Tetrahedron Letters,Vol.28,No.24,pp 2705-2708,1987 0040-4039/87 $3.00 + .00
Printed in Great Britain Pergamon Journals Ltd.

BASE-INITIATED REACTIONS OF N-FLUOROPYRIDINIUM SALTS; A NOVEL CYCLIC CARBENE PROPOSED AS A REACTIVE SPECIES(1)

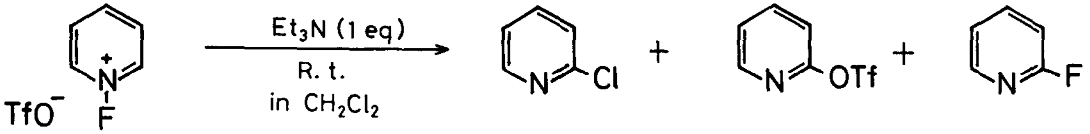
Teruo UMEMOTO* and Ginjiro TOMIZAWA
Sagami Chemical Research Center
Nishi-Ohnuma 4-4-1, Sagamihara, Kanagawa 229, Japan

A new type of base-initiated reactions of pyridinium salts was found and a novel cyclic carbene was proposed as the reactive species.

The reactions of pyridines, pyridine N-oxides, or pyridinium salts with bases have been studied extensively and it has been established that addition, addition-elimination, elimination-addition, ring-opening, or proton-abstraction followed by nucleophilic reaction occurs depending upon the nature of pyridine rings and bases.(2) On the other hand, it has well been known that singlet carbenes have a highly electrophilic character because of the vacant π-orbitals.(3) It has also been pointed out that, if assisted by strong electron donors such as nitrogens, the carbenes become nucleophilic.(4)

This paper describes a new type of reactions of pyridinium compounds containing a novel singlet carbene as a possible reactive species. Recently we reported the syntheses of a series of N-fluoropyridinium salts and demonstrated that they acted as widely applicable fluorinating agents because of a variable range of fluorinating power and easy handling.(5)

However, we found that, when N-fluoropyridinium triflate **1** was treated with triethylamine in methylene chloride, an exothermic reaction occurred immediately, giving 2-chloropyridine **2a** (62%) along with 2-pyridyl triflate 3

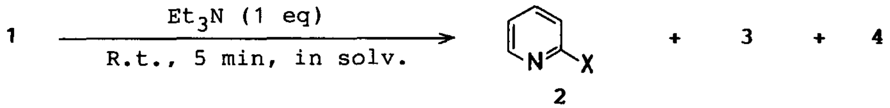


1 (Tf = CF_3SO_2) 2a 3 4

Table 1 Reaction of **1** with several kinds of bases in methylene chloride

Run	Base (1eq)	Time (min)	GC-Yield (%)		
			2a	**3**	**4**
1	Et_3N	5	62	21	5
2	Et_2NH	5	63	22	6
3	NaOMe	10	25	7	5
4	t-BuOK	10	35	5	7
5	$PhCH_2N^+Me_3OH^-$	180	34	3	6

Table 2 Reactions of 1 in several kinds of solvents



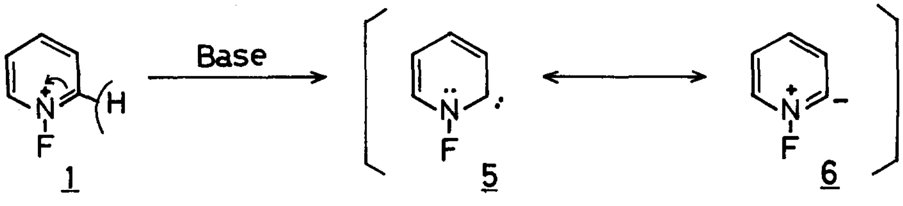
Run	Solv.	Yield (%)[a) 2]	3	4
1	CH_2Cl_2	62 (**2a**)[X=Cl]	21	5
2	CH_2Br_2	60 (**2b**)[X=Br]	27	4
3	THF	25 (**2c**)[X=$O(CH_2)_4F$] 5 (**2d**)[X=$O(CH_2)_4O(CH_2)_4F$]	33	6
4	Dioxane	15 (**2e**)[X=$O(CH_2)_2O(CH_2)_2F$]	36	6
5	CH_3CN	55 (**2f**)[X=$NHCOCH_3$]	7	3
6	Benzene	33 (**2g**)[X=Ph]	42	15
7	Furan	17 (**2h**)[X=2-Furyl] 13 (**2i**)[X=3-Furyl]	39	9
8[b)]	Acetone	25 (**2j**)[X=$OCFMe_2$] 25 (**2k**)[X=$OCMe=CH_2$]	14	5

