Tetrahedron Letters,Vol.25,No.36,pp 3923-3926,1984 0040-4039/84 $3.00 + .00
Printed in Great Britain

REACTION OF PYRIDINE N-OXIDES WITH TRIFLIC ANHYDRIDE: FORMATION OF N-SULFONYLOXY AND DIPYRIDINIUM ETHER SALTS

Zhen-Chu Chen and Peter J. Stang*
Chemistry Department, The University of Utah,
Salt Lake City, UT 84112

Abstract. Pyridine and picoline-N-oxides react with $(CF_3SO_2)_2O$ to give N-sulfonyloxy and dipyridinium ether triflate salts.

We have previously reported that the reaction of certain activated ketones or thioureas with triflic anhydride $[(CF_3SO_2)_2O, Tf_2O]$ leads to novel dication ether salts[1] 1 and dication disulfide salts[2] 2, respectively:

$$2R_2C{=}O \xrightarrow{Tf_2O} \underset{\underline{1}}{R_2\overset{+}{C}{-}O{-}\overset{+}{C}R_2 \cdot 2\overset{-}{O}Tf} \qquad 2(R_2N)_2C{=}S \xrightarrow{Tf_2O} \underset{\underline{2}}{(R_2N)_2\overset{+}{C}{-}S{-}S{-}\overset{+}{C}(NR_2)_2 \cdot 2\overset{-}{O}Tf}$$

Likewise it is known that DMSO[3] and HMPA[4] give 3 and 4, respectively, upon reaction with Tf_2O.

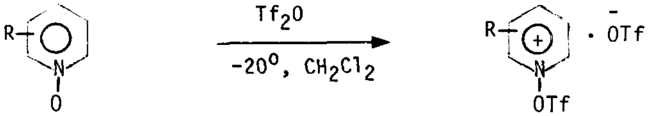
$$\underset{\underline{3}}{(CH_3)_2\overset{+}{S}{-}OTf \cdot \overset{-}{O}Tf} \qquad \underset{\underline{4}}{[(CH_3)_2N]_3\overset{+}{P}{-}O{-}\overset{+}{P}[N(CH_3)_2]_3 \cdot 2\overset{-}{O}Tf}$$

In order to broaden the scope of our previous investigations and, in particular, to prepare heteroatom linked salts, we report here on the reaction of pyridine- and picoline-N-oxides with Tf_2O.

Pyridine and related N-oxides are known to react with a variety of acylating agents and in the majority of cases the reaction involves an acylated intermediate of type 5.

5

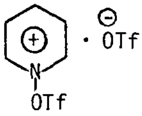
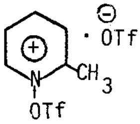
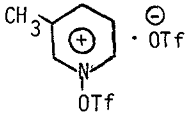
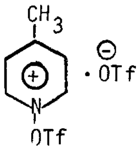
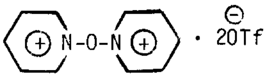
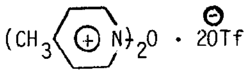
However, these intermediates are very reactive and unstable and hence have never been isolated, except in selected cases as picrates[5] or perchlorates[6]. In contrast reaction of these N-oxides with Tf_2O gives stable, crystalline, albeit very hygroscopic, sulfonyloxy salts, 6, in excellent isolated yields.



$\underline{6}$, $\underline{a}$:R = H
$\underline{b}$:R = 2 - Me
$\underline{c}$:R = 3 - Me
$\underline{d}$:R = 4 - Me

A typical experimental procedure is as follows: In a three-necked round-bottom flask equipped with an Argon inlet and outlet, magnetic stirring, thermometer and addition funnel were added 3.1g (11 mmol) of Tf_2O in 10 ml of dry CH_2Cl_2.

Table. Physical and Spectral Properties of Salts $\underline{6}$ and $\underline{7}$

Starting N-Oxide	Product	%Yield	M.P. (dec.)°C	M.W. Cld.	M.W. Exp.	^{19}F-NMR*
C_5H_5NO	 $\underline{6a}$	93	62-64	377	382	85.2, 96.2
$2\text{-}CH_3C_5H_4NO$	 $\underline{6b}$	87	61-63	391	392	85.3, 95.5
$3\text{-}CH_3C_5H_4NO$	 $\underline{6c}$	86	68-70	391	395	85.2, 96.1
$4\text{-}CH_3C_5H_4NO$	 $\underline{6d}$	90	60-62	391	395	85.2, 96.0
$2C_5H_5NO$	 $\underline{7a}$	89	102-104	472	471	85.2
$2(4\text{-}CH_3C_5H_4NO)$	 $\underline{7b}$	20	148-149	500	504	85.1

