mixture turned to yellow, the carbonyl compound (10 mmol), dichloromethylsilane (15 mmol) and PBr_3 (11 mmol) or NaI (15 mmol) were added to the solution. The resulting mixture was refluxed for indicated time (*Table*) until the disappearance of carbonyl compounds (monitored by TLC). Then it was cooled to room temperature, quenched with dilute hydrochloric acid (0.2 M) and extracted with diethyl ether (3 x 50 mL). The combined organic layer was washed with aqueous $NaHCO_3$ (30 mL) and saturated brine (30 mL), dried over anhydrous Na_2SO_4, and concentrated under reduced pressure. The residue was purified by column chromatography to afford the desired products.

Acknowledgement.- We are grateful to the Natural Science Foundation of Zhejiang Province, China (Project No. Y405124).

REFERENCES

1. a) B. Castro, *Org. React.* (N.Y.), **29**, 1 (1983); b) G. W. Brown, "*The Chemistry of the Hydroxy Group*", Chapter 11, p. 593, S. Patai (Ed.), Wiley-Interscience, London, 1971.

2. a) B. Borodin, *Liebigs Ann.*, **119**, 121 (1861); b) H. C. Hunsdiecker, *Ber.*, **75**, 291 (1942); c) R. K. Ingham, *Chem. Rev.*, **56**, 219 (1956); d) D. Crich, "*Comprehensive Organic Synthesis*", B. M. Trost and I. Fleming (Eds.), Pergamon: Oxford, **7**, 723 (1991); e) R. A. Sheldon and J. K. Kochi, *Org. React.* (N.Y.), **19**, 326 (1972).

3. M. L. Poutsma, " *Free Radical*", Vol. II, Chapter 14, J. K. Kochi (Ed.), John Wiley & Sons, New York, 1973.

4. R. D. Chambers, S. R. James, "*Comprehensive Organic Chemistry*", J. F. Stoddart (Ed), Pergamon Press, Oxford, **1**, 493, (1979), and references cited therein.

5. M. L. Corre, E. Gheerbrant and H. L. Deit, *J. Chem. Soc., Chem. Commun.*, 313 (**1989**).

6. G. W. Kabalka, Z. Wu and Y. Ju, *Tetrahedron Lett.*, **41**, 5161 (2000).

7. a) J. M. Aizpurua and C. Palomo, *Tetrahedron Lett.*, **25**, 1103 (1984); b) J. M. Aizpurua, B. Lecea and C. Palomo, *Can. J. Chem.*, **64**, 2342 (1986); c) R. C. Weast, "*Handbook of Chemistry and physics*", 57th ed. C. R. C. Press, Cleveland, Ohio. 1977-1978.

8. Z. F. Li, C. Q. Sheng, H. Y. Qiu and Y. M. Zhang, *Org. Prep. Proc. Int.* **39**, 429 (2007).

9. A. McKillop, D. Bromley and E. C. Taylor, *J. Org. Chem.*, **34**, 1172 (1969).

10. a) A. Lorenzo, P. Molina and M. Vilaplana, *Synthesis*, 853 (**1980**); b) R. N. Castle and J. L. Riebsomer, *J. Org. Chem.* **21**, 142 (1956); c) R. C. Fuson and H. G. Cooker Jr. *J. Am. Chem. Soc.* **62**, 1180 (1940); d) S. R. Landauer and H. N. Rydon, *J. Chem. Soc.*,2224 (**1953**); e) H. G. Bray, J. C. Caygill, S. P. James and P. B. Wood, *Biochem. J.*, **90**, 127 (1964); f) E. J Corey and J. E. Anderson, *J. Org. Chem.*, **32**, 4160 (1967).

****

PREPARATION OF NOVEL QUINO[3,4-C]-, QUINO[4,3-C], QUINO[5,6-C]-, QUINO[6,5-C]-, AND QUINO[7,8-C][2,7]NAPHTHYRIDINE

Submitted by (06/07/07) Charles F. Nutaitis* and Kimberly Smith

Department of Chemistry, Lafayette College, Easton, PA 18042
e-mail: nutaitic@lafayette.edu

Polycyclic aromatic hydrocarbons containing one or more nitrogen atoms in place of a carbon atom (azaPAH or azaarenes) are ubiquitous environmental pollutants emanating from various sources, including the fossil fuel industry, tobacco smoking, wood preservation, pesticides, cooked high-protein foods and pharmaceuticals. Like their carbocyclic counterparts, azaarenes have been shown to possess mutagenic and carcinogenic activity that can vary greatly between regioisomers.[1] As a result, there continues to be interest in developing synthetic methodologies for the preparation of a large variety of azaarene ring systems so that a more complete structure-activity profile can be deduced.

For the past 15 years, we have been investigating an intramolecular pyridyne cyclization strategy for the synthesis of the benzo[c][2,7]naphthyridine ring system **3**, a structural feature common to many natural products exhibiting biological activity.[2]

The pyridyne cyclization precursors **1** can be readily obtained from reductive amination of 5-bromonicotinaldehyde and the appropriate aromatic amine. Utilizing this methodology,