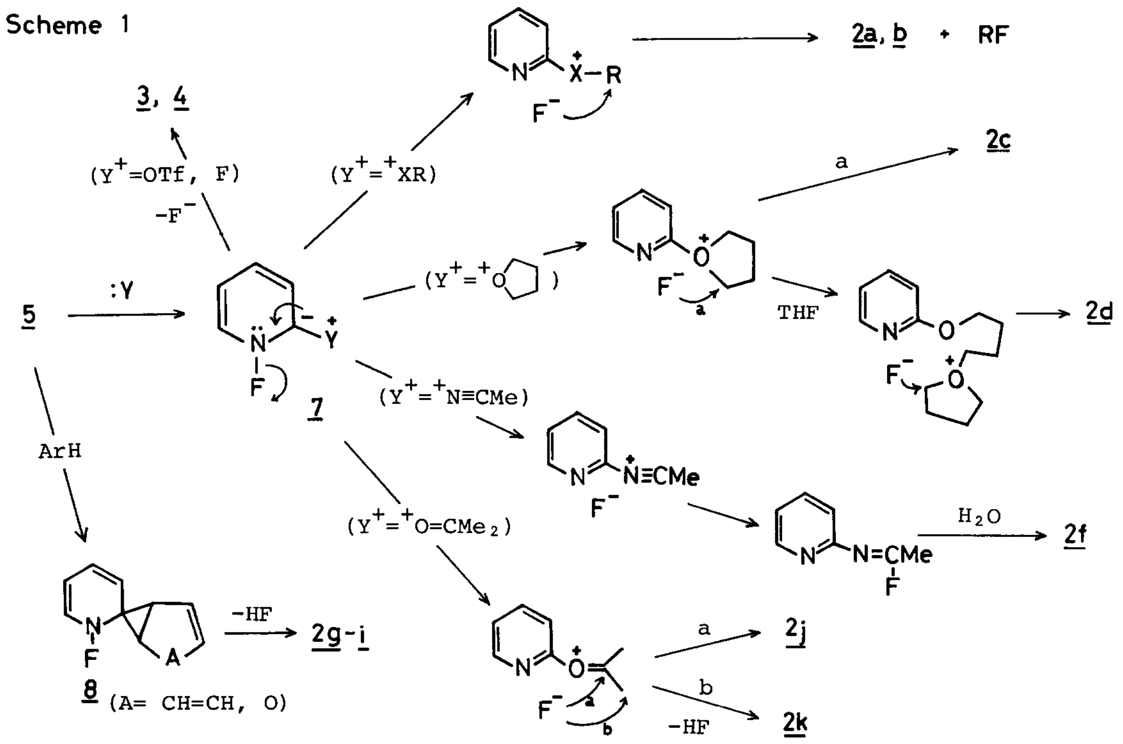
a) GC-yields except for **2d**, **2f**, **2g**, **2h**, and **2i** which are isolated yields. All the products showed spectral data in accord with the assigned structures.
b) 2 molar equivalent amount of Et_3N was used.

(21%) and 2-fluropyridine **4** (5%). We were surprized by the formation of **2a** in particular. The use of other bases gave the similar results (Table 1). The bases are essential for the reactions, because **1** is stable in the solvent. **1** was never or little substituted by the bases at the 2 or 4-positions, even though they have a strong nucleophilicity. In Runs 2 and 3 only, 2-diethylaminopyridine **2l** and 2-methoxypyridine **2m** were formed in very poor 1% and 9% yields, respectively. The same treatment of N-fluoropyridinium tetrafluoroborate[5a)] as in Run 1 gave **2a** (40%) and **4** (22%).

1 was treated with Et_3N in several kinds of solvents (Table 2). **1** reacted with haloalkanes, ethers, a nitrile, a ketone, and aromatics at halogen, oxygen, nitrogen, oxygen, and aromatic sp^2 carbon sites, respectively. It clearly demonstrates the electrophilicity of the reactions and indicates the presence of a reactive intermediate species which reacts even with neutral halogen and oxygen atoms. Thus, the reactions of N-fluoropyridinium salts are quite different from the known reactions[2)] of pyridines or their analogues.

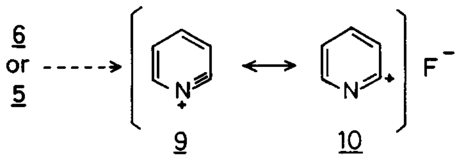
We propose a carbene **5** as the reactive species, derived by the proton-abstraction. It is well known that carbenes react with neutral halogen, oxygen, and nitrogen atoms to give ylides.[3)] It has also been shown from deuterium exchange studies that 2-protons of N-alkylpyridinium salts are considerably acidic.[2),6)] Since the fluorine atom is very electron-attracting while alkyl is





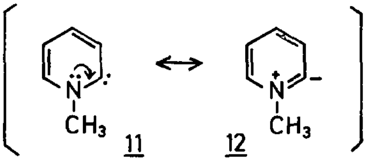
electron-releasing, it is quite reasonable that the 2-protons of **1** are readily removed by such bases. **5** has a ylide form **6** as a resonance structure which may undertake nucleophilic reaction.3) Since the reactions are distinctly electrophilic, **6** may be neglected. All the products are easily explained by the carbene mechanism (Scheme 1). **5** reacts with the heteroatoms to form ylides **7** followed by elimination of F^- which undertakes further reactions as shown in Scheme 1. **3** is produced similarly. A small amount of **4** is given by the reaction of **5** with F^- or HF generated as a by-product or by the attack of F^- to the 2-positions of pyridine rings of the intermediate onium ions shown in Scheme 1. **5** also reacts with an aromatic compound to form a 3-membered ring intermediate **8** which undergoes dehydrofluorination to give a 2-arylpyridine(s).