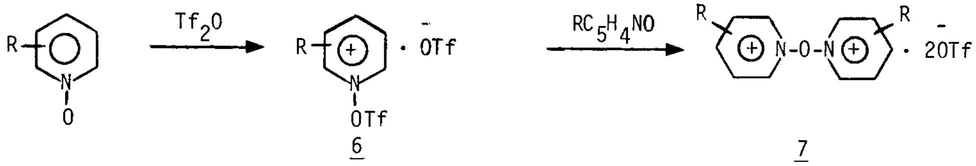
*In CD_3CN rel. to C_6F_6

The solution was cooled to -20°C and 0.95g (10 mmol) of pyridine-N-oxide in 5 ml of dry CH_2Cl_2 was added. Immediately upon addition a white crystalline precipitate formed. After completion of the addition the mixture was stirred for an additional 15 minutes then filtered under an Argon atmosphere in a "closed" system. The white ppt was washed with 5 ml of dry CH_2Cl_2 followed by 10 ml of dry ether then dried under vacuum yielding 3.5g (93%) of white crystalline 6a. Yields and properties of monosalts 6 are summarized in the Table.

Likewise, *inverse* addition of Tf_2O, as above, to *two* equivalents of N-oxide in cold CH_2Cl_2 gave a new crystalline white solid 7a and 7b in the case of pyridine- and 4-picoline-N-oxide, respectively, and a viscous oil in the case of 2- and 3-picoline-N-oxides. Physical and spectral data for 7 are also given in the Table.

The identity of salts 6 and 7 were established by physical, spectral and chemical means. In particular, titration with standardized aqueous NaOH established the molecular weight of these compounds. The infrared in nujol, although difficult to obtain because of the hygroscopic nature of these salts, clearly showed the characteristic triflate absorptions. Most important, the ^{19}F-NMR of monosalts 6 had two signals, as expected, in the covalent region at 96 ppm and the ionic region at 85 ppm while the dication ether salts 7 showed, but a single absorption at 85 ppm consistent with the absorption of ionic CF_3SO_3.

These observations are consistent with the initial formation of mono-cations 6 which in the presence of excess N-oxide undergo further reaction with the nucleophilic oxygen of the pyridine-N-oxide to give dication salts 7:



That monocation 6 is the precursor of 7 is confirmed by the reaction of isolated pure 6 with an equivalent of pyridine-N-oxide that yields a salt identical in all respects with the dications 7 formed directly as decribed above.

Mono salts 6 are extremely moisture sensitive and highly reactive towards nucleophiles. Hydrolysis of 6d, for example, with 20% sodium carbonate solution, followed by extraction with $CHCl_3$ gave recovered starting 4-picoline-N-oxide in nearly quantitative yield. Likewise, reaction of 6a-d with aniline at 0°C in acetonitrile gave the expected $CF_3SO_2NHC_6H_5$ in 86-91% isolated yields.

Hence, we have established that pyridine-N-oxides are excellent subsrates for the formation of both monocations 6 and nitrogen-linked dication ether salts 7. Mono cations 6 represent the first example of isolated "acylated" intermediates of tertiary amine-N-oxides from reaction with an anhydride and dications 7 are new heteroatom-linked examples of this novel class of carbenium ions.[1]

Acknowledgements. Financial support was provided by the NSF (CHE 81-03596). We thank Mr. J. Davis for assistance with the ^{19}F spectra.

References

1. Stang, P.J.; Maas, G.; Smith, D.L.; McCloskey, J.A. J. Am. Chem. Soc., 1981 , 103, 4837.
2. Maas, G,; Stang, P.J. J. Org. Chem., 1981, 46, 1606.
3. Hendrickson, J.B.; Schwartzman, S.M. Tetrahedron Lett., 1975, 273.
4. Aaberg, A.; Gramstad, T,; Husebye, S. Tetrahedron Lett., 1979, 2263.
5. Traynelis, V.H. Sr.; Gallagher, A.M. Martello, R.F. J. Org. Chem., 1961, 26, 4365.
6. Traynelis, V.H. Sr.; Pacini, P.L. J. Am. Chem. Soc., 1964, 86, 4917; Muth, C.W.; Darlak, R.J. J. Org. Chem., 1965, 30, 1909.

(Received in USA 29 May 1984)