1,2-Pyridynium or 2-pyridyl cation, **9** or **10**, may be assumed as an alternative species, generated via **6** or **5** by elimination of F^-. However, the leaving power of F is not so strong as to form unstable **9** or **10**. **10** was calculated to be less stable than phenyl cation7). Even though **9** or **10** was formed, it should combine with the considerably nucleophilic counter anion F^-, giving stable **4** as a main or sole product. However, the yields of **4** were trace or very low, and **2** or **3** yielded in plenty in spite of the nonnucleophilicity of the heteroatoms or $^-$OTf. The formation of fluorides **2c-e,j** rather than **4** indicates that the binding between the pyridine ring and the oxygen of THF, dioxane, or acetone occurred before the cleavage of the N-F



bond, supporting the carbene mechanism. Since **9** and **10** would be expected to react with furan in the modes of [2+4]cycloaddition at 2,5-positions and electrophilic substitution at 2-positions of the furan ring, respectively,8) both of them should give 2-isomer **2h**, but not 3-isomer **2i**. However, **1** produced both **2h** and **2i**. Accordingly, the ionic mechanism via **9** or **10** may be excluded.

Whereas a strong electron donor-assisted N-methyl carbene **11** or ylide **12** has a nucleophilic character,4),9) N-fluoro carbene **5** has the electrophilic character. It is clearly attributed to the great decrease of the electron density of the nitrogen site due to the strong electron-withdrawing effect of F. Besides, the N-F-containing carbene reaction would strongly be assisted by the release of the resonance energy on the following aromatization by elimination of F^- from **7**, giving stable 6π-aromatic pyridine derivatives.



11 12

1 was treated with alkaline (2 eq) to give 2-hydroxypyridine **2n** (50%) along with **3** (<1%) and **4** (<1%). The similar treatment of **1** with sodium methoxide (2 eq) in methanol gave **2m** (73%), **3** (3%), and **4** (1.5%). Our above consideration strongly suggests that **2n** and **2m** would not be formed by the addition-elimination mechanism,2) but by the carbene mechanism. On the other hand, it is interesting that the treatment of **1** with a large excess of diethylamine as a solvent did not afford **21** at all. The products were **3** (61%) and **4** (18%) only. The nonproduction of **21** again rejects the cationic **9** or **10** mechanism and might be explained by the carbene mechanism as follows. The attack of such a strongly electron-donating nucleophile as the amine to carbene **5** would result in the formation of the unstable, approximately 8π anti-aromatic ring system or unstable ylide **7**. Accordingly, **5** did not react with diethylamine, but with nonnucleophilic $^-$OTf and poorly electron-donating $F^-(F^-HN^+HEt_2)$ to give **3** and **4**.

We thank Miss Sumi Ishihara for her partial experimental assistance.

References

1) Presented at the 11th Symposium on Fluorine Chemistry of Japan, Abstract pp 34-35, Oct. 16, 1986 (Nagoya).
2) a) D.M.Smith, "Rodd's Chemistry of Carbon Compounds," Sec. Ed., ed by S.Coffey, Vol.IV (Heterocyclic Compounds-Part F), pp 56-226, Elsevier, Amsterdam (1976). b) "Heterocyclic Compounds - Pyridine and Its Derivatives," ed by R.A.Abramovitch, Vol. 14, Part 1-4, John Wily & Sons, New York (1974-5).
3) a) W.Kirmse, "Carbene Chemistry," Sec. Ed., Academic Press, New york (1971). b) R.Noyori, "Gendai no Yuki Kagaku - Karuben, Irido, Naitoren oyobi Benzain," ed by T.Goto, pp 1-70, Hirokawa Publishing Co., Tokyo (1976).
4) Dr.-Ing.H.-W.Wanzlick, Angew. Chem. Int. Ed. Engl., **1**, 75 (1962).
5) a) T.Umemoto and K.Tomita, Tetrahedron Lett., **27**, 3271 (1986). b) T.Umemoto, K.Kawada, and K.Tomita, Tetrahedron Lett., **27**, 4465 (1986). c) T.Umemoto and G.Tomizawa, Bull. Chem. Soc. Jpn., **59**, 3625 (1986).
6) a) K.W.Ratts, R.K.Howe, and W.G.Phillips, J. Am. Chem. Soc., **91**, 6115 (1969). b) J.A.Zoltewicz and G.M.Kauffman, J. Org. Chem., **34**, 1405 (1969).
7) R.Gleiter, R.Hoffman and W.-D.Stoher, Chem. Ber., **105**, 8 (1972).
8) G.R.Newkome and W.W.Paudler, "Contemporary Heterocyclic Chemistry," Chap. 7 and 10, John Wiley & Sons, New York (1982).
9) H.Quast and E.Schmitt, Justus Liebigs Ann. Chem., **732**, 43 (1970); Angew. Chem. Int. Ed. Engl., **4**, 691 (1965).

(Received in Japan 10 February 1987)